Associazione Italiana
Radioterapia e Oncologia clinica

34° Congresso Nazionale AIRO

Associazione Italiana
Radioterapia e Oncologia clinica
Giovani

13° Congresso Nazionale AIRO GIOVANI

Società Italiana di Radiobiologia

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AIRO 2024

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MILANO
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LIBRO degli ABSTRACTS
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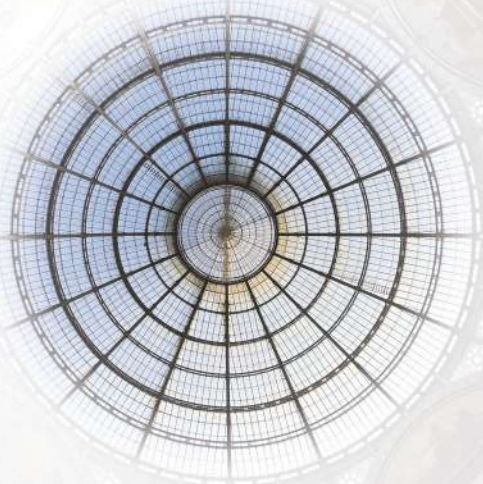

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IBISCO PHASE II TRIAL: EVALUATING IMMUNOLOGICAL AND PATHOLOGICAL RESPONSES TO ANTICIPATED STEREOTACTIC RADIOTHERAPY BOOST IN LUMINAL B BREAST CANCER RECEIVING NEOADJUVANT CHEMOTHERAPY.

Code: 274

Aims: Pathological complete response (pCR) following neoadjuvant systemic therapy is a key predictor of disease outcomes and survival in aggressive breast cancer (BC) subtypes, particularly in triple-negative and Her2-positive BC. Achieving pCR in Luminal B BC, however, remains challenging, highlighting the need for innovative treatment strategies. The IBISCO trial explores the efficacy of combining preoperative stereotactic radiotherapy (SBRT) boost with standard neoadjuvant chemotherapy (NAC) to improve pCR rates in this context.

Methods: IBISCO, a phase II trial, aims to increase pCR rates from 15% to 35% in Luminal B BC patients by integrating a preoperative SBRT boost with standard NAC (weekly paclitaxel for 12 weeks, followed by Epirubicine-Ciclofosfamide for 4 cycles). The primary endpoint is assessed using the Residual Cancer Burden index. Additionally, exploratory analyses include evaluating changes in the tumor- associated inflammatory microenvironment and tumor genomic profile post-SBRT. Standard clinical practice will guide surgery and adjuvant therapies post-neoadjuvant treatment.

Results: From February 2023 to January 2024, eight Luminal B BC patients, predominantly with cT2 tumors, were enrolled in the trial. The preoperative SBRT boost was scheduled between the 3rd and 4th paclitaxel administration. The SBRT treatments were delivered using the Volumetric Arc Modulated Therapy (VMAT) technique with flattening filter free and Deep Inspiration Breath Hold, ensuring optimal target coverage and minimal exposure to organs-at-risk (OaRs). The prescribed dose was 24 Gy in 3 fractions of 8 Gy each. A key focus was on sparing OaRs, especially the skin, to prevent surgical complications. In all cases, SBRT planning with VMAT was successfully implemented, maintaining a mean PTV/breast ratio of 6.18%. Only one patient required a reduction in CTV V95% below 98% to meet OaRs constraints. Importantly, no acute skin toxicities were observed (Table 1).

Conclusions: The preliminary results of the IBISCO trial suggest that the integration of a preoperative SBRT boost with NAC is not only feasible but also safe for treating BC. This approach, using advanced RT techniques, has shown potential in delivering precise and effective treatment without significant acute skin toxicities. The final results of the study are awaited to confirm these initial observations and potentially influence treatment strategies for this specific BC subtype.

Patient	Age	Site and breast quadrant	cTNM	Size T (mm)	Positive N (mm)	CTV (cm^3)	PTV (cm^3)	Volume Ratio PTV/ipsilateral breast (%)	Acute toxicity_1week after SBRT	Acute toxicity_3weeks after SBRT	CTV coverage V95%	PTV coverage V95%
1	65	R, upper-outer	cT2N0M0	37x30x33	0	18.0	37.4	4.5	G0	G0	99.9%	95.4%
2	49	R, lower-inner	cT(m)1N0M0	27x22, 12x12	0	11.9	21.4	9.2	G0	G0	96.6%	92.5%
3	56	R, upper-outer	cT2N1M0	30x22	1 (16 mm)	16.7	35.7	2.8	G0	G0	100%	98%
4	67	L, upper-inner	cT2N0M0	45x30	0	25.6	50.9	5.4	G0	G0	100%	94.5%
5	50	R, upper-outer	cT2N1M0	22x12	1 (15mm)	6.2	16.2	2.2	G0	G0	100%	97.8%
6	73	R, upper-outer	cT2N1M0	42x34x32	1 (14mm)	20.8	40.6	6.7	G0	G0	100%	93.4%
7	55	L, subareolar	cT2N0M0	29x34x28	0	15.2	32.9	4.0	G0	G0	99.9%	95.2%
8	35	L, upper-outer	cT2N0M0	24x27x26	0	13	31.0	14.6	IN TREATMENT	IN TREATMENT	99.1%	95.4%

Table 1. Target coverages. In red, the suboptimal coverages of the various targets.

Target	Coverage	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8
PTV_eval	V95>95%	95.4%	92.5%	-	94.5%	97.8%	93.4%	95.2%	95.4%
	V90>95%	99.5%	99.5%	-	99.2%	99.6%	98.3%	99.3%	99.4%
(PTV)	V95>95%	93.8%	63.3%	98%	93.6%	97.0%	93.1%	93.4%	80.8%
CTV_eval	V95>95%	99.9%	96.6%	-	-	-	-	-	99.1%
(CTV)	V95>95%	99.9%	86.7%	100%	100%	100%	100%	99.9%	98.1%
GTV	V95>95%	100%	97.4%	100%	100%	100%	100%	100%	99.9%

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INTENSITY MODULATED RADIATION THERAPY IN VULVAR CARCINOMA (VC): SURVIVAL OUTCOMES AND TOXICITY PROFILE ANALYSIS OF A MONO-INSTITUTIONAL EXPERIENCE.

Code: 511

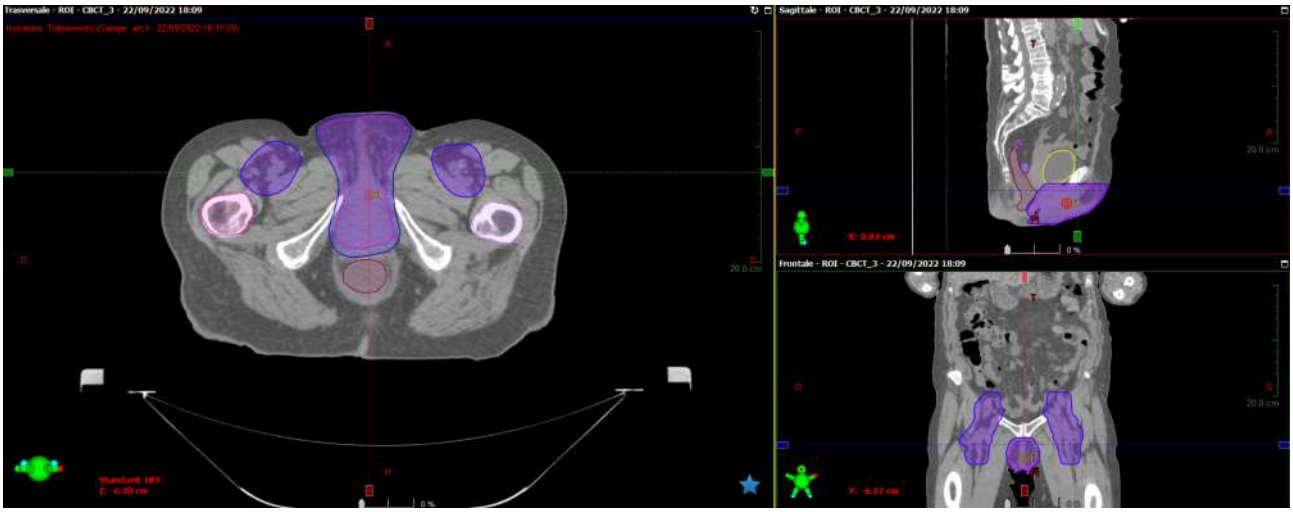
Aims: To evaluate outcomes and toxicity of cohort of VC patients (pts) treated with Intensity Modulated radiation therapy (IMRT).

Methods: We retrospectively analysed VC pts who underwent IMRT at our institution. Toxicities were graded using the CTAE v5.0. The Kaplan–Meier method was used to estimate the rates of survival outcomes. The risk factors were performed with the log-rank test. The chi-square test (or Fisher's exact test) for ordinal and nominal variables was used to evaluate the association between toxicities and treatment.

Results:22 pts were treated between March 2018 and June 2023. Median follow-up was 18 (IQR: 8-35). Median age was 77 years (IQR: 72-84). FIGO stage were IA in 11 pt, IB in 8 pts, II in 2 pts, IIIA in 4 pts, IIIB in 4pts, IIIC in 1 pts and IVA in 2 pts. Fourteen pts received adjuvant RT, and 8 received definitive RT. Median RT dose to the vulva/vulvar bed and loco-regional nodes were 55 Gy (range 45-64) and 50.4 Gy (range 45-64) delivered in 28 fractions (range 25– 33). Concurrent chemotherapy was used in 4 pts.
Median treatment time was 43 days (range 33-77). Due to intercurrent acute toxicities 2 pts interrupted temporarily RT for 4 and 5 days, respectively. Two and 8 pts experienced severe (G3) gynaecological (vaginal mucositis) and skin acute toxicity (erythema), respectively. We reported only one late skin sever toxicity (cutaneous fistula) in a pts with locally advanced tumor stage and 8 severe gyn toxicities (vaginal stenosis). Large pelvis RT fields were related to worst GI acute toxicity compared to small pelvis RT fields (p-value <0.01). Median OS was 37 months (95%CI:29-54). Six-months, 1 year- and 2 year- OS were 81.1%, 70% and 49%, respectively. OS for histological grade 1–3 was

statistically significant different (p- value <0.01). Adjuvant RT showed a trend toward better OS compared to definitive RT (Pvalue 0.08). Six pts had local failure, median time to local failure was 4 months (range 1-52). Six-months and 2 year- LC were 75% and 38%. Eight pts had progression with 6 months- 1 year- and 2 year-PFS were 77%, 66% and 33%. Histological grades were statistically related to PFS: 6 months-PFS was 100%, 56% and 33% for grade 1, 2 and 3, respectively with a p-value <0.01. Three patient developed lung metastasis and histological grade G1-3 was related to worst MFS (p.value 0.04).

Conclusions: IMRT for VC is well tolerated. Further studies with larger cohorts are encouraged to establish strategies to improve survival outcomes.



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EFFICACY OF TARGETED INTRAOPERATIVE RADIOTHERAPY (TARGIT- IORT) AS ANTICIPATED BOOST IN HIGH-RISK BREAST CANCER.

Code: 61

Aims: High risk breast cancer require a tumor bed boost dose. We reported clinical outcome of TARGIT IORT as anticipated boost modality in a large single-institute population.

Methods: All patients had an infiltrative breast carcinoma and at least one of the following risk factors: age<50years, grading G3, diffuse lymphvascular invasion or diffuse peritumoral ductal in situ carcinoma, positive nodes or lobular histology. Patients were treated with TARGIT-IORT as anticipated boost modality during lumpectomy with a dose 20Gy. Whole breast radiotherapy was performed with standard or hipo- fractionated schedule. Primary outcomes were 5-years in-breast tumor relapse risk and survival without in breast tumor recurrence, secondary analyses were regional- and distant recurrence-free survival, mastectomy-free survival, overall survival and tumor-related survival. Primary and secondary outcomes were estimated with Kaplan Meyer method. High grade toxicity events were collected and scored according to Common Terminology Criteria of Adverse Events scale 5.0.

Results: The study included 439 patients treated between 2002 and 2021. Median follow up was 89 months (range:6-245) and 82% of patients had a 5-year complete follow up. The estimated risk of 5 years in-breast tumor recurrence was 0.8% (95%CI=0.4%-1.2%) and 5-year survival without local relapse (event=death or local recurrence) was 96.4% (95% CI=95.5%-97.5%). Survival analysis results for secondary endpoints were reported in Table 1. Only 5/23 (23%) local relapses were inside the previous index quadrant. High grade toxicity (CTCAE Grade 3-4) events were rare (incidence=1.1%) and consisted in 1 case of skin fistula, 2 cases of severe fibrosis and 2 radiation induced angiosarcomas.

Conclusions: TARGIT-IORT was an effective modality to deliver an anticipated boost in high-risk breast cancer patients.

Table 1: five-years Kaplan Meyer estimates of survival measures

Outcomes	Kaplan-Meyer estimates (95%CI)
5 years regional recurrence free survival	99.5 (99.2-99.8)
5 years distant recurrence free suvival	97.5% (96.7-98.3)
5 years mastectomy-free survival	99.2 (98.8-99.6)
5 years overall survival	97.2% (96.6-97.8)
5 years tumour related survival	98.7% (98.1-99.3)
5 year not tumour related survival	98.5% (97.9-99.1)

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ELDERLY AND FRAIL PATIENTS WITH MUSCLE-INVASIVE BLADDER CANCER: IS SBRT A SAFE AND FEASIBLE APPROACH WHEN NO OTHER LOCAL OPTIONS ARE AVAILABLE?

Code: 113

Aims: As of today, 20–30% of bladder cancer patients present with potentially curable disease but are considered too frail to undergo radical treatments and SBRT targeting macroscopic bladder tumor could represent a valuable palliative treatment approach. The present study aims to report the feasibility and safety of this approach in a monocentric cohort of frail and elderly bladder cancer patients not eligible for curative treatments.

Methods: Data of patients who underwent SBRT to the gross disease or to the tumor bed after transurethral resection of bladder tumor (TURBT) from 2017 to 2021 at the European Institute of Oncology IRCCS, Milan, Italy were retrospectively considered. SBRT was delivered with image-guided radiation therapy (IGRT) using three different linear accelerators. Schedules of treatment were 30 and 25 Gy in 5 fractions (both every other day, and consecutive days). Treatment response was evaluated with radiological investigation and/or cystoscopy. Toxicity assessment was carried out according to Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer (RTOG/EORTC) v2.0 criteria.

Results: A total of 16 patients were included in the study (Table 1), of them 11 received SBRT on the macroscopic target volume and 5 on the tumor bed after TURBT. No grade (G) >2 acute toxicities were described after treatment for both groups. Regarding late toxicities, only one patient in the group receiving SBRT on the macroscopic disease reported G4 GU toxicity. Ten patients had available follow-up status, of them six had complete response, one had stable disease, and three had progression of disease. The overall response rate and disease control rate were 60% and 70%, respectively.

Conclusions: To the best of our knowledge, this is the first report of SBRT for bladder cancer in a frail and elderly population. Our preliminary data demonstrate that the treatment is technically feasible, with an acceptable toxicity profile. These outcomes emphasize the potential of this approach in a non-radical setting and could help to provide more solid indications in this underrepresented setting of patients.

Group 1 (n = 11)		**Median (IQR)**
Median age	*years*	81.6 (79.8 – 86.4)
		n
Gender	*male*	8
	female	3
ACCI	*6*	1
	7	1
	8	1
	9	4
	10	1
	11	2
	12	1
Histologic type	*Urothelial*	10
	other	1
T stage	*ycT1*	1
	cT2	3
	ycT2	3
	ycT3b	2
	cT4a	1
	ycT4a	1
N stage	*cN0*	6
	ycN0	2
	cN1c	1
	ycN3	2
M stage	*cM0*	5
	ycM0	1
	ycM1a	2
	cM1b	1
	ycM1b	1
	cMx	1
Group 2 (n = 5)		**Median (IQR)**
Median age	*years*	83.0 (73.7 - 85.5)
		n
Gender	*male*	3
	female	2
ACCI	*7*	1
	8	2
	11	1
	12	1
Histologic type	*Urothelial*	5
T stage	*ycT2*	2
	ycTx	3
N stage	*cN0*	4
	cNx	1
M stage	*cM0*	4
	cM1b	1

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THE EFFICACY OF STEREOTACTIC BODY RADIATION THERAPY FOR SYSTEMIC TREATMENT-FREE OLIGORECURRENT RENAL CELL CARCINOMA: SURVIVAL OUTCOMES AND PREDICTIVE FACTORS

Code: 112

Aims: Renal cell carcinoma (RCC) has been historically considered a radioresistant tumor; however, encouraging results have been recently reported about stereotactic body radiation therapy (SBRT) delivered both on the primary tumor and on metastatic sites. This study aims to assess the effectiveness and survival outcomes of SBRT in systemic treatment-free patients with oligorecurrent RCC.

Methods: We retrospectively analysed data of patients treated with SBRT on oligorecurrent sites from RCC. All patients were treated with Volumetric modulated arc therapy (VMAT) technique with ablative intent. Endpoints of the analysis were overall survival (OS), local control (LC), distant metastases free survival (DMFS), time to systemic therapy and pattern of toxicity. Univariate analysis and multivariate Cox regression (backward conditional) model were carried out.

Results: From 2006 to 2022, 61 patients were treated with SBRT on oligorecurrent metastases. SBRT was delivered on a single metastasis in 35 (57.4%) patients, 18 (29.5%) patients were treated on 2 metastases and in 8
(13.1%) patients 3 to 5 metastases. Lesions were in a single organ in 52 (85.2%) patients, in 2 organs in 8 (13.1%) patients and in 1 patient in 3 organs. After a median follow up of 26.8 months, median OS and LC were not reached. One and three-years OS rates were 88.2% (95%CI 76.8–94.2) and 65.6% (95%CI 50.0–77.4), respectively; rates of LC at 1 and 3 years were 94.7% (95%CI 84.5–98.2) and 86.5% (95%CI 71.6-93.9), respectively. Presence of bone disease and number of metastases were confirmed to be independent predictor of OS. Median DMFS was 14.7 months, with 1- and 3-years rates of 56.7% (95%CI 42.7–68.5) and 31.6% (95%CI 19.2–44.8). Treatment of lung metastases was associated with a significant improvement in DMFS compared to other sites of disease. Median time to systemic therapy activation was 60.8 months; older age and treatment of lung metastases were associated with longer delay of systemic therapy, while the presence of bone disease was associated with an earlier onset. In term of toxicity, SBRT was well tolerated with only 2 (3.3%) patients experiencing G3 acute toxicity.

Conclusions: SBRT can be safely and effectively delivered on oligometastatic patients affected by recurrent RCC, despite the traditional radioresistance. Patients with older age and lung metastases are most likely to benefit from SBRT by delaying time to systemic therapy, while the presence of bone disease may request a more intense regimen of treatment.

Patients' characteristics

	Patients, No (%) **N=61**
Age (years) - Median - Range	 66 42 - 88
Sex - Male - Female	 51 (83,6%) 10 (16,3%)
Performance status - 0 - 1 - 2	 40 (65,6%) 19 (31,1%) 2 (3,3%)
Primary tumor treatment - Total nephrectomy - Other	 56 (91,8%) 5 (8,1%)
Primary tumor histology - Clear cells - Papillar - Others	 52 (85,2%) 7 (11,5%) 2 (3,3%)
Metastatic presentation - Synchronous - Metachronous	 6 (9,8%) 55 (90,2%)
Bones metastases - Yes - No	 12 (19,7%) 49 (80,3%)
Number of treated organs - 1 - 2 - 3 or more	 52 (85,3%) 8 (13,1%) 1 (1,6 %)
Number of irradiated metastases - 1 - 2 - 3 or more	 35 (57,4%) 18 (29,5%) 8 (13,1%)
Irradiated lesions sites - Lung - Brain - Adrenal gland - Pancreas - Others	 24 (39,3%) 12 (19,7%) 8 (13,1%) 6 (9,8%) 14 (23%)
BED10 (Gy) - Range - Median - >100 - <100	 35,7 - 120 78,7 19 (31,1%) 42 (68,9%)

Median OS was not reached. One and three years OS rates were 88.2% (95%CI 76.8 – 94.2) and 65.6% (95%CI 50.0 – 77.4).

	Univariate			Multivariable		
	HR	95%CI	P value	HR	95%CI	P value
Age	1.04	0.99 – 1.08	0.062	-	-	-
Gender, Male	1.11	0.32 – 3.80	0.867	-	-	-
ECOG PS	1.69	0.86 – 3.34	0.127	-	-	-
DFI	1.00	0.99 – 1.01	0.569	-	-	-
Time to SBRT	0.99	0.97 – 1.00	0.416	-	-	-
Bone disease	**3.39**	**1.29 – 8.86**	**0.013**	**3.06**	**1.10 - 8.50**	**0.031**
N mets	**2.53**	**1.58 – 4.04**	**0.000**	**2.37**	**1.25 – 4.50**	**0.008**
N Organs	**2.83**	**1.15 – 6.93**	**0.022**	1.15	0.33 – 3.92	0.818
Lung mets vs other	0.36	0.13 – 1.01	0.054	-	-	-
BED10	0.98	0.96 – 1.00	0.056	-	-	-
Local relapse	1.19	0.27 – 5.15	0.813	-	-	-

Median LC was not reached. Rates of LC at 1 and 3 years were 94.7% (95%CI 84.5 – 98.2) and 86.5% (71.6 – 93.9).

	Univariate			Multivariable		
	HR	95%CI	P value	HR	95%CI	P value
Age	0.99	0.92 – 1.07	0.959	-	-	-
Gender, Male	-	-	-	-	-	-
ECOG PS	0.45	0.06 – 3.41	0.443	-	-	-
DFI	0.97	0.94 – 1.01	0.189	-	-	-
Time to SBRT	0.98	0.95 – 1.02	0.459	-	-	-
Bone disease	2.59	0.46 – 14.37	0.274	-	-	-
N mets	2.01	0.77 – 5.23	0.150	-	-	-
N Organs	1.71	0.20 – 14.71	0.622	-	-	-
Lung mets vs other	0.24	0.02 – 2.12	0.203	-	-	-
BED10	0.96	0.92 – 1.00	0.074	-	-	-

Median DMFS was 14.7 months, with 1 and 3 years rates of 56.7% (95%CI 42.7 – 68.5) and 31.6% (95%CI 19.2 – 44.8).

	Univariate			Multivariable		
	HR	95%CI	P value	HR	95%CI	P value
Age	0.98	0.95 – 1.01	0.330	-	-	-
Gender, Male	1.84	0.71 – 4.71	0.202	-	-	-
ECOG PS	0.98	0.55 – 1.72	0.947	-	-	-
DFI	0.99	0.99 – 1.00	0.451	-	-	-
Time to SBRT	0.99	0.98 – 1.00	0.256	-	-	-
Bone disease	**2.75**	**1.30 – 5.77**	**0.008**	**2.14**	**1.00 – 4.58**	**0.048**
N mets	**1.59**	**1.07 – 2.36**	**0.021**	**1.97**	**1.27 – 3.06**	**0.002**
N Organs	1.04	0.41 – 2.66	0.924	-	-	-
Lung mets vs other	**0.40**	**0.20 – 0.80**	**0.009**	**0.32**	**0.15 – 0.67**	**0.002**
BED10	0.99	0.97 – 1.00	0.206	-	-	-
Local relapse	1.54	0.59 – 4.00	0.375	-	-	-

Median time to systemic therapy was 60.8 months. RAtes at 1 and 3 years were 85.9% (95%CI 73.7 – 92.7) and 55.4% (95%CI 37.1 – 69.6).

	Univariate			Multivariable		
	HR	95%CI	P value	HR	95%CI	P value
Age	**0.95**	**0.91 – 0.99**	**0.019**	**0.91**	**0.87 – 0.96**	**0.001**
Gender, Male	5.44	0.72 – 41.12	0.101	-	-	-
ECOG PS	0.83	0.36 – 1.93	0.680	-	-	-
DFI	0.98	0.97 – 1.00	0.068	-	-	-
Time to SBRT	0.98	0.96 – 1.00	0.130	-	-	-
Bone disease	**4.50**	**1.64 – 12.35**	**0.003**	**6.46**	**2.10 – 19.80**	**0.001**
N mets	1.58	0.95 – 2.65	0.077	-	-	-
N Organs	0.62	0.14 – 2.64	0.526	-	-	-
Lung mets vs other	**0.39**	**0.15 – 0.99**	**0.048**	**0.30**	**0.11 – 0.81**	**0.019**
BED10	0.98	0.97 – 1.00	0.185	-	-	-
Local relapse	2.25	0.63 – 8.01	0.208	-	-	-

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DEVELOPMENT AND EXTERNAL VALIDATION OF A DL-BASED CTV SEGMENTATION MODEL ON A LARGE MULTICENTRIC DATASET IN THE CASE OF WHOLE-BREAST RADIOTHERAPY TREATMENT

Code: 235

Aims: To optimize the radiotherapy treatment and reduce toxicities, OARs and CTV must be segmented. The aim of this work is to create for the first time an advanced in-house DL 3D model able to automatically segment right and left CTV breast together thanks to the availability of a large single- institute patients' cohort (611 patients: 332 right, 279 left). Moreover, the model has been internally and externally validated on the multicentric MIKAPOCo cohort of 8 institutes (including Institute 3, the same center on which training was performed) on 978 patients (526 right, 452 left).

Methods: The dataset (3D CT images) consists of 611 patients, who underwent breast-conserving surgery followed by radiotherapy, whose CTV delineation was performed by different clinicians. A pre-
processing (es. crop, resize, scaling, data augmentation), aimed to uniform all the images, followed by a 3D- Unet able to segment both right and left CTV was implemented. The model performance of the validation set was addressed through the following metrics: Dice Similarity Coefficient (DSC), Hausdorff distance (HD) and its 95th percentile variant (HD 95). The same procedure was applied to the external validation dataset.

Results: The best 3D model achieved high performance on the validation set after 178 epochs (DSC: 0.901; HD: 20.9 mm; HD 95: 9.6 mm). The predicted segmentation well matches the clinicians' contours on the skin and chest side, while it is more uncertain, as expected, on the lateral and cranio-caudal side. Along the cranio-caudal axis, the predicted contours are more extended than clinical ones (caudal: 4.5 mm, IQR: 1.5-9.0; cranial: 10.5 mm, IQR: 4.5-21.0), as expected given the different strategies used by clinicians. The same metrics applied on internal and external data showed an overall agreement and model transferability for all but one center considered (see Fig. 1). Institute 9 is the most discrepant one, with clinical contours definitely smaller than the other centers and Institutes 10, 7, 1 showed a variability larger than the one of internal validation set.

Conclusions: We have constructed a 3D Unet for CTV segmentation trained on a single-institute large cohort. The training performance was accessed through validation metrics, obtaining DSC: 0.901 and HD 95: 9.6 mm. The model was internally and externally validated on 8 centers, showing an agreement with the training results, with the exception of Institute 9. Moreover, with the exclusion of patients with silicone implants, the model performance will further increase.

Figure 1: DSC, HD, HD_95 and VD (divided by the side of the CTV) trend across different institutes, being Institute 3 the training one. VD negative means larger CTV prediction. Box plots are shown with median (solid line) and mean values (dashed lines). Outliers are shown with dots. Black line shows the best metric values obtained for validation and gray line the median expected VD (zero).

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ADJUVANT HIGH-DOSE-RATE VAGINAL BRACHYTHERAPY (HDR-VB) AS MONOTHERAPY IN EARLY STAGES ENDOMETRIAL CANCER (EC) WITH INTERMEDIATED AND INTERMEDIATED HIGH RISK FACTORS WITH A SCHEDULE OF 25 GY IN 5 WEEKLY FRACTIONS OF 5 GY. AN UPDATE

Code: 506

Aims: to evaluate the toxicity and the outcome in I-II FIGO stage EC treated with high-dose-rate-brachytherapy (HDR-VB) with schedule of 25 Gy in 5 weekly fractions of 5 Gy.

Methods: From 2014 to 2019 seventy-one consecutive EC patients (pts) received adjuvant HDR-VB. The median age was 65 years (38-87yrs). All pts underwent primary surgery, 56,3% with and 43,7% without lymphadenectomy. Endometrioid was the prevalent histology (95,8%). FIGO stage distribution was: IA 25,4%, IB 67,2% and II 7,4%.Tumor grade G1-2 was in 55 (77,5%) and G3 in 16 (22,5%) pts. Lymph- vascular space involvement (LVSI) in 8 (11,3%) pts. The pts risk was: 6 (8,5%) low, 48 (67,6%) intermediate,1 (19,7%) intermediate-high and 3 (4,2%) high. Brachyvision treatment planning system and GammaMed device (HDRIr192) were used to plan and treat the pts.The median vaginal cylinder diameter was 3 cm. All pts were treated with schedule of 25 Gy in 5Gyx 5 weekly/fr at 0,3-0,5 cm depth from the vaginal surface. The CTV was the upper half of vagina (median =4.5 cm). Bladder, rectum and bowel were the OARs. Vaginal, gastro-intestinal and genito-urinary toxicity was graded according CTCAE 5.0 scale.
Late toxicity and recurrence were evaluated against age, grade, LVSI, stage, risk group, BMI, number of nodes removed, dose prescription depth. The Kaplan-Meier method was used to estimate rates of six-years LC,OS, DFS and CSS.

Results: The median follow-up was 74,3 months (14-109 months). Tumor relapsed, within the first 3 yrs, in 10 (14%) pts: 3 (4,2%) vaginal, 1 (1,4%) pelvic, 5 (7%) distant and 1(1,4%) pelvic both distant. Late
toxicities G2 were: 1 (1,4%) costipation, 1 (1,4%) incontinence, 2 (2,8%)vaginal dryness and 8 (11,3%) vaginal stenosis. Age, BMI, >10 nodes removed, dose prescription depth, risk group,LVSI were not correlated with toxicity at univariate analysis. Only the stage IA and IB versus stage II (p=0.0001) were significantly correlated with DFS: 92,7% and 26,6% respectively. The 6-year OS, DFS, CSS and LC were 94,7%, 93%, 96,9% and 97,1% respectively.

Conclusions: There are no prospective data on the best schedule of VB alone in EC, however our experience, produced similar results of other studies. We reported 3 (4,2%) vaginal recurrences and 8 (11,3%) late G2 vaginal stenosis.No late G3-G4 toxicities were registrated. Furthermore, our study population experienced a high vaginal control rate of 97,1%, with fractionation scheme of 25 Gy in 5Gy x 5 weekly fr.

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EVALUATION OF TREATMENT TIME INFLUENCE ON THE BIOLOGICAL EFFECTIVENESS OF BRAIN RADIOSURGERY TREATMENTS

Code: 331

Aims: Brain radiosurgery (SRS) planning does not take into account the overall treatment time (OTT) even if it is well known from early cell survival studies that treatment protraction causes a loss of biological effective dose (BED). The study aimed to assess the time-dependence in biological effectiveness of linac-based single-isocenter SRS using the BED-OTT model proposed by Jones and Hopewell in 2018 for radionecrosis endpoint. A comparison with SRS-dedicated platforms with longer treatment times was added.

Methods: This retrospective analysis included 34 single-lesion (SL) and 24 multiple-lesion (ML) SRS cases, focusing on the number of arcs (n) and OTT. A 30-second inactive time between arcs was considered (dose record and following arc setup). The study employed half-times for fast ($t_{1,1/2} = 0.19$ h) and slow ($t_{2,1/2} = 2.16$ h) repair of sublethal damage with equal weight in the repair kinetics. The suggested α/β of 2.47 Gy was used. BED-OTT values were calculated for prescription doses (18/21 Gy), as an approximation of brain maximum dose, and for the common 12 Gy. BED-OTT was compared to the simple linear-quadratic (LQ) model ($\Delta[\%]$ = BED-OTT – BED-LQ). In order to compare treatment times between SRS-dedicated platforms, BED-OTT values were also calculated for 21 Gy and 60 min- and 120 min-OTT, with 1 or 5 interruptions.

Results: Results recorded median OTT of 3.4 min and 4.8 min for SL and ML cases, respectively, with corresponding median Δ of -2.6% and -4.1%. On the other hand, a 60 min-long delivery of 21 Gy with 1 or 5 interruptions would correspond to a Δ of -25.8 % and -27.4%. A 120 min-long delivery of 21 Gy with 1 or 5 interruptions would lead to a Δ of -36.7% and -37.8%. The 12 Gy-BED-OTT registered a median Δ of -2.4% and -3.7% in SL and ML cases, respectively. For a 60- and 120-minute delivery with 1 interruption, Δ for 12 Gy-BED-OTT would be -23.9% and -34.1%, respectively. Results are summarized in **Table 1**.

Physical Dose	*BED_{LQ} [Gy]*	
21	199.5	
18	149.2	
12	70.3	
Cases	OTT [min]	
SL	3.4 [2.3 – 5.9]	
ML	4.8 [3.7 – 9.3]	
Physical Prescription Dose	BED_{OTT} [Gy]	$\Delta[\%] = BED_{OTT} - BED_{LQ}$
SL (34)	-	-2.6 [-1.7 – -4.3]
SL – 21 Gy (26)	194.7 [191.0 – 195.9]	-2.4 [-1.8 – -4.3]
SL – 18 Gy (7)	145.3 [144.0 – 146.7]	-2.6 [-1.7 – -3.5]
ML (24)	-	-4.1 [-2.6 – -6.2]
ML – 21 Gy (19)	192.0 [189.6 – 194.4]	-3.7 [-2.6 – -5.0]
ML – 18 Gy (5)	141.5 [140.0 – 144.7]	-5.1 [-3.0 – -6.2]
SRS-dedicated platform		
21 Gy – 60 min		
1 interruption	148.1	-25.8
5 interruptions	144.9	-27.4
21 Gy – 120 min		
1 interruption	126.2	-36.7
5 interruptions	124.1	-37.8
Physical Constraint Dose (12Gy)	BED_{OTT} [Gy]	$\Delta[\%] = BED_{OTT} - BED_{LQ}$
SL	68.6 [67.5 – 69.2]	-2.4 [-1.6 – -4.0]
ML	67.6 [66.2 – 68.6]	-3.8 [-2.4 – -5.8]
SRS-dedicated platform		
12 Gy – 60 min		
1 interruption	53.5	-23.9
5 interruptions	52.5	-25.4
12 Gy – 120 min		
1 interruption	46.4	-34.1
5 interruptions	45.7	-35.0

Table 1 – Comparison of obtained BED values obtained with the linear-quadratic model (BED_{LQ}) and the model including the overall treatment time (OTT) proposed by Jones and Hopewell (BED_{OTT}). In both models, the considered α/β = 2.47 Gy. Abbreviations: SL single-lesion cases, ML multiple-lesion cases, (#) number of cases

Conclusions: With simple equations, this study compared the BED time-dependency between linac-based and dedicated- platforms SRS and showed that calculated BED values were higher for both maximum brain dose and 12 Gy in the former group. An investigation on clinical outcome correlations should help guide decision-making and possibly leads to adjustment in doses. By incorporating the BED model and evaluating treatment time dependencies, the study provides valuable insights for optimizing SRS protocols and potentially enhancing patient care.

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SALVAGE STEREOTACTIC REIRRADIATION FOR LOCAL RECURRENCES OF SPINAL METASTASIS

Code: 149

Aims: Local recurrences of spinal metastases after radiotherapy have been historically difficult to manage due to concerns about severe spinal cord toxicity. We report our institutional experience on salvage robotic stereotactic radiotherapy (sSRT) to previously irradiated spinal metastases, investigating safety and efficacy.

Methods: From January 2018 to September 2023, 21 metastatic spinal segments in 20 patients who received sSRT, following imaging-confirmed local relapse at a site previously treated with radiotherapy, were retrospectively identified. Primary tumor was of prostate in 11 pts, lung in 3 pts, kidney in 5 pts, and thyroid in 1 patient. sSRT sites were: cervical (9.1%), thoracic (54.5%), lumbar (31.8%), and sacral (4.6%). For the first RT course, median dose and number of fractions were 25.3 Gy in 5 fractions (range, 18-45 Gy in 1-30 fractions). Median time from first irradiation to sSRT was 30.9 months (6.9-81.8).
Median sSRT dose and number of fractions were 25 Gy in 5 fractions (range, 15-30 Gy in 1-5 fractions). Equivalent dose in 2-Gy fractions (EQD2) to evaluate late toxicity was calculated for both RT course using an α/β of 3. Median EQD2 for late toxicity was 103.5 Gy (81.1-220.5). Local control (LC) for each treated segment was calculated from the date of the sSRT and estimated using the Kaplan-Meier method. Toxicity was assessed with CTCAE version 5.0 criteria.

Results: Starting from sSRT, median follow-up was 14.1 (1-50.3) months. One pt reported pain flare one day after RT with spontaneous pain relief. No neurological toxicities or vertebral compression fractures were observed after sSRT. Of the 10 pts who reported pain (median VAS 5, range 5-8), 70% presented a complete pain response after sSRT. Local relapse free survival (LRFS) was 82.5% at 12 months and 66% at 36 months.

Conclusions: We observed negligible toxicity and good LC rates following sSRT in patients with local relapse after previous RT. Prospective clinical studies are needed to determine toxicity and the optimal salvage dose and fractionation.

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HIGH-DOSE PROTON THERAPY IN SKULL BASE CHORDOMA AND CHONDROSARCOMA: CLINICAL OUTCOME AND TOXICITY IN A LARGE COHORT SERIES

Code: 122

Aims: Skull base chordomas (C) and chondrosarcomas (CS) are locally aggressive tumors located adjacent to critical structures. Radiotherapy is used both as adjuvant therapy after surgery and as radical treatment. The aim of our retrospective study is to report the experience of the Trento Proton Therapy Centre in terms of toxicity profile and clinical outcome.

Methods: Between June 2015 and December 2023, 81 patients (pts) with skull base C and CS were irradiated with proton therapy (PT). Mean age was 50 years (range:3.7-84.1). There were 67 C (82.7%), and 14 (17.3%) CS. Tumor sites were: clivus (n= 74), petroclival region (n=5), and anterior cranial fossa (n=2). Sixty-three pts were treated at first diagnosis and 18 subjects after recurrence. Surgery was performed at least once in all but 2 patients; 72 cases had gross residual disease before PT, while 9 cases were without gross disease. Seven cases were re-irradiations.

Results: All but two pts completed their treatment (distant disease progression and general conditions decline). All pts were treated with active beam scanning PT. Single field optimization (SFO) and multifield optimization (MFO) were used in 38 and 43 pts, respectively. Mean high-risk (HR) PTV volume was 57.5 cc (range 2.2-335.8); mean low-risk (LR) PTV volume was 102 cc (range 19.3–432). Mean prescribed total dose was 71.5 GyRBE (range 54-74 GyRBE) for HR PTV and 54.0 GyRBE (range 50-59.5 GyRBE) for LR PTV. No acute or late ≥ Grade (G) 4 side effects were recorded. G3 ore more acute and late toxicities occurred in 2% of the pts. Radio-necrosis (RN) has been observed in 12 pts (14.8%) with a median time of 16 months after the end of PT (11 pts showed brain RN, 1 pt intra-tumoral RN); in 8 pts (66,6%) RN was asymptomatic (G1), and in the remaining cases (33.4%) it was managed with steroid therapy (G2). At the median follow-up of 37 months (range: 1- 68) 8 out of nine patients treated without gross disease are alive without any relapse. Regarding the 72 pts with gross disease: 54 (75%) are alive with locally controlled disease, 6 (8%) are alive with local and/or distant progression, 7 (10%) died of local disease, 2 (3%) died of local and distant progression and 3 (4%) died of other causes. Median time of local relapses was 20.2 months (range 1.0 - 53.8 months).

Conclusions: PT allows to deliver high doses of radiation therapy in a very critical setting. Results are encouraging but a longer follow-up is needed to gain more robust data for late toxicity and long-term disease control.

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GUIDING METASTASES-DIRECTED THERAPY WITH PROSTATE-SPECIFIC MEMBRANE ANTIGEN (PSMA) PET/CT IMPROVES THE ONCOLOGICAL OUTCOME OF OLIGOMETASTATIC PROSTATE CANCER PATIENTS.

Code: 545

Aims: To verify the impact of next-generation imaging compared to conventional imaging as a guide for metastases-directed therapy (MDT) in a real-world multicentric cohort of oligometastatic prostate cancer (PCa) patients.

Methods: We retrospectively recruited 256 de-novo oligometastatic or oligorecurrent PCa patients submitted to image-guided MDT in six tertiary-level cancer Centers. Inclusion criteria were: (i) histologically-confirmed diagnosis of PCa; (ii) imaging evidence of ≤5 pelvic or extra-regional nodal (M1a), or bone metastases (M1b); (iii) upfront MDT delivered through SBRT±systemic therapy guided by either bone scan and CT/MRI (conventional imaging), [18F]F-Fluorocholine, [68Ga]Ga-PSMA-11 or
[18F]-PSMA-1007; (iv) availability of the subsequent clinical follow-up. Progression after MDT was defined as either biochemical recurrence (PSA raise ≥2 ng/dL and 25% above nadir), radiological or clinical progression, subsequent treatment changes, or death. Clinical, laboratory and imaging parameters were assessed as predictors of Progression-Free Survival (PFS, primary endpoint of the study).

Results: Clinical characteristics of patients enrolled at the time of MDT are shown in table 1.

Table 1: Clinical characteristics of patients enrolled at the time of metastasis-directed therapy.

		Overall (n=256)	Conventional imaging-guided MDT (n=13)	[18F]F-Fluorocholine-guided MDT (n=163)	PSMA-guided MDT (n=80)	*p-value*
Pre-imaging clinical characteristics						
Age		73.18±6.99	72.38±8.17	73.38±7.09	72.89±6.64	0.803
Initial AJCC stage						
	Stage I	12 (4.7%)	1 (7.7%)	9 (5.5%)	2 (2.5%)	**<0.001**
	Stage II	57 (22.3%)	0 (0.0%)	37 (22.7%)	20 (25.0%)	
	Stage III	142 (55.5%)	3 (23.1%)	91 (55.8%)	48 (60.0%)	
	Stage IV	45 (17.5%)	9 (69.2%)	26 (16.0%)	10 (12.5%)	
ISUP grade						
	ISUP 1	38 (14.8%)	1 (7.7%)	25 (15.3%)	12 (15.0%)	0.551
	ISUP 2	59 (23.1%)	1 (7.7%)	38 (23.3%)	20 (25.0%)	
	ISUP 3	62 (24.2%)	4 (30.7%)	35 (21.5%)	23 (28.8%)	
	ISUP 4	41 (16.0%)	1 (7.7%)	29 (17.8%)	11 (13.7%)	
	ISUP 5	56 (21.9%)	6 (46.2%)	36 (22.1%)	14 (17.5%)	
Primary treatment						
	Surgery	187 (73.0%)	3 (23.1%)	116 (71.2%)	68 (85.0%)	**<0.001**
	Radiotherapy (± ADT)	53 (20.7%)	3 (23.1%)	40 (24.5%)	10 (12.5%)	
	Medical therapy	16 (6.3%)	7 (53.8%)	7 (4.3%)	2 (2.5%)	
CRPC at MDT		58 (22.7%)	9 (69.2%)	37 (22.7%)	12 (15.0%)	**<0.001**
Treatment at MDT		109 (42.6%)	12 (92.3%)	65 (39.9%)	32 (40.0%)	**0.001**
PSA pre-MDT		3.76±6.22	9.18±15.83	3.99±5.29	2.41±4.72	**0.001**
Time of oligometastatic disease						
	De novo	50 (19.5%)	8 (61.5%)	24 (14.7%)	18 (22.5%)	**<0.001**
	Oligorecurrent disease	206 (80.5%)	5 (38.5%)	139 (85.3%)	62 (77.5%)	
Imaging findings						
Number of metastases						
	1 lesion	174 (68.0%)	7 (53.8%)	111 (68.2%)	56 (70.0%)	**0.024**
	2 lesions	56 (21.9%)	2 (15.4%)	40 (24.5%)	14 (17.5%)	
	3 lesions	18 (7.0%)	3 (23.1%)	11 (6.7%)	4 (5.0%)	
	4 lesions	6 (2.3%)	1 (7.7%)	1 (0.6%)	4 (5.0%)	
	5 lesions	2 (0.8%)	0 (0.0%)	0 (0.0%)	2 (2.5%)	
Site of metastases						
	Lymph node	175 (68.4%)	3 (23.1%)	119 (73.0%)	53 (66.3%)	**0.001**
	Bone	81 (31.6%)	10 (76.9%)	44 (27.0%)	27 (33.7%)	
SUVmax				8.02±6.32	9.71±8.77	0.112
MTV				3.06±2.92	2.81±3.54	0.592
TLG				17.09±20.60	12.75±17.93	0.145
MDT parameters and clinical follow-up						
MDT total dose (per lesion)		33.35±4.20	30.54±5.46	33.32±3.78	33.88±4.62	**0.028**
MDT BED (per lesion)		121.72±29.99	105.67±17.04	127.09±31.76	113.10±25.01	**0.037**
Follow-up (months)		37.14±24.75	17.90±14.37	44.75±25.25	24.75±17.40	**<0.001**

MDT was guided by conventional imaging, choline PET/CT, or PSMA PET/CT in 5.1%, 63.7% and 31.2% of patients, respectively. After MDT, PSA nadir was 2.58±8.97 ng/mL. The median follow-up was 30.8 months. At the univariate analysis, predictors of PFS were: castration resistance status at the time of MDT (p=0.013), PSA pre-MDT value (p<0.001), oligorecurrent compared to de-novo oligometastatic disease (p=0.030), number of metastatic lesions (p=0.038), presence of bone metastases (p=0.006), and PSA nadir after MDT (p<0.001). Notably, the use of either conventional imaging or choline PET/CT compared to PSMA PET/CT significantly predicted PFS (p<0.001 for both). The multivariate analysis confirmed imaging modalities guiding MDT and the PSA nadir as the sole independent predictors of PFS (p<0.001 for both).
Patients receiving MDT guided by conventional imaging, choline PET/CT, or PSMA PET/CT showed significantly different median PFS (5.8 vs. 13.1 vs. 34.5 months, respectively, p<0.001).

Conclusions: The use of next-generation imaging with PSMA PET/CT favorably impacts the oncological outcome of oligometastatic PCa patients treated with MDT.

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A MULTICENTER HIGH-QUALITY DATA REGISTRY FOR ADVANCED PROTON THERAPY APPROACHES: RESULTS FROM THE POWER REGISTRY

Code: 300

Aims: The paucity and low evidence-level data represent one of the main issues for the establishment of solid indications on proton therapy (PT). The POWER registry aims to prospectively and systematically collect data on patients treated with PT to expand the existing knowledge of suitable indications, feasibility, and clinical outcomes.

Methods: Patients with any tumor histology, site, and type of oncologic disease (benign and malignant disease) eligible for PT (according to international, national, and institutional recommendations), and able to provide informed consent were included in the registry. The collection is planned for a 5-year duration.
Three levels of data collection have been implemented: (i) clinical research; (ii) radiological research; (iii) biological and translational research. Quality-of-life questionnaires (general, specific for site, for age>70 years old, sexual activity, appreciation) were administered to all patients at baseline and at the end of treatment. A carbon footprint questionnaire was collected at the end of treatment. Pseudoanonymized data of PT patients will be collected and stored in a dedicated platform (Clinical Data Platform) for scientific purposes.

Results: From 29th November 2023 to 9th February 2024, 14 patients with a median age at enrollment of 55 years (range 34-77 years) have been included. All of them were treated with the IBA Proteus®ONE system. Population characteristics are shown in **Table 1**.

Table 1. Summary of patients' characteristics.

Pt ID	Age at treatment	Cancer site	Cancer type	Imaging	Treatment	Questionnaires
1	38	Gyn	Cervix SCC	MRI, PET-CT	R	QoLg, QoLs, ApQ, CFP
2	77	Gyn/Uro	Bladder UC	MRI, PET-CT	R	QoLg, QoLs, SaQ, AQ, ApQ, CFP
3	60	HN	Maxillar SCC	MRI	R	QoLg, QoLs ApQ, XQ, DQ, CFP
4	48	HN	Tongue SCC	MRI	F	QoLg, QoLs, XQ, DQ
5	66	HN	Oral SCC	MRI	R	QoLg, QoLs, XQ, DQ
6	53	HN	Maxillar ACC	MRI	R	QoLg, QoLs,XQ, DQ
7	56	Rectal	Rectal AC	MRI, PET-CT	R	QoLg, QoLs SaQ, ApQ, CFP
8	53	Anal	Analcanal SCC	MRI, PET-CT	R	QoLg, QoLs
9	60	CNS	GBM	MRI	R	QoLg, QoLs
10	55	CNS	Meningioma	MRI	F	QoLg, QoLs, ApQ CFP
11	65	CNS	Meningioma	MRI	F	QoLg, QoLs
12	55	Spinal	Neurinoma	MRI	F	QoLg, QoLs
13	34	Spinal	Melanoma	MRI,	F	QoLg, QoLs
14	61	Abdominal	Liposarchoma	MRI, CT	F	QoLg, QoLs

List of abbreviations: F = first treatment, R = re-irradiation, HN = head &neck, CNS = central nervous system, SCC = squamous cell carcinoma, ACC = adenoid cystic carcinoma, AC = adenocarcinoma, GBM = glioblastoma multiforme, MRI = magnetic resonance imaging, PET-CT = positron emission tomography-computed tomography, QoLg = quality of life general, QoLs = quality of life specific, AQ = age>70y, ApQ = appreciation, SaQ = sexual activity, XQ = xerostomia, DQ= dysphagia, CFP = carbon footprint.

Twenty diagnostic imaging data (15 MRI, 4 PET-CT, 1 CT), 14 simulation CT and corresponding PT treatment plans, set-up verification images, as well as 14 baseline blood samples (complete blood count with leukocyte formula) have been collected. At the time of the analysis, 5 patients completed the PT course and answered an additional questionnaire to investigate the environmental impact of PT in terms of its carbon footprint. Considering accommodation and transport costs sustained by patients, on average 315 euros were spent. The average home-institution mileage was about 430 km.
All patients complete the PT course without interruption due to treatment-related toxicity.

Conclusions: The POWER Registry is a high-quality scientific tool recently implemented at our Division. It aims to collect data of all patients treated with PT in order to provide reliable and robust real-world data for future clinical, radiomic, biological, and translational studies

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SBRT IN ELDERLY WOMEN WITH EARLY BREAST CANCER UNSUITABLE FOR SURGERY AND ELECTED TO RECEIVE PRIMARY ENDOCRINE THERAPY ALONE: PRELIMINARY RESULTS

Code: 344

Aims: To evaluate maximum tolerated dose (MTD) for Stereotactic Ablative Body Radiotherapy (SABR) for unresected breast cancer in elderly patients elected to receive primary hormone therapy alone.

Methods: This is a prospective, single institution, open-label, phase I study of dose escalation SABR performed according to time-to-event Keyboard (TITEKeyboard) design. We will enroll and treat 30 patients, in cohorts of size 10 patients, over 75 years, unfit for surgery or who decline surgery, with histologically confirmed diagnosis of early breast cancer (cT1-2 N0 M0), Luminal like A or B. Treatment dose levels will be 40Gy, 42.5Gy and 45Gy deliveredwith 5 fractions on everyother-day scheme. Primary end-point was the MTD, defined as the dose level associated with a ≤ 20% rate pre-specified treatment-related dose
-limiting toxicity (DLT). DLT was defined as any grade 3 or worse toxicity (CTCAE v.5.0) occurring within 6 months from the start of treatment. Co-secondary endpoints were patients reported quality of life (QoL), evaluated using the combined EORTC QLC-C30 and QLQ-BR23 questionnaires, breast cosmesis and primary tumor better response in terms of locoregional control (LRC) and clinical response (CR).
Cosmesis evaluation are carried out before treatment, at last day of treatment and at every clinical examination with Harris scale scoring system and with Breast-Q v2.0 questionnaire.

Results: From February 2021 to January 2024 we have enrolled and treated 10 pts at I dose level of 40Gy/5fx and 5 pts at intermediate dose level of 42.5Gy/fx with excellent tolerance to treatment (Tox: 0%≥G3; 7% G2; 27% G1; 66% G0). 12 pts achieved a follow-up of at least 6 months without reaching the MTD. Median time to cCR is 6.7 months and 8.4 months for rCR. QoL questionnaires reported an improvement after treatment for the majority of patients while all pts showed an excellent cosmesis. In this small number of patients no differences were observed in the EORTC QLC-C30 and score and the breast cancer-specific score (QLQ-BR23) from the baseline at 6 months follow-up.

Conclusions: These are preliminary data on the first dose level in an ongoing phase I study, that will be updated at AIROcongress. In elderly patients eligible for hormone therapy only and unsuitable for surgery, SBRT could improve locoregional control by means of a short and highly effective treatment without any interruption of systemic treatment. The study is still enrolling patients at second dose level.

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POSSIBLE STRATEGIES IN QUALITY ASSURANCE TO OPTIMIZE TREATMENT DELIVERY FOR INTERVENTIONAL RADIOTHERAPY (BRACHYTHERAPY) HEAD AND NECK REGION.

Code: 46

Aims: Quality assurance (QA) holds critical significance in the field of head and neck (H&N) interventional radiotherapy (IRT - brachytherapy), as has previously been discussed in the GEC-ESTRO ACROP recommendations. Four key phases of the IRT process have been identified: implant check, treatment planning, dose calculation, and treatment delivery. Aim of this report is to investigate the possible strategies to specifically implement treatment delivery in interstitial IRT, thereby ensuring the most accurate therapy for H&N cancer patients.

Methods: We collected all patients treated by IRT at our institutional Interventional Oncology Center through our electronic database for H&N cancer, covering a period from January 2022 to December 2023. We focused specifically on anatomical sub-sites with treatment schedules lasting beyond 5 days and therefore we considered only patients diagnosed with either nose vestibule or eyelid cancers which usually receive 14 fractions twice a day (with an overall treatment time of 9 days). The delivery of each fraction was in accordance with our institution's quality assurance program, detailed in Figure 1A. The Oncentra Brachy TPS (v.4.6.2, Elekta) was used to measure the length between the two buttons on each tube, comparing data between the initial CT scan and the midcourse scan.

Results: Our study encompassed 30 patients treated by interstitial IRT for nose vestibule or eyelid cancers. The procedure for these patients was performed involving an average of 6 plastic tubes per implant. In total 420 fractions were delivered and 360 measurements of the button-to-button distance were recorded using midcourse simulation. In most cases, data analysis showed no significant differences in the mean button distance between the first CT scan and the subsequent midcourse CT with the mean values of 35.2±10.5mm and 35.9±10.5 mm respectively, so apparently the overall result is consistent. However, in 10% of the cases, a replanning was deemed necessary as shown in Figure 1B. This decision was based on the threshold criterion that any mean variation in button distance exceeding 1 mm indicated a level of uncertainty necessitating the revision of the plan.

Conclusions: The administration of IRT for H&N cancers is a complex procedure that necessitates comprehensive training for the entire multi-professional team involved. Ensuring quality assurance is of utmost importance, not only for patient safety but also o increase the probability of attaining the desired clinical outcomes.

1A

Deviation to prevent	Timing	Action
Catheter-transfer tube misconnection	First fraction	Using different catheters' lengths
Catheter displacement	Every fraction	Visual check of catheters performed using marks
		Transfer tubes in antigravity position
	Midcourse	New simulation CT

1B

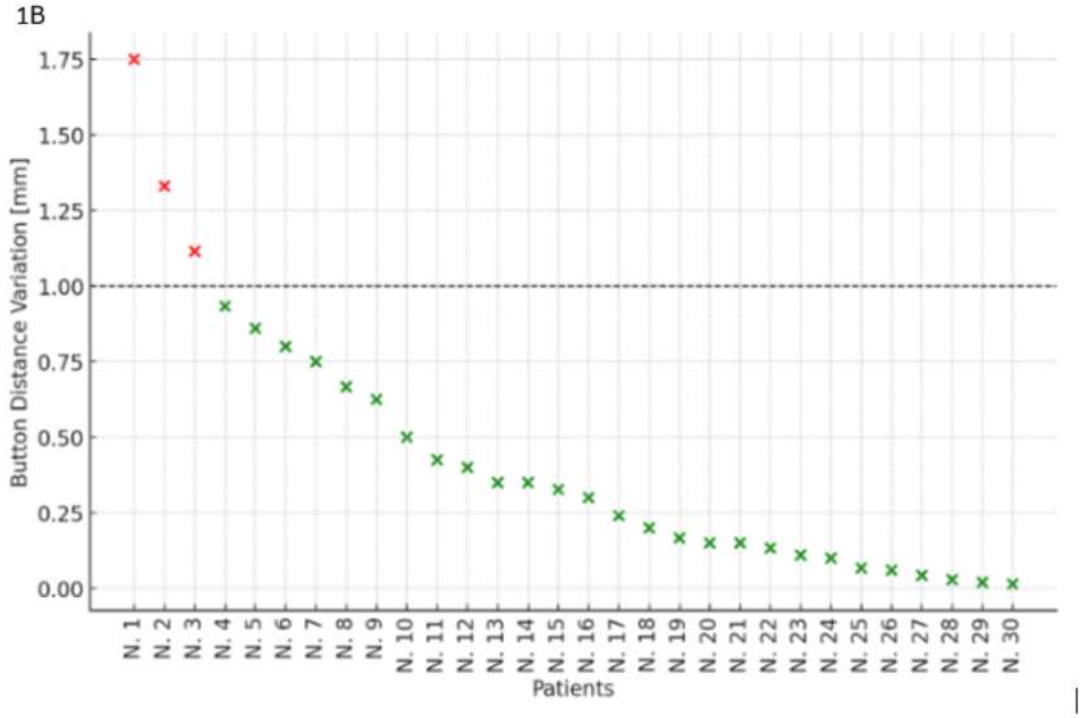

Figure 1: A) Summary of the quality assurance controls performed during the treatment delivery. B) Button Distance Variations for each patient: values exceeding the cutoff value (indicated in red) necessitate a revision of the treatment plan. Values below the cutoff threshold (green) do not require a reevaluation of the plan.

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SIMULTANEOUS INTEGRATED BOOST (SIB) PLANNING APPROACH IN CARBON ION RADIOTHERAPY FOR HEAD AND NECK ADENOID CYSTIC CARCINOMA (SIBACIRT): A PROSPECTIVE PHASE II TRIAL (NCT05733910).

Code: 62

Aims: investigate whether a Simultaneous Integrated Boost (SIB) planning approach in Carbon Ion Radiotherapy (CIRT) for head and neck adenoid cystic carcinoma (HNACC) patients can
significantly reduce toxicity without affecting Local Control, compared to the standard sequential (SEQ) planning strategy.

Methods: SIBACIRT is a monocentric, single arm prospective phase II clinical trial. The study duration is 36 months. Forty-two patients with HNACC (unresectable or after surgery) will be enrolled and treated with CIRT using a SIB approach, with a total dose to High Risk Clinical Target Volume (CTV) of 65.6 GyRBE in 16 fractions (4.1 GyRBE/fraction) and Low risk-CTV simultaneously receiving a total dose of 54.4 GyRBE (3.4 GyRBE/fraction) or 48 GyRBE (3 GyRBE/fraction) depending on different prognostic factors.
The primary endpoint will be acute and subacute toxicity (within 180 days after the end of treatment), graded using CTCAE version 5.0. Secondary endpoints will be: 1) local control assessed at least 12 months after starting of treatment; 2) development of multivariate predictive models, including clinical and dosimetric parameters, for different toxicity endpoints; 3) Quality of Life (QoL) according to EORTC QLQ C30 and QLQ 43 questionnaires, assessed at baseline, at the end of treatment and every 6 months after the end of treatment.

Results: In absence of published clinical trials, SIBACIRT will provide for the first time clinical controlled data about an innovative SIB approach with CIRT. Data will be compared to clinical outcomes in the CNAO historical series of HN-ACC patients treated with SEQ CIRT approach and a total dose of 65.6 Gy[RBE].

Conclusions: SIBACIRT results will be important to assess if a SIB strategy can provide clinical significant reduction of toxicities and improvement of patients' QoL without affecting LC, thus enhancing the potential benefits of CIRT in treating radioresistant and difficult to treat tumors.

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STEREOTACTIC MR-GUIDED RADIOTHERAPY OF CARDIAC TUMOURS/METASTASES - INITIAL DATA FROM THE MULTICENTRE SHARP STUDY

Code: 280

Aims: For inoperable cardiac metastases or primary cardiac tumors failing to respond to systemic therapy, treatment options are limited. Currently, there is limited data on the efficacy and toxicity of cardiac irradiation, which is mainly based on case reports. The multicenter prospective Stereotactic Heart Ablative RadiotheraPy (SHARP) study aims to investigate the toxicity and feasibility of stereotactic MR-guided radiation therapy (MRgRT) of inoperable cardiac/peri-/paracardial masses.

Methods: Patients were enrolled from September 2022 at 4 centers (Heidelberg, Rome, Zurich, Munich). The treatment involves stereotactic adaptive MRgRT in 5 fractions with doses of 6-8 Gy, prescribed to the 80% isodose. The primary objective is to assess acute tolerability and feasibility of irradiation.
Additionally, local control and toxicity are monitored for 1 year. Toxicity is assessed using the CTCAE 5.0 scale.

Results: A total of 23 patients were included. Patient characteristics are shown in table 1. One patient has completed the 1-year follow-up, while one patient discontinued irradiation due to reduced general condition (transferred to palliative care, not radiation-associated). The mean follow-up of the remaining 22 patients is currently 175 days. Regarding serious adverse events (SAEs), one patient developed G2 pneumonitis after 3 months, and another experienced ventricular fibrillation after 2 weeks (unclear if RT- associated, due to pre-existing condition). Acute toxicity at 3 months included mild to moderate side effects G1-2 (dyspnea, fatigue, pain). One patient reported therapy-related G3 fatigue after 6 months, and another had G3 chest pain at screening. At 3 months, 10 lesions (44%) reported complete response 4 (17%) and partial response 6 (26%), 7 remained stable (30%), and 6 (26%) were not evaluated (end of study, missing imaging).

Conclusions: MRgRT is a tolerable treatment modality for cardiac malignancies that are inoperable or have not responded to systemic therapy. This offers promising opportunities for patients who previously had no treatment options.

		N (%)
Patients		**23 (100)**
Gender	Male	14 (61)
	Female	9 (39)
Mean age at screening years (range)		61 (26-90)
Inclusion per site	Heidelberg	4 (17.5)
	Rome	5 (21.7)
	Zürich	7 (30.4)
	LMU	7 (30.4)
Average Follow Up (from RT-End)		175 Days
Median Follow-Up (from RT-End)		167 Days
Primary Histology	Sarcoma	4 (17.4)
	Thymoma	3 (13.1)
	CRC	3 (13.1)
	Melanoma	3 (13.1)
	NSCLC	2 (8.7)
	HCC	2 (8.7)
	Mesothelioma	2 (8.7)
	RCC	1 (4.3)
	Testicular tumour	1 (4.3)
	Pulmonary carcinoid	1 (4.3)
	HNSCC	1 (4.3)
Tumor response	CR	4 (17.4)
	PR	6 (26.1)
	SD	7 (30.4)
	PD	0
	Not assessed	6 (26.1)
RT dose fractionation (Gy)	5 x 6	2 (8.7)
	5 x 7	16 (69.5)
	5 x 8	3 (13.1)
	Not assessed	2 (8.7)
GTV to PTV margin (mm)	3 4 5 Not assessed	9 (39) 5 (22) 4 (17) 5 (22)
Dosimetric data *[available from 18/23 (78.3%) patients]*		
Average GTV Volume cc (range)		72.5 (0.5 – 308.0)
Average GTV D98% Gy (range)		37.18 (29.8 – 45.1)
Average PTV Volume cc (range)		107.7 (2.6 – 409.0)
Average PTV D98% Gy (range)		34.7 (29.1 – 40.6)
Average Heart excl. PTV Dmean Gy (range)		7.35 (1.2 – 14.9)
Average RT duration		
min (range)		56 (23 – 95)

Table 1: Patient cohort

CRC: colorectal carcinoma; NSCLC: non-small cell lung cancer; HCC: hepatocellular carcinoma; RCC: renal cell carcinoma; HNSCC: head and neck squamous cell carcinoma; CR: complete response; PR: partial response; SD: stable disease; PD: progression disease; RT: radiation therapy: GTV: gross tumor volume; PTV: planning target volume

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EARLY RESULTS OF RADIOMICIART TRIAL (NCT05081531): A PROSPECTIVE MONOCENTER STUDY OF MULTI-IMAGING ADAPTIVE RT FOR LOCALLY ADVANCED HEAD- NECK CANCER

Code: 92

Aims: Patients with head and neck cancer (HNC) may develop significant anatomical changes
during radiotherapy (RT). Adequate dose coverage and sparing of organs at risk can be guaranteed by re- planning with adaptive radiotherapy (ART). Advanced imaging modalities play a role in the customization of the RT as shown the use of ART and radiomic. The RadiomicART trial evaluates a machine learning-based radiomic approach to predict outcome and toxicity of HNC patients treated with ART by CT, MRI and PET-scan.

Methods: Patients with locally advanced HNC treated with radical RT from October 2021 to September 2023 were analyzed. Target volumes were delineated on CT and adjusted on MRI and FDG-PET-scan. The total dose was 66/60/54 Gy in 30 fractions with VMAT-SIB. For the whole sample, 95% of the prescribed dose covered at least 95% of the PTV. At week 3 after the start of RT, CT simulation, MRI and FDG-PET-scan were repeated for re-planning. In week 4, the new plan began (figure 1). We performed the comparison between the original plan and the re-simulation (adaptive plan) through CT, MRI and FDG-PET showing the variation of PTVs and collected early data on toxicity during follow-up.

	Baseline			Replanning		
	Median volume (cc)	Mean volume (cc)	Range (cc)	Median volume (cc)	Mean volume (cc)	Range (cc)
GTV-T	22,85	29,61	2,6-118,7	20,45	26,48	2,2-87,5
GTV-N	6,3	19,78	0-215,9	4,35	14,11	0-174,2
Right parotid	29,85	32,71	11,9-70,3	27,2	29,39	9,7-68,2
Left parotid	31,15	32,73	14,7-71,8	28,35	29,35	12,9-68,8
Right submandibular gland	9,3	10,7	5,1-29,5	8,45	8,23	4,3-12,4
Left submandibular gland	9,1	9,67	0,9-15,1	7,5	7,89	4,1-13,3

Table 1. Median and mean volumes of GTV-T, GTV-N, parotids and submandibular glands at basaline and re-simulation.

	Month 3				Month 6				Month 12			
Adverse effect	G1	G2	G3	G4	G1	G2	G3	G4	G1	G2	G3	G4
Asthenia	20%	4%	0	0	21%	3%	0	0	14%	4%	0	0
Dysphagia	22%	22%	0	0	39%	3%	0	0	27%	10%	0	0
Dysgeusia	49%	9%	0	0	34%	11%	0	0	34%	4%	0	0
Xerostomia	62%	20%	0	0	61%	3%	3%	0	69%	0	0	0
Weight loss	18%	9%	0	0	8%	11%	0	0	10%	4%	7%	0
Submental edema	9%	0	0	0	11%	0	0	0	0	0	0	0
Skin fibrosis	11%	0	0	0	16%	0	0	0	4%	0	0	0

Table 2. Adverse effect of RT at 3, 6 and 12 months.

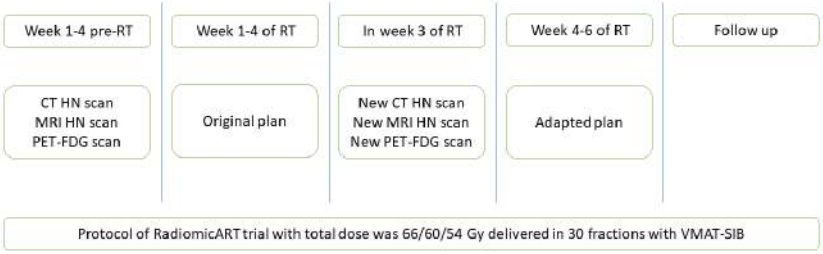

Figure 1. Protocol of RadiomicART for adaptive Radiotherapy.

Results: 51 patients were enrolled and completed the scheduled radiotherapy treatment. Median GTV-T and GTV- N at baseline and replanning were 22.85 cc (2.6-118.7) vs 20.45 cc (2.2-87.5), and 6.3 cc (0-215.9) vs 4.35 cc (0-174.5), respectively. Mean GTV-P were 29.61 cc vs 26.48 cc, and mean GTV-N 19.78 cc vs 14.11 cc, at basaline and re-simulation. Median right parotid volumes at baseline and replanning were 29.85 cc (11.9-70.3) and 27.2 cc (9.7-68.2) and left parotid were 31.15 cc (14.7-71.8) and 28.55 cc (12.9-68.8), respectively. Besides, median right submandibular glands volumes at baseline and replanning were 9.3 cc (5.1-29.5) vs 8.45 cc (4.3-12.4), and left gland were 9.1 cc (0.9-15.1) vs 7.5 cc (4.1-13.3). At the time of analysis, the most common grade 3 adverse events during follow up were xerostomia (3%) and weight loss (7%) (Table 2). Grade 2 xerostomia at 3, 6 and 12 months follow up was respectively in 20%, 3%, and 0% of treated patients.

Conclusions: The early results of the study showed a notable volume reduction of both primary tumor and nodal metastases, and main OARs at re-simulation compared to baseline. This results emphasize the need for monitoring and adaptation of treatment plans in HNC to optimize therapeutic efficacy and minimize adverse effects.

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LADIES PROJECT: LARGE DATABASE IN ENDOMETRIAL CANCERS FOR A PERSONALIZED TREATMENT

Code: 91

Aims: To evaluate the role of radiotherapy in the treatment of endometrial cancer (EC) in a retrospective multicentre Italian study.

Methods: A large database was set up. Inclusion criteria were: accrual between 2010 and 2020, treatment with surgery, post-operative external beam radiotherapy and/or interventional radiotherapy (IRT) preceded or not by adjuvant chemotherapy. Oncological outcomes and acute and late toxicity were correlated with treatment type and risk group.

Results: A total of 1848 patients, from 16 Italian centres were analyzed (median age 65 years, range 27-88). After surgery, all patients received radiation therapy (Table 1) and 31% also chemotherapy.
Patients were stratified on the basis of standard risk factors, merging intermediate and high-intermediate risk classes into one intermediate group and including advanced and oligometastatic disease in the high- risk group. The low-risk group encompassed 124 patients, the intermediate-risk 1140, and the high risk 576.
Table 2 reports oncological outcomes of the 3 risk groups.
When risk groups were correlated with RT treatment type, multivariate analysis showed that patients in the intermediate risk category had a 2.5-fold increased risk of local relapse if treated with IRT alone, compared to the reference treatment (EBRT+IRT). For the patients belonging to high risk group, the type of treatment did not significantly impact on the outcome as only < 10% of patients received IRT alone.
EBRT+ SIB were associated with acute gastrointestinal, genitourinary, skin and haematological toxicity while the IRT alone showed a low impact in all the examined patterns.

Conclusions: This retrospective study provided insights into Italian use of adjuvant radio- and chemotherapy for EC. The results are in accordance to actual guidelines. External beam and vaginal IRT remain integral aspectsof adjuvant therapy for EC, but molecular study are necessary to personalize the treatment and avoid over- or under-treatment.

Table 1. Distribution of patients according to Radiotherapy (RT) treatments.

RT	EBRT	EBRT + BOOST EBRT sequen.	EBRT + BOOST EBRT concom.	EBRT + IRT	IRT escl.	TOT
N patients	217 (11.7%)	45 (2.4%)	304 (16.4%)	772 (41.7%)	510 (27.5%)	1848

Table 2. 5-years oncological outcomes in the 3 risk groups.

Risk Group	Local Relapse free survival	Distant Metastasis Free survival	OS	CSS
Low	100.0%	94.1%	94.0%	97.1%
Intermediate	94.3%	86.4%	93.6%	95.7%
High	86.2%	74.1%	80.7%	83.6%
Total	92.4%	83.4%	90.0%	92.5%

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CORRELATION BETWEEN RADIOLOGICAL AND PATHOLOGICAL RESPONSE IN EARLY STAGE BREAST CANCER PATIENTS TREATED WITH A SINGLE FRACTION RADIOSURGERY IN THE PRE-OPERATIVE SETTING: ANALYSIS OF A PHASE 2 CLINICAL TRIAL.

Code: 69

Aims: The objective of this study is to correlate pathological and radiological response for early stage breast cancer patients treated with pre-operative single fraction radiosurgery (SRS). Radiological and pathological results have been analysed in order to assess if breast MRI scan or Mammography with contrast enhancement (CE) can predict a complete pathological response.

Methods: We run a phase II clinical trial enrolling women older than 50, with proven breast invasive non special type carcinoma, hormonal receptors positive/HER2 negative, any grade, tumor size < 3cm, unifocal, with no nodal involvement, candidates to conservative surgery. The Gross Tumor Volume (GTV) comprises the tumor. The Clinical Target Volume (CTV) is equal to GTV. The Planning Target Volume (PTV) is created by adding a 3mm margin to CTV. The total dose is 30-36 Gy prescribed to the 95% of the PTV. Patients had a breast MRI scan 3 months after radiosurgery (SRS) and underwent surgery at 4 months. The radiological response is described as no evidence of disease (NED) or partial response if any residual tumor was detectable (rPR). The pathological response is defined as complete response (pCR), partial response (pPR) or stable disease. Pathological "major response" comprises patients with pCR and patients with residual disease < 10%.

Results: From January 2022 to January 2024, 52 patients had pre-operative SRS and subsequent conservative surgery. Of those, 41 (89%) had breast MRI scan with contrast enhancement (CE) and 5 (11%) had Mammography with CE (CEM). For 29 patients (63%) pre-operative scans reported NED, but pathological results revealed the rate of major response was confirmed only in 14/29 patients (48%). Radiological results describe any residual disease in 17 cases (37%).
Pathological results confirmed in 16/17 of them (94%) residual disease.

Conclusions: This analysis was conducted for the purpose of determining if breast MRI or CEM are able to identifypatients having a complete response to SRS in order to possibly avoid surgery. Our, data do not support this hypothesis. However, MRI and CEM are very sensible in identify patients with residual disease. We suggest patients having pre-operative SRS should be tested with a re-biopsy.

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UPDATE OF A SINGLE INSTITUTIONAL EXPERIENCE OF THE RADIATION THERAPY ONCOLOGY GROUP (RTOG) 8502 QUAD SHOT REGIMEN USING IMRT IGRT FOR INCURABLE HEAD AND NECK CANCER (HNC).

Code: 611

Aims: Update of a single institutional experience of the Radiation Therapy Oncology Group (RTOG) 8502 "QUAD shot" regimen using IMRT IGRT for incurable head and neck cancer (HNC).

Methods: From March 2021 to January 2024 we recruited 30 consecutive patients with incurable head and neck cancer (HNC), 9 females (30%) and 21 males (70%).
Mean age was 77 (range 65-91) years.
The performance status was established on first visit with the ECOG scale and the weight of each patient was recorded at the beginning and at the end of the radiotherapy cycle.
All patients were treated with at least one cycle of the RTOG 8502 regimen. Treatment plans included the use of IMRT and VMAT with 6 MV photons generated by a linear accelerator.
Megavoltage cone beam or KiloVoltage cone beam (MVCB or KVCB) was used for image-guided radiation therapy (IGRT).
Two daily fractions of 3.7 Gy were delivered with an interval of at least 6 h for 2 consecutive days, totaling
14.8 Gy over 4 fractions. This was repeated every 3–4 weeks for a total of three cycles. No concurrent systemic therapy was performed.

Results: The number of completed cycles was 1 in 3 patients (19%) and 3 in 27 (81%). Tumor response was achieved in (80%) patients and symptom relief in (100%) patients.
A total of 80 % of subjects had ECOG-2 and the others had had ECOG -3.
All patients who received two or more treatments cycles achieved overall response. Median overall survival (OS) was 6 months.
Body weight before and after radiotherapy course had an average increase of 3 kg (range 0-6.1 kg). Grade 1 toxicity was observed in 80% of patients, but no acute Grade ≥ 1 or late toxicity was observed.

Conclusions: Our data are confirmed to be in agreement with those of the literature: the RTOG 8502 "QUAD shot" protocol using IMRT is efficacious for incurable HNC with highly reduced toxicity. Treatment with multiple cycles is recommended for better treatment response and/or survival.

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COMPARISON OF TRANS-VAGINAL ULTRASOUND (TVUS) AND MAGNETIC RESONANCE IMAGING (MRI) TO EVALUATE TUMOR RESPONSE AFTER EXTERNAL BEAM RADIOTHERAPY (EBRT) AND TO PERFORM BRACHYTHERAPY (BT) BOOST PRE-PLANNING IN LOCALLY ADVANCED CERVICAL CANCER

Code: 363

Aims: The aim of this study was to perform a blinded comparison between TVUS and MRI for the assessment of tumour volume at diagnosis and before brachytherapy (BT) boost, in a cohort of 31 locally advanced cervical cancer patients (pts).

Methods: 31 consecutive biopsy-proven cervical cancer patients (pts) referred to our department were prospectively included in this analysis. Patients underwent pelvic MRI and TVUS at diagnosis, before receiving pelvic EBRT with concomitant chemotherapy, before starting brachytherapy boost and after the end of treatment. TVUS evaluation was added to the usual imaging based on the patient's voluntary acceptance; for this reason, not all pts underwent ultrasound evaluation in the three different treatment phases. Five patients had not yet completed the whole treatment course at time of data recording. The following parameters were evaluated: tumour volume estimated on each MRI and TVUS study, with volume calculated by using a rotational ellipsoid based on the three spatial axes (CC, AP, LL) and determined by dedicated physicians, radiologists and gynaecologists; post EBRT and post-treatment Delta-tumor volume; parametrial and vaginal fornix infiltration.

Results: Defining MRI as a reference parameter, a comparison was made with the analyzed TVUS parameters, defining for each of them sensitivity, specificity and accuracy in the three treatment phases. It was not always possible to obtain ultrasound evaluation data at the end of therapy; therefore, data are not complete for the whole series. The results of our analysis showed good sensitivity, specificity and accuracy (Tab.). For the evaluation of post-EBRT and post-treatment Delta-tumor volume a REML (restricted maximum likelihood) analysis was performed. A statistically significant concordance of 0.8 (95% CI 0.64-0.91; $p < 0.0001$) between TVUS and MRI was found. The greatest agreement was detected in the comparison of the difference in volumes between diagnosis and at the end of EBRT (0.91 – 95% CI 0.78 - 0.96; $p < 0.0001$).

Conclusions: The precondition for a safe and good quality BT treatment is to elaborate an optimal pre-planning. MRI has demonstrated clear advantages in terms of image quality. Based on our preliminary data, TVUSseems also to be potentially useful to evaluate tumour response after EBRT to perform BT pre-planning

Evaluated Parameters	Time	Sensibility %	Specificity %	Accuracy % (IC 95%)
Parametrial	Diagnosis	83	67	79,3 (IC 60.2 to 92.0)
	Post-EBRT	50	90	75 (IC 47.6 to 92.7)
	End of treatment	--	88	--
Vaginal fornix	Diagnosi	60	100	77,8 (IC 57.7 to 91.4)
	Post-EBRT	0	87	77,8 (IC 52.4 to 93.6)
	End of treatment	--	88	--

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URETHRA-SPARING SINGLE-DOSE ABLATIVE PROSTATE RADIOTHERAPY WITH REAL-TIME MOTION MANAGEMENT

Code: 196

Aims: To report the implementation of urethra-sparing linac-based Single-Dose Ablative Radiation Therapy (SDART) for unfavorable localized PCa with real-time intrafraction organ motion management (NCT04831983).

Methods: From June2021 to July2023, thirty patients with localized unfavorable-intermediate or selected high-risk PCa were enrolled to receive 24Gy SDART (BED1.5 = 408Gy). Patients were simulated with empty rectum and bladder filled by catheter. Fused CT and T2W 3D MRI image sets were used to delineate target and OARs. PTV consisted of CTV with 2-mm isotropic margin. A high-dose avoidance zone (HDAZ) was created by a 3-mm expansion around rectum, bladder, and urethra. Plans were optimized using 10MV-FFF single arc with minimum target dose defined by the OARs constraints and dose escalation to 24Gy away from HDAZ. During the treatment delivery, CBCT matching ensured accurate patient setup and an electromagnetic device allowed for real-time prostate motion monitoring. Treatment was interrupted and position was corrected when the prostate exceeded a 2-mm threshold. Acute toxicity was evaluated with CTCAEv5 3 months post-treatment.

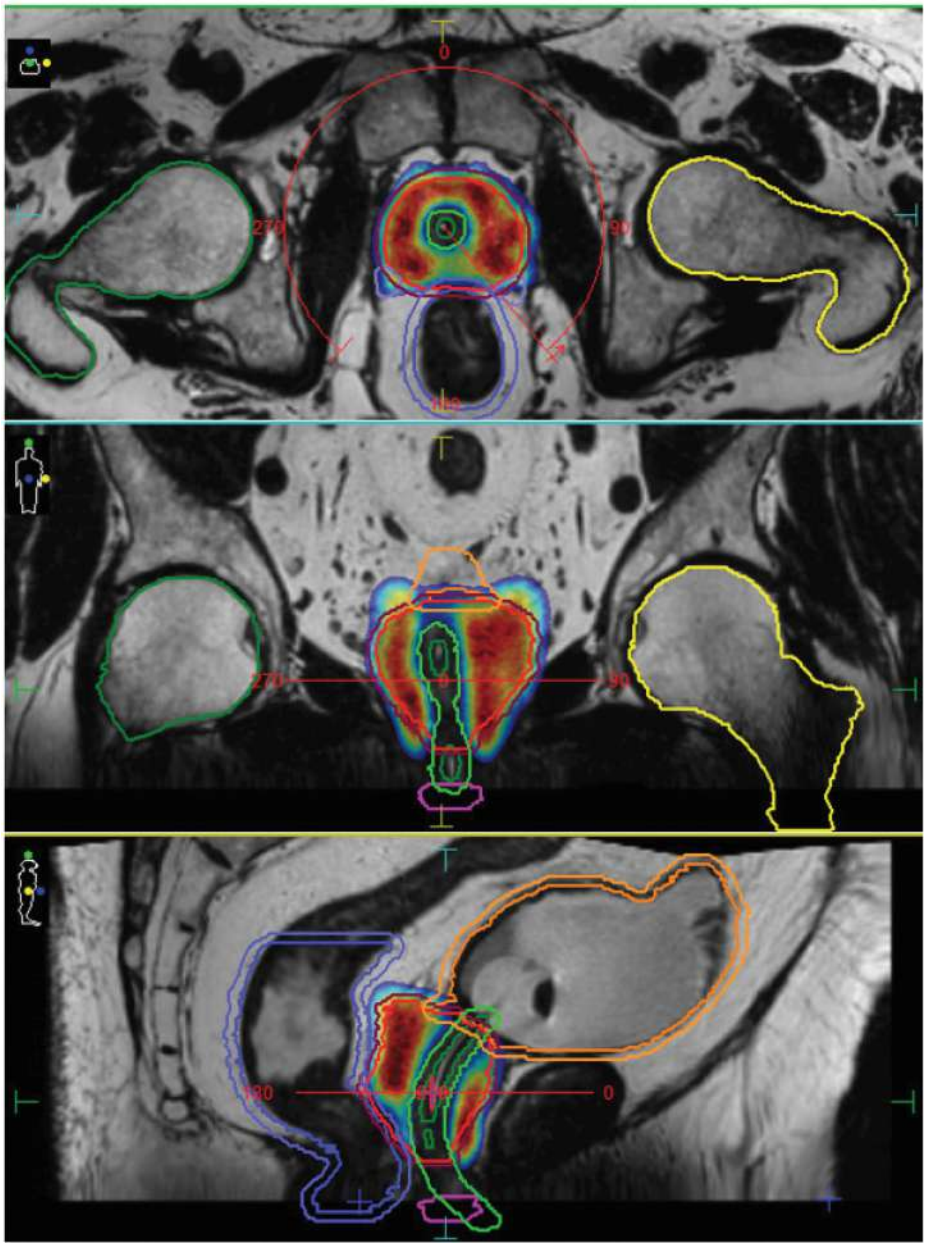
Results: All planning objectives were achieved. Median CTV and PTV were 50.8 cc [16.3–75.7] and 72.0 cc [25.6–100.6]. The average total monitor units per plan were 6910±592. All the treatment plans fulfilled a 2%/2mm gamma passing rate >95% objective using a 2D silicon diode array. The mean delivery time lasted 4.3±0.5 minutes [3.3–5.7]. The overall mean treatment time, from procedure inception to beam-off, was 15.9±8.4 minutes [6.9–35.5]. Intrafraction tracking was successfully carried out in all sessions and beam interruptions due to target motion beyond limits were needed in 17 patients (57%). The prostate was found within 2-mm from its initial position in 82% of the treatment time, i.e. in 77% of the time during the setup phase and in 93% during the delivery phase (beam on + interruptions). At 3-month follow-up, only one patient experienced GI side effects (G1), while GU toxicity was observed in eight patients (six G1 and two G2), mainly consisting of urgency, frequency, and dysuria.

Conclusions: Our preliminary findings offer encouraging perspectives on the safety of 24Gy SDART. The use of negative dose-painting and online motion tracking to limit the volume of rectal mucosa receiving criticaldoses and to accomplish urethra-sparing is feasible. Long-term results are awaited to confirm the efficacy of single fraction in the treatment of localized PCa.

Table 1. Plan goals and characteristics.

	median	mean	range	objective
Urethra PRV				
$D_{0.035cc}$ (Gy)	20.9	20.9	20.1 - 21.8	≤ 22.8
D_{1cc} (Gy)	19.1	19.0	18.2 - 19.2	≤ 19.2
Bladder PRV				
$D_{0.035cc}$ (Gy)	23.7	23.7	23.4 – 24.0	≤ 24
D_{1cc} (Gy)	22.6	22.6	21.9 - 22.8	≤ 22.8
$D_{50\%}$ (Gy)	4.1	4.0	1.3 - 10.0	≤ 12
Rectum PRV				
$D_{0.035cc}$ (Gy)	21.1	21.3	20.3 - 22.2	≤ 22.8
D_{1cc} (Gy)	19.2	19.1	18.6 - 19.2	≤ 19.2
$D_{50\%}$ (Gy)	3.9	3.9	2.2 - 6.9	≤ 12
Neurovascular bundles				
$D_{0.035cc}$ (Gy)	22.8	22.6	19.2 - 23.9	≤ 24
Penile bulb				
$D_{0.035cc}$ (Gy)	10.7	10.5	1.9 - 17.6	≤ 24

Figure 1. Dosimetric plans on the axial, coronal and sagittal planes using fused CT/MR image sets. Color-wash dose distributions are shown with a threshold of 80% of the prescription dose (19.2Gy) to show conformal avoidance of the organs at risk (urethral sparing effect by inverse dose painting is seen as a hole inside the gland).



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MULTICENTER STUDY OF PATIENTS WITH LOCALLY ADVANCED RECTAL CANCER UNDERGOING NEOADJUVANT RADIOCHEMOTHERAPY WITH OR WITHOUT RADIATION DOSE INTENSIFICATION: A COMPARATIVE ANALYSIS

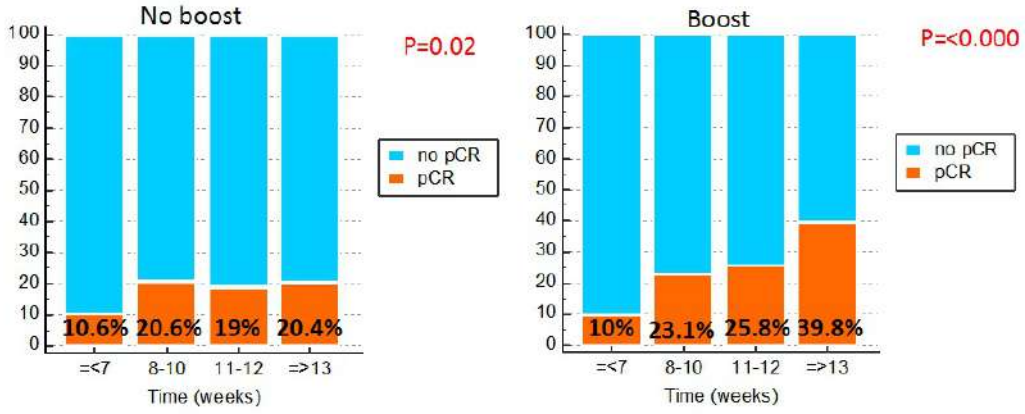
Code: 53

Aims: This is a multicenter retrospective study that aims to compare different levels of RT dose intensification in locally advanced rectal cancer (LARC) patients.

Methods: Twelve centers participated in the study. The primary objective was to evaluate whether the increase in radiotherapy (RT) dose is associated with an increase in the rate of pathological complete response (pCR). The secondary objectives are to evaluate the relation between treatment dose and interval to surgery and compare downstaging, acute and late RT-related toxicity, perioperative toxicity, local and distant recurrence, and overall survival (OS) between the 2 regimens.

Results: The results on 1039 patients are herein reported. Patients were treated with concomitant RCHT with (373) or without (666) an RT boost. The dose boost range was 53.8-60 Gy. Patients were operated on after a median time of 10 weeks (IQ range 5-28). The median follow-up was 48 months. The overall pCR rate was 22.2% (231 patients). In the subgroup analysis pCR was 26.5% (99) and 16.9% (113) in the boost and no-boost groups, respectively (p=<0.000). The pCR rate stratified by interval to surgery (≤7, 8-10, 11-12, ≥13) was: 10.5%, 21.6%, 22%, 29.8%. In the subgroup analysis, the pCR stratified by interval to surgery was: 10%, 23.1%, 25.8%, 39.8% (p=<0.000), and 10.6%, 20.6%, 19%, 20.4% (p=0.02) for boost and no-boost group, respectively, and 95% of pCRs occurred within week 20 in the boost group and week 16 in the no-boost group (p=<0.000). In the univariate analysis (UVA), patients treated with boost had a higher rate of > grade 3 acute gastrointestinal (5.8% versus 1.5%; p=<0.000). Globally, local relapse was observed in 100 patients (9.6%) and the 5-year local relapse-free survival rate was 87.8%. The pCR was associated with an improved local control in the UVA (5-year 95% versus 85.7%; p=0.001). The median OS was 12.8 years, and the 5-year OS was 76.4%. In the univariate analysis RT boost did not correlate with survival (p=0.12), but having a pCR did (5-year OS: 93.3% versus 72.4%; p=<0.000), as well as baseline staging (p=0.000) and pathological stage (p=<0.000). The 5-year metastases-free survival was 72.1%.

Conclusions: RT dose-intensified regimens in LARC might significantly increase the pCR rate, even if at the cost of higher acute toxicity. While pCR seems only partially improved by prolonged time to surgery in the no-boost group, a progressive and significant pCR improvement in patients treated with boost over time was observed.



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IMAGINGRING M A NOVEL DEDICATED MOBILE SYSTEM FOR HDR GYNECOLOGICAL BRACHYTHERAPY PLANNING: OUR EXPERIENCE

Code: 500

Aims: Brachytherapy (BT) represents a therapeutic option for both definitive and adjuvant treatment of cervical and endometrial cancers. The standard BT planning procedure include the simulation CT to perform the contouring and calculate dose distributions. The opportunity to perform 3D adaptive treatment planning and dosimetry for each BT fraction is critical to improving the precision and safety of high radiation doses delivery to the tumor target. For this purpose, a dedicated mobile CBCT scanner has been installed in our hospital. Here we present a primary evaluation of the imaging performance and protocols for image- guided gynecological BT planning.

Methods: The ImagingRing m (IRm) scanner has 121 cm diameter ring gantry with X-ray source (60–120 kV) and detector (43.2× 43.2cm^2 flat panel) rotating independently along the gantry. In comparison to existing CBCT system, the IRm is innovative because it features non-isocentric imaging, dynamic collimation, legs with motorized wheels, battery-powered mobility and wireless remote controlling via tablet-PC. As initial stage, a phantom study was conducted to evaluate 3D imaging performance with focus on pelvis protocols. For the 3D imaging quality test, the Catphan 600 was used. Images were acquired by using three pre- loaded protocols. No manual adjustments have been made to scan settings (kV, prefiltering, mAs, field of view). Image quality metrics were evaluated. CT numbers accuracy and linearity, image uniformity, noise, spatial resolution, low-contrast detectability were all assessed in order to compare the scan protocols.

Results: Concerningly the CT number linearity of eight insert, no significant differences were observed between the protocols. The image uniformity values were found to be within ±4 Hounsfield units (HU), with a range of 9.1–12.3 HU for standard deviations. The resolution level was 21 line-pairs-per-centimeter (lp/cm) on average. For image low-contrast detectability, the minimum diameter of distinguishable contrast holes reached 1 mm at a 0.5% resolution.

Conclusions: The IRm may be a significant issue for adaptive gynecological BT planning. The ability to conduct an in- room planning imaging at the moment of the applicator insertion has impact on patient's perception in terms of comfort. Regarding to the image quality concerns, further investigations are required to identifythe optimal clinical practice for obtaining good image quality at a reasonable radiation dose.

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STANDARDIZED ADJUVANT RADIOTHERAPY FOR 1-2 MACROMETASTATIC SENTINEL LYMPH NODES WITHOUT AXILLARY DISSECTION IN BREAST CANCER CONSERVATIVE SURGERY: PRELIMINARY RESULTS OF A PROSPECTIVE OBSERVATIONAL STUDY (AXILL-ART)

Code: 163

Aims: The trend of surgery in early stage breast cancer with limited axillary involvement (1-2macrometastatic sentinel lymph nodes (SLN)) aims at reducing the treatment burden by performing breast conservative surgery (BCS) with sentinel node biopsy (SNB) alone. Although lymphedema is more prevalent after axillary dissection vs SNB, adjuvant radiotherapy (ART) might increase this incidence. Moreover, in this setting of patients, regional node irradiation (RNI) has become extremely heterogeneous.
At the European Institute of Oncology, the AXILL-ART study aims to evaluate the incidence of ipsilateral arm lymphedema 1 year after the completion of ART in patients receiving standardized RNI.
Here we are presenting a preliminary dosimetric analysis of this prospective observational study.

Methods: Inclusion criteria are described in Table 1. The RNI volume has been defined according to tumour biology: patients with Luminal A/Luminal B and Her2+/TN cancers received RNI to the 1st-2nd and 1st-4th axillary levels, respectively.
All patients received hypofractionated ART (15 fraction) with Tomotherapy with 2.67Gy/fr both to the whole breasts (*PTV breast*) and axillary nodes (*PTV nodes*) and 3.2Gy/fr for simultaneous integrated boost (SIB).
Any increase in arm circumference of at least 10% either in the lower arm or the upper arm, or both, compared with the contralateral arm has been classified as lymphedema.

Results: From 01/2019 to 12/2023, 49 patients have been recruited with 46 concluding ART+RNI according protocol stratification. Among those, 14, 29, 1 and 2 had Luminal A, Luminal B, Her2+ and TN types, respectively. SIB was administered to 44 patients.
In the whole population, the median V95% of *PTV breast*(+/-SIB) and *PTV* nodes was 97.81% and97.06%, respectively. Data of incidental dose to the L3/L4 was available for 31/43 patients receiving L1-2 RNI, with a median value of Dmean 31.53Gy/5.59Gy and Dmax 40.91Gy/20.96Gy, respectively.
One-year follow up evaluation was available for 33 patients, with lymphedema reported in 2 cases (6%).

Table 1: Inclusion criteria for the AXILL-ART protocol

Histological proven invasive breast cancer
Breast conserving surgery with no axillary dissection
T1-T2
pN1a with no more than 2 positive sentinel nodes
Negative surgical margin (no tumour cell on ink)
PS <2
Age >18
Written informed consent

Conclusions: In a well selected population of patients receiving BCS and SNB with 1-2 macrometstatic SLN, 1-year lymphoedema rate was acceptable. Nevertheless, target coverage was always respected in the entire population. Standard ART after SNB with limited axillary involvement are encouraged with respect to the indication and extension of treatment volumes. Longer follow up is needed in order to evaluate oncological outcome.

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EVALUATION OF CLINICAL AND DOSIMETRIC PREDICTIVE FACTORS IN CARDIAC TOXICITY IN RADIOTHERAPY FOR STAGE III NON-SMALL CELL LUNG CANCER

Code: 351

Aims: The aim of this study was to investigate predictors of early heart damage in patients with locally advanced non small cell lung cancer (LA-NSCLC) undergoing chemoradiotherapy (CRT).

Methods: This trial is a prospective, observational cohort study including patients with stage III NSCLC who underwent concomitant CRT. Radiotherapy was delivered with a median total dose of 60 Gy with conventional fractionation. The 3D technique or Intesity-modulated radiotherapy (IMRT) was used. Manual contouring of the target and organs at risk (OAR) was performed from the simulation CT images. The differences in cardiac dosimetry, clinical and treatment factors between patients who have experienced cardiac and no-cardiac events (CV) were assessed by means of T-test and Chi-Quadro. Dosimetric parameters and clinical or treatment factors that resulted different between patients who experienced CV and those who did not ($p<0.05$) were included in the univariate regression analysis. Variables with a $p<0.1$ at univariable analysis and without significant cross-correlations were entered into multivariate logistic regression. ROC curves were used to assess the cut-off point for the risk of developing CV events.

Results: This analysis included 34 patients with stage III NSCLC. The median age was 69.5 years (range 43-87). The median follow-up was 27.8 months. 62% of patients were in stage IIIA. All patients were treated with concurrent CRT, platinum-based regimen was used in 65% of cases. No patients died of CV complications. Eight patients (23.5%) had a CV event: four atrial fibrillation, two supraventricular tachycardia, one atrioventricular block (second degree), and one patient presented heart failure. No patients presented coronary events. Table 1 describes the heart dosimetric parameters, clinical and treatment factors analyzed. Table 2 shows univariate and multivariate analysis results. At univariate analysis the predictors of increased risk of CV events were the volume of PTV, the total dose, the volume of heart receiving 30-45-50 Gy and the atrium Dmean. In the multivariate analysis the strongest predictor of CV events was V45 Gy (cut-off value 11%), even if the statistical significance was not reached ($p=0.059$, OR=2.112, 95%IC=0.972-4.588).

Conclusions: Several dosimetric parameters were associated with an increased incidence of non-coronary CV events in our patients' cohort. The strongest predictor was V45 Gy (cut-off value 11%). Further prospective evaluation in a larger cohort of patients is warranted.

Table 1. Heart dosimetry parameters, clinical and treatment factors between patients who experienced cardiovascular events and those not

	EVENTI CARDIOVASCOLARI POSt RT (0 NO/1 SI)	Mean	Std. Deviation	Std. Error Mean	p-value
CUOREDmax	0	62.45	10.38	2.03	.512
	1	59.94	3.61	1.27	
CUOREDmedia	0	11.89	5.86	1.15	**.032**
	1	17.72	8.06	2.85	
V5	0	48.33	23.92	4.69	.089
	1	64.19	27.10	9.58	
V30	0	13.40	8.86	1.73	**.009**
	1	24.67	13.53	4.78	
V45	0	5.68	4.09	.80	**.007**
	1	10.79	5.24	1.85	
V50	0	3.85	3.25	.63	**.030**
	1	7.00	4.02	1.42	
VSDmax	0	19.91	15.01	2.94	.071
	1	29.70	15.19	5.37	
VsxDmedia	0	4.31	4.93	.96	.117
	1	8.26	7.20	2.54	
LADDmax	0	20.99	14.49	2.84	.086
	1	32.2	15.78	5.57	
LADDmedia	0	7.95	6.56	1.28	.070
	1	12.29	8.88	3.14	
V15 LAD	0	16.51	23.85	4.97	.142
	1	29.37	31.58	11.16	
V15 Vsx	0	9.40	20.15	4.20	.237
	1	9.66	10.11	3.57	
Dmedia Atrio dx	0	15.48	12.46	2.60	**.019**
	1	29.99	18.72	6.62	
Dmax nodo seno atriale	0	39.98	21.28	5.01	**.032**
	1	52.96	6.38	2.60	
BMI	0	27.82	4.69	.92	.160
	1	26.38	2.51	.88	
PACK/YEAR	0	50.25	34.84	6.83	.414
	1	71.40	40.71	14.39	
ETA'	0	69.54	9.84	1.93	.158
	1	69.25	9.02	3.18	
ASCVD %	0	22.30	15.07	3.37	.942
	1	21.96	8.77	3.92	.
VOLUME (PTV)	0	310.02	140.40	27.53	**.031**
	1	442.40	160.50	56.74	.
DOSE TOTALE	0	58.79	3.40	.66	**.019**
	1	52.15	12.70	4.49	
DIABETE	0	11			.328
	1	2			
DISLIPIDEMIA	0	11			.112
	1	6			
FAMILIARITA	0	9			.352
	1	4			

Abbreviations:

Table 2. Univariate and multivariate logistic regression analysis

	Univariate p	OR	95%IC	Multivariate p	OR	95%IC
Heart Dmean	**0.048**	1.147	1.001-1.314	-		
Heart V30Gy	**0.025**	1.106	1.012-1.208	-		
Heart V45Gy	**0.019**	1.297	1.044-1.613	0.059	2.112	.972-4.588
Heart V50Gy	**0.043**	1.286	1.008-1.640	-		.000-2.456
Right Atrium Dmean	**0.033**	1.066	1.065-1.130	0.861	.990	.884-1.109
Seno-atrial node maximum dose	0.180	1.049	0.978-1.124	-		
VOLUME (PTV)	0.05	1.006	1.000-1.011	0.122	1.011	.997-1.025
Total dose	0.09	.866	.733-1.023	0.181	.737	.471-1.153

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DELTA RADIOMICS CAN PREDICT COMPLETE PATHOLOGICAL RESPONSE IN RECTAL CANCER PATIENTS UNDERGOING NEOADJUVANT CHEMO-RADIATION: A PROSPECTIVE EVALUATION

Code: 367

Aims: The present study was designed to evaluate MRI delta texture analysis (D-TA) in predicting the outcome in terms of the complete pathological response of patients with locally advanced rectal cancer undergoing neoadjuvant chemoradiotherapy (C-RT) followed by surgery.

Methods: We performed a retrospective analysis on 69 patients with locally advanced rectal adenocarcinoma undergoing C-RT and radical surgery in two different centers between January 2015 and December 2019 and a small prospective evaluation on 14 patients from June 2023 to December 2023. The gross tumor volume (GTV) was evaluated at both baselines and after C-RT MRI and contoured on T2, DWI, and ADC sequences. Multiple texture parameters were extracted with LifeX Software, and D-TA was calculated as the percentage variations in the two time points.
A prediction model was trained using a neural network approach (Multilayer Perceptron Network, MPN, SPSS v24.0©) combining delta radiomics features in a training dataset. It was then evaluated on the other retrospective set and the small prospective one using the Receiver Operative Characteristics Complete pathological response (pCR, with no viable cancer cells: TRG 0) was chosen as the statistical end-point. ROC Curves were calculated on the three different datasets.

Results: In the whole retrospective cohort, 16 patients (23,2%) showed a pCR and 4/14 patients in the prospective cohort (28,5%). The MPN showed an AUC for pCR of 0.77 in the Training Dataset and respectively 0.88 in the retrospective Validation Dataset and 1 in the small prospective dataset.

Conclusions: Our results suggest that D-TA has a significant role in the prediction of pCR, thus this method may lead to select patients who may potentially be selected for a deintensification strategy. However, further analysis with larger prospective trials is warranted.

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DEVELOPMENT OF A PREDICTIVE MODEL FOR PATIENTS WITH BONE METASTASES REFERRED TO PALLIATIVE RADIOTHERAPY: SECONDARY ANALYSIS OF A MULTICENTER STUDY (THE PRAIS TRIAL)

Code: 144

Aims: The decision to administer palliative radiotherapy (RT) to patients with bone metastases (BMs), as well as the selection of treatment protocols (dose, fractionation), requires an accurate assessment of survival expectancy. In this study, we aimed to develop three predictive models (PMs) to estimate short-, intermediate-, and long-term overall survival (OS) for patients in this clinical setting.

Methods: This study constitutes a sub-analysis of the PRAIS trial, a longitudinal observational study collecting data from patients referred to participating centers to receive palliative RT for cancer-induced bone pain. Our analysis encompassed 567 patients from the PRAIS trial database. The primary objectives were to ascertain the correlation between clinical and laboratory parameters with the OS rates at three distinct time points (short: 3 weeks; intermediate: 24 weeks; prolonged: 52 weeks) and to construct PMs for prognosis. We employed machine learning techniques, comprising the following steps: i) identification of reliable prognostic variables and training; ii) validation and testing of the model using the selected variables. The selection of variables was accomplished using the LASSO method (Least Absolute Shrinkage and Selection Operator). The model performance was assessed using receiver operator characteristic curves (ROC) and the area under the curve (AUC).

Results: Our analysis demonstrated a significant impact of clinical parameters (primary tumor site, presence of non- bone metastases, steroids and opioid intake, food intake, and body mass index) and laboratory parameters (interleukin 8 [IL-8], chloride levels, C-reactive protein, white blood cell count, and lymphocyte count) on OS. Notably, different factors were associated with the different times for OS with only IL-8 included both in the PMs for short- and long-term OS. The AUC values for ROC curves for 3-week, 24-week, and 52-week OS were 0.901, 0.767, and 0.806, respectively.

Conclusions: We successfully developed three PMs for OS based on easily accessible clinical and laboratory parameters for patients referred to palliative RT for painful BMs. The implementation of these tools into clinicalpractice warrants further investigation through subsequent studies.

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PREDICTIVE VALUE OF CLASSICAL PROGNOSTIC FACTORS OUTPERFORMS SUV-MAX IN LOCALLY ADVANCED CERVICAL CANCER: FINDINGS FROM A COMPREHENSIVE OBSERVATIONAL STUDY ENCOMPASSING TUMOR, PATIENT, AND TREATMENT-RELATED DATA (THE ESTHER STUDY)

Code: 415

Aims: Despite advances in cervical cancer treatment, locally advanced cervical cancer (LACC) remains challenging. Traditional factors like FIGO stage and tumor size inform prognosis, but PET-related parameters' role is unclear due to conflicting literature. This study explores the correlation between pre-treatment SUV-max from FDG-PET scans and outcomes in LACC patients.

Methods: LACC patients from 2007-2021 (ESTHER study) received concurrent chemoradiation (CRT) with Cisplatin and BRT boost. Pre-treatment factors and SUV-max were analyzed for their impact on local control (LC), distant metastasis- free survival (DMFS), disease-free survival (DFS), and overall survival (OS) using univariate and multivariate analyses.

Results: 173 patients, median 36-month follow-up (range: 3-151 months), were included. Older age was related to lower DMFS (univariate p=0.049, multivariate p=0.002) and OS (univariate p=0.003, multivariate p<0.001). Higher Hb levels (?12 g/dL) correlated with improved LC (univariate p<0.001, multivariate p=0.002), DFS (only univariate p=0.007), and OS (univariate p=0.040, multivariate p=0.023). FIGO stage III-IV correlated with worse LC (p=0.005), DMFS (p=0.021), DFS (p=0.003), and OS (p=0.032) compared to FIGO stage I-II in univariate analysis. Multivariate analysis confirmed negative correlations with DMFS (p=0.002), DFS (p<0.001), and OS (p=0.003). Total CRT plus BRT dose correlated with improved OS (univariate p=0.012, multivariate p=0.038). No significant SUV-max correlation with outcomes was observed (Table 1).

Conclusions: SUV-max prognostic value in LACC remains uncertain. Considering post-treatment parameters and other FDG- PET indices may provide insights. Achieving adequate irradiation doses and addressing anemia are critical for better LACC outcomes.

Table 1: multivariable analysis; only statistically significant values are shown.

Parameter	Values	Patients	LC			DMFS			DFS			OS		
		No	HR	95%CI	P	HR	95%CI	p	HR	95%CI	p	HR	95%CI	p
Age (years)	<55	77				1	rif.	**0.002**	1	rif.	**0.023**	1	rif.	**<0.001**
	55≥age<70	62				1.443	0.663–3.141	0.356	0.842	0.446–1.591	0.597	2.004	0.884–4.543	0.096
	≥70	34				4.291	1.892–9.732	**<0.001**	2.224	1.130-4.375	**0.021**	5.666	2.337–13.511	**<0.001**
Total dose (Gy)	≤ 75	129										1	rif.	
	> 75	44										0.425	0.189–0.955	**0.038**
FIGO stage	I-II	77				1	rif.	**0.002**	1	rif.	**<0.001**	1	rif.	**0.003**
	III	73				4.123	1.824–9.320	**<0.001**	2.718	1.430–5.168	**0.002**	3.671	1.722–7.822	**<0.001**
	IV	23				4.383	1.529–12.562	**0.006**	4.246	1.872–9.635	**<0.001**	2.555	0.825–7.912	0.104
Hb	<10	16	1	rif.	**0.003**							1	rif.	**0.053**
	10≤Hb<12	42	0.567	0.205–1.569	0.275							0.524	0.183–1.502	0.229
	≥12	115	0.181	0.062–0.524	**0.002**							0.298	0.106–0.844	**0.023**

Legend: 95%CI: 95% Confidence Interval; DFS: disease free survival; DMFS: distant metastasis free survival; FIGO: International Federation of Gynecology and Obstetrics; Hb: hemoglobin; HR: hazard-ratio; LC: local control; OS: overall survival.

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CORRELATION OF NEW INFLAMMATORY BIOMARKERS WITH SURVIVAL OUTCOMES IN STAGE III NSCLC: RESULTS FROM THE MULTICENTRE ANALYSIS OF NEUTRALITY TRIAL

Code: 387

Aims: Many inflammatory biomarkers have been recognized as prognostic indexes in NSCLC, mainly in metastatic setting. Neutrality trial aims to analyze the impact of these indexes on survival outcomes of stage III NSCLC patients treated as per Pacific regimen, especially investigating the role of neutrophil-to- lymphocyte ratio (NLR), the systemic inflammatory index (SII, NLR x platelets) and more recently developed parameters as the dNLR (neutrophil to leukocytes - neutrophil ratio) and the Lung Immune Prognostic Index (LIPI).

Methods: Neutrality trial is a retrospective multicenter observational study (ESR-19-20410). Blood count tests were collected from the beginning of systemic treatments and at established timepoints during therapy. Two cohorts of patients were identified: those treated with radio-chemotherapy alone, and those who received Durvalumab within the Expanded Access Program. This preliminary analysis focuses only on the latter population. Different cut-offs of NLR, dNLR and SII were considered, based on the median values observed in our population. Three LIPI index groups were considered: good (dNLR≤;3 and LDH ≤ UNL), intermediate (dNLR>; 3 or LDH ≥ UNL) and poor (dNLR>; 3 and LDH ≥ UNL). A Cox-Regression analysis on the different parameters modeled as time-variable indexes was performed.

Results: Data of 96 patients from 34 Italian Centers were evaluable and are detailed in Table 1. Median follow up was 35.6 months. Baseline NLR value significantly correlates with PFS: using a cut-off of 5, the HR was
1.93 CI (1.12-3.30), p: 0.017; when considered as a continuous variable, for each NLR increase of 1 point, the HR was 1.07 CI (1-1.14), p: 0.04. Also baseline SII and dNLR significantly correlate with PFS, with an HR of 1.67 CI (0.94-2.96) p: 0.08, and 2.14 CI (1.14-4.02) p: 0.018, respectively. Furthermore, the LIPI was found to correlate with PFS, with a longer interval in the good group compared to the intermediate (p: 0.004) and the poor (p: 0.039), as expected. Positive trends were found also for OS, especially for baseline values: an HR of 1.59 (p 0.15) for a NLR cut-off of 5, and an HR of 1,67 (p 0.09) and 1.49 (p 0.19) for dNLR and SII, respectively.

Conclusions: Neutrality trial confirmed the prognostic role of blood inflammatory indexes also in stage III NSCLC treated as per PACIFIC regimen. Further analyses are still ongoing, with the aim of driving a more personalized intensity of treatment, starting from the early phases of therapy.

Table 1: Patients Characteristics

	Patients (%) **96**
Sex	
M	62 (64.5%)
F	34 (35.5%)
Smoke	
Yes	85 (88%)
No	9 (12%)
Age years	
Median	68 y
Range	44-83
Histology	
Adenocarcinoma	54 (56%)
Squamocellular	39 (41%)
Others	3 (3%)
PD-L1 Expression	
0	12 (12.5%)
1-49	41 (43%))
≥ 50	30 (31%)
Not tested	13 (13.5%)
Stage Disease	
IIIA	35 (36.5%)
IIIB	48 (50%)
IIIC	13 (13.5%)
ECOG PS	
0	59 (61.5%)
1	35 (37.5%)
2	1 (1%)
Radiotherapy	
Concomitant	49 (51%)
Sequential	47 (49%)
DTF	
60 Gy	73 (76%)
66 Gy	5 (5%)
60-66 Gy	4 (4%)
< 60 Gy	14 (15%)
Time to Durvalumab	
< 40 days	16 (17%)
40-90 days	58 (60%)
> 90 days	22 (23%)

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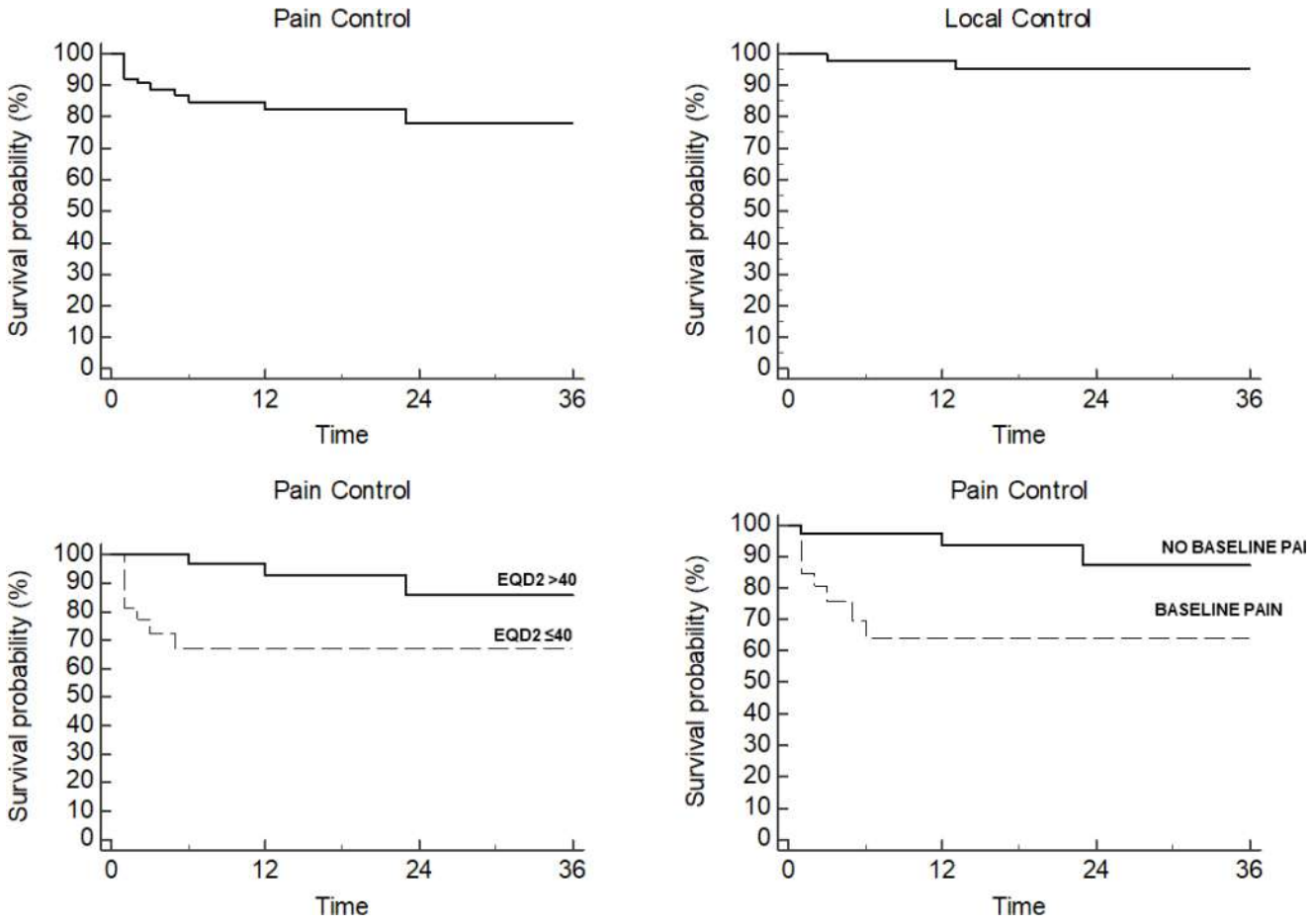
TREATING NON CONVENTIONAL BONE METASTASIS: ANALYSIS OF LOCAL CONTROL AND PAIN RELIEF OF RIB LESIONS TREATED WITH STEREOTACTIC BODY RADIOTHERAPY

Code: 380

Aims: Following reports of improved efficacy in vertebral metastases, Stereotactic Body Radiotherapy (SBRT) has been increasingly applied for local palliation and disease control in non-spinal bone metastases. However, its use in the management of rib metastases (RM) has been traditionally limited due to purported risk of iatrogenic fracture, possibly resulting in impaired pain control.
For this reason, SBRT in this setting has been scarcely reported in literature. The aim of our study is to evaluate pain control and local failure rates in RM treated with SBRT.

Methods: We collected data from a cohort of RM patients treated from October 2014 to December 2023 with SBRT (minimum allowed dose for inclusion was 16Gy/1 fraction, 24Gy/2 fractions, 24Gy/3 fractions, 30Gy/5 fractions). Clinical and treatment-related data were collected. Pain Control (PC) was defined as absence of pain or its reduction allowing for lowering pain medication intake, without a subsequent pain relapse. Local Failure (LF) was defined as radiologic progression on follow-up (FUP) imaging. Univariable analysis with the log-rank test and multivariable analysis with the Cox model were performed to investigate predictors of PC and LF.



Results: Data from 55 patients accounting for 64 RM were collected. Median age was 70 (range 37-78) years. Median FUP was 14 (2-74) months. Most represented primary tumors were prostate (41%,n=26) and non-small cell lung cancer (21%,n=13). Baseline pain before SBRT was reported in 26 (41%) lesions, requiring daily opioid intake in 12 cases (20%). SBRT was delivered with volumetric arc IMRT (92%, n=59) and robotic-arm (8%, n=5) Linac using the following regimens: 16 Gy/1 fraction, 24 Gy/2 fractions, 24-30 Gy/3 fractions, 30-55 Gy/5 fractions. Median EQD2 (assuming an ?/?=10) was 47 Gy (range 35-96.25). PC was 87% at 6 months and 82% at 1 year. Age> 70 (p=0.002), EQD2 ?40 Gy (p=0.009) and baseline pain (p=0.004) were correlated with impaired PC although only EQD2 ?40 Gy (0.007) and baseline pain (0.012) proved significant at multivariate analysis. LF rate was 2.0% at 6 months and 4.8% at 1 year. No predictive factors of LF were identified at statistical analysis. Pain flare wasobserved in 1 patient. No rib fractures were reported.

Conclusions: SBRT for RM is associated with low rates of local failure and durable pain control. Administration of SBRT before the onset of symptoms and use of dose intensive regimens may result in improved pain control.

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REIRRADIATION: AN IDEAL WORKFLOW FROM LITERATURE TO EVERY-DAY CLINICAL PRACTICE.

Code: 448

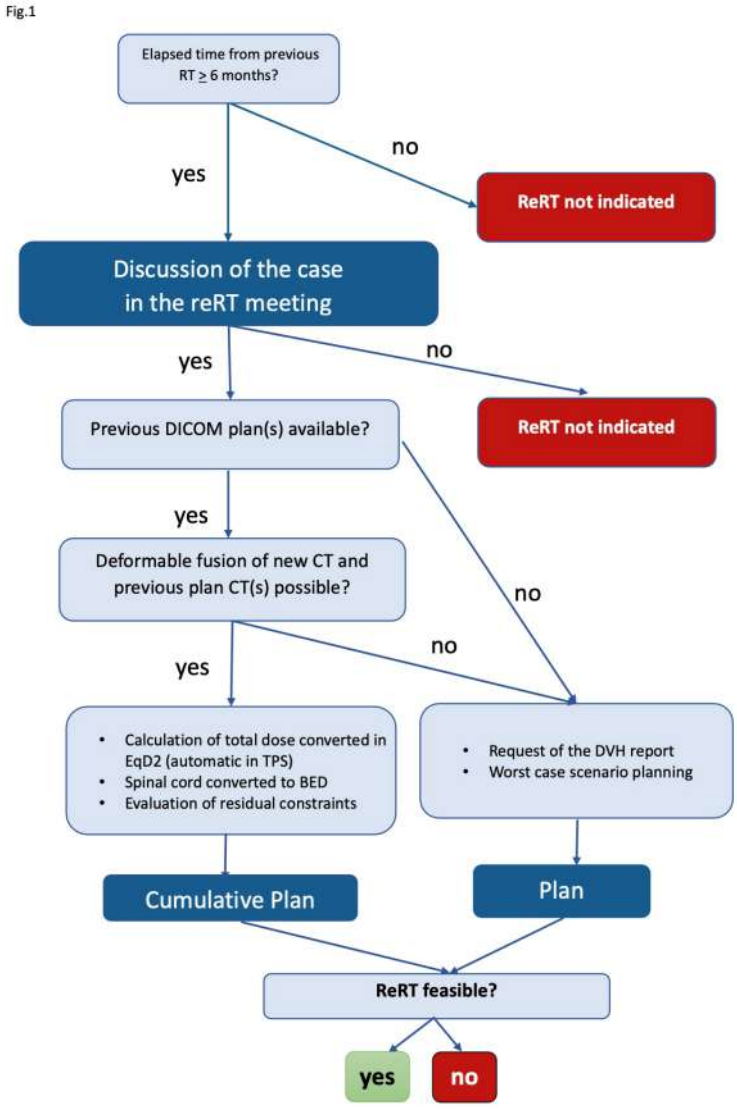
Aims: Reirradiation (reRT) is a pivotal tool in the field of radiation oncology. This study aims to introduce an innovative and comprehensive framework designed for the application in curative-intent retreatments.

Methods: An extensive and critical review of the current literature, focusing on proposed workflows, recommendations, and dose constraints has been performed from 10/10/2023 to 12/01/2024 by a dedicated working group of our Division (4 MDs, 4 physicists, 1 Biomedical Engineer). This framework accommodates both scenarios (Andratschke N 2022): retreating the same target area (R1-type reRT) and addressing adjacent targets where there might exist a cumulative toxicity risk due to previous treatments (R2-type reRT).

Results: The literature analysis has allowed us to 1) draw an internal document collecting pillars of reRT (classification, radiobiological consideration, etc); 2) collect α/β values for various tumors and dose constraints for different OAR; 3) propose a workflow that addresses the critical considerations necessary in the evaluation process for reRT, making it a valuable tool in everyday clinical practice (Fig. 1).
The entire process highlighted some of the key elements of our proposed model, which should be considered for every reRT:
• Comprehensive Treatment Review: includes access to patient's previous RT plans with 1) DICOM format and dose conversion in EqD2 (through TPS tools) of both first and subsequent RT plans for an accurate image registration and dose summation or 2) paper format for worst-case scenario planning
• Detailed Dosimetric Analysis and Data Reporting: this involves an evaluation of the deliverable dose to the target volume and the constraints to OAR, considering the dose received by the neoplastic tissue and by the OARs. Specific reports have been drawn for different districts (brain, head and neck, torax, abdomen/pelvis, prostate), outlining the cumulative doses received by the organs across different treatments, which is then documented in patient's medical records.
• Dual Physician Review and Validation: the reRT plan undergoes rigorous review and validation by two independent physicians, reinforcing the safety of the proposed plan.

Conclusions: Our study presents a model ensures a robust and secure quality assurance process throughout the evaluation, planning, and execution phases of retreatment in radiotherapy. This model stands as a commitment to patient safety, treatment efficacy, and innovation in the field of radiation oncology

Fig.1



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RADIATION THERAPY-DEPENDENT ORAL MUCOSITIS: HOW THE ORAL DYSBIOSIS MAY PREDISPOSE TO OPPORTUNISTIC FUNGAL INFECTIONS AND ORAL MUCOSITIS

Code: 9

Aims: Oral mucositis (OM) is a common acute side effect of radiation therapy (RT) in head-neck cancer patients (HNCPs). We performed an observational prospective study evaluating oral microbiota milieu and oral lipidomics before, during and after RT.

Methods: We recruited HNCPs>18 years old. Non-naïve chemotherapy patients who have received antibiotic therapy in the two weeks prior to baseline were excluded. We monitored oral microbiome and lipidomics in correlation with RT-dependent OM at 0, 7, 15 days from the beginning of the radiation-treatment and 1 month, 2 months post-RT treatment, using oral swab and oral saliva for metagenomics and lipidomics respectively. In addition, to understand the possible therapeutic effects of specific oral commensals we established an in vitro 3D tongue organoid model.

Results: 25 patients (median age 70 years) were recruited. 11 patients underwent RT at the primary site, and 14 at primary tumor site and neck lymphatic drainage. Median total RT dose to the primary tumor was 66 Gy (interquartile 60-66 Gy). Only 8 patients received cisplatin and 1 patient cetuximab. Most frequent acute RT-related side effects were: OM, dry mouth, dysphagia, fatigue; their appearance was related to the radiation dose. DNA-sequencing for 16S and 18S was performed and community diversity analysis was executed for the prokaryotic and eukaryotic population. RT-related oral fungal infection due mainly to *Candida albicans*, *Aspergillus fumigatus* and *Malassezia* was evident during therapy. Importantly, the oral microbiome shows for each patient a specific signature, although profound changes occur during RT.
The untargeted lipidomics analysis performed on saliva samples revealed different behaviours among patients in terms of global lipid fingerprinting at T0 (before treatments), T1-3 (during treatments), and T4-5 (after treatment). When a high variation was observed during treatment, observed modifications suggested patients' classifications based on the most affected lipid classes (glicerophospholipids, glicerolipids, or both).
Organoid exposure to selected bacteria restores the oral eubiome, showing that Lactobacillaceae increased epithelial regeneration, where the release of IL-22 is pivotal.

Conclusions: The present study represents an important tool to better delineate the oral myco/microbiome affected by RT, eventually leading to new mechanistic insights in advanced targeted therapy or OM prophylaxis in cancer.

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SINGLE INSTITUTIONAL EXPERIENCE WITH PALLIATIVE VOLUMETRIC RADIOTHERAPY WITH SIMULTANEOUS ABLATIVE BOOST (SAB): A FEASIBILITY STUDY OF RADICAL DOSE ESCALATION TO THE CENTRAL PART OF LARGE TUMORS WITH AN INTEGRATED BOOST IN THE ABLATIVE /PALLIATIVE TREATMENT SETTING

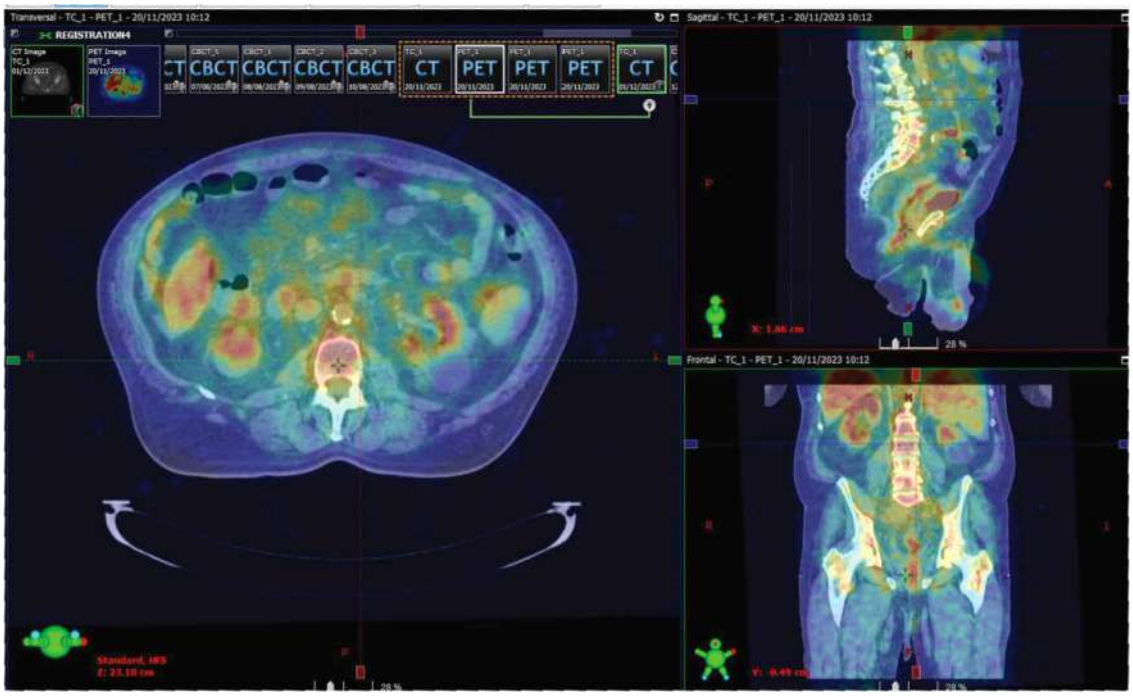
Code: 43

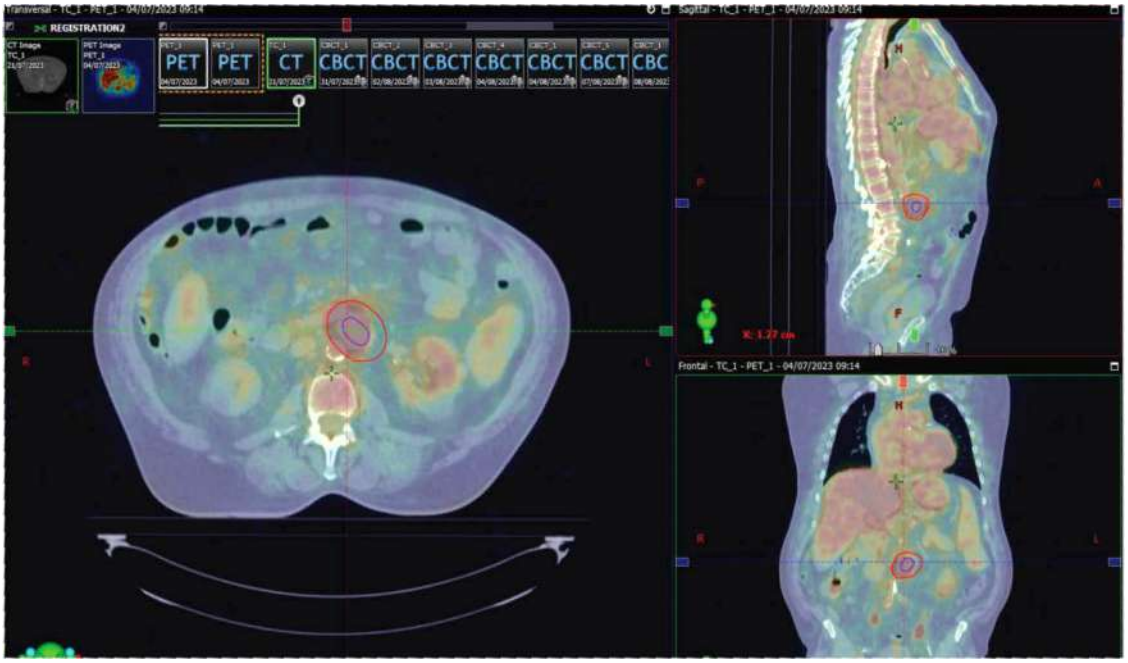
Aims: AIMS: For patients with large tumors, palliative radiotherapy (RT) often is the only local treatment option. To prevent toxicity the administered doses are low. Dose escalation to the tumor could be an option to better symptom control and prolong local control rates. In this retrospective study we used a very pragmatic approach with a simultaneously ablative boost (SAB) to an almost geometrically defined tumor core to achieve this. The primary endpoint was to demonstrate feasibility and tolerability.

Methods: METHODS Patients with solid tumors >10 cm³ in volume with different histologies were eligible in this retrospective observational mono institutional study with two fractionation schedules:
5 fractions (fx) (5 x 4 Gy with a SAB of 5 x 9 Gy) and 10 fractions ((10 x 3 Gy with a SAB of 10 x 4,80 Gy) .
The objective of dose escalation in this study was to deliver a dose >120% of the prescribed dose to the gross tumor volume (GTV) tumor core and to reach a maximum of at least 200% in the 80% of tumor core.

Results: RESULTS: From May 2021 to dec 2023 we evaluated 67 patients who were divided into 4 sub-groups according to the location of the disease (primitive tumor, nodes, visceral metastases and bone metastases. 24 (35.8%) patients were treated with a 10 fractions regimen. 43 patients were treated with the shorter five fraction regimen.
The medium planning target volume (77 PTV tot) was 563.2 cm3 (range 14.5–3083.7 cm3) and the medium core volume was 93.99cm3 (range 1–787 cm3).
RT was overall well tolerated by all patients. The median follow-up was 7 (3-30 MO)

Conclusions: Palliative radiotherapy with SAB to the tumor core seems to be a feasible and well- tolerated treatment for large tumors. The higher doses oF 45 Gy in 5 fx (or 48 Gy in 10 fx) did not cause unexpected G3 side effects at 30-60-90 days follow-up period. Treatment delivery and short-term follow- up was successful for about 85% of patients. Further research is needed for more information on efficacy and long-term toxicity.





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A PHASE 3 STUDY OF PEMBROLIZUMAB PLUS CHEMORADIOTHERAPY FOR HIGH-RISK LOCALLY ADVANCED CERVICAL CANCER (LACC): RESULTS FROM ENGOT-CX11/GOG-3047/KEYNOTE-A18

Code: 318

Aims: Standard therapy for LACC includes EBRT with CCRT then brachytherapy, which may benefit from the addition of immunotherapy. Pembrolizumab (pembro) showed efficacy and manageable safety in patients (pts) with cervical cancer. The ENGOT-cx11/GOG-3047/KEYNOTE-A18 study (NCT04221945) assessed pembro + CCRT for high-risk LACC.

Methods: Pts with newly diagnosed, previously untreated, high-risk LACC (FIGO 2014 stage IB2-IIB with node- positive disease or stage III-IVA) were randomized 1:1 to 5 cycles of pembro 200 mg or placebo (pbo) Q3W + CCRT then 15 cycles of pembro 400 mg or pbo Q6W. CCRT included 5 cycles (optional 6th dose) of cisplatin 40 mg/m2 QW + EBRT followed by brachytherapy. Pts were stratified by EBRT type, disease stage, and total radiotherapy dose. Primary endpoints were PFS per RECIST v1.1 by investigator or histopathologic confirmation and OS.

Results: 1060 pts were randomized to pembro + CCRT (n=529) or pbo + CCRT (n=531). At IA1 (data cutoff: Jan 9, 2023), median follow-up was 17.9 (range 0.9-31.0) mo. Treatment exposure is listed in the table.
Pembro + CCRT significantly improved PFS vs pbo + CCRT (HR, 0.70 [95% CI, 0.55-0.89; P=0.0020). 24-month PFS rates were 67.8% vs 57.3%, respectively; median PFS was not reached in either group. PFS benefit was generally consistent across all prespecified subgroups. With only 103 events (42.9% maturity), pembro + CCRT had a favorable trend in OS (HR, 0.73 [95% CI, 0.49-1.07]); these data have not crossed the boundary of statistical significance at this interim analysis. Treatment-related AEs (TRAEs) were less common in the pembro monotherapy phase vs pembro + CCRT combination therapy phase (72.7% vs 94.5%); corresponding results in the pbo arm were 60.0% vs 95.7%. Safety profiles were generally consistent with those previously reported for pembro monotherapy and chemoradiotherapy. There were no safety concerns and AEs were manageable with pembro + CCRT. TRAEs during combination therapy with pembro + CCRT led to discontinuation of cisplatin, pembro, EBRT, and brachytherapy in 10.4%, 1.5%, 0%, and 0% of pts, respectively; rates with pbo + CCRT were 10.8%, 0.9%, 0%, and 0.2%, respectively.

Conclusions: Pembro + CCRT significantly improved PFS and had a favorable trend in OS vs pbo + CCRT in pts with high-risk LACC. Pembro + CCRT had a manageable safety profile with most TRAEs reported during the combination phase of therapy. Pembro + CCRT has potential as a new standard of care for this high-risk population.

Table. CCRT Exposure in Patients Who Completed Radiation Treatment

	Pembrolizumab Plus CCRT	Placebo Plus CCRT
Cisplatin, n	518	522
<5 administrations, n (%)	65 (12.5)	62 (11.9)
5 administrations, n (%)	368 (71.0)	355 (68.0)
6+ administrations, n (%)	85 (16.4)	105 (20.1)
Radiation treatment to cervix, n	518	522
Total physical dose	76.0 (73.3–78.7)	75.9 (73.0–78.3)
Total EQD2 dose	87.2 (82.8–91.7)	87.1 (83.3–91.6)
EBRT to cervix, n	518	522
Total physical dose	45.0 (45.0–50.0)	45.0 (45.0–50.0)
Total EQD2 dose	44.3 (44.3–50.0)	44.3 (44.3–50.0)
EBRT to lymph nodes, n	438	432
Total physical dose	56.0 (55.0–57.5)	56.0 (55.0–57.5)
Total EQD2 dose	55.9 (55.9–58.9)	56.0 (55.9–58.9)
HDR brachytherapy		
Total physical dose	29.1 (26.8–31.0)[a]	29.0 (27.1–31.2)[b]
Total EQD2 dose	40.9 (37.0–45.1)[b]	40.9 (37.8–45.0)[b]
PDR/LDR brachytherapy, n	15	4
Total physical dose	35.2 (29.8–39.6)	36.6 (33.3–39.6)

Total physical and EQD2 doses shown are median (interquartile range) Gy.
[a]n = 489.
[b]n = 490.

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A PROSPECTIVE MULTICENTER PHASE II STUDY (MITO- RT3/RAD) ON THE EFFICACY OF STEREOTACTIC BODY RADIOTHERAPY FOR LYMPH NODES METASTASES OF OLIGOMETASTATIC OVARIAN CANCER.

Code: 161

Aims: The MITO-RT3/RAD trial (Trial Registration NCT04593381) is a prospective, multicenter phase II study aimed at identifying potential predictors of response and clinical outcome after stereotactic body technique (SBRT) treatment in ovarian cancer (OC). The study hypothesis was that radiotherapy (RT) delivered by pre-defined SBRT treatment schedules and shared constraints could improve the rate of complete response (CR). Herein we report data on lymph nodes metastases treated according to protocol.

Methods: Lymph nodes oligometastatic, persistent or recurrent OC patients were enrolled. The endpoint of the study was the CR rate to SBRT on "per-lesion" basis. The best response was evaluated by CT scan or PET/CT, every 3 months.
Sample size was quantified based on the previous study reporting a rate of CR to SBRT of around 70.0% on average. Based on the optimal two-stage design by Simon, we tested the null hypothesis that the true rate of CR to treatment would improve from 70.0% to the clinically relevant alternative of 85.0%, using an α error of 0.05 (two-sided) and a β error of 0.1. Thus, the first step was planned to treat 25 lesions; if ≥18 lesions achieved a CR, the study would enroll patients up to a total of 79 lesions. The regimen would be considered active if a CR was obtained in ≥61 lesions. Considering a dropout rate of 10.0%, at least 90 lesions should be treated.

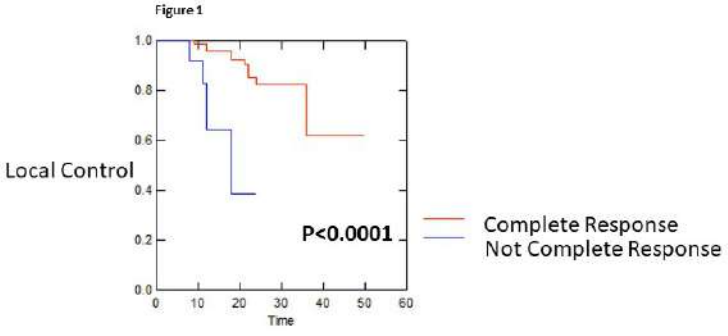
Results: Fifteen radiation oncology institutions participated in this trial, which enrolled patients between September 2019 and October 2023. According to study design, we treated 25 lesions (15 patients) in the first step, of which 24 achieved CR. Consequently, we proceeded to the second step, treating 79 lesions (51 patients), of which 68 achieved CR. While waiting for sufficient follow-up to be achieved for the 90 lesions as per study design, additional patients were enrolled, resulting in a total of 148 patients with 246 lesions.
Patients and lesions characteristics are reported in Table 1. CR and partial response, and stable disease were observed in 184 (74.8%), 45 (18.3%), and 16 (6.1%) lesions, giving a rate of clinical benefit of 99.2%. For the first 90 lesions with more mature follow-up, CR was significantly associated with a betterlocal control (LC) rate (82.5% versus 38.8%, p<0.0001).

Conclusions: Radiotherapy delivered by pre-defined SBRT treatment schedules and shared constraints improved the CR rate, leading to an excellent LC.

Table 1

	N. (%)
Patients	148
Lesions	246
Age, years	
Median (range)	61 (37-86)
ECOG	
0	130 (87.8)
1	18 (12.2)
Type of BRCA mutation	
Wild Type	73 (49.3)
BRCA-1	36 (30.3)
BRCA-2	12 (8.1)
BRCA-1 and BRCA-2	2 (1.5)
VUS	5 (3.4)
Unknown	5 (3.4)
Missing	21 (14.2)
Comorbidities	
None	51 (34.5)
>0	97 (65.5)
Histotype	
High grade serous cell	126 (85.1)
Endometrioid	6 (4.1)
Clear cell	8 (5.4)
Mixed	3 (2.1)
Undifferentiated	1 (0.6)
Mixed mullerian/sarcinosarcoma	1 (0.6)
Other	3 (2.1)
N. of previous surgery	
Median (range)	2 (0-5)
N. of lines of previous chemotherapy	
Median (range)	2 (0-7)
N. patients under PARPi maintenance	
No	59 (39.9)
Yes	89 (60.1)
N. patients undergoing previous in site radiotherapy	142 (95.9)
No	6 (4.1)
Yes	
Anatomical district	
Abdomen	109 (44.6)
Pelvis	75 (30.5)
Thorax	51 (20.7)
Neck	11 (4.4)
GTV	
Median, range (cm³)	3.56 (0.3-577.0)
PTV	
Median, range (cm³)	9.1 (1.0-97.9)
Total dose, Gy	
Median (range)	40 (24-50)
N. of fractions	
Median (range)	5 (3-8)
$BED_{10,00}$	
Median (range)	72 (38-125)

Figure 1



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ROLE OF DOSIMETRIC INDECES IN RADIONECROSIS ONSET AFTER STEREOTACTIC RADIOTHERAPY ON SURGICAL CAVITY OF RESECTED BRAIN METASTASES

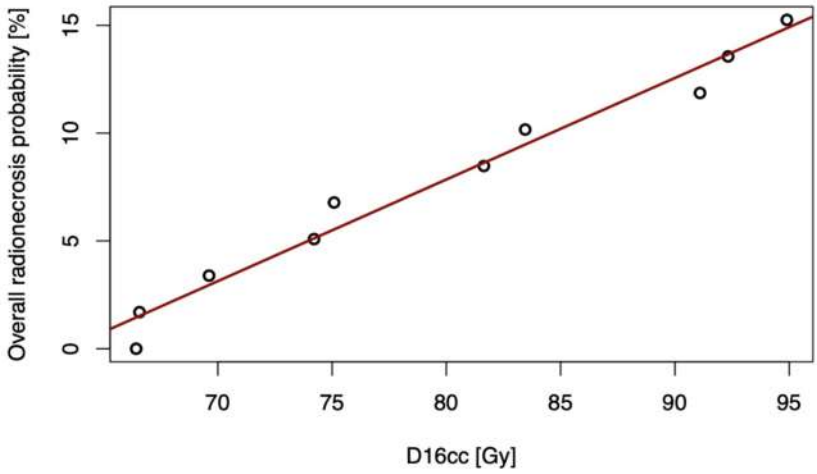
Code: 533

Aims: Brain metastases (BMs) are the most common intracranial tumours in adults. The two main types of treatment are surgery and radiotherapy. Whole brain radiotherapy (WBRT) was employed as an adjuvant local treatment.
However, because of its neurocognitive impairment, its use has progressively declined, giving way to postoperative stereotactic radiotherapy (pSRT). One of the most significant side effects of brain SRT is radionecrosis (RN). The objective of this retrospective study is to identify relevant dosimetric parameters associated with RN risk that can guide the radiation oncologist's clinical practice.

Methods: Adult patients treated with pSRT between 2015 and 2022 were included. Responses were assessed according to the RANO-BM. RN was studied by analyzing MRIs performed by a team of neuroradiology experts. Treatments were fractionated into 3, 5 (pSRT) or 10 fractions (WBRT in case of retreatments), with variable dose normalization.
Cumulative dose-volume histograms were collected for each patient. In case of multiple treatments or retreatments, the sum of DVHs was considered. All histograms were converted to an equivalent dose using an ?/? ratio of 2 Gy (EQD2). The impacts of Vdose and Dvolume on RN risk were analyzed.

Results: A total of 59 patients with 67 cavities were included in the analysis, with a median age of 59 years. Forty of the cavities were treated with 3 fractions of pSRT and the remaining with 5 fractions. When a whole brain retreatment was performed, it was administered in 10 fractions. Radionecrosis was observed in 10 surgical cavities, accounting for 14.9% of the total. Thirty-four patients underwent brain retreatment: of these, 3 developed radionecrosis (8.8%). We identified a D volume of 16cc that was significantly linearly related to the overall probability of radionecrosis. The median D 16cc for patients with RN was 81.6 Gy. The median radionecrosis free survival found was of 31 months. We observed a trend where the development of RN was more closely associated with non-homogeneous dose distribution (prescription at 80% isodose).

Conclusions: This study explored dosimetric parameters that can predict radionecrosis following pSRT. We identified a linear correlation between D16cc values and the likelihood of RN, aiming to offer practical guidance on risk levels for the development of RN. This parameter can also be employed to assess single or multiple treatments, either by converting DVHs to EQD2 or by summing DVHs from repeated treatments.



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DOES SBRT HAVE A ROLE IN OLIGOPROGRESIVE OR OLIGOPERSISTENT METASTATIC COLORECTAL CANCER? A SINGLE-CENTER STUDY.

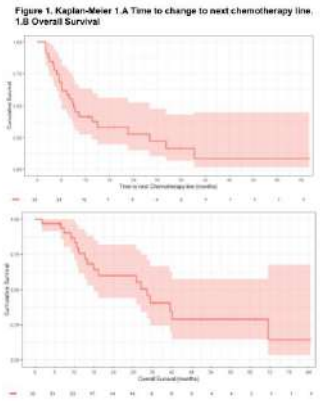
Code: 416

Aims: The aim of this study is to assess the effectiveness of Stereotactic Body Radiotherapy (SBRT) in delaying the initiation of subsequent systemic therapy in patients (pts) with metastatic colorectal cancer (mCRC).

Methods: We identified mCRC pts treated with systemic therapy in a single institution. We selected patients who underwent SBRT in the oligometastatic or oligopersistent setting. For these pts, we calculate the time to change systemic therapy as the interval from the SBRT to the need to start the subsequent therapy line. Overall survival (OS) served as the secondary endpoint, calculated from the time of SBRT to either the last follow-up or death, using the Kaplan-Meier method. Statistical analysis was performed by Rstudio.

Results: In this preliminary analysis, 93 mCRC pts treated with SBRT in an oligoprogressive or oligopersistent setting were identified in a prospectively collected database. At the time of this analysis, radiotherapy data were available for 33 patients (35%). Median age was 61 (range 36-81) years, with a predominance of males (64%). Only 3 (9%) pts were bulky at diagnosis. Pts received SBRT from December 2016 to May 2023. The median dose was 50 (range 25-60) Gy, and 91% of pts received 3
(33%) or 5 (51,5%) fractions. The biological effective dose was 100 (range 37,5-180) Gy_{10}. SBRT was administered to oligopersistent disease in 7 (22%) patients and to oligoprogressive disease in 26 (78%) patients. A total of 49 metastatic lesions were treated, with the most common sites being the lungs (36.7%), liver (30.6%), lymph nodes (26.5%), and other sites (6.2%). With a median follow-up of 19 months (range 2-86), 24 (72,7%) pts changed the line of systemic therapy. The median time to change was 8 (range 2-69) months.

Figure 1 displays the Kaplan-Meier curves for time to change the next chemotherapy line and OS. At 12 months, the probability of changing systemic therapy was 59% (95% confidence interval [CI] 0.26-0.63),and the one-year OS rate was 83% (95% CI 0.71-0.98).



Conclusions: This preliminary analysis suggests that SBRT for metastases in patients with oligoprogressive or oligopersistent mCRC leads to a median delay of 8 months in initiating the next line of systemic therapy. Integrating data from all 93 patients will yield a deeper understanding of radiotherapy practices and outcomes within this population. Further study should confirm these findings.

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STEREOTACTIC BODY RADIATION THERAPY FOR LUNG AND LIVER OLIGOMETASTASES FROM BREAST CANCER: DEFINITIVE RESULTS OF A PROSPECTIVE NON- RANDOMIZED PHASE II TRIAL

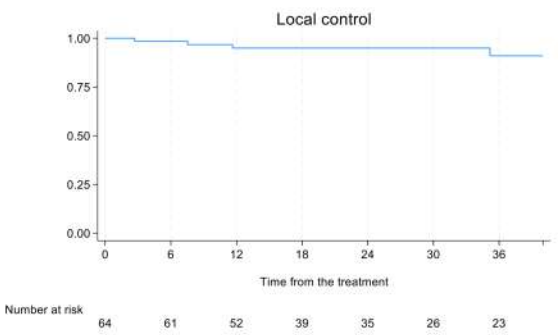
Code: 322

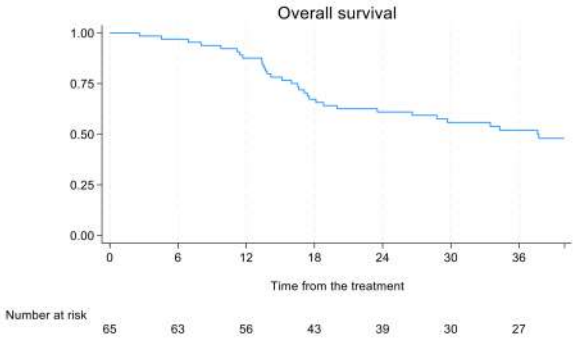
Aims: To report mature results for local control and survival in oligometastatic breast cancer patients treated with stereotactic body radiotherapy (SBRT) on lung and/or liver lesions in a phase II trial.

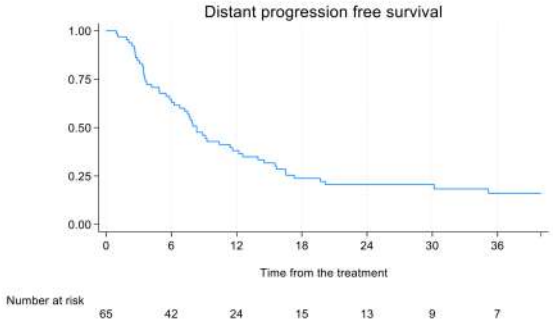
Methods: This is a prospective non-randomized phase II trial (NCT02581670) which enrolled patients from 2015 to 2021. Eligibility criteria included: age >18 years, ECOG 0-2, diagnosis of breast cancer, less than 5 lung/liver lesions (with a maximum diameter <5 cm), metastatic disease confined to the lungs and liver or extrapulmonary or extrahepatic disease stable or responding to systemic therapy. The primary end-points were local control (LC) and treatment- related toxicities. The secondary end-points included overall survival (OS), distant metastasis-free survival (DMFS), systemic therapy free survival (STFS).

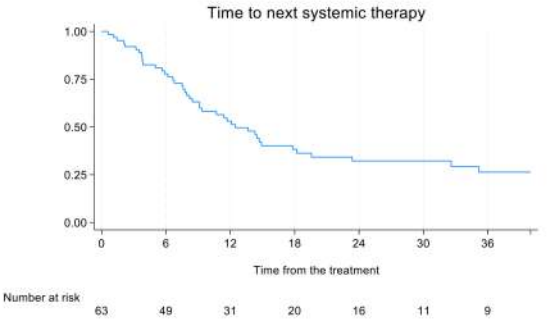
Results: The study population included 64 patients with a total of 90 lesions treated with SBRT. Patients and disease characteristics are shown in table 1. Treatment was well tolerated; safety results have already been presented. \
After a median follow up of 29 months (range 3-93), 5 patients had a local relapse. LC at 1 and 2 years was 94.9%, 91% at 3 years. Median local control was not reached. During follow up, 37 patients died (56.9%). Median OS was 16.5 months, OS at 1, 2 and 3 years was 87.5%, 60.9% and 51.9%, respectively. Most patients experienced a distant relapse (55, 84.6%). Median DMFS was 8.3 months, DMFS at 1, 2 and 3 years was 38.1%, 20.6% and 16% respectively.
Forty-five patients (69.2%) changed or started a new systemic therapy due to disease progression. Median STFS was 12.5 months, STFS at 1, 2 and 3 years was 53%, 32.2% and 6.4% respectively. At univariate analysis, local response to SBRT was found to be statistically linked with better OS (p 0.001 CI 95% 1.36-3.19), DMFS (p 0.030 CI 95% 1.03-2.13) and STFS
(p 0.030 CI 95% 1.04-2.52). Additionally, a better outcome was seen for extra-target disease reaching statistical significance for DMFS (p 0.040 CI 95% 1.02-3.04).

Conclusions: SBRT is a safe and valid option in oligometastatic breast cancer patients, with very high rates of local control. An optimal selection of patients is likely needed to improve survival outcomes and reduce the rate of distant progression.









Age median (range)	61 (32-87)	
Molecular classification	n.	%
Luminal A	18	28%
Luminal B	18	28%
HER2 enriched	14	22%
Triple negative	13	20%
Time from diagnosis to metastases (days)	1701.4	
Type of metastatic disease	n.	%
Synchronous	15	23%
Metachronous	49	77%
Previous local ablative treatments (LAT)	n.	%
No	44	69%
Yes	20	31%
Lines of systemic therapies before SBRT	n.	%
0	5	8%
1	23	36%
2	13	20%
≥3	23	36%
N. of radiated lesions	**n.**	**%**
1	44	69%
2	15	23%
3	4	6%
4	1	2%
Site of irradiated lesions	**n.**	**%**
Lung	23	36%
Liver	40	63%
Both	1	2%
Disease extra SBRT target	**n.**	**%**
Yes	23	36%
No	41	64%
Concomitant systemic therapy	**n.**	**%**
Yes	54	84%
No	10	16%
BED median (range)	**139.983**	**100-262.5**

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STEREOTACTIC RADIOSURGERY FOR POSTOPERATIVE METASTATIC SURGICAL CAVITIES: A NATIONAL SURVEY

Code: 226

Aims: The Central Nervous System Study Group of the Italian Association of Radiotherapy and Clinical Oncology proposed a nationwide survey, with the purposes to investigate: the management of postoperative RT in patient with single/multiple brain metastasis, the definition of treatment doses and volumes, the treatment timing and follow-up.

Methods: In 2023, the survey was distributed online to 24 members expert in brain cancer. The questionary was divided into 4 sections: general aspects (5 questions), clinical aspect (6 questions), treatment volumes (13 questions), techniques-doses-timing (6 questions).

Results: The response rate was 100%. In case of patients with single surgically removed brain metastases, all participants (100%) voted for stereotactic radiosurgery (SRS) or stereotactic fractionated radiotherapy (SFRT) on surgical bed. For asymptomatic patients with multiple brain metastasis and one surgically removed, 87% voted for SRS/SFRT on surgical bed and the other metastasis. The characteristics most considered for the indication to this treatment were: cumulative volume of intracranial disease (77%) and patient performance status (77%). The 68% voted that the correct timing for treatment could be within 30 days from surgery. SFRT treatment was voted by 95% of participants as preferred treatment approach vs SRS. The 86% of responders voted that GTV should include the surgical bed and any areas of contrast enhancement. While there is more variability in the definition of the CTV margin, especially in clinical situations such as contact with the dura and/or sinus venosus (1-5 mm was voted by 59%; 5-10 mm by 36%; >10mm by 5%). The indication for immuno- or target-therapy was voted as “not influencing the timing of SRS/SFRT treatment” by 81% participants in case of single metastasis and 59% in case of multiple metastasis. Regarding the follow-up, 86% of the responders voted that the contrast MRI every 60-90 days should be mandatory.

Conclusions: There was a strong agreement in the clinical aspects regarding the management of patients with single or multiple brain metastasis. A heterogeneity was highlighted in the treatment timing and volume definition. Following these crucial points, a virtual contouring lab of 5 cases and an educational webinar were promoted in the same project. The achievement of a National Consensus may represent an interestingfuture goal.

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RADIOPATHOMICS MODEL TO PREDICT EARLY RESPONSE IN LA-NSCLC PATIENTS UNDERGOING CHEMORADIATION

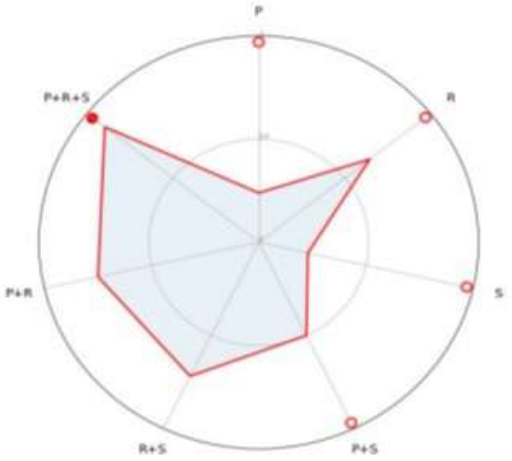
Code: 360

Aims: We aimed to evaluate the power of pre-treatment CT-based radiopathomic features to predict radiochemotherapy (RTCT) treatment outcomes. We developed a multimodal dataset that combines features computed from radiomics, clinical data, medical and histopathology images routinely collected to predict clinical outcomes.

Methods: Patients with LA-NSCLC were enrolled in a prospective trial and underwent concurrent definitive RTCT with an adaptive approach from 2012 to 2014.
Semantic features divided into demographic data,TNM stage and histological evaluation and mutations;2)Radiomic features, extracted from CT scans performed before starting chemoradiation; radiomic features were extracted from 3D ROIs given by CTV; 3) Pathomics features: hystological slides of lung cancer tissue biopsy stained with haematoxylin and eosin were digitized obtaining whole slide images (WSI) using NanoZoomer 2.0 RT (Hamamatsu) at a magnification power of 20x at a resolution of
0.5 µm per pixel. WSIs were loaded on QuPath software and re-evaluated by an expert lung pathologist that selected representative number of tumor areas, named Regions of Interest (ROIs). Tumor areas, avoiding fibrosis, necrosis or histological artifacts within the ROIs, defined as "crops", were segmented. Within this context different multimodal late fusion rules and two patient-wise aggregation rules leveraging the richness of information given by CT images, whole-slide scans and clinical data were analyzed.

Results: Overall 50 patients, 35 patients had available histological slides and were included in this analysis. In this latter group,13 (37.1%) patients achieved a significant target reduction during treatment and an adaptive planning performed. We investigate 8 different multimodal late fusion rules and two patient-wise aggregation rules in comparison to unimodal approach.The fusion-based multimodal paradigm, achieving an AUC equal to 90.9%, outperforms each unimodal approach, suggesting that data integration can advance precision medicine. Figure1 shows a radar chart plotting the performances in terms of AUC of the various unimodal and multimodal approaches. The combination of 3 modality resulted in the highest performance of the model.

Conclusions: We propose a deep learning framework for integrating multimodal data for prediction of early response to treatment. This approach has the potential to advance clinical decision support systems, and could represent an effective and innovative step forward in personalised medicine.



Modalities Combinations	AUC rank
P+R	0.64
R+S	0.61
P+S	0.31
P+R+S	0.91

Figure 1. Radar chart showing the performance in terms of AUC of the unimodal and multimodal approaches, where P stands for Pathomics, R for Radiomics, and S for Semantic. The filled circle represents the flow with the highest rank, whilst blank circles represent unimodal or multimodal approaches with statistically different performances from the best approach according to Friedman test with the Iman-Davenport amendment followed by the pairwise Bonferroni-Dunn post-hoc test ($p < 0.1$).

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INTEGRATING GENETIC INFORMATION INTO VOXEL-BASED ANALYSIS FOR ASSESSING LATE URINARY TOXICITY AFTER RADIOTHERAPY FOR PROSTATE CANCER: AN INNOVATIVE APPROACH

Code: 65

Aims: The study proposes a new approach to voxel-based analysis VBA including patient-specific factors, allowing HRs at a patient level. This approach considers 3D dose distributions and single-patient dose- modifying factors to account for inter-patient variability. The first application is bladder dose-surface maps (DSMs) incorporating a polygenic risk score (PRSi) *[Franco et al. 2021]*.

Methods: We studied prostate cancer patients (PCa) who underwent radical RT in an international prospective cohort. Endpoints were G2+ urinary frequency and G1+ haematuria (follow-up for 8y). The PRSi for frequency/haematuria involved 13 validated SNPs. DSMs were cut anteriorly, aligned at the most caudal slice and normalized lateral extent to the maximum bladder diameter. In the cranial-caudal direction, we fixed the most caudal 1.5 cm (~ the bladder neck) and normalized the rest to the median height.
Multivariable Cox-NTCP regression was used to assess the PRSi's contribution, based on Equivalent Uniform Dose (EUD) corrected for fraction and derived from bladder dose-surface-histograms. The HR for the PRSi was used to compute an effective EUD corresponding to one point in PRSi (PRSi_EUD_1). The EUD associated with its PRSi (PRSi_EUD) is the patient-specific PRSi times the PRSi_EUD_1. This quantity is established by incorporating PRSi_EUD into the DSM, assigning a dose to each voxel based.
PRSi-modulated DSMs showed non-uniform shielding towards higher doses for PRSi>0, lower for PRSi<0, no change for PRSi=0. VBA was performed using Cox regression on PRSi-modulated DSMs and the BH correction was applied to manage multiple tests.

Results: 674 PCa with DSM and PRSi revealed toxicity of 4.8% for G2+ frequency and 7.5% G1+ haematuria. PRSi was associated with toxicity, with mean values of 0.61/-0.40 for frequency and 0.38/-0.02 for haematuria. PRSi-modulated VBA revealed specific areas influencing dose-response relationships **(Fig.1)**, leading to an increase in HRs for both frequency (upto 0.06 higher/1Gy) and haematuria (upto 0.03)

Conclusions: A new method for incorporating single-patient genetic risk into VBA was developed. This approach generates PRSi-modulated dose maps, allowing for the inclusion of other patient-specific risk factors. The analysis identified bladder subregions linked to late toxicities, showcasing the enhanced sensitivity at avoxel level with PRSi modulation.
REQUITE funded by EU GA 601826, RADprecise by ERAPERMED2018-244, PerPlanRT Italian MoH ERP-2020-23671125

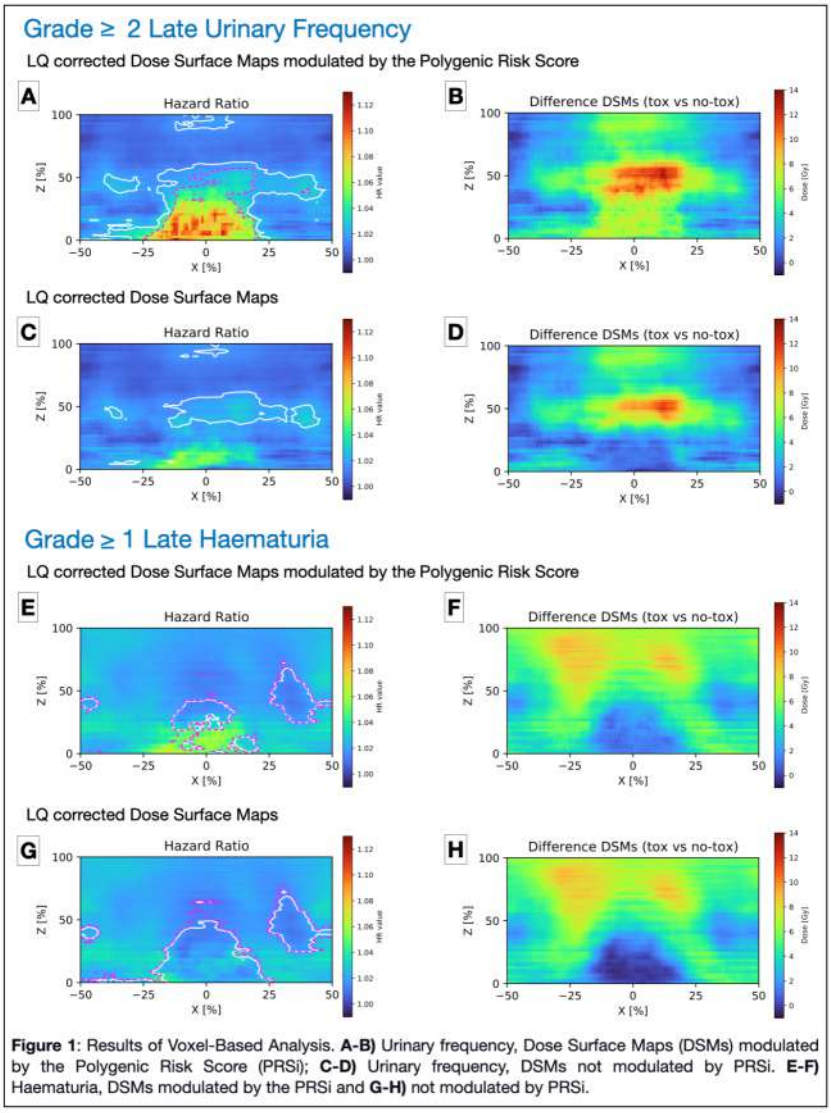

Figure 1: Results of Voxel-Based Analysis. **A-B)** Urinary frequency, Dose Surface Maps (DSMs) modulated by the Polygenic Risk Score (PRSi); **C-D)** Urinary frequency, DSMs not modulated by PRSi. **E-F)** Haematuria, DSMs modulated by the PRSi and **G-H)** not modulated by PRSi.

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FIRST ITALIAN EXPERIENCE WITH IMAGINGRING MOBILE: PRELIMINARY EVALUATION ON THE ACCURACY OF FLAP APPLICATOR POSITIONING IN CONTACT HIGH DOSE RATE BRACHITERAPY TREATMENT OF NON-MELANOMA SKIN CANCER

Code: 449

Aims: To assess the accuracy and the feasibility of positioning flap applicators on the skin patients provided by the real-time guided imaging system, which allows the entire workflow to be performed in one room.

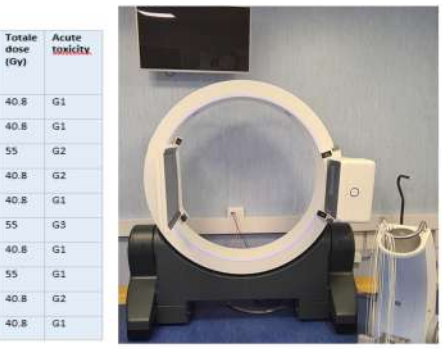
Methods: By the end of November 2023 a brand-new system has been introduced in our radiotherapy unit: the ImagingRing Mobile (Elekta ImagingRing v 2.5.2). This system brings CT imaging directly to the patient and avoids the need to displace applicators, improving patient comfort without compromising image quality. This in-room imaging allows for rapid adaptation of brachytherapy plans to each patient's current anatomy. We retrospectively analysed a total of 10 patients with non-melanoma skin cancer treated from November 2023 to January 2024. The patients underwent contact HDR-RT using flap applicators and remotely after loaded Ir-192 sources. Flap applicators, both customized directly to the target surface and attached to a customized thermoplastic mask, were used depending on the anatomical site. Treatment planning was performed using Oncentra brachy 4.5.4. Each simulation-CT scan was acquired by ImagingRing Mobile system. Reference CBCT scans were acquired and then every other day. The CBCT acquisition parameters were as follows: (Elekta ImagingRing v 2.5.2) 80 kVp, 8-20 mA, short scan SFoV. All CBCT scans were fused with the reference one using MIM software 7.3.2. On each scan, a ROI corresponding to the applicator was created, and then the agreement between all ROIs was calculated by comparing the contours.

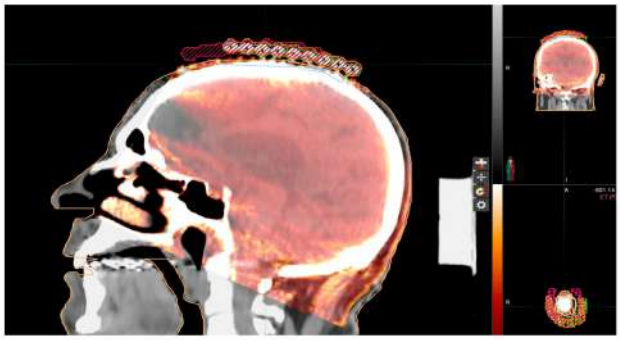
Results: A total of 114 CBCT scans were fused and evaluated. When the Mean Distance to agreement between the two contours (MDA mm) was > 3 mm the treatment was replanned. The range of variation in mm detected was from 30 mm to 1 mm.
The treatment was well tolerated by all patients; acute toxicity recorded at the end and 10 days after treatment was mostly G1-G2, and only in one case of reirradiation G3 according to CTCAE v5.

Conclusions: The addition of ImagingRing Mobile to the brachytherapy suite improves patient safety and comfort, the efficiency of HDR treatment, and simulation time as there is no need to transfer the patient from the CT scan to the treatment room. Additionally, the implementation of ImagingRing Mobile for brachytherapy allows for immediate visualization of the applicator positioning and precise delivery of the treatment. Imaging ring allows Image Guided Brachytherapy.

Table 1

Gender	Age (year)	Histology	Lesion Site	Setting	Dose prescription	Number of catheters	Totale dose (Gy)	Acute toxicity
M	82	SCC	scalp	adjuvant	3.40 Gy/die daily	9	40.8	G1
M	73	SCC	leg	adjuvant	3.40 Gy/die daily	10	40.8	G1
M	75	SCC	ear	definitive	2.75 Gy/die daily	6	55	G2
M	69	MERKEL	cheek	adjuvant	3.40 Gy/die daily	8	40.8	G2
F	75	SCC	scalp	adjuvant	3.40 Gy/die daily	6	40.8	G1
M	77	REC SCC	nose	definitive	2.75 Gy/die daily	6	55	G3
M	55	SCC	finger	adjuvant	3.40 Gy/die daily	6	40.8	G1
M	86	BCC	Front/nose	definitive	2.75 Gy/die daily	4 x 2	55	G1
F	77	SCC	nose	adjuvant	3.4 Gy/die daily	6	40.8	G2
M	76	SCC	cheek	adjuvant	3.4 Gy/die daily	6	40.8	G1





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EARLY BIOCHEMICAL OUTCOMES FROM A PROSPECTIVE TRIAL TESTING STEREOTACTIC SALVAGE RADIOTHERAPHY FOR MACROSCOPIC PROSTATE BED RELAPSE AFTER SURGERY - STARR (NCT05455736)

Code: 345

Aims: Prostate bed salvage radiotherapy (SRT) is the cornerstone treatment for biochemical recurrence after radical prostatectomy (RP). PSMA PET/CT or Magnetic resonance imaging (MRI) often allow to detect macroscopic recurrence within prostate bed. Dose escalation to improve disease control in this scenario through stereotactic salvage radiotherapy (SSRT) has been suggested as a potential way to improve disease control. STARR trial (NCT05455736) is a prospective trial evaluating biochemical relapse rate and toxicity after SSRT on prostatic bed macroscopic recurrence.

Methods: Patients affected by macroscopic recurrence within the prostate bed after RP were enrolled within a prospective multicenter study. Macroscopic recurrence was detected with a Choline or PSMA CT-PET or through MRI, performed with a post prostatectomy PSA PSA >0.2 ng/ml. Regional or distant metastatic disease were exclusion criteria.
Treatment was administered for a total dose of 35 Gy in 5 fractions every other day. PSMA or Choline CT- PET and MRI were used for target volume delineation. Concurrent Androgen Deprivation Therapy (ADT) was not allowed. biochemical response (BR) and Complete biochemical response (CBR) were defined as a PSA nadir < 0.2 ng/mL and <50% of baseline, respectively.

Results: Sixty one patients were enrolled between March 2021 and November 2023. The current analysis included 44 enrolled patients with > 3 months of follow up. Acute genitourinary and gastrointestinal toxicity occurred in 3 (2 G1 and 1 G2), and 4 patients (2 G1 and 2 G2), respectively. Late genitourinary and gastrointestinal toxicity were identified in 7 (all G1) and 1 patients (G2), respectively. Three months BR and CBR were detected in 38 (86.4%) and 20 (45.5%) cases, respectively. After a median follow up of 11 months (95%CI 8-15), 6 recurrences were detected (2 biochemical and 4 metastatic recurrences detected through PSMA PET-CT) The estimated median biochemical progression-free survival was not reached and median radiological progression-free survival was 25 months (95%CI 21-25 months), respectively.
Forty patients (90.9%) were free from ADT at the end of follow up, for a median ADT free survival of 26months (95% CI 20-26 months).

Conclusions: SSRT demonstrates feasibility and safety, revealing promising results in terms of biochemical outcomes, biochemical, radiological progression free and ADT free survival, with an optimal tolerability profile.

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Prostate re-irradiation after previous definitive or salvage radiotherapy (RE-START). A study on behalf of Italian Association of Radiotherapy and Clinical Oncology (AIRO)

Code: 37

Aims: Re-irradiation is an emerging treatment option for local relapse after definitive therapy of prostate cancer. A national registry endorsed by Italian Association for Radiation Oncology (AIRO) was instituted in 2023. Here are presented the results of the first retrospective cohort included.

Methods: All patients were affected by intraprostatic or prostate bed macroscopic recurrence after previous radical or postoperative radiotherapy, detected by PET CT or Magnetic resonance imaging. All treatment schedules providing at least 5 Gy per fraction were allowed. Patients with metastatic or regional nodal disease, residual severe toxicities from previous treatments or <6 months of follow-up after re-irradiation were excluded from the analysis.

Results: 302 patients were included. Stereotactic body radiotherapy (SBRT) was administered in all patients, for a median total dose of 30 Gy in 2-5 fractions. Concomitant ADT was administered in 58,5% of patients.
After 42 months of median follow up (95% CI 37-48 months), rate of acute GI and GU toxicity was 11.2% (29 G1 and 5 G2 events, respectively), and 22.5% of patients (56 G1 and 12 G2 events, respectively), respectively. Late GI and GU toxicity was recorded in 20.2% of patients (38 G1, 17 G2, 5 G3 and 1 G4 events, respectively) and 38.4% (68 G1, 34 G2, 6 G3 and 8 G4 events, respectively), respectively. Biochemical relapse free, metastasis free and overall survival (BRFS, MFS and OS) data were available for 287, 291 and 296 patients, with 171, 77 and 65 events, respectively. Median BRFS,
MFS and OS were 30 months (95% CI 24-34 months), not reached (95% CI NR-NR) and 98 months (95% CI 81-142). At univariate analysis, baseline high risk disease (p=0.01), time between end of first radiotherapy course and relapse<36 months (p=0.0004), concomitant ADT (p<0.0001) and PSA at relapse<1 ng/ml (p=0.001) were all significantly associated to BRFS, and persisted as independent prognostic factors at multivariate analysis. None of the abovementioned factors was significantly associated with MFS. Only time between end of first radiotherapy course and relapse<36 months was significantly associated to OS (p=0.02).

Conclusions: Toxicity rate after reirradiation was mild, and clinical outcomes in terms of BRFS, MFS and OS werepromising, even after more than 3 years of median follow up. Data including results updated with a prospective cohort included in RE-START trial are awaited.

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OLIGOMETASTATIC MESOTHELIOMA TREATED WITH ABLATIVE RADIOTHERAPY (OMAR): MULTI- INSTITUTIONAL DATABASE: ON BEHALF OF THE AIRO "BIOLOGY AND TREATMENT OF OLIGOMETASTATIC DISEASE" AND "THORACIC ONCOLOGY" STUDY GROUPS

Code: 25

Aims: The aim of this retrospective multicentric study is to evaluate whether Stereotactic Ablative Radiotherapy (SABR) can have an impact on disease course in patients with unresectable pleural mesothelioma (PM) with radiological progression after ≥ 1 line of chemotherapy at a maximum of 3 pleural (or extrapleural) sites.

Methods: Adult patients (≥18 years) affected by PM, treated from 2011 to 2021 with stereotactic radiotherapy for a maximum of three pleural or extrapleural sites are analyzed. SABR had to be delivered with ablative purposes (50Gy EQD2/10 delivered in a maximum of 12 fractions as per Oligocare definition). Primary endpoint is time to new systemic therapy (TTNS). Secondary endpoints are local control (LC), progression free survival (PFS), overall survival (OS), acute and late toxicity RT related.

Results: From 6 Italian RT centers, 48 patients were enrolled in the study. Patients and treatment characteristics are shown in table 1.
Treatment was generally well tolerated. Only 8 patients (19.5%) experienced some kind of acute toxicity, no G3 or G4 toxicity was recorded. Most common side effects was thoracic pain G1 (4 patients) or G2 (2 patients). One patient experienced esophagitis G2, while one other cough and dyspnoea G1. Late toxicity profile was good with chronic pain reported by 4 patients (two G1, one G2 and one G3). Median follow up was 20.8 months (range 2.2-92.4).
27 patients (65.8%) started or changed systemic therapy due to disease progression during follow up. Median TTNS was 12.8 months. TTNS free survival at 1 and 2 years was 53% ± 7.9% and 25.2% ± 7.2%, respectively.
At last follow up, 21 (51.2%) patients died all but one due to neoplastic disease. Median OS was 37.1 months. OS at 1 and 2 years was 87.3% ± 5.3% and 77.2% ± 7.6%, respectively.Four patients had a local recurrence (9.7%), all relapsed also in distant sites. Generally, 36 patients (87.8%) relapsed outside of RT field, most of them in pleural sites. Median local control was not reached. LC at 1 and 2 years was 97.5% ± 2.5% and 93.8% ± 4.4%, respectively.
Median PFS was 7.9 months. PFS at 1 and 2 years was 31.6% ± 7.5% and 7% ± 4.4%, respectively.

Conclusions: SABR is a safe and effective approach for the treatment of oligorecurrent/oligoprogressive PM, although cronic thoracic pain is reported by 10% of patients. Time to new systemic therapy is prolonged up to 12 months. Ten percent of patients are free from disease at 2 years and more than half are alive at 3 years.

Patient and primary disease		
Variable	Number	Percentage
Sex: male	32	66.6%
female	16	33.4%
Age (median/range)	68 years (38-86)	
Smoking status: Never	21	43.8%
Former	22	45.8%
Active	5	10.4%
Histology: Epithelioid	43	89.6%
Biphasic	1	2.1%
Sarcomatoid	4	8.3%
Clinical TNM staging: Ia	8	16.7%
Ib	23	47.9%
IIIa	2	4.2%
IIIb	15	31.2%
Surgery: Pleurectomy	23	47.9%
Extrapleural pneumonectomy	3	6.3%
No	22	45.8%
Chemotherapy: Neoadjuvant	20	41.7%
Adjuvant	6	12.5%
First line	22	45.8%
Adjuvant RT: Yes	8	16.7%
No	40	83.3%
Metastatic disease characteristics		
Disease Free Interval (median/range)	1.9 years (0-11)	
Oligometastasis classification:		
Oligorecurrence	26	54.2%
Oligroprogression	22	45.8%
Relapse timing: during/after first line CT	37	77.1%
After second/third line CT	11	22.9%
Extratarget disease: Yes	19	39.6%

No	29	60.4%
SBRT		
Number of irradiated lesion(s): 1 2 3	32 13 3	
Irradiated site(s): Pleura Lung Nodes Other	39 6 7 1	
PTV volume (cc)	Median 45.2 (range 14.4-332.5)	
BED (median/range)	72 Gy (57.6-115.5)	
BED biologically effective dose		

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OUTCOME ANALYSIS OF ENRT VS SBRT FOR LYMPH NODE RELAPSES IN GYNECOLOGICAL CANCERS

Code: 139

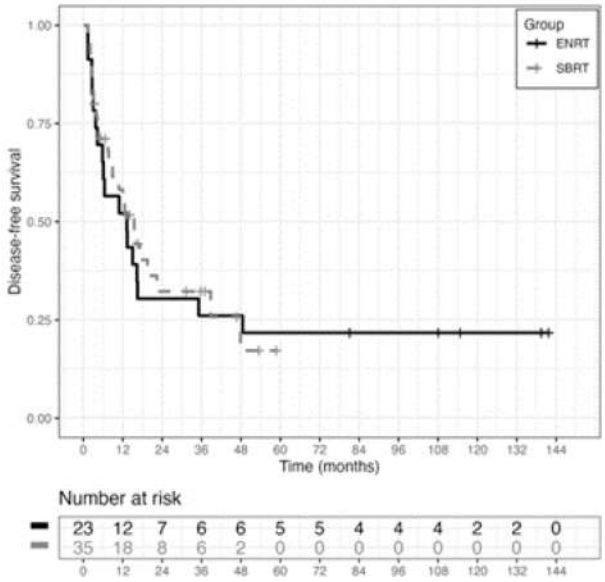
Aims: Extended nodal radiotherapy (ENRT) of the interested chain was prescribed as salvage treatment for lymph node (LN) relapses in Gynecological tumors (GT), lately, with a Simultaneous Integrated Boost (SIB) of positive LN. Recently stereotactic body radiotherapy (SBRT) has been proposed, with promising results. There is, to date, no comparison between the two options; we analyzed the outcomes and toxicity of salvage ENRT with SIB vs SBRT for LN relapse in patients of our Institute.

Methods: From 02/2007 to 04/2023, 58 GT pts with LN relapse were treated with fluoro-deoxy-glucose positron emission tomography/computed tomography (PET/CT) guided-salvage RT in our Institution: 23 pts received ENRT and Simultaneous Integrated Boost (SIB) to PET positive LN, and 35 pts SBRT to positive PET/TC LN. Primary tumors in the ENRT and SBRT groups were, respectively: ovarian in 52.2% vs 45.7% pts; endometrial in 39.1% vs 25.7% pts; cervix, vagina and vulva in 8.7% vs 28.6% pts. More than 150 positive LN's were treated. In the ENRT group the LN chain PTV (pelvic, para-aortic or extra abdominal), was treated with a prophylactic dose, and a SIB with a median Biological Equivalent Dose (BED) of 76.5 Gy (Interquartile range, IQR 74.4; 78.8) to PET positive LN. In the SBRT group a median BED of 72 Gy (IQR 59.6;76.5) was prescribed. Toxicity was assessed using CTCAE version 5 criteria.

Results: Median follow-up was 81.1 (IQR 48.5; 117.2) and 37.0(IQR 21.3; 58.4) months for ENRT vs SBRT, respectively. Local relapse was registered in 8.7% and 14.3% in ENRT and SBRT groups, respectively; regional relapse in 34.8% vs 34.3%, and distant relapse in 78.3% vs 57.1%. Overall Survival (OS) was not statistically different (60.9% ENRT vs 65.7% SBRT). Kaplan Meier estimate of disease-free survival (DFS) is presented in Figure 1. Maximum acute and late toxicity (genitourinary, gastrointestinal and other), based on treatment site, was of grade (G) 2, except for one patient with acute G3 erythema, and one patient with late bone insufficiency fracture, both in the ENRT group.

Conclusions: While for prostate cancer ENRT apparently provides superior DFS vs SBRT, the two therapeutic options obtain similarly good results in terms of DFS, with acceptable toxicity, for GT. OS remains low for both modalities, as already observed. Prospective studies with adequate samples are needed to provide more complete information concerning the treatment of GT.

Fig. 1: DFS



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THE PROMISING EFFECTS OF LATTICE RADIOTHERAPY FOR LARGE, FUNGATING, OR ULCERATING BREAST CANCERS: A PROSPECTIVE SINGLE-CENTER STUDY

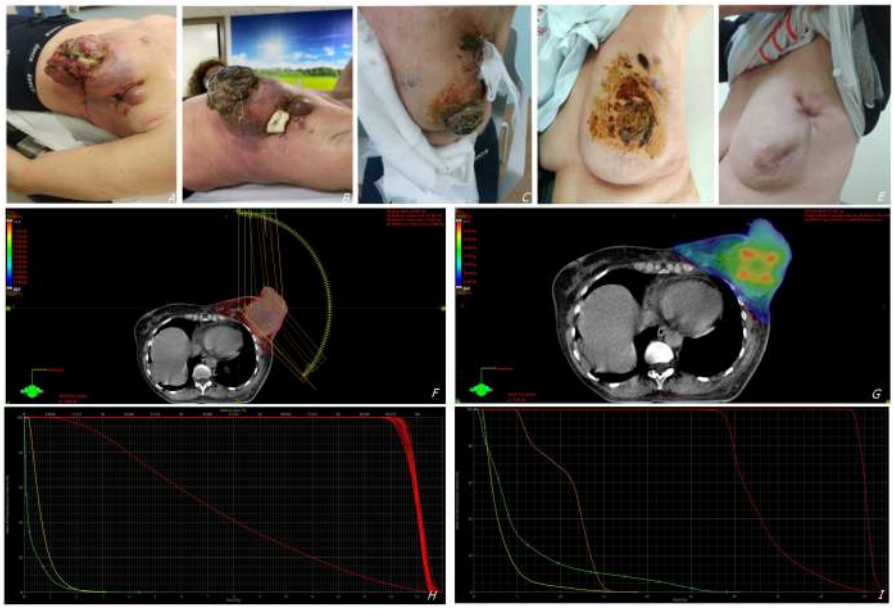
Code: 172

Aims: To evaluate the safety and efficacy of lattice radiotherapy (LRT) for large, inoperable breast cancers.

Methods: In this prospective study, patients who underwent LRT for breast tumors that were ulcerating/fungating/extensively eroding the chest wall, and were ineligible/unwilling for surgery, were enrolled between May 2021 and Nov 2023. The baseline Eastern Cooperative Oncology Group (ECOG) status, pre- and post-LRT numerical rating scale (NRS), and post-LRT changes in quality of life (QoL) were recorded. Survival outcomes were reported at 6 months and 1-year. Median rates of survival and dosimetric parameters were calculated. Kaplan-Meier curves for overall survival (OS), cancer-specific survival (CSS) and failure of local control (LC) were constructed.

Results: From May 2021 to November 2023, 10 patients (8 females) underwent LRT. The median age was 76 (range 57–99) years and the median ECOG performance status was 2.5 (range 1–4). The planned schedule was completed by 9/10 patients, accounting for a 90% compliance rate. Among patients with pain (n=7), NRS rapidly reduced from 7 (range 5–10) to 3 (range 1–6). The median equivalent uniform dose for the LRT plan was 0.71 Gy (0.09–1.59). The actuarial rates of 6-month LC, CSS, and OS were 75%, 89%, and 61%, respectively, with only LC rate changing to 50% at 1 year. Two patients had local relapse at the six- month and 1-year follow-up, respectively, after having achieved a complete response at three months, and two others died of COVID-19 infection and ischemic stroke.

Conclusions: LRT was found to be effective and safe in palliating symptoms among patients with large inoperable breast tumors. To our knowledge, this is the first clinical report describing the safety and efficacy of LRT treatment of primary breast cancers. Our preliminary study shows the promising effects of LRT for large, fungating, ulcerating breast tumors in the mitigating distressing symptoms. The effects of LRT on survival need to be examined in larger studies.



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EXPLORING PAIN MANAGEMENT IN BREAST CANCER: KEY FINDINGS FROM THE ARISE STUDY

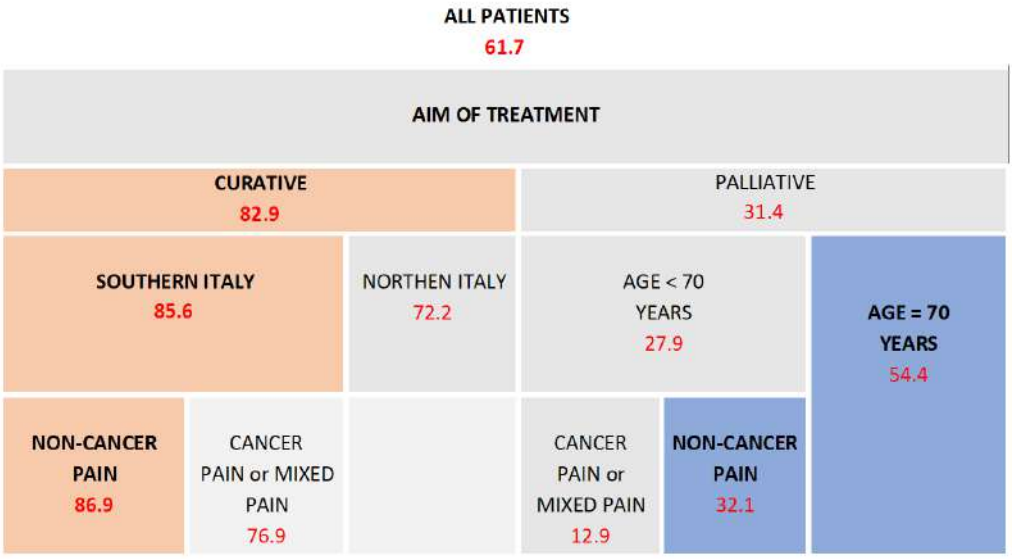
Code: 104

Aims: This ARISE study secondary analysis aims to delve into the complexities of pain management in breast cancer patients undergoing radiotherapy (RT) in Italy, seeking to understand the factors that contribute to the prevalent inadequacy in pain management. It aims to identify and analyze predictive variables for pain management adequacy and establish the relationship between these variables and the effectiveness of pain control.

Methods: This observational study engaged 2,104 participants from 13 Italian RT departments, focusing on 426 breast cancer patients reporting pain. Advanced statistical methods, including the Least Absolute Shrinkage and Selection Operator (LASSO) and the Classification and Regression Tree (CART) analysis, were employed to identify significant predictive variables for pain management adequacy. Data collection involved a standardized form capturing personal, health-related information, specifics about cancer, pain intensity, and medication.

Results: The analysis showed that 61.7% of patients experienced suboptimal pain management. Factors identified as significantly influencing pain management adequacy included the type of pain, patient age, the objective of RT, and the geographical location of the RT center. Notably, patients undergoing curative RT exhibited a higher incidence of inadequate pain management (PMI<0) compared to those undergoing palliative RT (82.9% versus 31.4%). Geographical variations were evident, with patients treated in northern Italy showing better pain management compared to those in central-southern Italy (72.0% versus 85.6%). Furthermore, the analysis focusing solely on breast cancer patients with non- neoplastic pain highlighted the geographical location of the RT center and age as significant factors impacting pain management adequacy.

Conclusions: The ARISE study underscores a significant inadequacy in pain management among breast cancer patients undergoing RT in Italy, influenced by a complex interplay of treatment-related, demographic, and regional factors. The study's findings emphasize the need for enhanced, personalized pain management strategies and highlight the importance of considering a multifaceted approach that includes patient demographics, pain characteristics, and regional healthcare practices. Future research should expand on these findings, incorporating broader, more diverse cohorts and integrating more objective pain measurement tools to improve pain management and patient outcomes in breast cancer care.



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EXPLAINABLE MACHINE LEARNING MODEL TO PREDICT OVERALL SURVIVAL IN PATIENTS TREATED WITH PALLIATIVE RADIOTHERAPY FOR BONE METASTASES

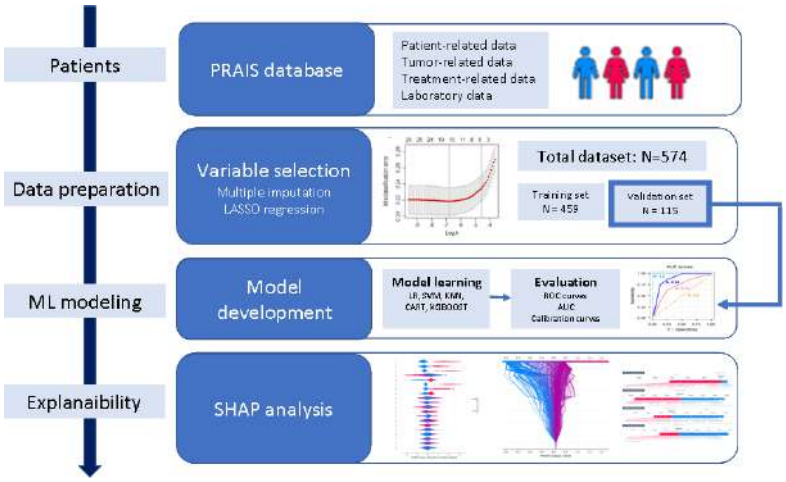
Code: 552

Aims: The estimation of prognosis and life expectancy is critical in the care of patients with advanced cancer. To aid clinical decision-making, we build a prognostic strategy combining a machine learning model with explainaible artificial intelligence to predict one-year survival following palliative radiotherapy (RT) for bone metastasis.

Methods: Data collected in the multicentric PRAIS trial were extracted for 574 eligible adults diagnosed with metastatic cancer. The primary end point was the overall survival at 1-year (1y-OS) after the start of RT. Candidate covariate predictors consisted of 15 clinical and tumor related pre-RT patient characteristics, 7 dosimetric and treatment-related variables and 49 pre-RT laboratory variables. Machine learning models were developed and internally validated using the Python package. The effectiveness of each model was evaluated in terms of discrimination and calibration. A SHapley Additive exPlanations (SHAP) explanaibility analysis to infer the global and local feature importance and to understand the reasons for correct and misclassified predictions was performed.

Results: The best-performing model for the classification of 1y-OS survival was the XGBoost algorithm, with AUC and F1-score values equal to 0.805 and 0.802, respectively. The SHAP technique revealed that higher chance of 1-year survival is associated with low values of interleukin8, higher values of hemoglobin and lymphocytes count and the non-use of steroids.

Conclusions: An explanaible machine learning approach can provide a reliable prediction of one-year survival after radiotherapy in patients with advanced cancer. The implementation of SHAP analysis provides an intelligible explanation of individualized risk prediction, enabling oncologists to identify the best strategy for patient stratification and treatment selection.



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FURTHER CLARIFICATION OF PAIN MANAGEMENT COMPLEXITY IN RADIOTHERAPY: INSIGHTS FROM MODERN STATISTICAL APPROACHES

Code: 103

Aims: The primary objective of this study was to assess the adequacy of analgesic care in radiotherapy (RT) patients, with a secondary objective to identify predictive variables associated with pain management adequacy using a modern statistical approach, integrating the Least Absolute Shrinkage and Selection Operator (LASSO) algorithm and the Classification and Regression Tree (CART) analysis.

Methods: This observational, multicenter cohort study involved 1,387 patients reporting pain or taking analgesic drugs from 13 RT departments in Italy. The Pain Management Index (PMI) served as the measure for pain control adequacy, with a PMI score <0 indicating suboptimal management. Patient demographics, clinical status, and treatment-related factors were examined to discern the predictors of pain management adequacy.

Results: Among the analyzed cohort, 46.1% reported inadequately managed pain. Non-cancer pain origin, breast cancer diagnosis, higher ECOG Performance Status scores, younger patient age, early assessment phase, and curative treatment intent emerged as significant determinants of negative PMI from the LASSO analysis. Notably, pain management was observed to improve as RT progressed, with a greater discrepancy between cancer (33.2% with PMI<0) and non-cancer pain (73.1% with PMI<0). Breast cancer patients under 70 years with non-cancer pain had the highest rate of negative PMI at 86.5%, highlighting a potential deficiency in managing benign pain in younger patients (Table 1).

Conclusions: The study underscores the dynamic nature of pain management during RT, suggesting improvements over the treatment course yet revealing specific challenges in non-cancer pain management, particularly among younger breast cancer patients. The use of advanced statistical techniques for analysis stresses the importance of a multifaceted approach to pain management, one that incorporates both cancer and non- cancer pain considerations to ensure a holistic and improved quality of oncological care.

Table 1: Predictive model for inadequate pain management: Red numbers represent the proportion of patients with inadequate pain management (PMI < 0), while the figures in brackets represent the total number of patients within each respective group. (RT: radiotherapy; ECOG: Eastern Cooperative Oncology Group Performance Status).

ALL PATIENTS 46.1 (1387)							
CANCER PAIN 33.2 (941)				NON-CANCER PAIN 73.1 (446)			
AIM OF TREATMENT				PRIMARY TUMOR			
Curative RT 48.0 (250)		Palliative RT 28.0 (691)		Breast cancer 83.8 (210)		Other cancers 63.6 (236)	
Before RT	During RT	ECOG PS 0-1	ECOG PS 2-4	Age < 70 years	Age = 70 years	Before RT	During RT
55.6 (108)	42.3 (142)	33.0 (269)	25.0 (422)	86.5 (141)	78.3 (69)	69.0 (106)	59.0 (130)

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ROLE OF [11C]-METHIONINE POSITRON EMISSION TOMOGRAPHY FOR DELINEATION OF CLINICAL TARGET VOLUME FOR REIRRADIATION THERAPY PLANNING IN RECURRENT DIAGNOSED GLIOBLASTOMA

Code: 140

Aims: Reirradiation for recurrent glioblastoma (GBM) have been investigated in the litterature and no clear evidences exist regarding the clinical target volume (CTV) optimal definition and the use of metabolic imaging using aminoacid tracers, other than MRI. For this reason, we investigated the role of
[11C]-Methionine PET (MET-PET) in a cohort of adults patients with recurrent GBM treated with Radiation therapy and TMZ chemotherapy. Objectives of the present study were to evaluate how it could modify the CTV delineation, and if it could detect eventually tumor cells not otherwise visible.

Methods: Patients with recurrent GBM, and an interval time (IT) from previous RT > 6 months were included. Simulation CT scan, MRI with different sequences and a 11CMETPET were performed in all patients and images were co-registrated one with each other to define the CTV. Two different target volume were defined: Biological target volume (BTV) corresponded to the pathological uptake on MET-PET, and CTV defined as the abnormalities volume on MRI. Correlations between BTV and CTV were recorded.

Results: From September 2013 to January 2024, 121 patients were reirradiated for recurrent GBM. The median age was 52 years, and majority had KPS 90-100. The median IT between first radiotherapy and reirradiation was 27 months (range 8-212 months). The overlap between BTV and CTV showed low correlation between the two volumes, with CTV not always fully included BTV. In all cases the BTV included the whole CTV, while in 50% part of BTV was outside the CTV. The location of MET-PET uptake was mainly observed on post contrast T1 MRI and in some cases on FLAIR MRI abnormalities.

Conclusions: MET-PET allowed to detect areas at higher risk of recurrent. A challenging issue is represented by integration of morphological and functional imaging to contour CTV in the setting of reirradiation. This results are promising and could permit to better define the target reducing the dose at organs at risk and increasing the possibility of a dose escalation for a higher local control.

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EXPLORING NEOADJUVANT FOLFIRINOX COMBINED WITH CHEMORADIATION FOR LOCALLY ADVANCED PANCREATIC CANCER: A PHASE II STUDY

Code: 64

Aims: To evaluate the margin-negative (R0) resection rate in borderline resectable and locally advanced unresectable pancreatic ductal adenocarcinoma (PDAC) after induction FOLFIRINOX followed by chemoradiation (CRT).

Methods: In this single-arm, phase 2 clinical trial, patients with locally advanced PDAC underwent pre-treatment CT scan, 18FDG PET-CT scan and a staging laparoscopy to detect occult metastases. Patients received four cycles of FOLFIRINOX regimen. Patients without disease progression at restaging proceeded to long- course CRT with concurrent gemcitabine (600 mg/m² weekly). Four weeks after the completion of CRT, patients underwent CT scan and PET-CT scan. Surgery was considered for patients with technically resectable tumours. The primary objective was R0 resection rate with a prespecified alternate hypothesis of 55%. Secondary objectives included progression-free survival

(PFS), overall survival (OS), local progression-free survival (LPFS), metastasis free-survival (MFS), and safety. Adverse events were recorded using the NCICTC scale. The trial is registered as NCT05399394.

Results: A total of 65 patients were evaluated, including 3 patients with early systemic staging (Figure 1). Twenty- two patients (34.9%) were excluded due to evidence of metastatic disease, leaving a total of 40 patients enrolled. Of these, 17 patients (48.6%) had locally advanced unresectable tumours, while 18 patients (51.4%) had borderline resectable disease. Four patients (10%) had disease progression after induction chemotherapy. Surgical exploration was performed in 19 patients, all of whom underwent radical resection. R0 resection was achieved in all 19 of the 35 eligible patients (54.3%). Median follow-up was
15.6 months (range, 8.5 to 72.9). Median OS and median PFS in patients who completed CRT were 18.6 months and 13.5 months, respectively. OS, PFS, LPFS and MFS at one-year were 87.6%, 59.3%, 81.5% and 69%, respectively (Figure 2). Resected patients had a significantly longer median OS compared to non- resected patients (28.2 months vs. 13.2 months, p=0.004). Median PFS for resected patients was 17.5 months compared to 9.5 months for non-resected patients (p=0.001). Treatment-related grade 3 to 4 toxicities included piastrinopenia (29.4%), neutropenia (5.7%), nausea and vomiting (5.7%).

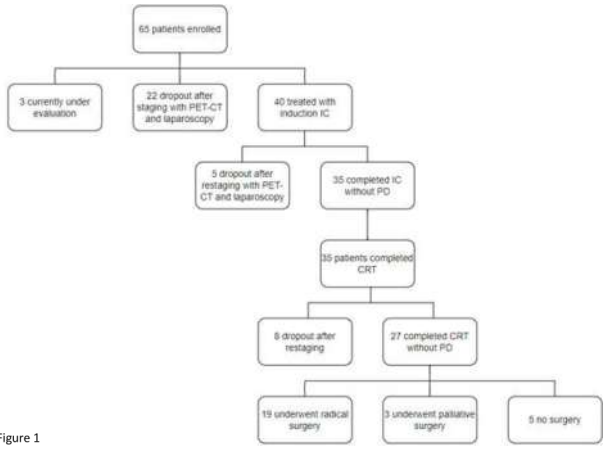

Figure 1

Patients (N=35)						
	Median (months)	1-yr (%)	2-yrs (%)	3-yrs (%)	4-yrs (%)	5-yrs (%)
OS	18.6	87.6	36.0	22.4	17.0	1.0
PFS	13.5	59.3	13.4	-	-	-
LPFS	19.0	81.5	59.4	59.4	44	44
MFS	17.5	69.0	22.6	22.6	22.6	22.6

Figure 2

Conclusions: FOLFIRINOX followed by long-course CRT in borderline resectable and locally advanced unresectable PDAC resulted in high R0 resection rates and prolonged median PFS and median OS.

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Pulsed-dose-rate Brachytherapy (Interventional Radiotherapy) following Intensity-Modulated Radiotherapy with or without chemotherapy for cervical cancer: oncological outcome and toxicity analysis of 155 patients

Code: 569

Aims: Brachytherapy (BT) boost after radio-chemotherapy (RCT) is a standard of care in management of locally advanced cervical cancer (LAAC).We analyse the survival outcomes and toxicity rate of patients treated with Intensity Modulated Radiation Therapy (IMRT) followed by Pulsed-Dose-Rate Brachytherapy (PDR- BT) for cervical carcinoma in our institution.

Methods: From March 2011 to June 2021, 155 consecutive patients with histologically proven cervical carcinoma FIGO stages IB-IV underwent PDR-BT following IMRT treatment.Radiation treatment was delivered to a median total dose of 50,4 Gy (range, 45 - 50,4 Gy). Weekly concomitant chemotherapy was administered to 150 patients.
Endocavitary or hybrid endocavitary-interstitial PDR-BT boost was administered to 105 (67,7%) and 50 (32,3%) patients, respectively.
The median total dose of PDR BT was 30 Gy (range, 22 - 35 Gy).Local control (LC), nodal (NFS) and metastatic (MFS) recurrence-free survival as well as progression-free survival (PFS) and overall survival (OS) were analyzed.Late genitourinary (GU) and gastrointestinal (GI) toxicity were defined as toxicities occurring after six months from the end of BT and they were described by the Common Terminology Criteria for Adverse Events (CTCAE) v5.0.

Results: After a median follow-up of 62 months (range, 5-156 months),we observed 22 cases of local relapse,23 cases of regional failure (pelvic or paraaortic lymph-nodes) and 38 distant metastases.The 5-years LC, NFS, MFS, PFS and OS were 84.4%(95% CI: 78.6-90.7%), 85.4%(95% CI: 79.891.4%), 74.4%(95% CI:
67.5-81.9%), 64.5%(95% CI: 57.2-72.7%) and 63.9%(95% CI: 56.1-72.8%) respectively.Twenty-two
cancer-related deaths were registered.Gentourinary (GU) and gastrointestinal(GI) acute toxicity of any grade was observed in 63 (40%, 95% CI: 27-56%) and 37(23%, 95% CI: 13-39%) patients, respectively. Late toxicity data was available for 152 patients.Overall, 14(9%) patients had grade ≥ 2 urinary toxicity, 36(23,2%) patients experienced grade ≥ 2 rectal toxicity and 18(38,3%) patients grade ≥ 2 vaginaltoxicity. Six patients (3,8%) had grade 4 rectal toxicity requiring colostomy.Type of BT and total dose delivered could be correlated to an increased risk of toxicity however we did not find statistically significant correlations between the independent variables and the onset of late grade 4 toxicity.

Conclusions: PDR BT as boost after chemoradiotherapy is an effective procedure in the definitive treatment for cervical cancer with favorable outcomes and toxicity profile.

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STEREOTACTIC BODY RADIOTHERAPY FOR SPINAL OLIGOMETASTASES: A SURVEY ON PATTERNS OF PRACTICE ON BEHALF OF THE ITALIAN ASSOCIATION OF CLINICAL ONCOLOGY AND RADIOTHERAPY (AIRO)

Code: 51

Aims: The Study Group for the Biology and Treatment of the OligoMetastatic Disease on behalf of the Italian Association of Radiotherapy and Clinical Oncology (AIRO) has conducted a national survey with the aim to depict the current patterns of practice of stereotactic body radiotherapy (SBRT) for spinal oligometastases

Methods: The Surveymonkey platform was applied to send a 28-items questionnaire focused on demographic, clinical and technical aspects related to SBRT for spinal oligometastases. All the AIRO members were invited to fill the questionnaire. Data were then centralized to a single center for analysis and interpretation.

Results: 53 radiation oncologists fulfilled the survey. A complete agreement was observed in proposing SBRT for spinal oligometastases, with the majority considering up to 3 concurrent spine oligometastases feasible for SBRT (73.5%), regardless of spine site (70%), vertebral segment (85%) and morphological features of the lesion (71.7%).
Regarding dose prescription, fractionated regimens resulted as the preferred option, either in 3 (58.4%) or five sessions (34%), with a substantial agreement in applying a margin larger than 1 mm (almost 90% of participants), and using both MRI and PET imaging to improve target volume and organs-at-risk delineation (67.9%)

Conclusions: This national italian survey illustrates the patterns of practice and the main issues for the indication of SBRT for spinal oligometastases. A consistent agreement in clinical indications was reported, with a slight heterogeneity in terms of dose prescription and fractionation schemes.

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ULTRA HYPO RT IN ELDERLY PCA PATIENTS WITH AGGRESSIVE DISEASE: STILL A SPACE FOR CURATIVE APPROACH?

Code: 461

Aims: Longer life expectancy has led to an increase in number of elderly patients (pts) with localized PCa. Elderly pts often present a high prevalence of comorbidities which makes difficult to propose RT including both prostate, pelvis and associated long-term ADT. The aim of the present study is to evaluate the efficacy and safety of personalized UHRT+/- ADT in this cohort of pts.

Methods: Men aged ≥75 years with localized PCa who underwent curative UHRT between 2012 and 2021 were retrospectively included. Continuous variables were summarized as mean, median and interquartile range (IQR), while frequency analysis was performed for categorical variables. Toxicities were collected according to RTOG scale and biochemical PFS was analysed with KM
method.

Results: A total of 227 pts was included. Median age at diagnosis was 79.4 years (IQR 77.9 – 81.4) with a median Charlson Comorbidity Index of 4 (IQR 3-4). The majority of the pts (52%, 119) was diagnosed with high risk, while the remainings (48%, 108) were unfavorable intermediate risk.
All pts underwent UHRT on prostate in 5 fx every other day with a dose/fx within 6.5 and 7.25 Gy. Ninety-nine pts (43.6%) received a boost on DIL with a total dose within 37.5 Gy and 40 Gy. Concomitant ADT was administered to 166 pts (73%) with a median duration time of 12.0 months (IQR 6.0 – 12.0). General cohort characteristics are summarized in **Table 1.**

Pts characteristics	n (%)
Risk class	
Unfavourable intermediate	108 (48.0)
High	111 (49.0)
Very High	8 (3.0)
ADT	
Yes	166 (73.0)
No	61 (27.0)
cT	
1	78 (34.4)
2	119 (52.4)
3	29 (12.7)
4	1 (0.5)
Staging	
CT scan	200 (88.1)
Bone scan	163 (71.8)
Abdomen MRI	8 (3.5)
Whole Body MRI	6 (2.7)
Cho-PET	32 (14.1)
PSMA-PET	4 (1.8)
NA	23 (10.1)
Prostate Dose (Gy)	
35	125 (55.1)
36.25	102 (44.9)
DIL (Gy)	(n=99)
37.5	83(84.0)
40	16 (16.0)
Acute maximum GU toxicity	
G0	126 (55.5)
G1	81 (35.7)
G2	17 (7.5)
G3	1 (0.4)
G4	2 (0.9)
Acute maximum GI toxicity	
G0	206 (90.7)
G1	15 (6.7)
G2	6 (2.6)
G3	0
G4	0
Late maximum GU toxicity	(N=194)
G0	143 (74.0)
G1	31 (16.3)
G2	17 (9.2)
G3	1 (0.5)
G4	0
Late maximum GI toxicity	(N=194)
G0	169 (87.1)
G1	15 (7.8)
G2	9 (4.6)
G3	1 (0.5)
G4	0
Last follow-up	(n=198)
NED	157 (79.3)
AWD	39 (19.7)
DIED for other causes	2 (1.0)

After a median follow-up of 1.92 years (IQR 1.12 – 3.15), 42 pts (21%) experienced a biochemical recurrence and 30 pts (15%) developed a clinical progression of disease.One 2 and 3 years biochemical DFS rates were 98.2%, 87.3% and 78.2%, respectively. No statistical difference was found between pts aged 75-80 years and $\geq$80 years (p = 0.52).
At last follow up, 157 pts (79.3%) were alive with no evidence of disease, 39 (19.7%) were AWD and 2 (1%) died for other causes than PCa.
The majority of pts reported no acute GI (90.7%) and GU (55.5%) toxicity. Three pts (1.3%) experienced a G$\geq$3 GU toxicity while no G$\geq$3 GI were registered. Data about late toxicities were available for 194 pts: 74% and 87.1% of the pts reported respectively a G0 GU and GI toxicity. One patient (0.5%) reported a G3 GU maximum late toxicity, while 1 patient (0.5%) experienced a G3 GI toxicity.

Conclusions: Optimal biochemical control and safe GI/GU toxicity profiles demonstrate that personalized ultra UHRT +/- short ADT course should be considered as a treatment option in this setting of pts.

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TRANSFORMING PATIENT CARE PATHWAYS THROUGH INTER-PROFESSIONAL COLLABORATION AND TECHNOLOGICAL INNOVATIONS

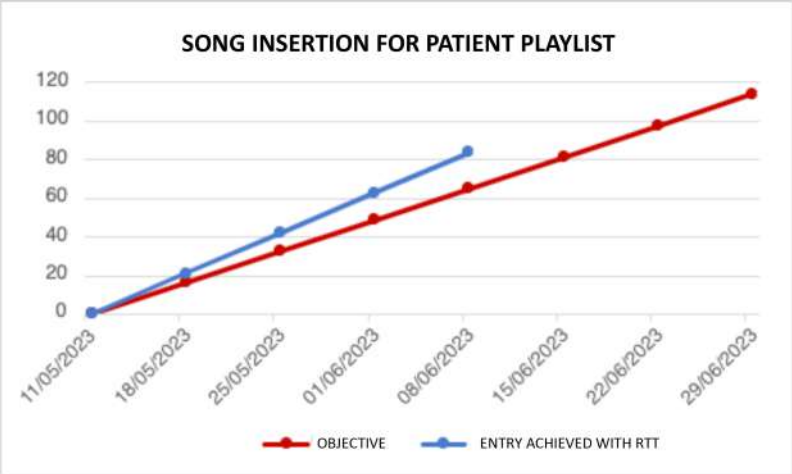
Code: 604

Aims: The intersection of patient-centered care (PCC) initiatives and emerging digital technologies presents promising prospects for improving patient experiences and treatment efficacy. This study investigates the evolving responsibilities of Radiotherapy Technologists (RTTs) within an inter-professional framework, aiming to streamline patient care pathways before, during, and after interventional procedures.

Methods: Based on experiences at Fondazione Policlinico Universitario A. Gemelli IRCCS, three pioneering PCC projects are examined: the Happy protocol, Musica Amica Mia and IHelp Project. These initiatives highlight the crucial role of RTTs in addressing patients' holistic needs, alleviating anxiety, and promoting patient engagement through educational interventions and technological advancements. Additionally, a novel project focuses on collecting Patient Reported Experience Measures (PREMs) and Patient-Reported Outcome Measures (PROMs) from patients undergoing multimodal therapies. Portable monitoring tools (Internet of Things -IoT devices), including wearables and a dedicated app, seamlessly integrate real-world data into clinical practice.

Results: The analysis underscores RTTs' significant contributions in managing patient needs and enhancing engagement in care pathways. Moreover, continuous data collection facilitated by IoT devices allows for the application of artificial intelligence (AI) algorithms to predict treatment toxicity and identify high-risk patients. The IHelp project involved 88 patients and RTTs conducted educational interviews with patients to stress the importance of their participation in the monitoring process for personalized therapy. Daily interaction with RTTs ensured proper utilization of IoT and App technology. Additionally, RTTs played a pivotal role in implementing the Musica Amica Mia project, curating personalized playlists for patients undergoing radiotherapy or Interventional radiotherapy to mitigate anxiety and stress.

Conclusions: In conclusion, collaborative efforts among healthcare professionals, coupled with digital technology integration, are pivotal for advancing patient-centered care and treatment outcomes. As interventionalradiotherapy progresses, the role of RTTs becomes increasingly crucial. Hence, specialized training for RTTs focusing on patient engagement and education is imperative. Furthermore, harnessing AI-driven predictive models based on real-world data presents unparalleled opportunities for personalized patient care.



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LEPTOMENINGEAL DISEASE (LMD) FOLLOWING POSTOPERATIVE RADIOSURGERY IN RESECTED BRAIN METASTASES: LONG TERM FOLLOW UP OF A PHASE 2 STUDY

Code: 248

Aims: The risk of leptomeningeal disease following SRS on the tumor bed in resected brain metastases (BMs) was reported up to 28%, in retrospective studies. We evaluated LMD in patients enrolled in prospective phase II study treated with surgery followed by hypofractionated radiosurgery (HSRS) on the tumor bed in oligometastatic patients with single large brain metastases (BMs).
Local control (LC), occurrence of new BMs (BDF), overall survival (OS), and prognostic factors related to LMD were analyzed too.

Methods: Patients aged >18 years with a primary diagnosis of solid tumors, Karnofsky performance status >70, oligometastatic disease, a single brain lesion ≥2.1 cm in maximum diameter or <2 cm with conditioning mass effect, neurologic deficits, or massive edema were included. Surgery was performed with the aim to maximally remove the tumor according to functional boundaries. HSRS was performed within 1 month of surgery and total dose was 30 Gy in 3 fractions was delivered.

Results: Between June 2015 and May 2018, 101 patients were enrolled. Patients and tumor characteristics are shown in Table 1. Two year LC, BDF and OS were 87%, 50.4% and 49.5%, respectively, confirming the results also at long-term follow up. New BMs occurred in 51 patients (50.5%), of whom 20 (19.8%) development leptomeningeal disease. In patients with LMD, median OS and 6-month, 1-year, and 2-year OS rates were 16 months, 95%, 75%, and 20%, respectively. In patients with new BMs and without LMD, median overall survival time and 6-month, 1-year, and 2-year overall survival rates were 20 months, 93%, 80.6%, and 38.7%, respectively. Tumor volume (P=0.0252), lesion's diameter (P=0.0131), leptomeningeal disease (P=0.0133) significantly influenced overall survival. According to logistic regression analysis, the infratentorial site (P=0,0480) and meninges not surgically removed (P=0,0196) influenced the development of LMD. Radionecrosis (RN) occurred in 36 patients. Grade 2 or 3 RN was recorded in 25 (24.7%) and 11 (10.9%) cases, respectively. Neurocognitive functions remained stable or, in some cases, improved.

Conclusions: Surgery followed by HSRS on the tumor bed is an effective and safe approach. Leptomeningeal disease conditioning a worse prognosis. Preoperative HSRS could represents an alternative approach to reduce this complication.

	No. patients 101	%
Gender		
Male	43	42.6
Female	58	57.4
Primary tumor		
Breast	28	27.8
NSCLC	46	45.5
Malignant Melanoma	8	7.9
Others	19	18.8
Median IT diagnosis-BMs occurrence (months)	22 (range 0-269)	
Median age at BMs treatment (years)	56 (range 28-79)	
KPS at BM occurrence		
70	3	3.0
80	19	18.8
90-100	79	78.2
Extracranial metastases at BMs occurrence		
Yes	35	34.7
No	66	65.3
No. BMs		
1	88	87.1
2	10	9.9
3	2	2.0
4	1	1.0
Site		
Sovratentorial	78	77.2
Infratentorial	23	22.8
Meningeal resection		
Yes	20	19.8
No	81	80.2

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IMPACT OF ADHERENCE TO ESMO GUIDELINES ON SURVIVAL OUTCOMES IN RECTAL CANCER: A PROCESS MINING ANALYSIS OF REAL-WORLD PATIENT DATA

Code: 312

Aims: The guidelines provide a resource to ensure optimal patient care based on the latest scientific evidence, playing a significant role in standardizing and improving the quality of care, guiding clinical decisions, enhancing patient outcomes, and setting the direction for future research. Concurrently, process mining has emerged as a tool to evaluate guideline adherence in rectal cancer treatment protocols, using data from Electronic Health Records(EHRs)to identify patterns, uncover hidden inefficiencies and refine healthcare processes.This research assesses the effects of adhering to the 2017 European Society of Medical Oncology(ESMO) guidelines on survival outcomes in rectal cancer patients, using process mining on retrospective data.

Methods: We analyzed a Real World Data(RWD) monocentric cohort of non-metastatic rectal cancer patients treated from January 2000 to December 2021. Patients were categorized in ESMO risk classes as early, intermediate, locally advanced, and advanced risk groups. Process mining examined guideline adherence and identified treatment deviations. Deviations were classified as overtreatment (radiotherapy(RT)≥55Gy, intensified chemotherapy (CT) with oxaliplatin (Oxa) or undertreatment (RT<45Gy).Survival outcomes, as overall survival(OS), disease-free survival DFS), local control (LC) and metastasis-free survival(MFS), were analysed according to ESMO guidelines adherence.

Results: 2219 patients met the inclusion criteria, with an overall adherence of 14.1%. 17.8% early-stage patients, 14%intermediate,18%locally advanced, and 7.7%advanced patients were adherent. Amongst the groups, survival analysis indicated no significant difference for early group. In the intermediate group, 5-year OS(5yOS) was notably higher in patients who received overtreatment (85.9% with increased RT dose and 86.8% with Oxa-CT, p<0.01).Locally advanced patients non-adherent to guidelines also showed improved 5yOS, particularly with increased RT and Oxa-CT. For locally advanced patients, those non-adherent to guidelines showed improved 5yOS of 87.1% with RT overdosage and 86.9% with Oxa- CT(p<0.001).Advanced patients also benefited from RT dose escalation in terms of 5yOS(p<0.001)(Table 1).

ESMO class of risk		5yOS	p-value	5yMFS	p-value	5yLC	p-value	5yDFS	p-value
EARLY	*Adherent*	100%		94,1%		100%		94,1%	
	No Adherent	81,9%		87,2%		89,9%		71,5%	
	• *Oxaliplatin*	91,8%	p=0.59	86,5%	p=0.426	95,4%	p=0.347	75,1%	p=0.456
	• *RT dose = 55 Gy*	85,3%	p=0.371	87,1%	p=0.56	89,3%	p=0.363	74,3%	p=0.321
	• *RT dose < 45 Gy*	100%		100%		100%		100%	
INTERME-DIATE	*Adherent*	62,9%		66,6%		86,3%		43,5%	
	No Adherent	84,1%		85,6%		93,8%		72,3%	
	• *Oxaliplatin*	86,8%	**p=0.001**	86,3%	p=0.019	94,5%	p=0.307	76,4%	**p<0.001**
	• *RT dose = 55 Gy*	85,8%	**p=0.001**	83%	p=0.064	93,8%	p=0.048	72,1%	**p=0.003**
	• *RT dose <45 Gy*	71,4%		100%		85,7%		71,4%	
LOCALLY ADVANCED	*Adherent*	74.9%		78%		86.6%		62.5%	
	No Adherent	85.1%		83.7%		94%		73.7%	
	• *Oxaliplatin*	86.9%	**p<0.001**	85,9%	**p=0.028**	95.6%	**p=0.001**	78%	**p<0.001**
	• *RT dose≥55 Gy*	87.1%	**p<0.001**	82.8%	p=0.34	93%	p=0.191	72.9%	**p=0.005**
	• *RT dose<45 Gy*	69.1%		85.6%		95%		65.2%	
ADVANCED	*Adherent*	72.4%		70.8%		89.9%		58.4%	
	No Adherent	67.4%		73.6%		87.5%		53.6%	
	• *Oxaliplatin*	73.4%	p=0.614	91.1%	p=0.097	94.3%	p=0.412	68.3%	p=0.42
	• *RT dose≥55 Gy*	74.2%	**p<0.001**	72.4%	p=0.907	90.4%	**p=0.007**	58.7%	**p<0.001**
	• *RT dose <45 Gy*	42.4%		68.3%		72.8 %		33.2%	

Table 1: Survival outcomes for different ESMO risk groups, comparing adherent and non-adherent patients. p-value calculated using log-rank test. (significant values p<0.05 in bold)
RT: radiotherapy; OS: overall survival; DFS: disease-free survival; MFS: metastasis-free survival; LC: local control; 5y: 5 years

Conclusions: This study shows that process mining of RWD in rectal cancer allows improvement of clinical guidelines. It ighlights the discrepancy between standard guidelines and actual survival outcomes, underscoring the need for dynamic, patient-specific guidelines that support personalized treatment approaches in oncology.

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STEREOTACTIC ABLATIVE RADIOTHERAPY (SABR) IN EARLY-STAGE NON-SMALL CELL LUNG CANCER: RESULTS ON 20 YEARS OF EXPERIENCE

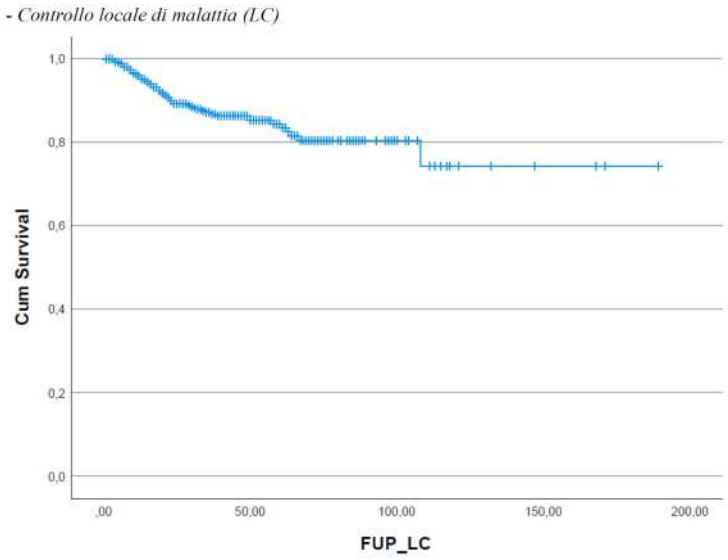
Code: 603

Aims: The aims of this study are to analyse the oncological outcomes and safety of SABR in the definitive management of ES-NSCLC.

Methods: This retrospective study included patients with ECOG PS ≤ 2 affected by T1-2N0M0 NSCLC treated with SABR between 2003 and 2021 at our Institution. Surgery was contraindicated or refused by patients. The primary endpoints were Local Control (LC), Nodal Control (NC), Systemic Control (SC) and Overall Survival (OS). Secondary endpoints were acute and late clinical toxicities. Pulmonary toxicity was defined with the CTCAE 5.0 grading. Post-SABR radiological changes were evaluated with the
Ronden classification. Survival analyses were performed with Kaplan-Meier method. Cox regression model was used to assess associations between covariates and these clinical outcomes.

Results: 637 patients with a mean age of 76 years were included in this analysis. 87% had a smoke exposure, 52% respiratory comorbidities, 6% heart failure. 47% of patients had no histological confirmation of the pulmonary lesion. Patients were treated according to a "risk adapted" fractionation schedule: 255 (40%) received 3 fractions, 231 (36%) received 5 fractions and 121 (19%) received 8 fractions. With a median follow-up of 16 months, 1 and 2-year LC rates were 96 % and 89%, respectively (**Figure 1**). The rates of NC were 93% at 1 year and 86% at 2 years, while systemic control rates were inferior (1, 2-year SC: 86.5% and 73.5%). The median OS was of 43 months (1, 2- year OS: 89% and 72%). Death was documented in 442 (69.4%) patients, mostly (55.3%) for non-neoplastic causes. In a Cox multivariable analysis, age at treatment (HR: 1.05; p=0.001), smoking habit (HR:1.33; p=0.032), pre-existing heart failure (HR: 2.11; p = 0.028) and the surgery exclusion (HR: 1.15; p=0.043) were associated with worse OS. Only 16 cases (3%) of acute severe pneumonitis of grade 3 or higher were detected and 7% chronically. 273 patients (43%) displayed early imaging abnormalities: 23% diffuse consolidations, 27% patchy consolidation, 17% diffuse Ground Glass Opacities (GGOs), 33% patchy GGOs. The modified fibrosis was the most frequent pattern of chronic radiological outcome (55%).

Conclusions: Our results confirm the optimal disease local control reached by SABR in patient with ES-NSCLC. Thisanalysis corroborates the excellent safety profile of SABR in light of the very low rates of clinical- radiological pulmonary toxicity events



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PERSONALIZED SBRT BY SINGLE FRACTION EIGHT-GRAY PALLIATIVE RADIOTHERAPY WITH MODULATED INTENSITY FOR PAIN REDUCTION: THE SAINT STUDY - A SINGLE ARM PHASE 2 COHORT ANALYSIS FOR WORST PROGNOSIS PATIENTS

Code: 221

Aims: Palliative Radiotherapy for painful bone metastases represents a crucial clinical, scientific and organizational issue. Intensified, stereotactic radiotherapy (SBRT) is often applied but clear evaluation of result is controversial since most of the experiences are conducted outside clinical trials and clinical benefit is not always univocal.
In most of the studies a prognostic score is not applied to stratify patients, although usually suggested as needed.
Aim of this single institutional prospective trial is to evaluate the efficacy and safety of an intensified SBRT schedule for patients with painful bone metastases at worst prognosis. (Clinicaltrial.gov identifier: 0011201)

Methods: A monocentric study was conducted, applying SBRT by intensified single fraction eight-gray palliative radiotherapy for patients with painful spinal lesions.
Patients were stratified by a validated prognostic score (Mizumoto score) discriminating 3 level of prognosis (good, intermediate, worse): only patients at worse prognosis (inferior to 6 months) were enrolled.
SBRT schedule was delivered as simultaneous integrated boost of: 8 Gy to the entire vertebral body + 10-15 Gy to the GTV; boost dose to GTV was allowed in the range of 10 to 15 Gy respecting the Spinal Canal Constraint of 10 Gy maximum dose.
Primary endpoint was palliative effect at 1 month, according to International Chow's criteria (thus, not only according the NRS response).

Results: From 2019 to 2023, 31 patients were enrolled, treated on 33 spinal CTVs. All patients were stratified byMizumoto Score as worse prognosis.
Dose to entire vertebral body was 8 Gy for all treated lesions; boost dose (in SIB) to the GTV was 15 Gy for 20 CTVs (60,6%), 12 Gy for one CTV (3%) and 10 Gy for 12 CTVs (36,4%).
Median follow-up was 2 months (range 1-26 months). At 1 month, three out 31 patients were dead.
At 1 month follow-up evaluation (primary endpoint) the distribution of pain response was: complete 45%, partial 52% (i.e.: overall response 97%), indeterminate 3%, progression 0%. No acute/subacute Grade >3 toxicity related to the schedule was reported.

Conclusions: Pain response at 1 month according "SAINT" protocol reported rates of overall response 97% (versus conventional response by literature of approximately 60-65%) and complete response 45% (versus conventional 20-25%). This schedule is effective and will be evaluated in randomized trial versus standard, even for patients at worse prognosis, if compliant.

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PERSONALIZED PAIN REDUCTION WITH BONE METASTASES STEREOTACTIC RADIOTHERAPY: A PHASE III RANDOMIZED MULTICENTRIC TRIAL (PREST TRIAL): INITIAL ANALYSIS ON TECHNICAL FEASIBILITY

Code: 230

Aims: Palliative Radiotherapy (PRT) for painful bone metastases represents a clinical and scientific issue. Intensified SBRT is often applied but clear evaluation of result is difficult since most experiences are outside clinical trials. In most of the studies a prognostic score to stratify patients is not applied, although usually suggested as needed.
Only 7 Phase 3 trial are available, with controversial results.
The PREST trial is a multicentric Phase 3 trial facing standard PRT versus SBRT for patients selected by prognostic score. Aim of this preliminary evaluation is to weight its technical feasibility.
(Clinicaltrial.gov identifier: 0013663/18)

Methods: In PREST trial patients with painful spinal metastases (stratified by a validated prognostic score selecting patients at better prognosis) are either randomized to conventional PRT delivering 20 Gy in 5 fractions or to SBRT by SIB (21 Gy in 3 fraction of 7 Gy to the entire vertebral body+30 Gy in 3 fraction of 10 Gy to the GTV).
The experimental arm requires one or more CBCT at each session.
Primary endpoint is palliative effect on the CTV at 3 months, according to International Chow's criteria (thus, not only according the NRS response).
We collected technical IGRT characteristics (linear and angular errors and number of required CBCT) and toxicity of the first 10 patients enrolled in SBRT arm, to check feasibility.
Only the first 10 patients progressively enrolled in experimental arm were considered for this analysis.

Results: Global trial enrollment started on 2020. Mean number of CBCT per daily fraction was 1,8.Median displacement for set-up (in cm) accounted for: 0.2835 Vertical, 0.088 Longitudinal, 0.263 Lateral. Median angular set-up error (in degrees) accounted for: 0.516 Pitch, 0.1635 Roll, 0.166 Rtn.
Current median follow-up is 6 months (range 3-26 months) - enrollment ongoing-.
All patients completed each SBRT session with full compliance. No toxicity of CTCAE Grade >3 was reported at 1 and 3 months.
At 3 months follow-up evaluation (primary endpoint) the distribution of pain response in SBRT arm was: complete 88%, partial 0% (i.e.: 88% overall), indeterminate 12%, progression 0%.

Conclusions: SBRT by experimental arm of PREST Trial seems feasible. Toxicity and Pain efficacy must be evaluated at the end of accrual.
The preliminary 3 month response rate, (respect the literature standard of 25% complete and 60% overall) will be evaluated for sample size adaptation at interim analysis.

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NEOADJUVANT STEREOTACTIC MR-GUIDED ADAPTIVE BOOSTED SHORT-COURSE RT FOR LOCALLY ADVANCED RECTAL CANCER (SMART-SIB): CAN DOSE-ESCALATED RT RIVAL INTENSIFICATION OF CHEMOTHERAPY IN TOTAL NEOADJUVANT TREATMENT?

Code: 205

Aims: The purpose of this study is to evaluate efficacy and tolerability of dose-escalated short course radiotherapy (RT)using sterotactic MR-guided adaptive technique (SMART-SIB), included in a neoadjuvant therapy protocol for locally advancced rectal cancer.

Methods: Patients (pts) with histological proof of newly diagnosed, primary, locally advanced adenocarcinoma of the rectum (cT3-4 cN0-2 cM0), underwent SMART-SIB using a hybrid MR-LInac (MRIdian Viewray). The prescribed dose was 25Gy (5Gy/fr) to the mesorectum with a simultaneous integrated stereotactic boost to the rectal lesion of (40Gy) at 80% isodose, corresponding to 60Gy in EQD2 (alpha/beta = 10), delivered on 5 days (3fr/week). A MR-guided adaptive strategy was applied, consisting in daily on-table recontouring and replenning to control interfractional volume changes, combiden with a gating approach with a a cine-MR to manage intrafractional motion. Sequential chemotherapy was administered after RT (max numner of cycles: 4). Finally, total mesorectal excision was performed. Primary endpoint was evaluation of acute adverse effects, graded according CTCAEv.5. Secondary endpoint was pathological complete response rate (pCR).

Table 1. Patients characteristics, clinical stage and pathological response	n=46	%
Median age (yrs)	67 (range 35-81)	
Sex		
Male/female	29/17	63/37
Clinical T stage		
cT3	44	96
cT4	2	4
Clinical N stage		
cN0	12	26
cN1	17	37
cN2	17	37
Distance from anal verge		
< 5cm	15	33
5-10cm	17	37
10-15cm	12	26
High risk features		
MRF+	5	11
Lateral N+	5	11
Pathological Stage		
ypT0	17	37
ypT1	3	7
ypT2	17	37
ypT3	9	20
ypT4	-	-
ypN0	39	85
ypN1	5	11
ypN2	2	4
Pathological Response (sec. Mandard)		
TRG 1	17	37
TRG 2	17	37
TRG 3	10	22
TRG 4	2	4
TRG 5	-	-

Results: From October 2020 to January 2024, 46 patients (pts) underwent SMART-SIB. Mean follow-up time was 19 months (range 3-39). Sequential chemothery consisted of capecitabine for 26 (57%)pts; oxaliplatinum- based regimens were prescribed for 6 (13%) pts. Fourteen pts (30%) were unfit for chemotherapy due comorbidities and/or intolerance. All pts were completely resected (R0). Mean interval between completion of SMART-SIB and surgery was 9 weeks (range 2-21) no grade 3 or higher toxicity was recorded. Grade 2 proctitis with tenesmus and mild pain was the most reported GI symptom (30%).
Regarding GU symptoms, 2 pts (4%) reported grade 1 dysuria. A tumor and or /nodal downstaging occurred in all pts; 27 pts (27%) clinically staged cN+ had a pathological nodal complete response. The pCR was achieved for 17 (37% pts), it occurred with a prolonged time to surgery (>7 weeks) (Table 1).

Conclusions: Compared with recent total neoadjuvant treatments, with include several cycles of oxaliplatinum-based chemotherapy, SMART-SIB for locally advanced rectal cancer also seem to result in high pCR rate with limited toxicity, especially if followed by delayed surgery. Further larger randomized studies are needed to confirm these findings.

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VALIDATION OF A VMAT AUTO-PLANNING TECHNIQUE FOR SIB RADIATION THERAPY OF HEAD AND NECK (H&N) CANCERS.

Code: 588

Aims: Auto-planning (AP) systems are gradually entering clinical practice, proving to be a tool for workload reduction while achieving optimized and robust treatment plans. The aim of this study was to verify the application of a fully AP system, called mCycle, for H&N cancers.

Methods: 20 H&N patients (pts) were selected (5 nasopharynx, 4 oropharynx, 1 hypopharynx, 6 larynx, 1 oral cavity and 3 neck). 45% of pts had stage IV disease (7 IV A and 2 IVB), 40% stage III. 15 pts were candidated for curative treatments and 5 for post- operative treatments.
For each pts 3 different simultaneous integrated boost (SIB) dose prescriptions were investigated performing manual and AP calculation: 70-56 Gy, 66-56,1 Gy, 60 54.1 Gy.
The plans were compared by assessing differences in planning time, dosimetric quality and deliverability. The dosimetric quality was evaluated both qualitatively, performing a blinded score evaluation (1-5 for coverage and OAR sparing), and quantitatively, introducing a plan quality index (PQI) for the PTVs and the OARs. Through a signed-rank Wilcoxon test (significance level 0.05) the statistical significance of the analysed parameter was evaluated.

Results:
The AP significantly reduces the average planning time from about 2 hours (1:46±0:40, h:min) in manual mode to an average of 11±4 minutes.
The radiotherapist deemed all plans clinically acceptable, and in many cases (83%), the AP equal to or better than the manual plan.
The requests for PTVs coverage were, on average, well fulfilled in the AP for all 3 prescriptions, but for the first and third prescription the manual plans showed a slightly greater PTVs coverage.
Both plannings respect the constraints on the noble organs, but the AP yields superior results for the oral cavity, cochlea, eyes, larynx, lens, lips, constrictor muscles, lachrymal glands and thyroid. Considering the overall PQI, the values remain comparable across all prescriptions.
All the AP QA meet the acceptability requirement (>90%), The delivered time for the AP is about 1 minute longer.

Conclusions: AP proved to be a valuable tool that significantly reduces planning times, enhances OARs sparing keeping a good PTVs coverage even in advanced stage H&N cancers.
This validated AP system could represent a valid resource for the implementation of replanning also from an adaptive radiotherapy perspective.

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FAIR-AC (FATIGUE IN RADIOTHERAPY AND ACUPUNCTURE): A PHASE III MULTICENTRIC RANDOMIZED CONTROLLED TRIAL, FINANCED BY THE REGION OF TUSCANY, ON BREAST OR PROSTATE CANCER PATIENTS TREATED WITH RADIOTHERAPY.
2024 UPDATE

Code: 379

Aims: Acupuncture (A) and Traditional Chinese Medicine (TCM) are recognized by the world's leading scientific institutions in terms of efficacy and are compatible with allopathic medicine. Thanks to its action on endorphins, AMPc and mitochondria, A is a quick remedy for asthenia during chemotherapy and radiotherapy treatments. A has a marked effect on fatigue (F) in cancer patients (pts), particularly among breast (BC) and prostate cancer (PC) patients. FAIR-AC (FAtigue In Radiotherapy and ACupunture) is a phase III multicentric randomized controlled trial that evaluates the actual incidence of F in Italian BC and PC pts treated with radiation therapy (RT), and the role of A on F mitigation during RT treatment.

Methods: 400 consecutive pts affected with BC both after breast conservative surgery or mastectomy who will be referred for postoperative RT, and 200 consecutive pts affected with PC, referred for definitive or postoperative RT to three Radiation Oncology Units in Tuscany were planned to be enrolled in FAIR-AC trial. Stratification is made according to adjuvant and neo-adjuvant chemotherapy (CT) in BC pts, and to concomitant androgen deprivation therapy (ADT) in PC pts. Randomization (ratio 2:1) is used. In Arm 1 pts are treated with “standard care”, in Arm 2 with “standard care+A”. Specific and validated questionnaires investigate F and QoL.

Results: Between February 2022 and January 2024 214 pts were enrolled (131 BC and 83 PC), randomized and their clinical data collected on a customized web-based platform. 108 pts were assigned to the standard arm (SA) and 106 to the experimental arm (EA). Most BC pts received adjuvant endocrine treatment and moderately hypofractionated breast 3DCRT. VMAT/ IMRT with IGRT was planned for PC pts and RT volume encompassed prostate and seminal vesicles, standard doses and fractionation were prevalent. The study is still on-going and actively recruiting. The preliminary analysis shows not significant test values of both differences in mean fatigue levels at baseline, the result of correct randomization. A seems to have a role in reducing fatigue in the EA. Its tolerance profile is optimal, and no relevant adverse events havebeen signaled.

Conclusions: A is a safe and well tolerated treatment. If these results will be confirmed in the definitive analysis, it might be offered outside of clinical trials to prevent and reduce F to all BC and PC pts planned for RT. Definitive results might be available in less than a year.

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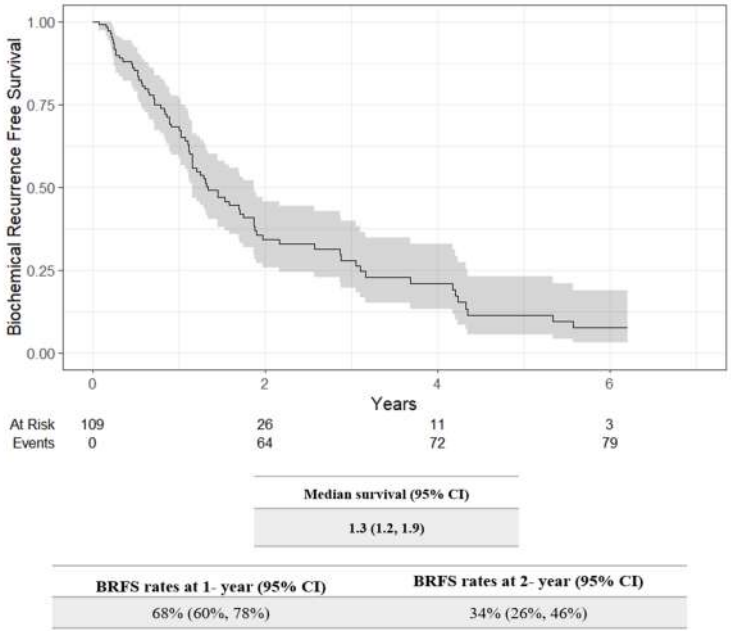
RE-IRRADIATION FOR ISOLATED LOCAL RECURRENCE OF PROSTATE CANCER: A MONOCENTRIC EXPERIENCE

Code: 570

Aims: This study aims to evaluate the safety and effectiveness of re-irradiation for local relapse in patients who underwent curative RT or salvage/adjuvant RT for prostate cancer (PCa).

Methods: Patients who underwent adjuvant/salvage RT following surgery or curative RT and exhibited evidence of isolated intraprostatic disease on MRI or PET choline were retrospectively considered for study inclusion. Re-RT was performed with image-guided RT (RapidArc®, VERO®, and CyberKnife®) with a dose of 25-35 Gy in 5 fx.

Results: A total of 120 patients, with a median age at salvage re-RT of 73 years, were included in this analysis. Of these, 83 patients (69%) received curative RT for the primary, while 37 patients underwent radical prostatectomy. The median PSA at re-RT was 3.7 ng/ml (2.2-5.5 ng/ml) and concomitant hormone therapy was administered to 32 (27%) patients. Disease staging was assessed by PET choline and MRI in 90 patients (75%) and 105 patients (88%), respectively. Thirty patients received 25Gy/5fx, 53 received 30Gy/5 fx, and 37 received 35 Gy/7 fx. Among those who received curative RT for the primary, 62 patients received partial prostate irradiation, targeting only the visible lesion, while 21 received treatment for the entire prostate. The median GTV was 17.2 cm^3 for patients undergoing re-RT to the prostate and 5.5 cm^3 for those who received re-RT to the prostate bed. At a median follow-up of 4.7 years, median time to biochemical recurrence was 1.3 years (95% CI 1.2-1.9 years), and biochemical recurrence-free survival rates at 1- and 2-year of 68% and 34%, respectively (**Figure 1**). A total of 19 patients experienced both intraprostatic relapse and metastatic relapse, 13 developed only metastatic relapse, and 37 had a local relapse. Among the 56 intraprostatic relapses, 17, 26, and 13 were observed in the 25Gy, 30Gy, and 35Gy groups, respectively. One Grade 2 acute GU event was recorded. Considering maximum toxicity after treatment, three Grade ? 3 late GI events (two resolved at the last follow-up) and twelve Grade ? 3 late GU events (seven resolved at the last follow-up) were reported.



Conclusions: Salvage re-RT for isolated local recurrence of PCa could represent a feasible treatment approach, but appropriate patient selection is mandatory. Further studies should focus on identifying the ideal prescription dose and the ideal candidates for this personalized treatment option.

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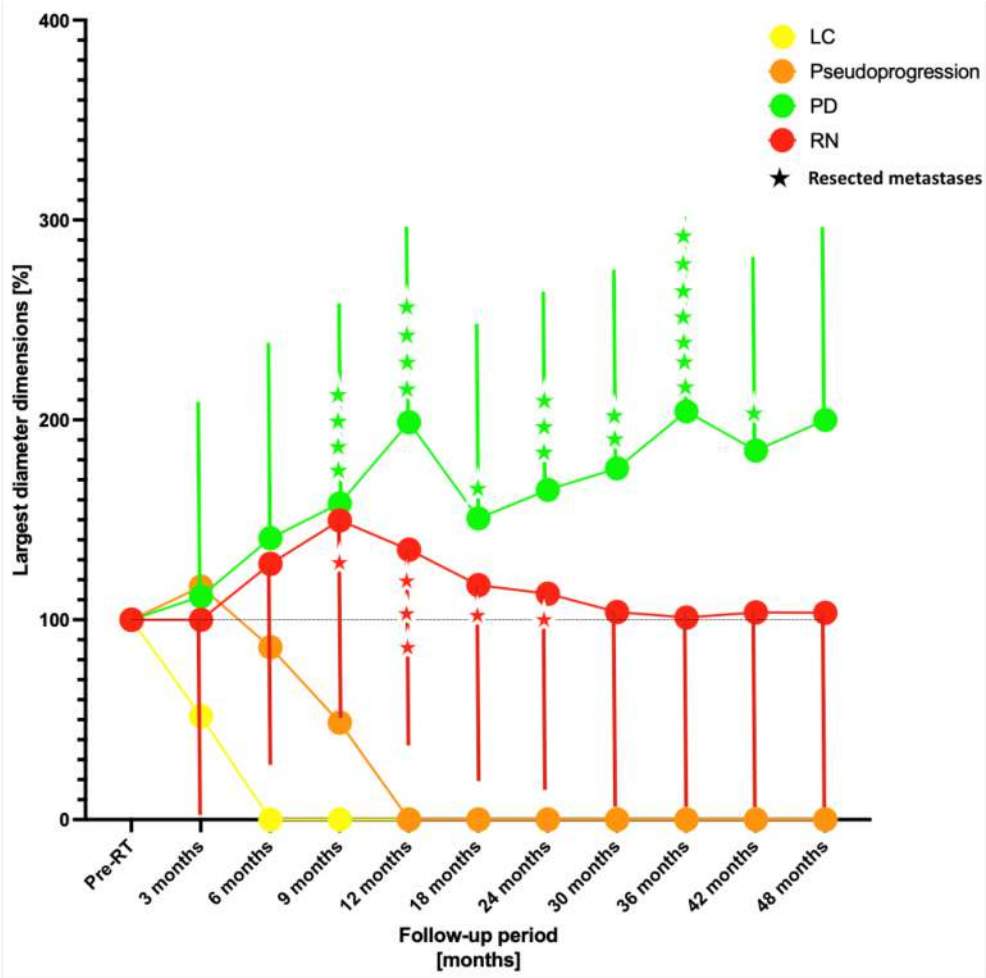
LONGITUDINAL VOLUMETRIC ANALYSES OF BRAIN METASTASES AFTER STEREOTACTIC RADIOTHERAPY

Code: 208

Aims: To test for a correlation between volumetric lesion changes and time of occurrence with pseudo- progression (PP), progression and radiation necrosis (RN) after stereotactic radiotherapy (SRT) of brain metastases (BMs) from solid primary malignancies.

Methods: Dimensional analysis was performed by measuring the largest diameter in contrast-enhanced T1-Mprage sequences before SRT and during follow-up. Patients with BMs with at least two post-treatment MRI scans were included (n=508), post-operative treatments excluded. Progression was defined using RANO-BM criteria. Radiology reports were used to define PP, progression, RN.

Results: With a median follow-up of 14 months (IQR, 5-54), local control was 85% at 1-year, 84% at 2-year and 84% at 3-year follow-up. Overall, median time to maximum shrinkage was 6 months (IQR, 3-9 months). 3-months post SRT, 20% of BMs showed an increase in largest diameter, 76% showed shrinkage, and 4% had no volume change. At 6months, 22% showed an increase and 78% shrinkage. Among those which showed an increased size at 6 months, 27% presented shrinkage at 3-months follow-up. Of the BMs without local recurrence, 8% showed PP and 7% RN. At 3-months follow-up, the controlled BMs size was 52% (IQR, 0-76%), while at 6 months it shrank to 0% (IQR, 0-61%). In pseudo-progressed BMs, median largest diameter was 117% (IQR, 102-159%) at 3-months, which shrank to 86% (IQR, 52-121%) after 6 months. In progressive BMs, median largest diameter was 112% (IQR, 79-149%) at 3 months and 141% (IQR, 99-228%) after 6 months. Volumes that developed RN had stable dimensions 3 months from SRT.
A volumetric increase to 128% (IQR 87-159%) occurred at 6 months. At 9 months follow-up, median size was 150% (IQR, 89-205%). At 12 months follow-up, shrinkage to 135% was observed (IQR 86-222%).



Conclusions: Locally controlled BMs showed a steady dimensional decline that reached a maximum shrinkage after 6 months. For PP, an initial increase in volume with a peak between 3 to 9 months, a steady decrease afterwards and maximum shrinkage after 12 months was observed. RN was a late event, showing a steep incline in size between 3 and 9 months, followed by a slow decline that did not reach the volumetric dimensions observed after SRT. [MG1] In most cases, progressive BMs showed an increase at 3 months, even though in 27% this occurred at different time-points after initial shrinkage

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QUALITY OF LIFE AND FINANCIAL TOXICITY IN HEAD AND NECK CANCERS PATIENTS TREATED WITH PARTICLE THERAPY: PRELIMINARY RESULTS OF A PROSPECTIVE STUDY (NCT05947149).

Code: 419

Aims: Quality of life (QoL) represents a fundamental issue in the care of head and neck cancers (HNCs). Many studies have focused on QoL in conventional radiotherapy (RT) but there is still a lack of data after particle therapy (PT). In addition, financial toxicity (FT) is very crucial in these pts both for the costs of medical care and for the symptoms reported after RT. Our aim is to collect QoL and FT data by means of questionnaires and to investigate their relationships with socio-demographic and clinical variables.

Methods: This prospective study will include pts with diagnosis of HNCs candidate to curative PT. Pts will be enrolled during CT simulation or at the first session of PT. Exclusion criteria are: re-irradiation, second tumor, psychiatric and neurological diseases which could impair compilation of questionnaires. Questionnaires EORTC QLQ-C30 will be administered at baseline, 3 and 6 months and 1 year after PT and PROFFIT questionnaire at baseline and 1 year after PT. Descriptive statistics were generated for demographic, clinical factors, QoL and FT. Associations with clinical and/or social factors were performed with t-test, anova one-way analysis or chi square test. R Pearson Correlation was used for correlation between age and socio-cultural factors.

Results: From May 2023 to February 2024 thirty-one pts have been enrolled. Patients' characteristics are listed in Figure 1. All pts completed the questionnaires at baseline before PT. Median score of global health status (QL2) was 66.7 (IQR: 58.3-83.3) according to QLQ-C30. Median PROFFIT-score was 23.8 (IQR: 14.28-52.38). PROFFIT-score was significantly associated with "Physical functioning" (PF2) (p=0.002), "Emotional functioning" (p=0.0004), "Social functioning" (p=0.013), "Financial difficulties" (p=0.00). PF2 (p=0.034) and QL2 (p=0.030) was associated with employment status, meaning that pts employed had a better score. PF2 was associated with educational status, meaning that pts with upper level of education had better score (p=0.048). There was no influence of systemic induction chemotherapy on QoL or FT.

Conclusions: To our knowledge, this is the first study focused on QoL and FT in HNCs candidate to PT. Employment and educational statuS seemed to be related to QoL. FT was significantly associated to certain functional scales of QLQ-C30. Further enrollments are required to validate these initial findings and follow up are fundamental to assess any changes in QoL and FT after PT.

Table 1. *Patients and treatment characteristics*

		Patients	
		n	%
Sex	Male	19	61.3
	Female	12	38.7
Age	18 - 60 years	20	64.5
	> 60 years	11	35.5
	Mean (sd)	49.8 (17.13)	
Caregiver	Yes	29	93.5
	No	2	6.5
Educational level	Primary school	2	6.5
	Lower secondary school	6	19.4
	Upper secondary school	16	51.6
	Degree	7	22.5
Employment status	Unemployed	9	29
	Employed	22	71
Marital status	Single	8	26
	Married/cohabiting	22	71
	Widowed	1	3
Comorbidity (CCI score)	2	14	45.2
	3	6	19.4
	4	4	13
	5	5	16
	6	2	6.4
Histology	Adenoid cystic carcinoma	12	38.7
	Poorly differentiated carcinoma	3	9.7
	Sinonasal undifferentiated carcinoma (SNUC)	3	9.7
	Mucoepidermoid carcinoma	2	6.5
	Epithelial-Myoepithelial carcinoma	2	6.5
	Neuroendocrine carcinoma	2	6.5
	Sinonasal adenocarcinoma SMARCB-1 deficient	1	3.2
	Intestinal Type Adenocarcinoma (ITAC)	1	3.2
	Basal Cell adenocarcinoma	1	3.2
	Carcinoma ex pleomorphic adenoma	1	3.2
	Mucosal melanoma	1	3.2
	Esthesioneuroblastoma	1	3.2
	Sinovial Sarcoma	1	3.2
Tumor subsite	Sinonasal and nasal cavity	20	64.5
	Major salivary glands	7	22.6
	Oral Cavity	2	6.5
	Oropharynx	1	3.2
	Nasopharynx	1	3.2
Particle RT	Protons	19	61
	Carbon ion	4	13
	Mixed beam	8	26
Total dose RT	Mean (sd)	67.9 (3.68)	

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SBRT FOR THE TREATMENT OF MEDIASTINAL AND HILAR LYMPHADENOPATHY

Code: 382

Aims: Mediastinal and hilar lymphadenopathy (MHL) are a frequent pattern of cancer spread, especially in, but not limited to, primary lung malignancies. Local treatments have traditionally included surgical resection or conventional RT, with or without systemic treatments. Recently, there has been interest in the application of SBRT for MHL, especially in the oligometastatic setting, to improve local control (LC) and achieve shorter treatment durations to minimize systemic treatment breaks.The use of mediastinal SBRT had historically been not feasible in view of the expected toxicity due to the proximity of critical structures such as the esophagus, trachea, proximal bronchial tree, great vessels and heart. Aim of this study is to evaluate LC, Progression Free Survival (PFS), Overall Survival (OS) and toxicities of patients treated on MHL by SBRT.

Methods: This is a retrospective study that analyzes a group of patients treated by SBRT on MHL in our center from 2007 to 2021 (97 patients with 113 MHL). The median age was 67 years. The single fraction was administered in the 23% of cases and multiple fractions in the 77 % of cases. The medium BED(10) was 81 Gy (range: 37.5-120 Gy). The primary most represented was lung in 50% of MHL treated. Fifty-one percent of MHL were classified as oligorecurrent lesions, 36% oligoprogressive, 4% oligometastatic, 9% oligopersistent. The concomitant systemic treatments were allowed.

Results: The LC was reached in 88% of MHL treated by SBRT with rates at 1-3- and 5- years of 90%, 84% and 84% respectively. The rates of PFS at 1-3- and 5- years were respectively 36%, 20% and 10%. The median OS for the patients alive was 36 months with rates at 1-3- and 5-years of 73%, 45% and 31% respectively. We have registered 4% of acute toxicities ≤2 and one case of toxicity G5, the patient died 3 days after treatment by esophageal bleeding, and one case of late toxicities G2.

Conclusions: SBRT appears to be a safe and an effective option with good results in terms of LC in the treatment of MHL, with an acceptable toxicity profile, able also to delay the indication of systemic therapies. Its use in clinical practice is still limited, and there is extensive heterogeneity in patient selection and fractionation schedules, however, more prospective studies are needed to confirm these results.

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DELAYED SURGICAL TIMING AFTER NEOADJUVANT TREATMENT FOR MIDDLE- LOW RECTAL CANCER: A CROSS-SECTIONAL ANALYSIS OF FIRST 64 PATIENTS FROM BRIDGE 1 AND TIMISNAR TRIALS.

Code: 537

Aims: Neoadjuvant chemoradiation therapy (nCRT) followed by surgery is the standard of care for locally advanced rectal cancer (LARC). However, the optimal surgical interval (SI) is still controversial. Retrospective studies have shown that regression of adenocarcinoma may be slow and increased rates of pathological complete response (pCR) may be related to a longer SI. In Italy, 2 randomized trials, BRIDGE-1 and TiMiSNAR, are currently ongoing with the aim of analyzing the impact of delayed SI on pCR, and secondly whether longer SI may be detrimental to disease-free survival (DFS) and overall survival (OS).

Methods: BRIDGE 1 and TiMiSNAR are 2 multicenter, prospective, randomized, controlled, non-blinded, parallel- group studies. Data of patients with LARC treated at the Fondazione Policlinico Gemelli and AOU SS. Antonio e Biagio e Cesare Arrigo, TiMiSNAR coordinating center in Alessandria, were shared in a database and analysed. All patients underwent nCRT with a total dose on gross tumor volume of 55Gy in 25 fractions. Concomitant chemotherapy included chronomodulated oral capecitabine or 5-fluoruracil in continuous infusion. In TiMiSNAR trial, patients were randomized to undergo surgery at 8 weeks or at 12-13 weeks in the observational and experimental arms, while in BRIDGE-1 trial at 9-13 and 13-16, respectively. All patients underwent surgery, with local excision contemplated in BRIDGE-1. pCR, OS and DFS were analyzed in correlation with SI.

Results: A total of 64 patients, 27 patients and 37 patients from BRIDGE 1 and TiMiSNAR trial, respectively, were selected: 46 (71.9%) patients underwent surgery after 12-13 weeks. Patients' characteristics are reported in Table 1. Overall, 28 patients (43,7%) obtained a pCR (8 and 20 in the short and long SI). At a median follow up of 30 months, the 3-year OS was 85% and the 3yDFS was 87.5%, with no differences between the two groups (p=0.56 and p= 0.80, respectively).

Conclusions: This preliminary analysis of the BRIDGE-1 and TiMiSNAR trials suggests an increase of pCR rate in the LARC patients underwent surgery after 12-13 weeks without a negative impact on survival outcomes. The results of both trials look forward confirming these results.

Table 1. Patients' characteristics and radiation and surgical outcomes

Patients	Bridge (27)	Timisnar (37)	Totale (64)
Male	16	19	35
Female	11	18	29
Median age (range)	65,8 (44-80)	66,7 (51-83)	66,8 (44-83)
cT stage			
2	1	1	2
3	25	36	61
4	1	0	1
cN stage			
0	2	8	5
1-2	25	29	44
Tumor location			
Low	7	13	20
Medium-high	20	24	44
Surgical interval			
<12-13	11	13	24
≥12-13	16	24	40
Surgical type			
LAR/Anterior resection	23	35	58
Abdominal perineal resection	2	2	4
Local excision	2	0	2
Pathological Complete Response			
Yes	12	16	28
No	15	21	36
TRG Mandard			
1-2	16	21	37
3-5	10	16	26
Adjuvant Chemtherapy			
Yes	7	14	21
Local Recurrence			
Yes	1	1	2
Distant Metastases			
Yes	2	4	6
Death			
yes	0	1	1

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PSMA GUIDED APPROACH FOR BIOCHEMICAL RELAPSE AFTER PROSTATECTOMY - PSICHE TRIAL (NCT05022914)

Code: 311

Aims: According to guidelines, next generation imaging (NGI) is often provided in the setting of a biochemical relapse (BR) after radical prostatectomy (RP). However, the best management in after PSMA PET re- staging is unknown, and prospective evidence is awaited. Here are presented results in terms of detection rate and early clinical outcomes after a PSMA PET/CT based tailored strategy in this scenario, within PSICHE (NCT05022914), a prospective multicentric trial.

Methods: Inclusion criteria consisted in BR after RP with or without postoperative radiotherapy, with a PSA ranging between 0.2 ng/ml and 1 ng/ml. All patients underwent [68Ga] Ga- PSMA-11 PET/CT imaging followed by a pre-defined treatment algorithm. Briefly, prostate bed salvage radiotherapy (SRT) was proposed to all patients with a negative staging or positive imaging within prostate bed. Observation was proposed in all patients in whom PSMA was negative and postoperative radiotherapy had already been performed.
Stereotactic re-treatment of macroscopic relapse could be proposed in case of post SRT PSMA positive findings within prostate bed. Stereotactic body radiotherapy (SBRT) was used for all patients with pelvic nodal recurrence or oligometastatic disease. Androgen deprivation therapy (ADT)+/- androgen receptor targeted agent (e.g Enzalutamide or Apalutamide) was provided in case of widespread metastatic disease.

Results: The current analysis included 174 patients. 69.5% of patients had PSMA negative or prostate bed macroscopic relapse. Pelvic or distant oligometastatic disease was detected in 22.4 and 5.7% of patients. Widespread metastases were reported in 2.3% of cases. Consequently, SRT, SBRT or upfront ADT were proposed in 59.8%, 28.2% and 2.3% of patients. Median follow up was 17 months, 50 patients had further PSA rise, for an estimated median biochemical relapse free survival of 25 months. PSMA detected distant metastases were found in in 27 cases. ADT was prescribed in 13 patients.

Conclusions: PSMA PET CT imaging had a significant impact on standard management. The provided treatment algorithm led to promising results. Many patients avoided unnecessary treatment toxicity and remained free from ADT at the end of follow up.

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REIRRADIATION IN GLIOBLASTOMA PATIENTS UNDERGOING SECOND LINE REGORAFENIB: A MONOCENTRIC, RETROSPECTIVE REAL-LIFE STUDY

Code: 547

Aims: The established standard of care for newly diagnosed Glioblastoma (GBM) involves surgery, radiotherapy (RT) and temozolomide (TMZ). Upon recurrence, no widely accepted treatment regimen exists. We report our experience with Regorafenib as a second line treatment for GBM, with a special focus in a subgroup of patients undergoing reirradiation during systemic therapy with progressive disease and an adequate performance status.

Methods: We conducted a retrospective analysis on data from our centre (Department of Radiation Oncology, Careggi hospital, Florence, Italy) The inclusion criteria encompassed a histologically confirmed diagnosis of GBM in accordance with WHO 2016 standards, a documented radiological relapse via magnetic resonance imaging (MRI) following Stupp treatment and the starting of second line treatment with Regorafenib between 01/01/2020 and 31/10/2023. We also analysed patients' progression-free survival (PFS), overall survival (OS) and the effect of brain reirradiation. Treatment response was performed according to RANO criteria, while adverse events (AEs) were assessed using CTCAE v.5. According to the original schedule, patients received Regorafenib 160 mg once daily for the rst 3 weeks of each 4-week cycle. Radiotherapy for the reirradiation was delivered with CyberKnife® and Gamma Knife.

Results: From January 2020 to October 2023, we analysed 51 GBM patients from our centre. Median age was
58.25ys (IQR 21-81), 62.7% were male and 45 (88.2%) were in good clinical condition with a Karnofsky performance score (KPS) scoring between 80 and 100. Patients taking steroids at baseline were 33 (64.7%). Median OS was 19 months, median PFS was 3 months. The median number of Regorafenib cycles per patient was 4 (IQR 2-20). Grade 3-4 related adverse events were reported in 17.6% of patients. A dose reduction or a suspension due to AEs was required in 23.5% of patients. In 8 patients an hypofractionated reirradiation was performed for a mean dose of 21Gy (range 14Gy-30Gy) for a mean number of 2.83 fractions (range 1-5 fractions). Reirradiation was performed either with Cyberknife (6 patients) or Gammaknife (2 patients). No relevant toxicity was observed in the subgroup of irradiated patients while undergoing their treatment with Regorafenib.

Conclusions: Regorafenib confirms its role as a promising therapeutic choice in recurrent GBM, while reirradiation inpatients undergoing Regorafenib treatment appears to be safe and well tolerated and should be investigated in a prospective trial.

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RADIOTHERAPY FOR PATIENTS WITH LUNG CANCER AND INTERSTITIAL LUNG DISEASE: A DELPHI CONSENSUS

Code: 202

Aims: Interstitial lung diseases (ILD) are a heterogeneous group of illnesses affecting the lung parenchyma. Patients with ILD have a greater risk of developing lung cancer and generally have a worse prognosis. Furthermore, ILD make the patient more prone to developing toxicities related to radiotherapy and combined treatment resulting from exacerbation of the ILD itself. To date, there are no clear recommendations or guidelines regarding the management of patients with lung cancer and ILD candidate to radiotherapy combined or not with systemic therapy. This work aims to create a consensus regarding ILD assessment, patient selection, risk/benefit index and clinical management of patients with lung cancer and ILD who are eligible for thoracic radiotherapy.

Methods:
The consensus process was first performed using the Estimate-Talk Estimate method. The items of interests were independently identified by a board of experts of 4 radiation oncologists, 2 pneumologists, 1 radiologist and 1 medical oncologist. Board members then individually drafted one or more statement for every one item. An extended panel of 24 experts (12 radiation oncologists, 6 pneumologists, 3 radiologists and 3 medical oncologists) expressed their degree of consensus according to UCLA appropriateness method by means of a 9-point numerical rating scale (1 = totally disagree to 9= totally agree). A median score ≥7 was represented the consensus threshold for each statement.

Results: Sixteen statements from10 items were formulated, all of them reaching the consensus agreement. The list of items and statements are reported in table 1.

ITEM	STATEMENT
1 – Role of HRCT in ILD	- HRCT chest scan represents the most accurate examination for the identification and definition of the pattern of interstitial lung disease (ILD) at diagnosis, during follow-up and in the evaluation of any complications.
	- Theradiologist, in HRCT chest scan, should define the morphological pattern of ILD, the characterization into fibrosing/non-fibrosing ILD and the UIP/non-UIP pattern.
2 - Risk stratification of exacerbation/progression of interstitial disease	- In light of the greater pulmonary toxicities in patients with ILD and undergoing RT, the indication for radiation treatment should be evaluated in a multidisciplinary setting and subject to an accurate pneumological stratification of the risk of exacerbation and progression.
3 - Definition of the risk of RT-related toxicity	- RT Complications in patients with ILD depend, in addition to dosimetric factors, on patient characteristics, disease location, respiratory function, premedication and concomitant therapies.
	- The method of risk quantification of toxicity, independently of clinically validated prognostic indexes, can not ignore an individual evaluation.
4 - Prediction of RT complications	- For patients candidates for stereotactic RT, the dosimetric factors predictive of a greater incidence of toxicity are mean dose (MLD), V5, V10 and V20.
	- For patients candidates for radical non-stereotactic RT, the dosimetric factors predictive of greater toxicity are mean dose (MLD), V5 and V20
5 – Prevention of RT complications	- Prevention of complications during RT for lung cancer in patients with ILD could be conducted with steroid, immunosuppressive and biological therapy (idiopathic inflammatory disease or secondary to connective tissue disease) or antifibrotic therapy (progressive fibrosing disease).
6 – Stereotactic RT in ILD	- Stereotactic radiotherapy can be considered in patients with ILD only after careful evaluation of the benefit/harm ratio within a multidisciplinary context in which are evaluated the type of ILD, the presence of symptoms related to respiratory comorbidity, the life expectancy of the patient, the presenting characteristics of the lesion to be treated, the possible toxicities, including fatal ones.
7 - RT in locally advanced disease	- In locally advanced disease, chemoradiotherapy in patients with ILD should be proposed only after careful evaluation of the benefit/harm ratio within a multidisciplinary context in which are evaluated the type of ILD, the presence of symptoms related to respiratory comorbidity, the patient's life expectancy, the presenting characteristics of the lesion to be treated, the possible toxicities, including fatal ones. However, the use of the highest technological standards is essential.
8 - RT and systemic treatment in ILD	- In the case of an integrated chemoradiotherapy treatment for patients with ILD, platinum salts, vinorelbine and weekly nab-paclitaxel can be taken into consideration; gemcitabine and three-weekly taxanes should instead be excluded.
	- Maintenance immunotherapy after thoracic chemoradiotherapy should not be excluded a priorifor patients with suspected ILD. It can instead be a therapeutic option for patients with advanced cancer and concomitant ILD, subject to close monitoring of respiratory function.
	- Thoracic radiotherapy for patients with ILD, treated with targeted therapy (tyrosine kinase inhibitors or drug-conjugated antibodies), is limited to the risk of pneumonitis related to these treatments.
9 - Follow up after RT treatment with or without systemic treatment	- The clinical and radiological follow-up of patients undergoing radiotherapy and affected by ILD should be carried out in centers with experience and in a multidisciplinary context.
	- The follow up should also be personalized to identify earlier any RT toxicity
10 – Role of TMD	- TMDs should identify specific evaluation/treatment/monitoring pathways for patients affected by lung cancer and concomitant ILD and candidates for radiation treatment.

Conclusions: The present work describes the results of a multidisciplinary consensus process regarding the role of thoracic radiotherapy for patients affected with both lung cancer and ILD. The resulting agreements may constitute a valuable tool for all the clinicians and to facilitate the decision-making process in this challenging context.

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STEREOTACTIC RADIOTHERAPY (SRT) WITH SIMULTANEOUS INTEGRATED PROCTECTION (SIP) PLANNING STRATEGY TO MANAGE UPPER ABDOMINAL LESION WITH CRITICAL OVERLAP WITH VISCERAL ORGANS: RESULTS OF A PROSPECTIVE STUDY.

Code: 220

Aims: One of the challenges of stereotactic radiotherapy (SRT) is to manage lesions abutted to bowel, duodenum and stomach. Treating such lesions with effective doses is difficult, given the intrinsic radiosensitivity of the organs at risk (OARs) and the consequent risk of severe toxicities. This study was designed to investigate if deliberated dose-reduction strategy consisting in tailoring dose in the area of overlap between PTV and critical OARs (simultaneous integrated protection, SIP approach) is safe and effective.

Methods: This is a prospective, mono-institutional, single arm study. Inclusion criteria were: tumor abutment with duodenum, stomach or small bowel, SRT schedule in 6 fractions with dose prescription reaching at least a biologic effective dose (BED) of 70Gy, per-protocol dose constraints were: (near) maximum dose, D2cc and D20cc to duodenum, stomach or small bowel 38Gy, 32Gy and 24 Gy. Primary endpoint were 1 year freedom from local recurrence (FFLR) and acute-late toxicity.

Results: From June 2019 to December 2022 85 patients meeting inclusion criteria were enrolled. Median age of the patients was 73 (range 28-93). Majority of patients presented in ECOG PS 0-1 and were treated on a pancreatic lesion (48), the main histological subtype was pancreatic ductal adenocarcinoma. Treatment was equally performed with V-Mat FFF, Helical IMRT FFF and Robotic technique. Median FFLR resulted not reached, 1 year FFLR resulted 90%. At univariate analysis, PTV_SIP more than 4cc, PTV-SIP/PTV ratio more than 20%, minimum dose to PTV_SIP less than 28Gy, median dose to PTV_SIP less than 29 Gy and minimum dose to PTV_dominant less than 30Gy are all associated with worse FFLR. Multivariable analysis confirms that patients with PTV_SIP more than 4cc to be associated with greater risk of local relapse (Odds Ratio 47, IC 5.8-380, p=0.000). One case of G4 acute toxicity occurred (splenic abscess), one case of acute G3 toxicity (duodenal stenosis) and 13 cases of G2 toxicity mainly represented by emesis and dyspepsia. No grade 3 or worse late toxicity occurred.

Conclusions:SRT exploiting SIP planning is safe while maintaining effectiveness. This study for the first time provide prospective evidence on clinical and dosimetric parameters associated with tumor control probability when SIP is used. PTV_SIP less than 4cc is independently associated with local control exceeding 95% at 2 years. Such findings serve as new guidance for physicians in determining treatment indications and scheduling for SRT.

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STEREOTACTIC BODY RADIOTHERAPY FOR LUNG-ONLY OLIGOMETASTATIC HEAD AND NECK SQUAMOUS CELL CARCINOMA: LONG-TERM CLINICAL OUTCOME

Code: 412

Aims: Oligometastatic disease in head and neck squamous cell carcinoma (HNSCC) is a rare setting. Local ablative therapies are the most adopted strategies although no evidence-based recommendations are currently published. The aim of our analysis was to update and report on long-term clinical outcomes of a cohort of HNSCC patients treated with stereotactic body radiotherapy (SBRT) for lung-only oligometastatic disease.

Methods: Eligible patients had 1 to 5 lung metastases. The oligometastatic pattern was classified as "de novo" (suitable for SBRT only) or "oligoprogressive" (after first line of systemic therapy). We evaluated time to progression (TTP) as the time from the last day of SBRT to disease progression or death from any cause. Predictive factors of better clinical outcome and survival analysis were performed by Cox regression and Kaplan Meier methods, respectively.

Results: A cohort of 50 patients was retrospectively evaluated. The median age was 68 years (range 37-86) and 45 patients had an ECOG PS 0-1. Oropharynx cancer (OPC) was the primary tumor subsite in 20 patients (40%) and HPV positive status was reported in 13 patients (26%). "De novo" oligometastatic pattern was observed for the majority of patients (80%). After a median follow up (from the end of SBRT) of 24,5 months (range 5-113), median TTP and overall survival (OS) were 17 months (95% CI 5.4– 28.6) and 46 months (95%CI 23.1– 68.9), respectively. The 2-years LC rates was 89%. At univariate analysis, patients aged > 70 years reported a better TTP (0.05). If compared to the p16 negative group of patients, HPV-related cohort reported a significantly better OS from the end of SBRT (p 0.002) (Table.1).

Conclusions: Our findings suggested that SBRT may improve clinical outcome prolonging time to progression in a properly selected cohort of HNSCC patients with lung-only oligometastatic disease. Distant metastases from HPV-related primary HNSCC should be tested for p16/HPV status.

		Primary site		Metastasis		Survival Outcomes		
Patients	Age at diagnosis	p16 status	HPV status	p16 status	HPV status	PFS (months)	TTP (months)	OS (months)
1	61	+	-	+	+	35	1	101
2	64	+	+	+	+	88	88	91
3	70	+	+	-	-	5	59	70
4	65	+	+	NA	NA	13	9	59
5	48	+	NA	+	-	106	17	130
6	74	+	+	+	+	8	4	90

Abbreviation: NA, not applicable; PFS, progression-free survival; OS, Overall survival; TTP, time to progression.

Table 1. HPV-related oropharyngeal cancer patients with histologically-confirmed lung metastasis

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FIGHTING XEROSTOMIA IN HEAD AND NECK PATIENTS TREATED WITH RADIOTHERAPY: THE CHALLENGING STRATEGY OF THE PAROTID GLAND STEM CELL SPARING

Code: 267

Aims: Despite the implementation of modern technologies, xerostomia is still one of chronic side effects most impacting the quality of life (QoL) of head and neck (H&N) patients (pts) treated with radiotherapy (RT). The parotid gland has a pivotal role in salivary production, especially during eating, and it encloses a stem cells-rich region (SCRR). The present work aims to present preliminary results on eventual association between the dose received from the SCRRs and the degree of long-term xerostomia in a cohort of oropharyngeal cancer pts.

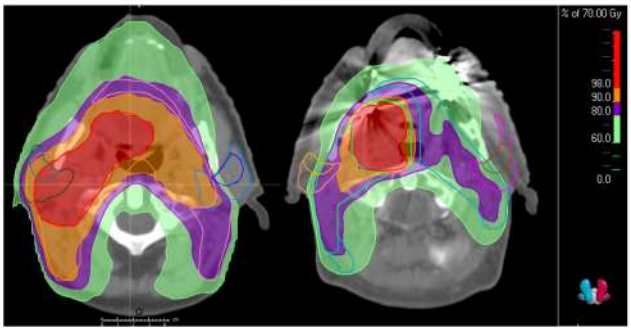
Methods: Pts treated with RT at our Department from 2012 to 2019 were retrospectively considered for study inclusion, in case of: (i) confirmed primary tumor of the oropharynx; (ii) RT with curative intent with volumetric modulated arc therapy (VMAT) technique, either combined or not with systemic treatment; (iii) physician-rated grade 2 (G2) or grade 0 (G0) chronic xerostomia one-year after RT, according to the Common Terminology Criteria for Adverse Events (CTCAE) v.4. The RT treatment plan was optimized following the standard procedure of our center, ensuring the clinical target volume (CTV) coverage, and striving to comply with the organs at risk (OARs) constraints (for the parotid gland: average dose.

Results: Sixteen pts (over 116 elegible pts) were included in the current preliminary analysis (9 with xerostomia G2 and 7 with xerostomia G0). The cumulative delivered dose was 70 Gy in conventional fractionation. The low sample size prevented any statistical tests, however, the dose received from the contralateral parotid gland and the contralateral SCRR was higher in G2 xerostomia pts than in G0 ones (Figure 1).

Conclusions: The present work confirms a trend between the dose received from either the contralateral parotid gland or SCRR and the onset of chronic xerostomia. Therefore, the future full data collection and consequent statistical analysis could better define the role of SCRR in develping long-term xerostomia.

Figure.1 Median dose received by OARs involved in saliva production (top) and dose distribution in pts with chronic G0 (left) and G2 (right) xerostomia.

	Xerostomia G0 (n = 7)	Xerostomia G2 (n = 9)
	Median dose (Gy)	Median dose (Gy)
SCRR (ipsilateral)	37.42	45.43
SCRR (contralateral)	25.61	35.92
Parotid gland (ipsilateral)	45.94	49.27
Parotid gland (contralateral)	22.5	31.22
Oral cavity	54.02	56.97



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BREAST DENSITY HISTOGRAM ANALYSIS: THE ROLE OF FAT IN OUTCOME PREDICTION AFTER WHOLE BREAST RADIOTHERAPY

Code: 299

Aims: The study aimed to define the role of breast densitometric state in association to local and distant progression free survival (LPFS, DPFS) and overall survival (OS) scored after the end of RT.

Methods: A large mono-Institutional cohort (n=1127) of early-stage breast cancer patients was enrolled between 2009-2017 and homogeneously treated with tangential fields delivering 40Gy/15fractions to the whole breast. The Clinical Target Volume (CTV) segmentations were available from RT plans. Volume, mean/median, SD, kurtosis, skewness, 10th/25th/75th/90th percentiles (P10, P25, P75, P90) were extracted from CTV Hounsfield Units (HU) histograms using a Python code. Only the range [-200,70]HU was investigated to avoid more high-density materials (clips, silicon). The extracted parameters were combined into Multivariate Cox regression (MCR) in association with LPFS, DPFS and OFS. One-thousand bootstrap simulations of the original cohort were performed. For each endpoint median and IQR ranges of p-values, hazard ratios (HRs) and AUC values were obtained. A prognostic index (PI) of risk was computed. A Kaplan Meier (K-M) test using the ROC Youden index as criterion was used to stratify patients with higher and lower risk.

Results: With a median follow-up of 6 years [IQR:4-8], the LP/DP/death number of events were 26/46/80.The best Cox model on LPFS included percentual volume of fat (VFAT%) and P10 of HU distribution (p=0.026, AUC=0.614 [IQR=0.585-0.643]). The K-M test done using PI_LPFS stratified patients with high ability (p=0.022, HR=2.678 [IQR=1.153-6.220]) (Figure 1a).The best Cox model on DPFS included Median and VFAT% of HU distribution (p=0.009, AUC=0.604 [IQR=0.574-0.632]). The K-M test performance obtained using PI_DPFS was quite good (p=0.004, HR=2.295 [IQR=1.303-4.042]) (Figure 1b).The Cox model on OS included VFAT% and P75 of HU distribution (p=0.0002, AUC=0.629 [IQR=0.600-0.658]). The K-M test done using PI_OS stratified patients according to their risk of death (p<0.0001, HR=3.037 [IQR=1.8544.976]) (Figure 1c).Adding the patient age as variable, the AUC increased up to 0.695 (IQR=0.667-0.722) showing that age and VFAT% are independently and associated to OS (p<0.0001). The PI_OS_age_corrected in K-M test better stratifies patients (p<0.0001, HR=13.338 [IQR=7.083-25.116]) (Figure 1d).

Conclusions: From this study we concluded that the prevalence of fat percentage in the breast was found to be protective for LPFS, DPFS and OS.

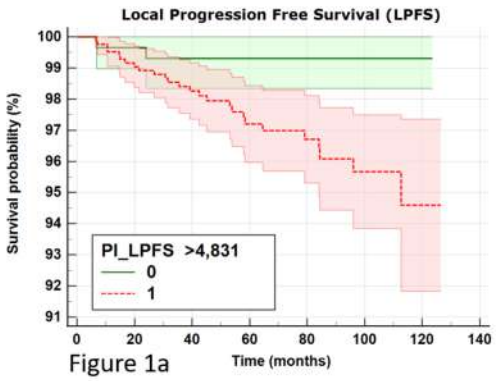

Figure 1a

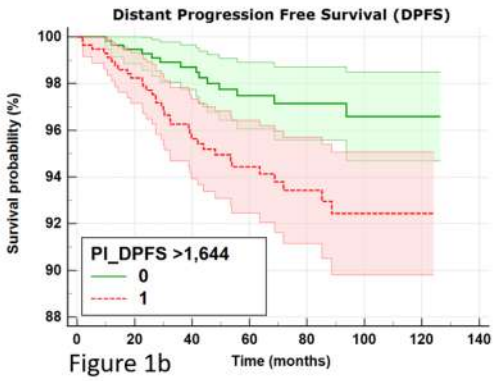

Figure 1b

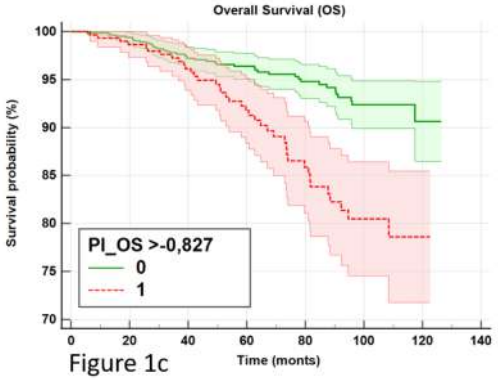

Figure 1c

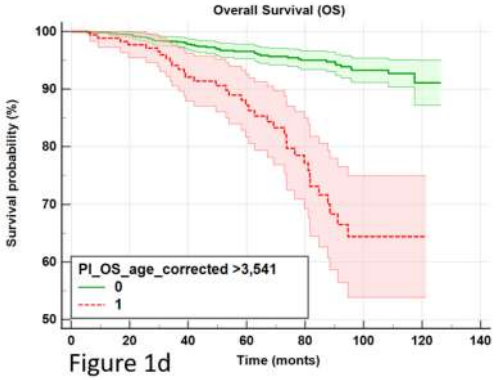

Figure 1d

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A NATIONAL SURVEY ON THE TREATMENT TRENDS FOR MULTIPLE BRAIN METASTASES: DOES CLINICAL PRACTICE REFLECT THE DATA?

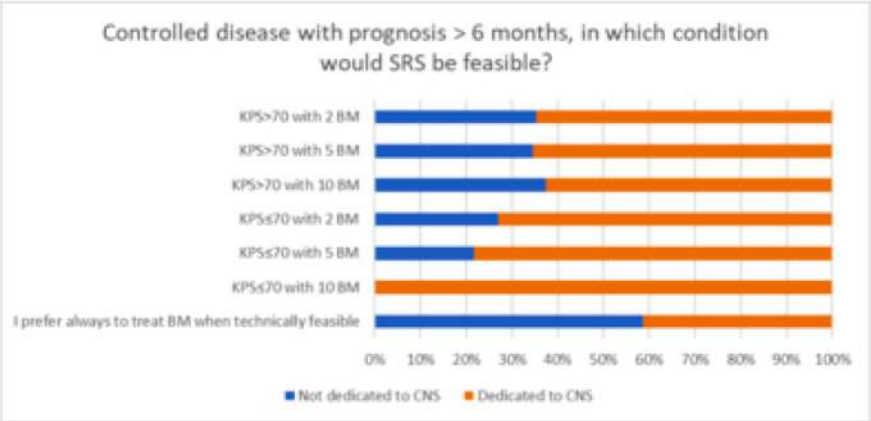
Code: 298

Aims: Recent studies have reported significant findings that are substantially influencing the approach to managing multiple brain metastases, particularly in cases of oligometastatic disease treated with novel drugs. This survey aims to examine the actual practices employed by the Italian Radiation Oncology community in the management of multiple brain metastases.

Methods: A comprehensive online survey comprising 31 questions was distributed to members of the Associazione Italiana Radioterapia e Oncologia Clinica (AIRO), including neurosurgeons. The questionnaire was structured into three sections: general information, clinical management, and technical aspects. Descriptive statistics were utilized to summarize participants' demographic characteristics, and responses regarding the factors influencing the use of Stereotactic Radiosurgery (SRS) were analyzed using frequencies and percentages. The results were presented through tables and charts to enhance data interpretation.

Results: A total of 186 individuals participated as respondents, with 133 (71.51%) successfully completing the questionnaire. The majority of respondents fell within the 30-40 age range (32.97%). Residents comprised 13.66% of participants, and 56.52% reported specific involvement in treating cerebral metastases. Prognostic scores for decision-making were not consistently employed. Stereotactic approaches were favored when dealing with over 10 lesions in controlled systemic disease with a prognosis exceeding 6 months and a Karnofsky Performance Status (KPS) above 70. If the disease is not controlled, the preference for stereotactic approaches decreases to around <10%. The option of a stereotactic approach becomes more favorable with an increasing number of brain metastases, particularly for specialists in brain diseases (Fig. 1), with no specific limit on the total treatment volume.
Hippocampal avoidance (HA) during Whole Brain Radiation Therapy (WBRT) is not routinely utilized, even when available. Technologies are assessed based on their categorization as mandatory, recommended, optional, not sufficient, and not recommended (Table 1).

Conclusions: Our initial analysis indicates a prevalent inclination among specialists dedicated to the central nervous system (SNC) towards favoring Stereotactic Radiosurgery (SRS) across a wide range of scenarios. Further, in-depth analysis will be conducted to more comprehensively address the ongoing trends in the management of multiple brain metastases.



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REAL-WORLD DATA OF PARTICLE BEAM RE-IRRADIATION IN GYNAECOLOGICAL MALIGNANCIES

Code: 326

Aims: Our study aimed to provide real-life data on the efficacy and safety ofproton beam radiotherapy (PBT) and carbon ion radiotherapy (CIRT) delivered as a rescue treatment for recurrent gynaecological cancer after definitive radiotherapy (RT).

Methods: This retrospective observational study included recurrent patients who received PBT or CIRT at the time of recurrence in the field of a previous RT treatment, according to National *LEA* guidelines. Clinical data at the time of diagnosis and at the time of recurrence were collected and analyzed. 1 and 2-year local control (LC) survival rate, the objective response rate (ORR), defined as the sum of complete response (CR) and partial response (PR), and the clinical benefit (CBR), the sum of ORR and stable disease (SD), were radiologically evaluated on per-lesion basis at the last follow-up. Toxicity was scored by the CTCAE 4.03 scale

Results: Between April 2017 and November 2023, 27 patients (median age 64.5 years, range 39-60) with 28 lesions were treated. Most patients had cervical (29.6%), endometrial (25.9%), and ovarian (22%) cancers followed by rarer and radioresistant histologies (melanomas, sarcomas) as primary tumours. The median clinical target volume (CTV) was 107 cc (range: 15-1381 cc). Lesions were treated with a median total dose of 43.5 Gy[RBE] (range:39-60 Gy[RBE]) for PBT (N=12 lesions) and 48 Gy[RBE] (range:39-68 Gy[RBE]) for CIRT (N=16 lesions). No concomitant systemic therapies were administered during re-RT. No progression after PBT was recorded and 3 cases of marginal recurrences after CIRT were experienced. The overall ORR was 68%, in particular, 75% for PBT and 62.5% for CIRT. The overall CBR was 89.3% with 100% for PBT and 81.3% for CIRT. The CBR for the 3 cases of recurrences after CIRT was maintained for a mean of 10.4 months. After a median follow-up of 12 months, 1 and 2 y- LC were 100% for PBT and 92 and 55%, respectively, for CIRT. No high-grade toxicities were recorded.

Conclusions: Data from this real-life dataset suggest that particle beam re-RT in a real-world setting of gynaecological recurrence is effective and well tolerated. The differences in terms of LC and ORR between CIRT and PBT are related to the histologies and the largest volumes treated with CIRT. Largest cohort and long-term follow-up are warranted.

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UNCOVERING THE RESPONSE OF OVARIAN CANCER CELL LINES TO LOW AND HIGH LET ACCORDING TO THEIR MUTATIONAL BACKGROUND

Code: 158

Aims: Within 2 years from diagnosis, up to 70% of ovarian cancer (OC) relapse and in this setting, radiotherapy (RT) has emerged as an active option. OCs exhibit a high degree of genomic instability, that might influence the response to treatment. This study aims to understand whether the LET might influence the response and motility of OC cells according to the molecular background.

Methods: Exponentially growing human OVSAHO (BRCA2-mutated[*M*] serous papillary OC), COV362 (BRCA1-*M* endometrioid OC), OVCAR8 (BRCA1-methylated high-grade serous OC), and OVCAR3
(BRCA-wild type[*WT*] high-grade serous OC) cells cultured in T25-T75 flasks were exposed to different single physical doses (0.5 Gy, 1 Gy, 2 Gy, 3 Gy, 4 Gy, 5 Gy and 6 Gy) of low (XRT) or high LET (CIRT) irradiation. We evaluated the *in vitro* OC cells' response by the clonogenic survival assay, migration through Boyden chamber assay and invasion using BioCoat Matrigel invasion chamber assay. We used unpaired Student's t-test with a 2-tailed to analyse any differences between each treatment among different groups.

Results: OVCAR3 (BRCA-*WT*) was the most XRT radioresistant cell line, while OVCAR8 (BRCA1 methylated) the most XRT radiosensitive. There was a greater significant radio-cytotoxicity after CIRT conditions for each cell line with a dramatic decrease in the number of OVCAR3 colonies after CIRT ($p< 0.001$). The ability of OCs to migrate decreased in a dose-dependent way both for low and high-LET. However, CIRT induced a more significant decrease in cell migration in each cell line, with a higher significant reduction in OVCAR3 (92% vs 78% at 2 Gy; 85% vs 41% at 4 Gy; 83% vs 37% at 6 Gy; $p < 0.0001$ for each condition). We observed a similar pattern regarding cell invasion with a reduction of invading cells after X- RT or CIRT, with a more significant effect after CIRT for each cell line but particularly for OVCAR3 (93% vs 76% at 2 Gy; 87% vs 39% at 4 Gy; 81% vs 35% at 6 Gy; $p < 0.0001$ for each condition).

Conclusions: BRCA-*M* status was a pattern of radiosensitivity, while the *WT* presented a significant XRT- radioresistance that can be overcome by the high-LET. CIRT exhibited a more substantial impact in limiting survival, migratory and invasive capabilities of OC cells with the greatest impact for BRCA-*WT*, emphasising its efficacy to increase the local control and reduce the risk of metastasis. This preliminarystudy might be the basis for creating a tailored RT strategy in an OC oligometastatic setting.

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EXTERNAL BEAM RADIATION DOSE TO BONE MARROW SUBREGIONS AND ACUTE HEMATOLOGIC TOXICITY IN ENDOMETRIAL CANCER

Code: 95

Aims: To identify dosimetric parameters associated with acute hematologic toxicity (HT) in endometrial cancer treated with Volumetric modulated arc therapy (VMAT-RT).

Methods: Patients with uterine adenocarcinoma treated in our Institution from March 2019 to November 2022 were retrospectively enrolled in this study.
All patients underwent adjuvant external beam radiotherapy with Volumetric modulated arc therapy strategy plus a brachytherapy boost on vaginal cuff. When indicated, adjuvant platin-based chemotherapy was administered after surgery in upfront or sandwich setting.
Pelvic bone marrow was contoured for each patient and divided into three subsites: lumbosacral spine (LSBM), ilium (IBM) and lower pelvis (LPBM).
The volume of each region receiving 10, 20, 30 and 40 Gy (V10, V20, V30, V40, respectively) and Dmean was collected.
Hematological toxicity during radiotherapy treatment was graded according to the CTCAE V 5.0. Regression models were used to test associations between dosimetric parameters and HT.

Results: Data from 99 patients were retrospectively analyzed. Adjuvant external beam radiotherapy was delivered to the pelvis with VMAT strategy for a total dose of 45 Gy, 1.8 Gy/fraction plus a brachytherapy boost on vaginal cuff for a total dose of 10Gy in 2 fraction weekly.
Thirty-one patients developed during radiotherapy treatment an HT > grade 2.
With a sensitivity of 32.2% and specificity of 88.2%, V20 Gy LSBM <50% is associated to a 10% risk of Grade 2 or worse HT and V20 Gy LSBM <68% is associated to a 20% risk of Grade 2 or worse HT (95%CI 0.50-0.74; p=0.04).
No association between hematological toxicity and V10-20-30-40 or Dmean of IBM and LPBM were observed.
Dosimetric parameters involving the lower pelvis had stronger association with hematological toxicity than those involving the ilium, even if not significant.

Conclusions: The volume of lombo-sacral pelvis receiving low-dose radiation (V20 LSBM >68%) seems to be associated with HT.
Future investigations should seek to confirm these findings through the inclusion of these parameters in the planning process.

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REIRRADIATION AND PET FET EVALUATION PRE AND POST-TREATMENT IN RECURRENT HIGH-GRADE GLIOMA

Code: 596

Aims: Most high-grade gliomas (HGGs) recur after initial multimodal therapy and re-irradiation (Re-RT) has been shown to be a valuable re-treatment option in selected patients. Diagnosis, treatment planning and follow-up of HGGs are based on magnetic resonance imaging (MRI): gadolinium contrast enhanced T1-weighted images (Gd-T1MR), T2 images, FLAIR images etc. Gd-T1MR could also occur after a recent surgery, RT or chemotherapy (pseudoprogression). In this case, amino-acid positron emission tomography (PET) has been proven to be able to non-invasively differentiate treatment-related changesfrom real tumor progression.We aimed to determine the predictive potential of 18F-fluoroethyl-tyrosine (18F-FET) PET acquired prior and after to hyperbaric re-irradiation (HBO-RT) of recurrent HGGs.

Methods: We carried out a retrospective analysis on eleven patients enrolled in a study evaluating the efficacy of Hypofractionated Stereotactic Radiotherapy (HSRT) after hyperbaric oxygen therapy for recurrent HGGs. The assessment of radiological and clinical response was based on MRI sequences obtained before and after HBO-RT according to RANO Criteria and concomitant 18F-FET was performed to support the differential diagnosis of PD or treatment-related changes. FET-based parameters and other factors included age, Karnofsky Performance Status (KPS), MGMT methylation status, ongoing use of steroids, planning target volume (PTV) were considered. Variables were evaluated against a dichotomic PFS outcome (progression within three months or later) by no parametric statistics.

Results: 11 patients (median age: 58 years; 39-71 years) with KPS higher than 80 were included in the present analysis; median overall survival was 17 months, while the median PFS was 6 months. Np FET parameters carried independent predictive information although there remained an insufficient tendency to significance for SUVmax (SUVmax p-value 0.173). Among considered patient-related parameters the ongoing use of steroids was the only parameter approaching significance (p-value 0.061), differently from age (p-value 0.490), KPS (p-value 0.500) and MGMT methylation status (p-value 0.567). Only PTV was significantly different between patients who experienced early progression and those who did not (p- value 0.0459).

Conclusions: In this small cohort of patients with recurrent HGG, treated with HBO-RT, FET PET parameters did not achieve conclusive predictive significance.

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FIVE-YEAR SURVIVAL AND SAFETY OUTCOMES FROM THE START-NEW- ERA NON-RANDOMISED PHASE II TRIAL

Code: 538

Aims: in early analysis of START-NEW-ERA non randomized phase II trial (1) stereotactic ablative radiotherapy (SAbR) had optimal local control (LC) and promising overall survival (OS) in absence of ≥G3 toxicity. We report 5-y efficacy and safety outcomes, approximately 3 years after the last enrolled patient.

Methods: Patients with unresectable locally advanced (LA) non-small cell lung cancer (NSCLC) unfit for concurrent radio-chemotherapy (RT-ChT) were enrolled. Neoadjuvant ChT was prescribed in fit patients. The tumor volume included primary tumor (T) and any regionally positive node/s (N). The co-primary study endpoints were LC and safety.

Results: Between December 31, 2015 and December 31, 2020 50 LA-NSCLC patients were enrolled. Histology was squamous cell carcinoma (SCC) and adenocarcinoma (ADC) in 52% and 48%, respectively. 40 (80%) patients had ultra-central tumor. Twenty-seven (54%) received neoadjuvant ChT and 7 (14%) adjuvant Durvalumab. Median prescribed dose was 45 Gy (range, 35-55) and 40 Gy (35-45) in 5 daily fractions to T and N, respectively. After a median follow-up of 63 months (range, 12-102), 19 (38%) patients had experienced local recurrence (LR). The median LR-free survival (FS) was not reached (95% CI, 28 to not reached). The 1-, 3- and 5- year LR-FS rates were 86±5%, 59±7% and 59±7%, respectively. At last follow- up, 27 (54%) patients were alive. Median overall survival (OS) was 55 months (95% CI, 43-55 months). The 1, 3, and 5-year OS rates were 94±3%, 70±6% and 50±7%, respectively. The median DFS was 13 months (range, 11-18). The 1, 3, and 5-year disease free survival rates were 56 ±7%, 24±6% and 21±6%, respectively. Only one (2%) patient developed grade (G) 3 toxicity. ADC (HR, 3.61;95% CI, 1.15-11.35) resulted significant predictor of better LC, while OS was significantly conditioned by smaller PTVs (HR, 1.004;95% CI, 1.001-1.010) and TNM stage (HR, 4.8;95% CI, 1.34-17).

Conclusions: This 5-year update analysis demonstrates robust and sustained clinical outcomes benefit with SAbR in LA- NSCLC patients with only one case of G3 toxicity suggesting the feasibility of using this approach in LA- NSCLC patients unfit for concurrent ChT-RT.

Reference: *1. Int J Radiation Oncol Biol Phys, Vol. 115, No. 4, pp.886-896, 2023*

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STEREOTACTIC ABLATIVE RADIOTHERAPY IN SYNCHRONOUS AND METACHRONOUS OLIGO-METASTATIC NSCLC: START-NEW-ERA OLIGO-M NON RANDOMISED PHASE II TRIAL

Code: 549

Aims: This is a non-randomised phase II trial (*Clinical Trial NCT06207292*) to assess efficacy and safety of SAbR in oligo-M NSCLC patients.

Methods: Synchronous and metachronous (oligo-recurrent, oligo-persistent and oligo-progressive) oligo-M NSCLC were enrolled. Ongoing systemic therapy was maintained until poly-M widespread. Oligo-M state and SAbR target were determined on the basis of PET-CT, including primary tumor (T), regional nodes (N) and oligo-M sites. The recommended doses in 5 fx were: 40-60Gy to T; 35-40Gy to thoracic regional N according to START-NEW-ERA Trial (1); 40-60 Gy to peripheral lung oligo-M; 40-50 Gy to central lung oligo-M; 35-45Gy to extra-thoracic N; 40-50 Gy to adreanal gland; 35-40 Gy to (GTV) spine according to Cox Guidelines and 35-50 Gy to non-spine bone oligo-M; 60-65Gy to liver. The co-primary end-points were progression-free survival (PFS), new and changing systemic therapy free-survival (n&cST-FS) and safety. The co-secondary end-points were local control (LC) and overall survival (OS).

Results: Between 2016 and 2023,70 synchronous (32=46%) and metachronous (38=54%) oligo-M NSCLC patients were enrolled. All analyses included patients with at least 6 months of follow-up after SAbR.18 (26%) and 52 (74%) were oncogene addicted (OA) and non-oncogene addicted (nOA) oligo-M NSCLC.36 (51%) and 13 (18%) had ongoing immunotherapy and targeted therapy, respectively; 21 (30%) oligo-recurrent received SAbR alone. 44 (63%) received SAbR to T and/or N. The median follow-up was 28 months (6-98). The median PFS was 6 months (5-13); the 1-, 2-, 3- and 4-year PFS was 40%, 28%, 22% and 20%. The median n&cST-FS was NR; the 1-, 2-, 3- and 4-year n&cST-FS was 72%, 59%, 59% and 53%. The median LC was NR; the 1-, 2-, 3- and 4-year LC was 89%, 85%, 80% and 72%.The median OS was 68 months (36-68); the 1-, 2-, 3- and 4-year OS was 83%, 75±6%, 64% and 56%. OS was significantly higher in OA respect to nOA NSCLC (p=0.0013), no difference was found in terms of PFS and n&cST-FS. No difference was found in synchronous versus metachronous oligo-M NSCLC in terms of PFS, n&cST-FS and OS. Only 1 with ongoing immunotherapy experienced lung G3 toxicity.

Conclusions: Oligo-M NSCLC treated with SAbR had good PFS, optimal n&cST-FS allowing to maintain and/or delay systemic therapy, and promising OS. Safety was met also in patients who received SAbR to primary tumor and/or thoracic regional nodes. Our clinical outcomes would suggest the efficacy of using this approach in clinical practice.

Reference: *(1) Int J Radiat Oncol Biol Phys. 2023 Mar 15;115(4):886-896*

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IMPROVING RESECTABILITY IN PANCREATIC NEOPLASM (IRENE-1): A PHASE II TRIAL ON NEOADJUVANT SBRT AND CHEMOTHERAPY.

Code: 207

Aims: Current guidelines recommend neoadjuvant Stereotactic Body Radiotherapy (SBRT) combined with chemotherapy (CHT) for locally advanced pancreatic cancer (LAPC). This phase II multicenter trial aimed to assess the resectability rate, local control (LC), toxicity, distant metastasis-free survival (DMFS), and overall survival (OS) following CHT with anticipated SBRT+CHT in LAPC.

Methods: Using the Gehan design, the study initially enrolled 14 patients. If at least one R0 resection was observed, the enrolment would continue to 25 patients to better estimate R0 resectability. SBRT (30 Gy in 5 fractions) was scheduled between the first and second cycles of CHT, with a minimum of 10 days after the second CHT cycle. CHT continued until week 20 post-SBRT, followed by re-evaluation via contrast- enhanced triphasic CT (tCT), based on RECIST criteria, for potential surgical intervention.

Results: The median follow-up and age of the 14 enrolled LAPC patients (2018-2022) were 24 months (range: 8-39) and 69 years (range: 50-84), respectively. Treatment included one cycle of CHT, SBRT (VMAT 30 Gy/5 fx), and five cycles of CHT post-SBRT. CHT regimens were gemcitabine + Nab Paclitaxel (14.2%) and FOLFIRINOX (85.8%). Median tumor diameter and CA19-9 levels pre- and post- treatment were 4.0 cm (range: 2.0-7.0 cm), 270.0 U/ml (range: 0.8-6129.0), and 53.0 U/ml (range:
0.8-278.8), respectively. Outcomes included five partial responses (38.5%), six stable diseases (46.1%), and two progressive diseases (15.4%). The resectability rate was 21.4%, with two R0 and one R1 resections. One case of Grade 3 late toxicity (gastric ulcer) was recorded. Median, 2-

year, and 3-year OS, LC, DMFS rates were 24, 20, and 10 months; 38.5%, 36.4%, and 31.3%; 19.2%, 36.4%, and 0.0%, respectively. Median OS was significantly higher in pancreatic body tumors compared to head tumors (38 vs 22 months, p=0.05).

Conclusions: Anticipated SBRT in combination with modern CHT regimens appears effective and well- tolerated, enhancing the resectability of unresectable LAPC. With two R0 resections achieved, the study will extend to 25 patients.

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IMMUNOTHERAPY (IT) OR TARGETED THERAPY (TT) COMBINED WITH STEREOTACTIC RADIOTHERAPY (SRT) FOR MELANOMA BRAIN METASTASES (BM): PRELIMINARY RESULTS FROM A MULTICENTRE RETROSPECTIVE STUDY ON BEHALF OF AIRO NEURO-ONCOLOGY (NO) GROUP

Code: 548

Aims: Despite guidelines for melanoma patients with asymptomatic BM would suggest to defer local therapy until the evidence of progression in favor of IT (Ipilimumab and Nivolumab) or TT (Dabrafenib and Trametinib), there is a lack of randomized evidence for oligo-BM. To define efficacy and toxicity of IT or TT with SRT, including radiosurgery (SRS) or hypo-fractionated SRT (HF-SRT), for melanoma BM in a multicentre retrospective study on behalf of AIRO NO Group.

Methods: Patients with melanoma BM receiving SRT + IT or TT (within 28 days) treated in 7 Italian Centres were preliminary analyzed.

Results: 94 melanoma patients with 193 (median 1; range, 1-12) BM received concurrent SRT + IT or TT. Median age and median PS were 63y (25-85) and 0 (0-2), respectively. 38 (40%) patients developed BM during TT or IT (oligo-progressive patients), while 56(60%) developed BM without an active treatment (oligo- recurrent patients); 85 (90%) received upfront SRT (i.e. at the time of radiological evidence of BM), while 9 (10%) delayed SRT (i.e. at the evidence of brain progression after upfront TT or IT). 64 (68%) received LINAC-based SRT, the others Cyberknife. 73 (78%) patients underwent SRS with a prescribed median dose of 24Gy (15-24), the remaining 21 (22%) HF-SRT with a median dose of 25Gy (21-35) in 3/5 fractions. Median volume of treated lesions was 0.98cc (0,09-35). All patients received IT or TT within 28 days of SRT (median time 10 days), 64 (68%) received IT, 30 (32%) TT. Median follow-up of 25 months (6-102). 11 (12%) patients developed local recurrence on at least one treated lesion. The median local- recurrence free survival (LR-FS) was not reached, 1-, 3-year LR-FS was 93%, 86%. 49 (52%) patients had intracranial progression outside the treated lesions. The median brain-progression FS (BP-FS) was 15 months (11-68), 1-, 3-year BP-FS was 51%, 42%. The median overall survival (OS) was 44 months (15-102), 1-, 3-year OS was 74%, 55%. 5, 11, and 3 patients developed G1, G2, and G3 radionecrosis (RN), respectively. No case >G3 RN was observed.

Conclusions: Our data confirm the efficacy of SRT and support the feasibility and safety of the combination of SRT+IT or TT, showing good tolerability (only 2% of patients developed G3 RN). We disagree with the "interpretation" that IT or TT alone approach should be considered as the first-line therapy in asymptomatic oligo-BM melanoma patients, suggesting that combined approach of IT or TT+SRT should be considered the first choice in this setting of patients.

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LONG-TERM RESULTS OF THE MIXED BEAM APPROACH FOR LOCALLY- ADVANCED NASOPHARYNGEAL CANCER

Code: 462

Aims: Management of locally advanced nasopharyngeal cancer (LANPC) is challenging due to poor rates of both local and distant control. The combination of intensity-modulated radiotherapy (IMRT) followed by intensity-modulated proton therapy (IMPT) boost yields the promise of improving patients' outcomes.
While results on acute toxicities have already been reported, aim of this work is to evaluate long-term radiation-related side effects and oncological outcomes, within a phase II study.

Methods: Inclusion criteria were histological diagnosis of either keratinizing/non-keratinizing/basaloid-squamous- cell primary LANPC (i.e., cT3–T4 cN0–N3 cM0), availability of dosimetric, oncological, and toxicity follow-up (FU) data, and written informed consent for research purposes. Acute and late toxicities were evaluated according to CTCAE v. 4.03, with toxicities of grade (G)≥3 considered severe. All patients (pts) received IMRT (total dose of 54-60 Gy, 2 Gy/die, 5 fractions a week) and subsequent boost with IMPT (total dose of 70-74 Gy [RBE], 2-3 Gy [RBE]/die, 5 fractions a week).

Results: Overall, 41 pts were included in the analysis. Median age was 49 (IQR: 40-58) years, and median Charlson Comorbidity Index was 3 (IQR: 2-4.5), with all pts having a performance status of 0 or 1. Histology was keratinizing in 3 cases, non-keratinizing in 34, and basaloid in the remaining 4. Stages were almost equally distributed between III and IVA according to the TNM 7th Edition. All pts received platinum-based concurrent chemotherapy and 26 pts received induction chemotherapy. Median total dose was 70 Gy. Considering severe acute toxicity, the most common was hematological (8 pts), followed by dysphagia (4), mucosal toxicity (2), and skin toxicity (1). No G4 toxicity was reported. After a median FU time of 44 (IQR: 29.3-69.3) months, most pts were alive with no evidence of disease (26/41, 63%), while four pts were alive with disease. Overall, 7 pts were deceased at last FU: the cause was LANPC in 4 cases, and other- non-oncological causes- in 3. Considering the higher degree of toxicity registered during the course of FU, three pts experienced G3 late toxicity. These were visual impairment, osteoradionecrosis, and nasopharyngeal stenosis. At the last FU, none of the pts described clinically-relevant toxicities.

Conclusions: After a median FU of almost 4 years, the mixed beam approach proves to be feasible, safe, and effective. Further prospectively collected series are needed to confirm our results.

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LOCALLY ADVANCED NSCLC: OVERVIEW OF PATTERN OF RECURRENCE IN DURVALUMAB ERA (LEOPARD TRIAL)

Code: 265

Aims: The treatment outcome of locally advanced non-small cell lung cancer (LA-NSCLC) has been improved over the past years, above all due to use of Durvalumab (Durva) after chemo-radiation (CRT) but local failure is still common for these patients (pts) and pattern of failure is still unclear.

Methods: We retrospectively evaluated the pattern of recurrence of LA-NSCLC pts after CRT and Durva, treated between January 2018 and December 2021 in 8 Italians centers. Primary endpoint is the pattern of recurrence, evaluated in terms of oligoprogression (OPD) versus pluri-station progression (PPD) and in field-recurrence versus out-field recurrence. Secondary endpoints are: PFS, OS, salvage therapy and toxicity.

Results: 167 pts with LA-NSCLC were identified. The median age for the cohort was 67 years and majority of pts were males (70 %). 88 (66.7%) pts had stage IIIA, while 44 (33.3%) had stage IIIB. 92 (70%) pts were treated with concurrent CRT. The median follow-up was 30 months. At last follow up time 60 (45%) pts experienced disease relapse/progression; of these, 39 (65%) pts experienced OPD. The most frequent site of relapse/progression was the brain, alone or in association with another organ (14), followed by lung (12), adrenal gland (4) and mediastinal lymphnodes (3). 22 experienced an in field relapse; of these 12 fell into the OPD category and the remaining 8 in the PPD category. The salvage therapy in OPD group was RT alone or in combination with systemic therapy in 24 pts; most of these underwent stereotactic RT (SRT). At last follow up, we have 27 pts who died, of which 20 from NSCLC and 7 from other causes. Median OS for the entire cohort was not reached. The estimated 1-, 2- and 3-year OS rate were 89 %, 76%, and 55%, respectively. The median PFS was 23 months. The estimated 1-, 2- and 3-year PFS rate were 64%, 48%, and 33%, respectively. No difference in OS were highlighted based on the type of relapse (ODP vs. poliPD) or the site of relapse (in field vs. outfield). A difference in PFS was shown between OPD and poliPD ($p<0.0001$) with a 1-year PFS of 33% and 19%, respectively; a difference in PFS between patients who have a relapse in the field compared to those who have an out-field relapse is also evident ($p<0.0001$) with a 1-year PFS of 40% and 20%, respectively.

Conclusions: OPD appears to be a very frequent event in these patients and opens future prospects for local treatments, such as SRT.

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VENTRICULAR TACHYCARDIA ABLATION THROUGH RADIATION THERAPY (VT-ART): A WIDE COHORT MULTICENTER ANALYSIS OF EFFICACY AND HOMOGENEITY OF APPROACH

Code: 595

Aims: Ventricular Tachycardia Ablation by Radiation Therapy (VT-ART) for ventricular tachycardia (VT) is promising. Definitive data on efficacy are lacking. Most of the available international literature accounts for less than 20 enrolled patients -pt-. Defining the best RT procedure is also an issue. Aim of this multicenter study is to evaluate VT-ART's homogeneity and efficacy on a large cohort

Methods: We collected pt undergone VT-ART for refractory VT, within a spontaneous network among Centers having performed preliminary experience for limited series, outside clinical trials. No restriction about pt selection and VT-ART treatment administration were applied. Collected variables focused on both treatment efficacy and procedural homogeneity

Results: Six Italian Centers collaborated, enrolling 23 pt. Not each of the data required by the promoting Center were available for all the sub-series, depending on the center's trend for default data collection. Based on the shared variables: range of recruitment was September 2019-October 2023; all pt were male; mean pt age was 69,7 years (range, 52-87). Pretreatment mean left ventricular ejection fraction was 33% (range22-50). All pt underwent at least one radiofrequency catheter ablation. Linac dedicated to SBRT was used in 11/21(52,4%) pt; 6/21 (28,6%) used MRgRT; 4/21 (19%) used conventional Linac. In 7/21 (33,4%) free breathing 4D simulation, and in 12/21 (57%) a gated breath hold (deep inspiration) was performed. Target delineation procedure varied among Centers. Although choosen references for constraints were similar among centers, the applied ones ranged 1-7 different guidelines. The mean CTV volume of the was 71,3 cc (range 8.9-238.5). The mean PTV margin provided was 3,3 mm (range 3-5).
For all pt, SBRT was performed with a dose of 25 Gy in single fraction; prescription isodose was 97% in 1/21, 95% in 3/21, 94% in 1/21, 80% in 15/21 pts, 75% in 1/21(mean 87,5%). PTV mean Dose was 27,6 Gy (23,4-29,7). Briefly, each of the 6 RT Centers applied its IGRT inner rule; online monitoring was performed through 4D gating control in all cases adding peculiar approaches in 2/6 Centers

Conclusions: The presented series is one of the largest collected. Feasibility of VT-ART seems confirmed. High homogeneity in dose prescription is confirmed. Main differences on details of delineation, treatment planning and procedural settings are reported. For brevity further details will be specified at the conference

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ORBITAL RADIOTHERAPY FOR GRAVES OPHTHALMOPATHY: SINGLE-INSTITUTIONAL EXPERIENCE OF EFFICACY AND SAFETY

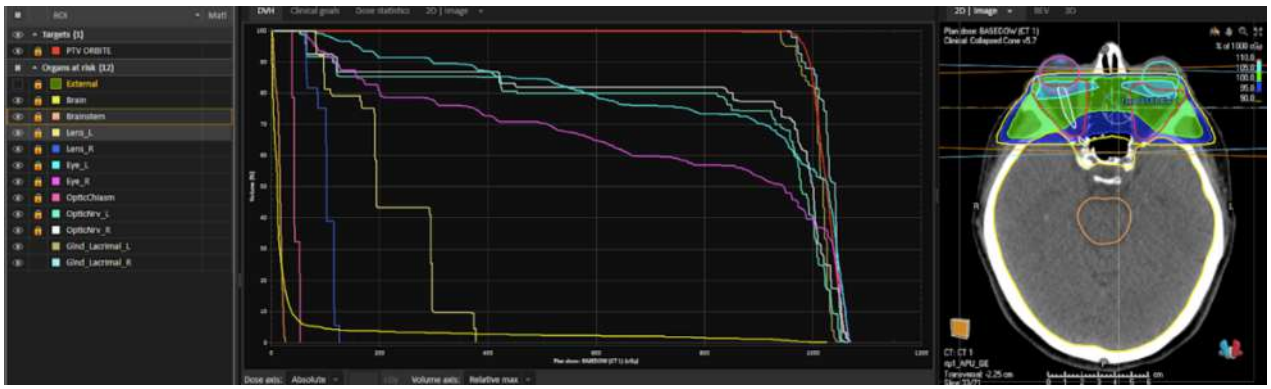
Code: 439

Aims: Graves' Ophthalmopathy (GO) is an autoimmune disease that mainly affects the retrobulbar soft tissues and represents the most frequent extrathyroidal manifestation in patients suffering from a particular form of hyperthyroidism (Graves-Basedow disease). Radiotherapy is effective especially during the active phase of the disease, in reducing the proliferation of fibroblasts and the production of glycosaminoglycans, responsible for edema. Its effectiveness increases when used in synergy with glucocorticoids administered intravenously. The aim of our study is to analyze the effectiveness and safety of radiotherapy in improving symptoms such as periorbital edema, reduction of vision, ocular motility and proptosis.

Methods: Between January 2002 and June 2023, 188 patients (125 women and 63 men) with GO were treated with retrobulbar radiotherapy using a schedule of 10 Gy/10 fractions and during SARS/COVID-19 pandemic 10 Gy/ 5 fr using 6 MV photon beam, with a 3D conformal technique administrated with 2 lateral fields, tilting the beams posteriorly with a personalized angle between 5 and 7 degrees to spare the lens and contralateral ocular areas. Radiotherapy was administrated during the 12 weeks of pulse steroid therapy (weekly hydrocortisone e.v. bolus). Patients were assessed with clinical exam, orbital MRi and, tyroid assessment (TSH, T3, T4, FT4 levels), proptosis measured with the Hertel exophthalmometer and CAS (Clinical Activity Score) > 4.

Results: In the acute phase, 30% of patients showed conjunctival hyperemia, which disappeared with the use of eye drops. No cases of xerophthalmia were observed Complete response to treatment was found in 80 patients (42.5.%), partial response or stabilization in 100 pts (53.3%) and progression in 8 (4.2%). In all patients except those who progressed, an almost complete reduction of CAD of at least 2 points, proptosis (reduced by more than 3 millimeters) and improvement in visual acuity was observed.

Conclusions: Radiotherapy is an effective and well-tolerated treatment in the case of GO. Better response rate is observed in case of association with the administration of glucocorticoids. Although the most commonly used fractionation schedule is that of 20 Gy/10 fr, in our clinical practice we have achieved comparable results with the 10 Gy in 5 or 10 fr schedule, with a lower incidence of toxicity.



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RETREATMENT FOR RESISTANT OR RECURRENT PAIN IN TRIGEMINAL NEURALGIA USING FRAMELESS LINAC RADIOSURGERY

Code: 54

Aims: Recurrent or resistant pain is a well know occurrence following surgical and radiosurgical treatments for Trigeminal Neuralgia. We reported pain control and complications in a large serie of patients (pts) undergoing Cyberknife radiosurgery retreatment as long as safety and efficacy of retreatments are poorly known.

Methods: The protocol for the first treatment aims to deliver an homogeneous radiation dose to an extended segment (6 mm) of the trigeminal nerve. Retreatments are performed on pts resistant to treatment (no pain improvement within 6 months) or with temporary clinical benefit and subsequent recurrent pain. A lower dose is typically prescribed for the second treatment to reduce the risk of sensory complications. Pain control and sensory complications are assessed using the dedicated BNI scales.

Results: 93 pts underwent retreatment for resistant or recurrent trigeminal pain were included. Mean age was 61,3 years (range 29-89). Mean interval between first and second treatment was 24.2 months (range 4-136 monts). 15 pts (16.1%) were retreated within six months for resistant pain. 25 pts (26.9%) within 12 months while 53 pts (57%) were retreated for recurrent pain at later time (12 to 136 months). Three pts required a third treatment. Mean dose delivered at the first treatment was 58.5 Gy (range: 30-75 Gy), prescribed to a mean 82.6% isodose (range 77-89). Mean dose delivered at the second treatment was 45.3 Gy (range: 30-63 Gy), prescribed to a mean 83.2% isodose (range:79-89). Mean volume at the first treatment was 28.8 mm^3 (range: 9-55) while 25.1mm^3 (range: 8-44.4) at the second. One year after the second treatment satisfactory pain control was achieved in 85 out of 93 pts (91.4%) and remained stable after 3 and 5 years. Sensory complications appeared in 27 pts out of 93 (29.3%) after 1 year and showed a mild improvement over the following years. Somewhat bothersome facial numbeness (BNI grade III) was found in 18 retreated pts (19.4%) while very bothersome facial numbess (BNI grade IV) developed in 3 pts (3.2%). No other neurological complication was found.

Conclusions: Radiosurgical retreatments for resistant or recurrent trigeminal pain are safe and effective and provide a high rate of long-term pain control.This comes at the price of a higher rate of sensory complications.
Further studies are needed to confirm results and assess wheter the rate of sensory complications can be reduced while preserving long-term pain control.

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LINAC-BASED STEREOTACTIC ARRHYTHMIA RADIOABLATION (STAR) FOR ATRIAL FIBRILLATION AND VENTRICULAR TACHYCARDIA: EXPERIENCE AND RESULTS OF A SINGLE CENTER

Code: 81

Aims: Stereotactic arrhythmia radioablation (STAR) is a novel therapeutic approach for cardiac arrhythmias including Ventricular Tachycardia (VT) and atrial fibrillation (AF). This analysis aims to investigate the safety and effectiveness of STAR for the treatment of paroxysmal atrial fibrillation (AF) in elderly patients (pts) and VT.

Methods: Pts who underwent cardiological assessment, resulting unable to receive other forms of therapy for VT, were enrolled to receive STAR-VT. For AF, instead, inclusion criteria were age >70 years, symptomatic AF, antiarrhythmic drug failure or intolerance. All pts underwent 4D cardiac computed tomography simulation. The Clinical Target Volume was identified in the area around pulmonary veins (PV) for AF, while for VT the contoured volume was strictly limited to regions of abnormal myocardium. Internal Target Volume (ITV) and Organs at Risk (OARs) planning risk volume (PRV) were generated to compensate for heart and respiratory movement. The Planning Target Volume (PTV) was defined by adding 0-3 mm to the ITV in all directions. STAR was performed with a total dose of 25Gy (single fraction). Treatment tolerance and effectiveness were evaluated during follow up.

Results: From September 2019 to September 2023, 21 pts were treated: 18 for AF and 3 for VT. With a median follow-up (FU) of 24 months (range 4–52), no acute toxicity Grade ≥3 was reported. Six pts had a Grade 1 oesophagitis 24 h after STAR; ten pts had an asymptomatic Grade 1 pericardial effusion, and one patient had a torsade de pointes treated effectively by electrical cardioversion and subsequent cardiac implantable cardioverter-defibrillator implantation. Most pts had a significant reduction in arrhythmia episodes. In the AF group, due to arrhythmias recurrences after STAR, five pts performed an electrophysiological study documenting successful PV isolation. Finally, a significant improvement in quality of life was reported according to EuroQol VAS (Visual Analogue Scale) (48 ± 15 at enrolment vs 75 ± 15 at 12 months FU; $P < 0.001$). In the VT group, one patient died after two years from STAR due to heart failure; in other two pts, after 4 and 10 months from STAR, no other arrhythmic episodes were documented by ICD.

Conclusions: The present data regarding STAR for VT and AF suggest its safety and potential role in increasing the quality of life, offering an alternative approach to medical needs. Indeed, more robust data are needed about safety and efficacy.

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PATIENT REPORTED OUTCOMES (PROs) IN ANAL CANCER PATIENTS TREATED BY INTENSITY MODULATED RADIOTHERAPY (IMRT)

Code: 512

Aims: Intensity modulated radiation therapy (IMRT) – based chemoradiation has confirmed its superiority in squamous anal cancer (AC) treatment in terms of tumor control improving treatment-related toxicities. However, the incidence of late toxicities continues to be a burden for survivors. In this study we prospectively analyze long term QoL of anal cancer patients (pts) through Patient-Reported Outcome (PROs).

Methods: Survivors from AC who had ended radiotherapy for at least one year were analyzed. QoL were analyzed using EORTC QLQ-C30 (cancer-specific) and QLQ-ANL27 (anal site-specific) questionnaires according to pts, tumor, and treatment characteristics. A scale from 1 to 4 is used to rate each question (not at all to very much) except for the overall health,where a scale of 1 to 7 was used (very poor to excellent).

Results: 52 pts were analyzed. Median follow-up was of 46 months (range 15,4-106 months). QLQ-C30 questionnaire indicated a mean global health status of 76,8 (SD 18,6), a mean physical functioning of 86,4 (SD 13,7), role functioning of 87.8 (SD 16,9), emotional functioning of 80 (SD 19,7), cognitive functioning of 85 (SD 19,2), and social functioning of 85 (SD 22).
For the QLQ-ANL27 questionnaire bowel function impairment was reported in 45% of pts. Bowel function issues relating to urgency and frequency were reported as "quite a bit" or "very much" in 19% and 10% of pts.The mean bowel function (non-stoma) was 27.4 (SD 21.5). Commonly reported symptoms included a need to be close to the toilet (mean 20,3, SD 29,1), cleaning oneself more often (mean 19,7 SD 27), and planning activities (mean 17,7 SD 29,7); 57.6% of pts reported not being sexually active and 44% reported that AC and its treatment had affected their sex life "quite a bit" or "very much".
35 females addressed on sexual function items with a mean score of 64,9 (SD 30). Prevalent responses as "not at all"/ "a little" options were identified for swelling in the legs or ankles (90.3%). At univariate analysis age >= 60 y showed a significant correlation with impairment of bowel function (p 0.02) and sexual function in female pts (p< 0.001).

Conclusions: Specific toxicities related to sphincter function and sexual dysfunction were primarily responsible for deterioration of the long-term QOL. This analysis shows that PROs could provide a greater understanding of patients' perception of treatment side effects. Future research aimed at reducing such toxicities is needed to further improve long-term QOL in anal cancer.

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QUANTITATIVE TUMOR VOLUMETRIC RESPONSES AFTER GAMMA KNIFE (GK) RADIOSURGERY FOR SPORADIC VESTIBULAR SCHWANNOMA (VS)

Code: 383

Aims: Stereotactic radiosurgery is the standard of care for treatment of VS, as well as exclusive treatment, adjuvant therapy after an incomplete surgery, or at relapse. Local control (LC) is the main focus of the treatment, excluding the need for further intervention. Preserving hearing function (HF) and facial nerve functionality (FNF) are also extremely important goals of the therapy, together with control of trigeminal and vestibular symptoms. The aim of this study is to evaluate the efficacy of SRS with GK in sporadic unilateral VS.

Methods: Patients (pts) with unilateral sporadic VS treated at our center with GK were included. All patients had evaluable pre- and postoperative T1-weighted contrast-enhanced magnetic resonance (MR); last available follow-up (FUP) tumor volumes were compared with baseline volumes. HF was determined with audiograms performed as per clinical practice; FNF, vestibular and trigeminal symptoms were scored with the House Brackmann Scale (HBS) and CTCAE 5.0 scale, respectively. An observational retrospective analysis was conducted.

Results: A total of 71 consecutive pts treated with GK between 2012 and 2019 were included. Median FUP time from GK was 67 months (36-122), with a minimum FUP of 36 months. Median age at GK time was 59 years (29-80). The median dose delivered was 12.5 Gy (12-13) at the isodose of 50%. Fifteen (21%) pts underwent SRS after surgery: 7 as adjuvant therapy and 8 at relapse. The median volume of lesions treated was 2,16 cc (0,09- 7,64) at GK time and 1,4 cc (0,07-5,19) at the last MR. In 60 cases (85%) we observed a reduction of lesions treated, with a mean volume decrease of 54% (15-95%); 4 lesions remained stable and in only 7 cases there was a volume increase, without the need of reintervention. At last FUP, HF was partially recovered in 38% of pts with complete HF loss at diagnosis (8 pts out of 21); for 72% of pts it remained stably impaired, while it was mildly reduced in only 1 pt out of 4 that had initially fully conserved HF. Tinnitus ceased in 79% of cases (15 out of 19) and 95% of pts had dizziness disappearance (21 out of 22). Three pts with initial altered FNF had a full recovery; we observed 3 new cases of FNF deficit, all in pts previously treated with surgery (HBH 2-4). Finally, 3 pts out of 4 that had initial trigeminal symptoms had a full recovery. Details of symptoms are listed in table 1.

Table 1

	At GK	Grade (HSB or CTCAE)	At last FUP	Grade (HSB or CTCAE)
Hearing function	Normal: 4	-	Normal:3 Mildly impaired:1 Complete loss: 0	-
	Mildly impaired: 46	-	Normal: 7 Mildly impaired: 33 Complete loss: 6	-
	Complete loss: 21	-	Normal: 0 Mildly impaired: 8 Complete loss: 13	-
Vestibular symptoms	Absent: 32	-	Absent: 24 Tinnitus: 7 Dizziness: 2	- All G1 All G1
	Tinnitus:19	all G1	Absent: 12 Tinnitus: 5 Dizziness: 3	- All G1 All G1
	Dizziness: 22	all G1	Absent: 17 Tinnitus: 4 Dizziness: 4	- All G1 G1=3, G2=1
Facial nerve functionality	Normal: 65	-	Normal: 62 Impaired: 3	- HBS 2=2 HBS 4=1
	Impaired: 6	HBS 2=1 HBS 4=3 HBS 5=2	Normal: 2 Impaired: 4	- HBS 2=2 HBS 3=1 HBS 6=1
Trigeminal symptoms	Absent: 67	-	Absent: 67 Present: 0	- -
	Present: 4	all G1	Absent: 3 Present: 1	- G1

Conclusions: To our analysis, GK treatment for sporadic VS is confirmed as a safe and effective option in terms of LC and symptoms management.

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IMPACT OF ADJUVANT RADIOTHERAPY ON FATIGUE IN BREAST CANCER PATIENTS: A 10-YEAR SINGLE INSTITUTIONAL EXPERIENCE IN 1002 PATIENTS.

Code: 413

Aims: Fatigue is one of the most common symptoms reported by cancer patients with negative consequences on patients' daily social life and quality of life, even after treatments. Herein we evaluated the impact of radiotherapy (RT) on the fatigue of breast cancer (BC) patients.

Methods: BC patients who received an adjuvant RT treatment between 2009-2019 and with at least one year of follow-up were retrospectively analyzed. Patient's characteristics including age and comorbidities, treatment factors such as Hormonal Therapy (HT), Chemotherapy (CT), RT dose and fractionation, and related toxicities were registered. Fatigue level was measured through the Cancer Linear Analogue Scale (CLAS) for quality of life (CLAS1), energy level (CLAS2), and ability to perform daily activities (CLAS3). These parameters were assessed before RT [T0], at one month [T1], and twelve months [T2]. Two Scores (ScRT10 and ScRT20) were obtained by subtracting the CLAS values at T1 and T2 from the T0 values. A decrease of ≥2 points in quality of life, energy level, and ability to perform daily activities was considered clinically significant for RT-related fatigue onset.

Results: 1002 patients were evaluated. Median age was 59 years (range, 27-85). RT was delivered in 16 or 25 fractions in 33% and 67%, respectively. HT and CT were administered in 95% and 54% of the overall population, respectively. At T1, the RT-related fatigue onset (decrease of CLAS1, 2, and 3 values) was observed only in 9.5%, 12.1%, and 12.4% of the overall population, respectively. Similarly, at T2, the RT- related fatigue onset was observed only in 12.7%, 16.1%, and 15.7% of patients, respectively. In the logistic regression investigating variables increasing the RT-related fatigue onset, we found that acute RT toxicity > G1 reduced the energy level at both T1 and T2 (p:0.042 and p:0.006, respectively), while HT mainly reduced the quality of life and ability to perform daily activities at T2 (p: 0.025 and p: 0.023, respectively). Surprisingly, previous CT administration was associated with reduced RT-related fatigue, as expressed by an increase in all CLAS values ($p<0.001$) (Table 1).

Conclusions: In a large BC series, RT-related fatigue onset was reported in a minority of cases. CLAS values were negatively affected by HT and treatment toxicity. The positive impact of CT on RT-related fatigue was probably due to the CLAS low values at T0 of chemo-treated patients that progressively increased during the RT course.

Table1. Clinical variables increasing RT-related fatigue (logistic regression)

		CLAS1		CLAS2		CLAS3	
Variables	**Yes/No increase**	**1 month [T1]**	**1 year [T2]**	**1 month [T1]**	**1 year [T2]**	**1 month [T1]**	**1 year [T2]**
Age <60 years	Yes	0.001	---	---	---	---	---
Standard Fractionation	Yes	---	---	0.038	---	---	---
Acute toxicity >G1	Yes	---	---	0.042	0.006	---	---
Hormonal Therapy	Yes	---	0.025	---	---	---	0.023
Prior Chemotherapy	No	<0.001	---	<0.001	0.010	<0.001	0.017
Smoking habit	Yes	---	0.001	---	---	---	---
Alcohol assumption	No	0.007	---	---	---	---	---

G: grade of toxicity

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BUTTERFLY GLIOBLASTOMA: CAN HYPOFRACTIONATED RADIOTHERAPY LEAD TO BETTER CHANCES OF SURVIVAL, IMPROVING QUALITY OF LIFE?

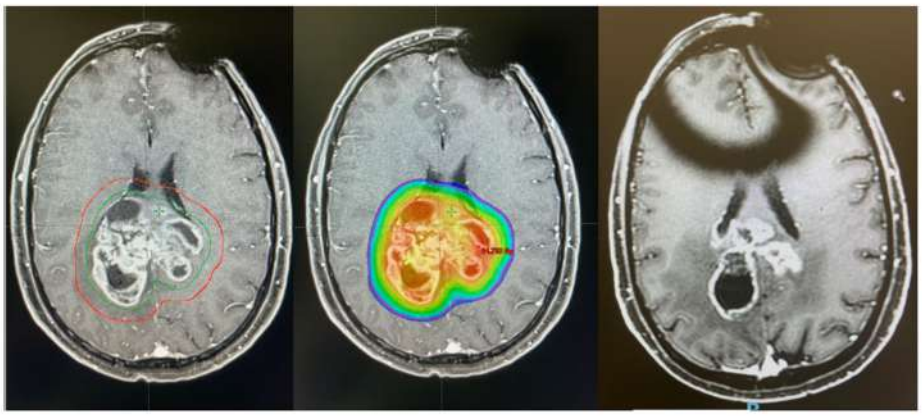
Code: 555

Aims: Butterfly glioblastomas (bGBM) are a rare type of malignant brain tumor, with a very poor prognosis, (median overall survival, OS, 3.3-6 months). Hypofractionated RT (Hypo- RT) could be evaluated for these patients to improve OS and quality of life (QoL). Thus, a retrospective analysis was performed.

Methods: Between January 2020 and June 2023, 164 high-grade gliomas were treated with radiotherapy. The bGBM were retrospectively evaluated. Hypo-RT scheduled as 52.5/40.5 in 15 fractions, 35GY in 10 fractions, or 25Gy in 5 fractions was used for these cases, and performed by Volumetric modulated arc therapy.

Results: Out of 164 patients, 62 were female, and 102 were male. Seventy-eight patients received a hypo-RT of 40.5/52.5 GY in 15 fractions, while 89 patients were treated with RT according to the STUPP protocol. RT was associated or not to concomitant Temozolomide. Ten cases out of 164 (6%) were identified as bGBM: 2 were female, and eight were male. Median age was 51 (range 39-70), and KPS was 50 (30-70). These patients were managed with biopsy (40%), or through surgical partial resection (60%). Regarding RT, with a median days between surgery and RT of 42, eight patients received hypo-RT in 15 fractions, one patient in 5 fractions, and one patient in 10 fractions. Only one patient with worsening clinical conditions could not complete RT (total dose of 17.5Gy in 5 fractions). For all patients, no acute toxicity greater than grade 3 was observed. Eight patients received concomitant TMZ during radiotherapy, while all patients received adjuvant TMZ (median cycles 10). For 80% of cases, recurrence was confirmed at 9-12 months (range 6-24), and in 4 cases, a reirradiation was performed and 3 patients underwent second line chemotherapy with Regorafenib or Bevacizumab. With a median follow-up time of 14 months (range 5-45), five patients died: 4 for progression disease and 1 for systemic infection during second-line chemotherapy with regorafenib. The median OS was 13 months. In terms of quality of life, clinical improvement was observed in all patients (median KPS after RT: 60). Post radiation patients have decreased incidence of symptoms like headache and seizures, and an improvement in motor functioning, weakness of leg and communication deficit.

Conclusions: Butterfly glioblastoma has a poor prognosis. Hypo-RT is a safe and effective weapon to offer in these cases, reporting favorable outcomes, a decrease symptoms and better QoL.



RMN preRT | Hypo-RT: 52.5Gy | RMN post-RT

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IMPACT OF ACUPUNCTURE (ACP) ON ACUTE DYSPHAGIA IN PATIENTS TREATED WITH RADIO-CHEMOTHERAPY FOR HEAD AND NECK SQUAMOUS CELL CARCINOMA: PRELIMINARY RESULTS FROM A RANDOMIZED PHASE 2 STUDY (NCT 05143268)

Code: 393

Aims: In HNSCC patients receiving curatively intended radio-chemotherapy (RCT) dysphagia, both disease- and treatment-related, is frequently assessed and this may result into malnutrition and clinical deterioration. Acupuncture (ACP) has been explored for xerostomia and pain relief, but its impact on dysphagia remains unclear. An Italian, multicentric, randomized phase 2 study aimed to assess the effect of ACP and standard treatment on swallowing function using the MDADI (MD Anderson Dysphagia Inventory) scale 2 weeks post RT completion. Here, we present preliminary results on ACP adherence and its safety in the experimental arm.

Methods: Patients diagnosed with HNSCC suitable for radical non-surgical treatment (RT alone, platinum based CTRT, RT+ cetuximab) from 6 Italian centers were eligible. Inclusion criteria were age ?18, ECOG PS 0-2, stage I-III for oropharyngeal cancer (OPC) HPV+, stage II-IVB for non-OPC HPV- carcinoma and accessibility to ACP service with oncological experience. Patients were randomly assigned in a 1:1 ratio to experimental arm (weekly ACP from 2 weeks before the beginning of RT up to 2 weeks after the end of treatment for a total of 11 sessions) or to standard arm. Patients were asked to fill in EORTC QLQ-C30, QLQ-HN43 and MDADI questionnaires at baseline and 2, 12 and 24 weeks after treatment. The use of ACP was hypothesized to yield a 10 point improvement in mean MDADI composite score compared with historical data (from 58 to 68; ?=0.05, beta=0.80, sample size=90).

Results: From June 2021 to November 2023, 91 patients were enrolled (ACP, n=44; standard arm, n=47). All were treated with IMRT and 71 with concomitant systemic therapy, whereas 81 underwent bilateral neck irradiation. Baseline characteristics of enrolled patients are reported (Tab. 1). Among those undergoing ACP and whose compliance data were available (n=38), adherence to ACP was excellent (100%), very good (99-75%), good (74-50%), poor (49-25%) and very poor (<25%) in 20, 6, 6, 3 and 3 cases, respectively. Most frequent reason for APC early discontinuation was worsening of clinical conditions requiring hospitalization (n=2) or supportive care (n= 4). None had side effects from ACP.

Conclusions: Our preliminary compliance results showed that weekly ACP is feasible and well tolerated in patients undergoing radiation-based treatment for locally advanced HNSCC. Its impact on acute dysphagia is still under investigation.

Table 1- Patients' characteristics

CHARACTERISTICS	N (%)
Total patients	91
Males	60 (66)
Females	31 (34)
Age (years)	
Mean	65.01
Range	48-84
Charlson Comorbidity Index (CCI)	
Mean	4.7
Range	2-8
Weight (kg)	
Mean	72.8
Range	47.7-117
Tobacco exposure	
Never smoker	36 (40)
<10 p/y	6 (7)
10-20 p/y	19 (21)
> 20 p/y	30 (33)
Alcohol exposure	
No/light drinking	75 (82)
Moderate drinking	12 (13)
Heavy drinking	4 (4)
Caregiver	
Absent	24 (26)
Present	67 (74)
Tumor primary	
Larynx	11 (12)
Nasopharynx	8 (9)
Oropharynx	70 (77)
Hypopharynx	2 (2)

HPV status	
Positive	51 (56)
Negative	25 (27)
Not Assessed	15 (16)
T stage	
Tx	1 (1)
T1	10 (11)
T2	46 (51)
T3	19 (21)
T4a	13 (14)
T4b	2 (2)
N stage	
N0	20 (22)
N1	38 (42)
N2a	13 (14)
N2b	6 (7)
N2c	8 (9)
N3	6 (7)
Stage Group	
I	25 (27)
II	25 (27)
III	24 (26)
IVa	15 (16)
IVb	2 (2)
Type of treatment	
RT alone	20 (22)
RT + platinum based CT	69 (76)
RT + cetuximab	2 (2)

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DOES CURATIVE RADIOTHERAPY IMPACT FATIGUE ONSET IN PROSTATE CANCER PATIENTS? AN ANALYSIS OF 1253 PATIENTS

Code: 385

Aims: Fatigue is a symptom frequently related to cancer and its different treatments. The negative impact on the physical and psychological health of cancer patients is well reported. In this study, the impact of radiotherapy (RT) on the fatigue of prostate cancer (PC) patients was evaluated in a large population.

Methods: PC patients undergoing a radical treatment between December 2002 and September 2022 were retrospectively evaluated. Patient's characteristics including age and comorbidities, Androgen-Deprivation Therapy (ADT), RT dose and fractionation, and related toxicities were registered. Fatigue level was measured through the Cancer Linear Analogue Scale (CLAS) for quality of life (CLAS1), energy level (CLAS2), and ability to perform daily activities (CLAS3). These parameters were assessed before RT (T0), and after one- (T1) and 12 months (T2). Two Scores (ScRT10 and ScRT20) were obtained by subtracting the CLAS values at T1 and T2 from the T0 values. A decrease of ≥2 points was considered clinically significant for RT-related fatigue onset.

Results: 1253 patients were evaluated. Median age was 72 years (range, 45-90). The vast majority (67%) had no or 1 comorbidity and 80% of patients had an optimal performance status (ECOG: 0). RT was performed as exclusive treatment in 61% of patients and the ADT was administered to 84% of patients. The treatment was administered using hypo-fractionated or stereotactic schedules in 86% of patients, while the remaining 14% received standard schedules. At T1, the RT-related fatigue onset (decrease of CLAS1, 2, and 3 values) was observed only in 10.8%, 14.3%, and 14.8% of the series. Similarly, at T2, the RT-related fatigue onset was observed only in 12.7%, 18.8% and 19.4% of patients. In the logistic regression investigating variables increasing the RT-related fatigue onset, concomitant ADT, late toxicities, and the alcohol assumption were significantly associated with a worsening of RT-related fatigue at T2 in CLAS3 ($p<0.005$). Furthermore, we observed a correlation between RT-related fatigue worsening of CLAS2 at T1 and acute genito-urinary toxicities (p:0.016). Other clinical variables increasing RT-related fatigue are reported in Table 1.

Conclusions: In a large PC series mostly treated with modern techniques, RT-related fatigue onset was reported in <15% of patients. Treatment-related toxicities and factors unrelated to RT, such as alcohol assumption and concomitant ADT, play a significant role in fatigue onset.

Table1. Clinical variables increasing RT-related fatigue (logistic regression)

Variables	Yes/No increase	CLAS1		CLAS2		CLAS3	
		1 month [T1]	1 year [T2]	1 month [T1]	1 year [T2]	1 month [T1]	1 year [T2]
Age	No	---	---	---	---	---	---
Hypofractionation	Yes	---	0.004	0.023	---	0.014	---
Pelvic Nodal irradiation	No	---	---	---	---	---	---
Comorbidities	No	---	---	---	---	---	---
GU acute toxicity >G1	Yes	---	---	0.016	---	---	---
GI acute toxicity >G1	Yes	---	---	---	0.045	---	---
ADT	Yes	---	0.056	---	---	---	0.010
Smoking habit	No	---	---	---	---	---	---
Alcohol assumption	Yes	---	---	---	---	0.010	0.043
Late toxicity > G1	Yes	---	0.017	---	---	---	0.017

GU: genito-urinary; GI: gastro-intestinal; G: grade; ADT: Androgen-Deprivation Therapy

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Discussioni Poster

BASELINE RADIOMIC FEATURES FOR OUTCOME PREDICTION IN PATIENTS WITH EARLY-STAGE NON- SMALL CELL LUNG CANCER CANDIDATE TO STEREOTACTIC BODY RADIOTHERAPY

Code: 440

Aims: Patients diagnosed with early-stage non-small cell lung cancer (ES-NSCLC) often undergo curative-intent SBRT without histopathological assessment. This results into the unmet need of identifying non-invasive prognostic biomarkers. This study investigates the role of image filtering in computed-based radiomics in this setting, using a single-center, homogenous cohort from a tertiary care cancer center.

Methods: The following inclusion criteria were used: 1) adults with radiological and/or histopathological diagnosis of ES-NSCLC per the AJCC TNM 8th, 2) curative-intent SBRT to a minimum BED of 100 Gy (?/?=10 Gy), 3) availability CT simulation scans, 4) minimum follow-up of 12 months and 5) written informed consent availability. Outcomes of interest were OS, PFS and LPFS. The open-source IBSI-compliant Pyradiomics software v3.0.1 was used for both image pre-processing and radiomic features (RFs) extraction. All in-built filters were enabled, including permutations. Following the exclusion of RFs with zero variance and high correlation, an iterative clustering algorithm and a multivariable Cox—LASSO Regression Model were applied. Univariate Cox PH models were used to test associations between clinical variables and the radiomic score; variables with p ? 0.10 were included in multivariate and retained if the p-value was confirmed as ?0.10.

Results: One hundred patients with a median age of 76 and a median Charlson Comorbidity Index of 7 were identified. The most requent stage was IA2 (n=46). Higher-order RFs were consistently retained in all predictive models (13/15, ~87%), and led to the identification of a radiomic score with excellent discrimination ability, especially for PFS and LPFS (log-rank p= 0.00014 and log-rank p=0.00064, respectively). All but two of the LASSO-selected RFs (~ 87%) derived from filtered images, and mainly from the wavelet category. Results of the multivariable analyses for OS, PFS and LPS are shown in **Table 1**. Model performances were satisfactory and ranged between 0.67 (test set, radiomic model, PFS) and 0.95 (test set, radiomic model, OS), with the radiomic or clinico-radiomic models outperforming the hybrid models.

Conclusions: Baseline RFs from filtered CT images can improve prognostic stratification; the use of filtering should be encouraged as it seems to bring potentially-relevant informative content. The frequent inclusion of high-order features in the models suggests a potential association between tumor density and the investigated oncological outcomes.

OVERALL SURVIVAL									
Characteristic	**Clinical Model**			**Radiomic Model**			**Clinico-Radiomic Model**		
N	HR	95% CI	p-value	HR	95% CI	p-value	HR	95% CI	p-value
BED_value									
< med 124.8 Gy	—	—					—	—	
>=med 124.8 Gy	0.08	0.01, 0.69	**0.022**				0.15	0.01, 3.11	0.221
radiomic_score_os				1.47	1.17, 1.86	0.001	1.46	1.12, 1.90	**0.006**
n = 96.0; N events = 6.00; statistic.log = 7.59; p.value.log = 0.006; statistic.sc = 8.30; p. value.sc = 0.004; statistic. wald = 5.25; p.value.wald = 0.022; statistic.robust = NA; p.value.robust = NA; R^2 = 0.076; r.squared.max = 0.356; c-index = 0.809; c-index SE = 0.033; Log-likelihood = -17.3; AIC = 36.7; BIC = 36.5; No. Obs. = 96									
PROGRESSION-FREE SURVIVAL									
Characteristic	**Clinical Model**			**Radiomic Model**			**Clinico-Radiomic Model**		
	HR	95% CI	p-value	HR	95% CI	p-value	HR	95% CI	p-value
FEV1%`	0.98	0.97, 1.00	**0.020**				0.99	0.98, 1.00	0.181
Shape									
Round	—	—					—	—	
Complex	0.30	0.13, 0.71	**0.006**				0.40	0.17, 0.96	**0.039**
Oval	0.21	0.06, 0.75	**0.016**				0.27	0.07, 0.97	**0.046**
radiomic_score *10				1.45	1.25, 1.68	**<0.001**	1.35	1.13, 1.61	**<0.001**
n = 76.0; N events = 26.0; statistic.log = 13.9; p.value.log = 0.003; statistic.sc = 15.5; p. value.sc = 0.001; statistic. wald = 14.1; p.value.wald = 0.003; statistic.robust = NA; p.value.robust = NA; R^2 = 0.167; r.squared.max = 0.910; c-index = 0.712; c-index SE = 0.044; Log-likelihood = -84.6; AIC = 175; BIC = 179; No. Obs. = 76									
LOCAL PROGRESSION- FREE SURVIVAL									
Characteristic	**Clinical Model**			**Radiomic Model**			**Clinico-Radiomic Model**		
	HR	95% CI	p-value	HR	95% CI	p-value	HR	95% CI	p-value
FEV1%	0.97	0.95, 1.00	**0.019**				0.98	0.95, 1.00	0.096
radiomic_score_local				7.15	3.07, 16.7	<0.001	6.31	2.32, 17.1	**<0.001**
n = 76.0; N events = 12.0; statistic.log = 6.49; p.value.log = 0.011; statistic.sc = 5.97; p. value.sc = 0.015; statistic.wald = 5.51; p.value.wald = 0.019; statistic.robust = NA; p.value.robust = NA; R^2 = 0.082; r.squared.max = 0.650; c-index = 0.732; c-index SE = 0.104; Log-likelihood = -36.7; AIC = 75.4; BIC = 75.9; No. Obs. = 76									

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RESULTS OF AIEOP LH-2004 PROTOCOL FOR CHILDREN AND ADOLESCENTS WITH HODGKIN LYMPHOMA: ANALYSIS OF SECONDARY MALIGNANT NEOPLASMS

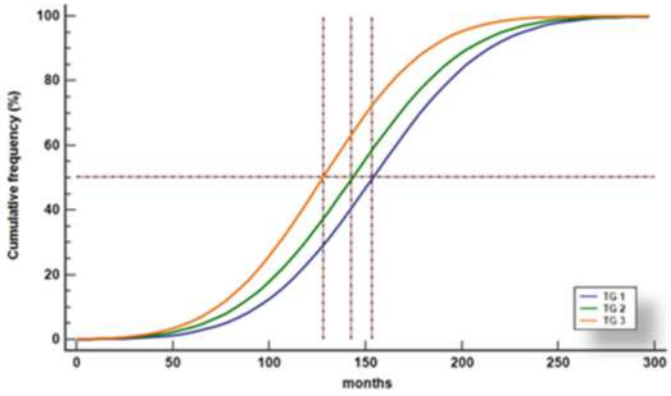
Code: 564

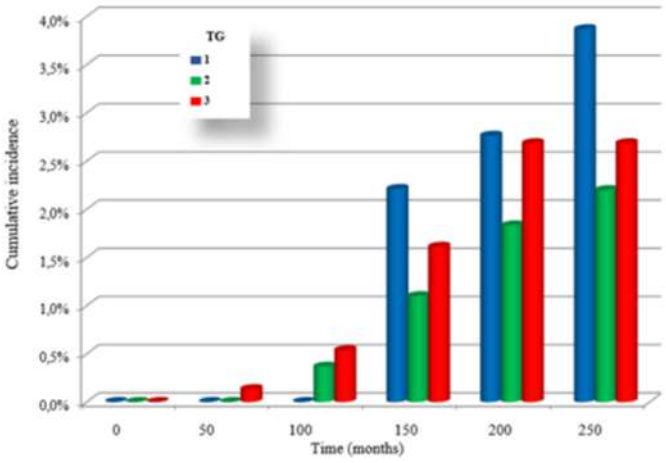
Aims: The AIEOP LH-2004 protocol for children and adolescents with Hodgkin lymphoma (HL) pursued the purpose of reducing the load of therapy, for pushing down late toxicities. It was the fourth Italian-based paediatric HL trial. Given the long-term follow-up, we analysed a specific long-term toxicity: the development of secondary malignant neoplasm (SMN).

Methods: From March 2004 to December 2017, the AIEOP LH-2004 protocol evaluated 1199 paediatric patients (pts) (median age 13.88 years, range 1.80-17.99), categorised according to the risk and response adapted strategy and the Cotswolds-modified Ann Arbor classification system in three therapeutic groups (TG). Pts assigned to the TG1 were in stage IA-IIA, did not have bulky lesions (mediastinum/thorax, M/T<0.33), nor lung hilum lymph nodes, with <4 lymphatic areas involved; pts not included in TG1 and TG3 were assigned to the TG2; pts assigned to the TG3 were in stage IIIB-IV or had bulky lesions (M/T≥0.33). Per protocol, local/involved field RT was delivered (IFRT). TG1 pts in CR after 3 ABVD cycles stopped the therapy, while those in PR received 25.2 Gy IFRT. TG2 pts in CR after 4 COPP/ABV cycles received 14.4 Gy IFRT; if PR, 2 IEP cycles followed the 4 COPP/ABV then, if CR, 14.4 Gy IFRT was delivered, while pts in PR received 25.2 Gy IFRT. TG3 pts received 4 COPP/ABV cycles: if CR, 2 more COPP/ABV cycles followed by 14.4 Gy IFRT were prescribed; if PR, 2 IEP cycles followed the 4 COPP/ABV then, if CR, 14.4 Gy IFRT was delivered, whilst pts in PR received 2 more COPP/ABV cycles and 25.2 Gy IFRT. The definition of SMN followed NCI criteria.

Results: In a median interval of 88 months (IQR 59-108), 33 pts developed 34 SMN. 2/33 pts did not receive RT and details about RT of a patient are missing. Thus, among 30 pts who underwent RT and subsequently developed SMN, 10 pts (33%) received a RT dose >20 Gy. 79.8% of SMN developed within the RT field. Cumulative frequency of SMN revealed that the 50% of the diagnoses occurred for TG1, TG2 and TG3, respectively, at 153.5, at 142.6 and at 128 months; cumulative incidence of SMN at 238 months were 3.9% for TG1, 2.2% for TG2 and 2.7% for TG3. The relationship between the TG and the development of reported SMN was described by ROC curves and was statistically relevant. Data about genetic predisposition toward SMN and familial cancer recurrence were not available.

Conclusions: Reduction of dose and volume of RT significantly reduced the cumulative incidence of SMN compared to previous Italian HL protocols.





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SAFETY AND SIDE EFFECTS OF ANAESTHESIA IN A SERIES OF PAEDIATRIC CANCER PATIENTS UNDERGOING RADIOTHERAPY: A MONOCENTRIC RETROSPECTIVE/PROSPECTIVE STUDY

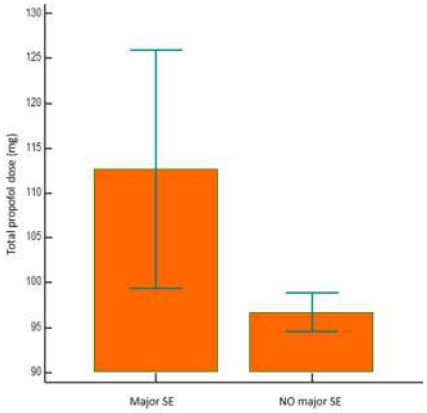
Code: 430

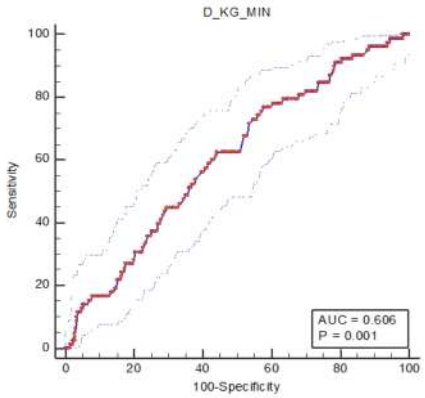
Aims: General anaesthesia (GA) is often employed in Paediatric Radiotherapy (RT) to provide immobility for the young patients (pts) during the simulation-CT and the sessions of RT. Each GA procedure is stereotyped and short-lasting. We retrospectively/prospectively analysed the anaesthetic-related complications of propofol with/without adjuvants - based GA procedures to study the safety and the risk factors associated, and to register related side effects (SE).

Methods: From January 2005 to December 2020, we retrospectively/prospectively analysed a monocentric series of paediatric cancer pts that underwent RT under GA. Pts were treated in supine position and a thermoplastic mask was used in the case of RT to the head-neck district. Vital signs were remotely monitored in the control room and video cameras were used to watch pts during the RT delivery. The waking up from GA was took place in the awakening room until full recovery of cognitive functions. A decrease up to 90% of the peripheral oxygen saturation was defined minor SE, whilst a decrease <90% of the peripheral oxygen saturation and/or a ≥30% reduction in heart rate compared to baseline was defined a major SE; cardiac and/or respiratory arrest and death were fatal SE.

Results: 71 paediatric cancer pts underwent to 1579 daily fractions of RT under GA. The most common districts of RT were the abdomen (32 pts), the craniospinal axis (13 pts) and the brain (13 pts). The mean number of fractions per pts was 12.5 (range 3-38), the mean duration of each session of GA was 45.5 min (range 10-105) and the mean total propofol dose was 159.17 mg (range 20-473.3 mg). In our series, total reported SE were 20.45%. Reported minor SE were 227 (14.37%): the frequency of minor SE increases as the number of RT fractions under GA increases with a statistically significant ($p < 0.001$) relationship coefficient $r=0.42$ (95% CI 0.21-0.60); a statistically significant relationship exists ($p = 0.0001$) also when RT is delivered to the spinal cord. Reported major SE were 96 (6.1%): the relationship with the initial bolus dose of propofol >100 mg was statistically significant ($p < 0.0001$). Furthermore, there was a statistically significant relationship ($p < 0.0001$) with total propofol dose/RT fraction >112 mg. No fatal SE occurred.

Conclusions: Propofol-based daily GA in paediatric cancer pts undergoing RT is a safe and reliable procedure as a valuable tool at the clinician's disposal. Our results are consistent with the Literature.





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SAFETY AND EFFICACY OF TRASTUZUMAB DERUXTECAN AND CONCOMITANT RADIATION THERAPY IN PATIENTS WITH METASTATIC HER2-POSITIVE BREAST CANCER

Code: 556

Aims: Radiation therapy (RT) is frequently required in oligometastatic or oligoprogressive Breast Cancer (BC), either with palliative or ablative intent. The combination of systemic treatments and RT is of particular interest, but few data are available to date. The aim of our study is to evaluate the safety of the use of T-DXd and concomitant RT in a consecutive series of HER2+ BC patients.

Methods: We retrospectively evaluated patients with metastatic HER2+ BC treated with T-DXd between May 2021 and August 2023 at two leading European institutions (University of Florence and Institute of Oncology, Ljubljana), receiving RT or not. Clinical data, acute and late toxicities and survival outcomes were collected. Primary end point was the association between RT and any adverse event grade(G) >2, evaluated according to Chi-square test.

Results: We included 52 patients, of whom 16 received RT within a month or during T-DXd, for a total of 17 treatments. At baseline, median age was 54 years old (range 34-88). After a median follow up of 6 months (range 1-24), 3 patients (18.8%) in the RT group and 5 (13.9%) in the no-RT group had died. Twenty-one patients (40.4%) received T-DXd as ≥IV line of anti-HER2 treatment, 16 (30.8%) as III line and 13 (25.0%) as II line. Only 2 patients (3.8%) with early metastatic disease relapse (<6 months after adjuvant anti-HER2 therapy completion) received T-DXd as I line treatment.
Median total RT dose was 30 Gy (range 8-48 Gy) with a median number of fractions of 3 (range 1-15). Median EQD2 dose was 50 Gy (range 16-104 Gy) and median BED 60 Gy (24-149 Gy). The most frequently treated site was bone (47.1%, N=8/17) followed by brain (29.4%; N=5/17). The development of G>2 toxicity and delivery of RT was not significantly correlated ($p = 0.83$).
Regarding toxicities of special interest for T-DXd, 3 cases of G3 fatigue have been reported in no-RT group and 1 in the RT group. Overall, only 1 case of G3 nausea was observed in the no-RT group. Grade 2 interstitial lung disease (IDL), that led to T-DXd discontinuation, was observed in 1 case in RT group and in 2 cases in no-RT group. No radionecrosis events were observed in 4 patients treated with intracranial RT.

Conclusions: Our data shows potential safety of RT and TDX-d combinations, without an increase in severe acute toxicity rates from the addition of RT. Data from larger series are needed.

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ANTI-HER2 AGENTS AND STEREOTACTIC RADIOTHERAPY FOR BRAIN METASTASIS IN HER2+ BREAST CANCER PATIENTS: HANDLE WITH CARE

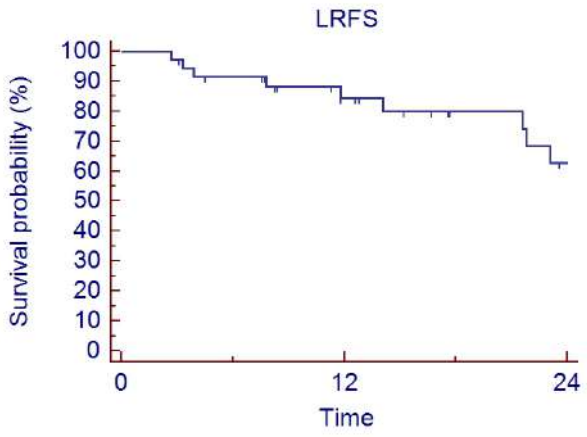
Code: 106

Aims: Patients (pts) with HER2+ breast cancer (BC) are commonly affected by brain metastasis (BM). Anti- HER2 agents have led to significant improvements of the outcomes of this population and new drugs with proven intracranial efficacy have recently become available. However anti-HER2 agents could be associated with an increased risk of symptomatic radionecrosis in pts treated with stereotactic radiotherapy (SRT). We reviewed outcomes of HER2+ BC pts undergoing SRT for BM in our Institute.

Methods: From 01/2018 to 06/2023, 219 BM were treated by robotic SRT in 21 HER2+ BC pts. SRT was delivered to a median of 2 (1 - 46) concomitant brain lesions. Median PTV was 0.92 (0.13-23.6) cc. Median prescribed RT doses was 30 (24-35)Gy in 3 (1-5) fractions, to a median isodose of 80 (69.5-80)%. Ten out of 21 pts underwent another previous RT course (9 SRT, one WBRT). Systemic therapies prescribed concomitant to SRT were: trastuzumab + pertuzumab in 36% of pts, trastuzumab in 31%, trastuzumab emtansine (T-DM1) in 17%, trastuzumab deruxtecan in 8%, lapatinib in 3%, capecitabine in 5%. Acute and late toxicity were registered according to CTCAE v 5.0.

Results: Median follow-up was 13 (3-70) months. Only grade (G1) acute toxicity (headache, nausea, dizziness) was observed in 28% of pts. Late toxicity (headache, dizziness, radionecrosis) was: 11% G1, and 28% G2.
Eight pts (38%) had radionecrosis diagnosed by perfusion MRI and/or methionine PET/MRI. Six of them were symptomatic: systemic therapies were trastuzumab in 3 pts, trastuzumab + pertuzumab in 3 pts and lapatinib in one patient. Four out of 6 pts underwent a previous RT course before SRT. Corticosteroids and/or bevacizumab were administrated to these pts, with benefit. Local relapse free survival (LRFS) at 6, 12 and 18 months was 91.5%, 84.3% and 82.6% respectively (figure 1).

Conclusions: SRT is a fundamental weapon for the management of BM, with a good efficacy and safety profile. Accurate pts selection and prospective studies are needed for optimizing combination of SRT and anti- HER2 agents.



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USE AND BENEFITS OF 0-7-21 HYPOFRACTIONATED RADIOTHERAPY SCHEME IN THE TREATMENT OF METASTATIC MELANOMA

Code: 504

Aims: The aim of our study is to evaluate feasibility and clinical outcomes (Local Control and Progression Free Survival) in metastatic melanoma patients treated with 0-7-21 hypofractionated radiotherapy scheme.

Methods: We selected and analyzed all patients with metastatic melanoma treated with 0-7-21 radiotherapy regimen in our center.

Results: From 2015 to 2023 11 (7 female and 4 male) patients who underwent to 0-7-21 scheme palliative radiotherapy were retrospectively analyzed. Median age at the time of the radiation treatment was 63 years (range 50-86). 6/11 patients were BRAF wild type, 2/11 BRAFV600K mutated and 3/11 not evaluated. All patients were also treated with immunotherapy: 3 Pembrolizumab alone; 3 Nivolumab alone; 1 Pembrolizumab, Nivolumab and Ipilimumab; 1 Encorafenib, Binimetinib and Pembrolizumab; 1 Ipilimumab and Nivolumab; 1 Pembrolizumab and Ipilimumab; 1 Vemurafenib, Ipilimumab, Pembrolizumab, Dabrafenib, Trametinib. All patients were treated with intensity modulated radiation therapy technique delivering a hypofractionated dose of 24 Gy in 3 fractions delivered on days 0, 7, and 21. Lymph node metastases were treated in 8 patients, skin metastases in 3 patients and brain metastases in 2 patients.
With a median Follow-Up of 12 months (range 2-24) LC was obtained in 91% of the cases at 12 months and median PFS was 12 months (range 2-24).

Conclusions: The '0-7-21' regimen especially in combination with immunotherapy was feasible and well tolerated. Clinical outcomes observed in this retrospective analysis show that this kind of fractionation could emerge as a valid therapeutic option in the palliative treatment of metastatic melanoma.

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HDAC3 INHIBITION OVERCOMES RADIORESISTANCE IN FUSION POSITIVE RHABDOMYOSARCOMA

Code: 98

Aims: Radiotherapy (RT) plays a critical role in the management of rhabdomyosarcoma (RMS) The high risk PAX3-FOXO1 fusion-positive subtype (FP-RMS) is often resistant to RT. We have recently demonstrated that inhibition of class-I histone deacetylases (HDACs) radiosensitizes FP-RMS both in vitro and in vivo. However, HDACs inhibitors exhibited limited success in human clinical trials on solid tumors possibly due to off-target effects. Hence, identifying specific HDAC isoforms that can be targeted to radiosensitize FP- RMS is imperative.

Methods: We performed in silico analysis, using transcriptomic and clinical data,to assess the impact of class-I HDACs expression in RMS patients' survival. siRNA-based screening was conducted to identify specific class-I HDACs involved in the response to irradiation by clonogenic assay. CRISPR/Cas9 technology was applied to confirm and dissect the involvement of HDAC3 in RMS radioresistance in vitro and in vivo. Annexin V and propidium iodide staining were used to study apoptosis and cell cycle, respectively; Immunofluorescence for γH2AX,Comet assay and western blots were performed to investigate DNA damage and repair.Drug discovery and design techniques were applied to develop MC4448 HDAC3 inhibitor.

Results: In silico analysis reveals that class-I HDACs are overexpressed in RMS patients, PDX and cell lines but, however, HDAC3 results the isoform that gives greater dependency to RMS cells and the only one whose expression correlates with a worse prognosis in P3F-RMS

patients. Among all class-I HDACs silenced by siRNAs, only HDAC3 inhibits colony formation in irradiated-FP-RMS cells. Moreover, HDAC3 knock- out (KO) FP-RMS cells exhibit PARP1- and caspase-dependent apoptosis and impaired stemness when irradiated compared to single treatments. Tumor growth in vivo was maximally inhibited in irradiated- HDAC3 KO tumors compared to single approaches. Mechanistically, HDAC3 loss-of-function also increases DNA damage in irradiated cells, augmenting H2AX phosphorylation and DNA double-strand breaks (DSBs) and counteracting irradiaton-dependent activation of ATM and DNA-Pkcs and Rad51 protein induction. Additionally, our new HDAC3 inhibitor, MC4448, shows specific anti-tumor effects and mirrors the radiosensitizing effects of HDAC3 depletion in vitro.

Conclusions: HDAC3 protects FP-RMS cells from DNA damage and apoptosis sustaining stemness and tumor growth in vivo in response to irradiation. HDAC3 inhibition could be a new promising strategy to overcome radioresistance in FP-RMS.

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HIGH-DOSE STEREOTACTIC BODY RADIATION THERAPY (SBRT) FOR ADRENAL GLAND METASTASES: OUTCOMES AND TOXICITIES

Code: 428

Aims: Adrenal glands are a common metastatic site from different primary tumors. In those settings where surgical resection is not feasible, because of technical difficulties or patient's comorbidities and/or disease characteristics, Stereotactic Body Radiation Therapy (SBRT) represents a safe alternative.

Methods: Forty-eight oligometastatic patients, treated at our Institution from 2017 to 2023 for 49 adrenal glands metastases, were studied retrospectively and included in the analysis.
Twenty-three patients (48%) had a lung cancer as primary tumour and the most representative histology in these patients was adenocarcinoma (20 patients, 87%).
All patients underwent SBRT delivered with VMAT/Rapid Arch technique and Flattening Filter- Free (FFF) beams.
Different fractionation schedules, all having an overall BED10 either equal or superior to 100 Gy, were used with a total delivered dose ranging 45-54 Gy in 3-6 fractions. Most common regimens were 45 Gy delivered in 3 fractions (83%) and 50 Gy delivered in 5 fractions (12%).

Results: The median BED10 was 112.5 Gy (range 100 – 112.5). With a median follow-up of 16.7 months, local control (LC) rates at 1 and 2 years were 94.6% (95CI 79.8 – 98.6) and 90.8% (95%CI 73.6 – 97.0), respectively. Median LC was not reached. None of the analyzed risk factors resulted to be predictive of LC.
One- and 2-year rates of Progression Free Survival (PFS) were 48.2% (95%CI 31.9 – 62.8) and 44.2% (95%CI 27.7 – 59.5), with a median PFS of 10.2 months.
Rates of 1- and 2-year OS were 69.0% (95%CI 53.3 – 80.4) and 50.8% (95%CI 34.7 – 64.8),
with a median OS of 31.3 months. Lung primary resulted to be a negative predictive factor for OS (HR 2.46, 95%CI 1.09 – 5.56; p=0.029). Median OS was 55.5 months for non-lung primary tumors, with respect to 16.7 months for patients with lung primary.
No grade 3 or greater toxicities were reported. Sixteen patients (33%) developed a low-grade toxicity. Only 2 patients (4%) reported a grade 2 toxicity, one developing G2 fatigue and the other G2 nausea. Fifteen patients (31%) complained of a grade 1 toxicity, experiencing either nausea, addominal pain, vomit, dyspepsia, or diarrhea.

Conclusions: High dose-SBRT delivered to adrenal gland metastases represents a safe and viable alternative to surgical resection with acceptable mild toxicities, in the absence of grade 3 or greater adverse events. Ensuring a BED10 of at least 100 Gy, by increasing the dose per fraction, enable to warrant optimal LC rates.

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SAFETY AND SURVIVAL OUTCOMES OF COMBINING TRASTUZUMAB- EMTANSINE (T-DM1) WITH INTRACRANIAL RADIATION THERAPY: A SINGLE CENTER EXPERIENCE

Code: 133

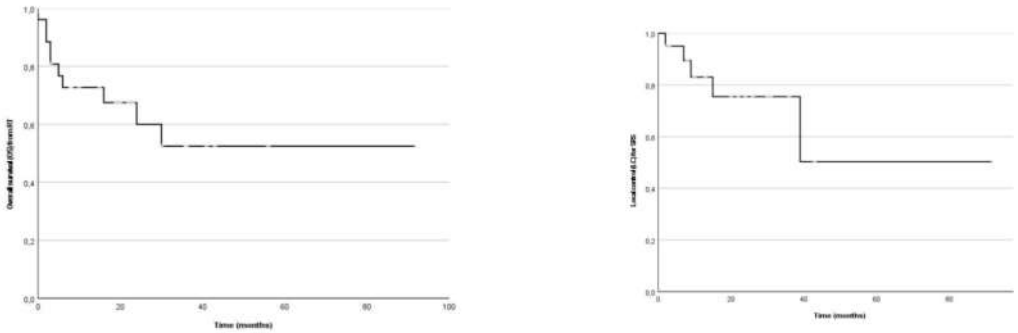
Aims: In patients with metastatic breast cancer (MBC) the combination of systemic therapies with locoregional treatments represents an effective strategy to tumor control. This monocentric study has the aim to evaluate the safety and survival outcomes of combining intracranial RT with T-DM1 in MBC settings

Methods: Patient data were retrospectively collected from January 2014 to June 2023. Characteristics of pts, brain metastases and treatment were recorded. Toxic effects were scored according to Common Terminology Criteria for Adverse Events (CTCAE v5.0). Statistical analysis of overall survival from intracranial RT (OS), Progression-free survival from intracranial RT (PFS) and local control of treated brain metastasis were performed by the Kaplan Meier method.

Results: A total of 26 pts with HER2-positive MBC were treated for brain metastasis at our institution. The median age was 51 years [range 31-81 years]. Seventeen pts received single fraction (15-24Gy) stereotactic radiosurgery (SRS) and 3 pts received hypofractionated (25Gy in 5 fractions) SRS. Gamma Knife-SRS, CyberKnife-SRS and Volumetric Modulated Arc Therapy (VMAT) were performed in 9 (34%), 7 (27%) and 4 (15%) pts. Six out of 26 (26%) pts underwent Whole Brain RT (WBRT). The median time interval between T-DM1 administration and RT (SRS/WBRT) was 16 days [range 3-27 days]. The median PFS from the first course of SRS/WBRT was 13 months [95% CI 7,5-18,5 months], whereas the median OS was not reached (Figure 1a). The 1- and 2-year LC of brain lesions treated with SRS were 83% and 75%, respectively (Figure 1b). Out of 20 pts treated with SRS, 4 had acute toxicity: G1 amnesia (1pt), G2 visual deficit (1 pt), G2 dizziness (1 pt), G2 brain oedema (1 pt). Only 1 pt (4%) experienced G3 radionecrosis after 8 months from SRS, requiring hospitalization and corticosteroid treatment. No chronic side effects were observed. One pt receiving WBRT, reported G2 brain oedema one month after RT

Conclusions: To date, prospective studies investigating the safety of combining T-DM1 with intracranial RT are still lacking. Therefore, although the toxicities found in our study are of low grade, caution is advised when combining T-DM1 with RT for brain metastases.

Figure 1. (a) Overall survival (OS) from intracranial RT (SRS/WBRT); (b) Local control (LC) of brain metastasis treated with SRS



a) OS **b) LC**

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PALLIATIVE METABOLISM GUIDED LATTICE RADIOTHERAPY IN PATIENTS WITH ADVANCED BREAST CANCER UNSUITABLE TO ABLATIVE APPROACH: A MULTICENTRIC STUDY

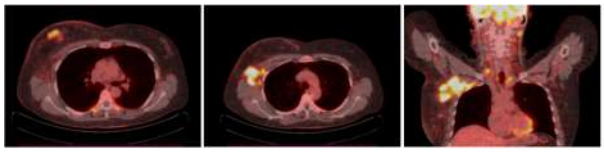
Code: 488

Aims: To evaluate clinical response (Local Control and Local Failure) and toxicities in patients with Stage III-IV breast cancer treated with "Metabolism-Guided" Lattice technique. The aim is to deliver a heterogeneous dose distribution characterized by alternating regions of high and low doses throughout a tumor with the goals of stimulating both bystander and abscopal effects.

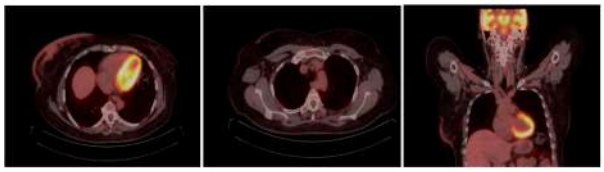
Methods: We selected all patients with locally advanced/metastatic breast cancer unsuitable to local surgery in the experimental centers (G. Martino Messina University Hospital, IOM Viagrande Foundation).

Results: From May 2021 to October 2023 14 patients (12 female and 2 male) with advanced breast cancer have been enrolled. The median age at the time of diagnosis was 70,5 years (range 49-99); all patients had a performance status (ECOG) 0–2; 11/14 patients received systemic therapy (hormonotherapy, chemotherapy or immuno-/targeted therapy).
All patients had contrast-enhanced CT and 18F-FDG-PET/CT. In the first therapy's phase we delivered high radiation doses within the tumor using “balls of dose”, called VERTEX, positioned at the edges of tumor areas with different metabolisms at the PET exam following a non-geometric model. The median total dose delivered on VERTEX was 15Gy (range 10-15Gy) in 1 fraction. In the second treatment phase a median total dose of 30Gy (range 20-40,05Gy) was delivered on Clinical Target Volume (CTV).
With a median Follow-Up of 7 months (range 1-32 months) LC has been obtained in 71,4% of the cases; we observed 42,8% of complete response. Toxicities data registered were low: radiodermatitis G1-G2 in 28,5% of the patients; 1 patient showed grade 3-4 toxicities.

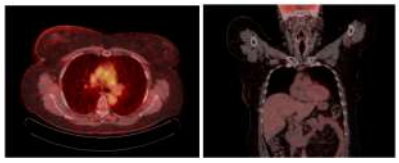
Conclusions: This approach is feasible and well tolerated with encouraging results in terms of local control and toxicities. These preliminary results seem to indicate that this kind of therapy could emerge as a therapeutic option in this setting of patients.



18 F-FDG PET uptake in the primary breast tumor, loco-regional lymph nodes and metastasis in the paratracheal lymph node



18 F-FDG PET uptake shows partial response in loco-regional lymph nodes and complete response in the paratracheal lymph node after seven cycles of Trastuzumab-Pertuzumab-Docetaxel



18 F-FDG PET scan shows a metabolic complete remission of breast solid tumor and locoregional node six months month after radiotherapy

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INTENSIFIED TOTAL MARROW IRRADIATION IN HIGH-RISK PATIENTS RECEIVING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTS

Code: 565

Aims: Patients with refractory leukemia or minimal residual disease (MRD) have a high risk of relapse after allo-HSCT. To lower this risk, one potential strategy is irradiation intensification, particularly at sites of disease, such as bone marrow. Therefore, patients with active or MRD in which the standard 13.5 Gy to the bone marrow were hypothesized to be not useful, we designed a conditioning regimen to deliver a higher dose. Here the toxicity profiles and survival outcomes are reported.

Methods: The conditioning regimen consisted in TMLI which was delivered in 5 days in 2 daily fractions by helical Tomotherapy. Using a simultaneous integrated boost (SIB) procedure, target volumes were the skeletal bones for TMI (total dose 20 Gy) and the major lymph node chains and the spleen for TLI (total dose 11.5 Gy). Patients with ALL also received 13.5 Gy to the brain. Following radiation therapy, chemotherapy was administered, including Thiotepa (2.5 or 3.75 mg/kg per day for 2 days), Fludarabine (30 mg/m2 per day for 5 days), Cyclophosphamide (15 mg/kg per day for 2 days). Haploidentical grafts consisted of 2 $x10^6$/kg Tregs, $1x10^6$/kg Tcons and a "megadose" (~circa $10x10^6$/kg) of purified CD34+cells. No post-transplant immunosuppression was given.

Results: From May 2020 to September 2023,10 pts (7AML, 3 ALL; 7 male and 3 female; median age 51 years) were recruited. Four patients underwent transplantation with detectable MRD, 6 with active disease. Dosimetric results are presented in Table 1. The majority of conditioning regimen-related adverse events occurring within 30 days after transplantation were graded as 1 to 2 according to the CTCAE (version 5.0). Oral and intestinal mucositis were generally mild and fully resolved in all patients. No cases of veno-occlusive disease (VOD) occurred. Only one case of transplantation-associated microangiopathy was observed. Acute GvHD occurred in 2 patient (20%), one Grade III and the other Grade IV; No patients developed moderate or severe chronic GvHD. 1(10%) pts died of transplant- related causes At a median follow-up of 26 months (range, 17-40 months), nine out of the ten patients (90%) remain alive. No disease relapse occurred in any of these patients.

Conclusions: Despite the high-risk diseases, none of the patients experienced relapse post-transplant. These data suggest that TMI dose escalation to 20 Gy is not only feasible with acceptable toxicity but also offers the potential to further enhance outcomes in patients with chemotherapy-resistant leukemia

TABLE - Summary of average organ dose (Gy) for patients treated with 20Gy TMLI.

Organ at risk	Average dose ± SD [Gy]
Bladder	10.40 ± 1.03
Esophagus	13.88 ± 0.56
Heart	8.47 ± 0.39
Small Bowel	7.67 ± 0.43
Large Bowel	8.94 ± 0.65
Kidneys	6.65 ± 0.23
Lens	3.38 ± 0.19
Lungs	10.43 ± 0.23
Oral Cavity	7.17 ± 0.45
Parotids	11.41 ± 1.01
Rectum	7.21 ± 0.68
Thyroid	10.14 ± 1.03

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PRELIMINARY RESULTS OF THE BLUE SKY STUDY: RADIOMICS AND CLINICAL FEATURES AS PREDICTIVE MARKERS IN STAGE III, UNRESECTABLE, PD-L1 POSITIVE NSCLC PATIENTS

Code: 520

Aims: Blue Sky Radiomics study (NCT04364776) is a multicenter, Italian observational trial aiming to investigate the prognostic and predictive role of radiomic and clinical features in patients affected by stage III, unresectable, PD-L1+ NSCLC treated with chemo-radiotherapy (CRT) and maintenance durvalumab.

Methods: We are reporting data on the first 70 patients included in the study so far. Contrast enhancement CT scans were acquired at the time of diagnosis (T0) and after CRT (T1). We extracted radiomic features from primary lung tumors segmented. The extraction method, through Pyradiomics, was previously published.
107 features were primarily selected, removing variables with correlation coefficients higher than 0.75. 20 features were used to build the models. We assessed the performance of the selected features +/- clinical factors (stage A vs. B-C, histology, PD-L1 level 50%, sequential vs. concurrent CRT) to predict PFS (12 months), local (thoracic) and brain relapse probability. In particular, we used two parametric models (Elastic Net -EN- and Support Vector Machine -SVM), and a non-parametric one (Random Forest-RF).

Results: The performances of EN, RF, and SVM models are shown in the table below
The best performances for PFS prediction are obtained with the EN model, considering the radiomic features and clinical factors as predictors (Accuracy=0.71, AUC=0.75). An AUC value of 0.75 is generally regarded as acceptable but not optimal. The radiomic features at T1 do not improve the predictions. For predicting distant relapses, elastic net models generally show better performances.
A higher AUC value was obtained for T0 radiomic features (AUC=0.77), and the accuracy was 0.75 for radiomic features and clinical features at T0 and for both cases at T1. Regarding the prediction of brain metastasis, the higher AUC value is obtained with EN and radiomic features as covariates (AUC=0.72) and with clinical factors as covariates (AUC=0.71). The accuracy level is generally high for different combinations of models, covariates, and time points (> 0.8).

Conclusions: We exploit the application of Machine Learning methods for estimating PFS and the probability of local relapses and brain metastases in patients with stage 3 unresectable NSCLC treated with PACIFIC regimen. The radiomic/clinical model did not reach enough accuracy to be used as prognostic/predictive in this cohort. Given the small dataset and a trend toward a positive signal, the next step could be testing the model in a larger cohort.

		T0						T1			
		Radiomic Features		*Clinical Factors*		*Radiomic Features + Clinical Factors*		*Radiomic Features*		*Radiomic Features + Clinical Factors*	
		Accuracy	AUC	Accuracy	AUC	Accuracy	AUC	Accuracy	AUC	Accuracy	AUC
PFS	Elastic Net	0.66	0.71	0.53	0.47	0.71	0.75	0.58	0.53	0.56	0.55
	Random Forest	0.61	0.59	0.61	0.56	0.64	0.55	0.59	0.57	0.60	0.53
	Support Vector Machine	0.70	0.66	0.61	0.48	0.67	0.63	0.57	0.51	0.50	0.44
Local Relapses	Elastic Net	0.69	0.77	0.50	0.76	0.75	0.62	0.75	0.75	0.75	0.71
	Random Forest	0.69	0.60	0.69	0.51	0.69	0.67	0.69	0.62	0.69	0.67
	Support Vector Machine	0.62	0.42	0.56	0.38	0.50	0.33	0.56	0.46	0.50	0.42
Brain Metastasis	Elastic Net	0.81	0.72	0.89	0.71	0.81	0.61	0.85	0.57	0.84	0.50
	Random Forest	0.89	0.66	0.89	0.53	0.89	0.64	0.85	0.68	0.89	0.65
	Support Vector Machine	0.81	0.46	0.89	0.50	0.80	0.45	0.85	0.49	0.83	0.47

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INFLAMMATORY MARKERS AS PROGNOSTIC TOOLS IN HIGH-GRADE SOFT TISSUE SARCOMA: A COMPREHENSIVE ANALYSIS OF NEOADJUVANT TREATMENT OUTCOMES

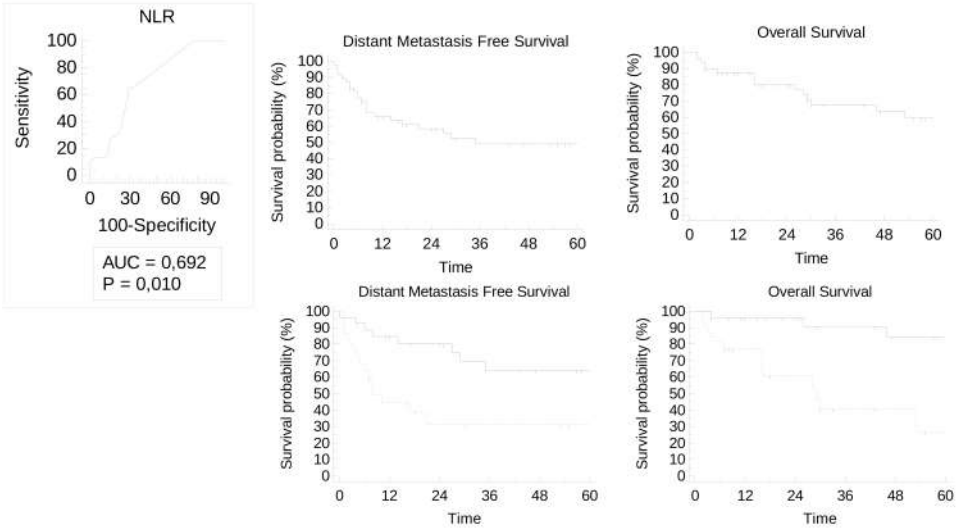
Code: 477

Aims: Half of the patients receiving curative treatment for localized high-grade soft tissue sarcoma (STS) experience distant relapse. We investigate the inflammatory state within solid tumors collecting immune-inflammatory markers that could result in a simple and efficient method for predicting outcomes in patients suitable for neoadjuvant therapy and surgical intervention.

Methods: Between 2010 and 2022 data of STS patients treated in preoperative setting were collected. Patients underwent preoperative chemoradiation followed by surgery for high-grade (FNCLCC 3), non-metastatic STS. We obtained the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII?=?NLR?×?platelets) from pretreatment blood samples. We analyzed biomarkers with the highest AUC for distant relapse. An optimal cutoff of NLR>3 was established using the Youden-J index (Specificity: 63.6%; Sensitivity: 70.4%). Kaplan-Meier methodology was used for Distant Metastasis Free Survival (DMFS) and Overall Survival (OS), while both univariate analysis (UVA) with the log-rank test and multivariate analysis (MVA) to evaluate the correlation between variables and outcomes.

Results: 49 patients with STS underwent preoperative chemoradiation. The median age was 55 years. Median values for NLR, SII, and PLR were 3, 748, and 141 respectively. ROC curve analysis favored NLR (AUC: 0.692) over SII (AUC: 0.67) and PLR (AUC: 0.588) for distant relapse. With a median follow-up of 28 months, 22 patients had distant relapse, and 16 deceased. The 1- and 3-year DMFS rates were 66% and 42%, respectively, while the 1- and 3-year OS rates were 88% and 67%. In UVA, only NLR>3 correlated with impaired DMFS (median 8 months vs NR, p=0.0054). Conversely, NLR>3 (median 29 months vs NR, p=0.0007), PS= 2 (median 3 months vs NR, p=0.0002), and trunk tumor location (median 26 vs NR, p=0.025) were associated with OS. In MVA both NLR>3 (p=0.006) and PS= 2 (p=0.031) were independently associated with survival.

Conclusions: NLR exhibited a higher AUC than SII and PL. Although the moderate sensitivity and specificity, an NLR>3 was notably correlated with both DMFS and OS in our study population. This suggests the need for additional investigation into the potential of immune inflammation biomarkers, emphasizing the significance of enhancing prognostic stratification for tailoring personalized patient care and follow-up strategies, particularly for those with higher risk of distant recurrence



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CASTRATE RESISTANT PROSTATE CANCER PATIENTS UNDERGOING FIRST LINE ABIRATERONE TRATMENT. A SUBGROUP ANALYSIS FROM ARTO TRIAL

Code: 486

Aims: ARTO (NCT03449719) is a multicentre, randomized phase II trial testing the outcomes after concomitant stereotactic body radiation therapy (SBRT) and abiraterone acetate (AA) in oligometastatic Castrate Resistant Prostate Cancer (CRPC) patients. Improved Progression free survival (PFS) and biochemical response were already shown within a previous published analysis. Here is presented a subgroup analysis exploring treatments received after progression and following outcomes.

Methods: Oligometastatic CRPC patients were randomized to receive either AA alone or associated with concomitant SBRT on all sites of disease. Time between Abiraterone start and first progression event and time between first and second progression event, death or last follow up were defined as PFS1 and PFS2. PFS1+PFS2 in patients treated with SBRT at oligoprogression vs patients undergoing second line systemic treatment were compared using Cox regression analysis.

Results: At last follow up, 77 out of 157 patients initially enrolled progressed after Abiraterone treatment (23 and 54 in the experimental vs control arm). Treatment at progression consisted in SBRT on oligoprogressive metastatic disease or second line systemic treatment in 23 and 40 patients, respectively. 14 patients did not receive any further treatment and were excluded from the current analysis. Fourteen patients had a second progression events. Patients undergoing SBRT vs second line treatment had a median PFS1+PFS2 time of 28 months (95%CI 25-34) and 23 months (95% CI 18-32), respectively (HR 1.09, 95% CI 0.29-4.12, p-value 0.898)

Conclusions: SBRT in oligoprogressive patients may achieve similar benefit if compared to second line systemic treatment. These data suggest that repeated SBRT may be a viable treatment option in selected patients.

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INCREASE OF PD-1 EXPRESSION IN CIRCULATING T LYMPHOCYTES AND SOLUBLE PD-L1 LEVELS AFTER RADICAL RADIOTHERAPY IN MALIGNANT PLEURAL MESOTHELIOMA: A NEW THERAPEUTIC APPROACH?

Code: 237

Aims: With this study we want to evaluate changes induced in T lymphocyte population and in levels of soluble PD-L1 by radical radiation treatment on chest wall (RHR) in Malignant Pleural Mesothelioma (MPM).

Methods: Our study population included patients affected by MPM treated with chemotherapy, non-radical surgery (microscopic or macroscopic residual disease) and RHR at a dose of 50 Gy in 25 fractions with boost to 60 Gy in 25 fractions on residual disease. The patients underwent blood tests on the first and last day of the radiation treatment and one month after the end of the same, for the evaluation of blood count and onco- immunological biomarkers. The PD-1 and Ki-67 expression in T lymphocytes were analyzed in peripheral blood samples by flow cytometry. Finally, soluble PDL-1 was evaluated by ELISA assay in serum samples.

Results: Samples from 35 patients suffering from MPM and treated with RHR between 2020 and 2023 at our center were analyzed. 80% (28 patients) had a disease of epithelioid histology. Higher levels of Lymphocyte-to-Monocyte Ratio (LMR) were associated with a better Overall Survival (p=0.006). At the end of RHR there was a statistically significant increase (p<0.001) in the percentage of T lymphocytes, helper and cytotoxic that express the PD-1 inhibition marker. This trend was maintained even one month after the end of the radiation treatment. After RHR, the proportion of T lymphocytes (both helper and cytotoxic) that expressed the Ki-67 proliferation marker also increased significantly (p<0.001). Eventually, after RHR, there was a significant increase (p<0.001) in the levels of soluble PD-L1 in the patients' serum. The main results are summarized in Table 1.

Conclusions: In this setting, the LMR seemed to have a positive prognostic role, and radiotherapy would appear to increase the populations of T lymphocytes (CD3, CD4, CD8) that express the PD-1 receptor, their proliferative rate and the serum levels of soluble PD-L1. This leads us to believe that there is a part of the immune response mediated by T lymphocytes against tumor cells which, although stimulated by the RHR, remains inhibited by the PD-1/PD-L1 pathway. These observations could lead to the identification of a known therapeutic target (drugs that act on the PD-1/PD-L1 cellular pathway) to support a maintenance immunotherapy after RHR as already happens in tumors of different histologies. Further studies are necessary to confirm these preliminary data.

Variable	N	p50 (mediana) (p25-p75)	p-value compared to preRT (test wilcoxon)
cd3pd1_pre-RT	27	33.50 (27.60-40.50)	
cd3pd1_post-RT	27	47.40 (39.80-55.00)	<0.001
cd3pd1_1 month post RT	10	54.65 (45.9-64.7)	0.007
cd4pd1_ pre-RT	27	35.00 (31.20-41.40)	
cd4pd1_ post-RT	27	52.10 (44.90-57.50)	<0.001
cd4pd1_ 1 month post-RT	10	73.55 (67-81.3)	0.005
cd8pd1_ pre-RT	27	40.90 (30.20-46.70)	
cd8pd1_ post-RT	27	47.90 (40.60-58.70)	<0.001
cd8pd1_1 month post-RT	10	58.5 (44.5-62.4)	0.012
cd3ki67_ pre-RT	27	4.41(3.87-5.66)	
cd3ki67_ post-RT	27	25.30 (12.50-34.30)	<0.001
cd3ki67_ 1 month post-RT	10	14.35 (6.32-24.2)	0.029
cd4ki67_ pre-RT	27	4.47 (3.33-5.78)	
cd4ki67_ post-RT	27	19.00 (9.64-23.10)	<0.001
cd4ki67_ 1 month post-RT	10	16.75 (10.52-20.25)	0.005
cd8ki67_ pre-RT	27	4.66 (3.32-5.77)	
cd8ki67_ post-RT	27	33.20 (14.00-62.40)	<0.001
cd8ki67_ 1 month post-RT	10	12.95 (5.27-21.55)	0.059
sPD-L1_pre-RT	35	85.68 (79.15-104.66)	
sPD-L1_post-RT	35	109.25 (99.52-117.84)	<0.001
sPD-L1_1 month post RT	10	108.29 (100.33-116.00)	0.012

Table 1. Expression of PD-1 on lymphocytes and proliferation marker Ki67 on lymphocytes before and after RT. Soluble PD-L1 levels in patient serum before and after RT.

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SAFETY AND EFFICACY OF RADIATION THERAPY IN ELDERLY NON- MELANOMA SKIN CANCER: A MONO-ISTITUTIONAL EXPERIENCE

Code: 573

Aims: Diagnosis of non-melanoma skin cancer (NMSC) is increasing, especially in very elderly patients with comorbidities, narrowing radical treatment options.The mayority of skin cancer patients are diagnosed with an advanced stage of disease, which impairs quality of life. Inoperable cases could be referred for locally exclusive radiotherapy, with palliative or radical intent. The current goal of Radiation Oncologist is to provide a treatment that ensures a good local control of disease, while maintaining a good quality of life for both the elderly patients and their family. The study presents a retrospective summary of this setting of patients, treated with definitive radiotherapy.

Methods: From January 2023 to Decemberr 2023 ten elderly patients with NMSC were treated with radiotherapy 2023 in the Radiation Oncology Unit Santa Maria alla Gruccia Hospital. The radiation dose was delivered both via an electron and photon beam. The dose range was adjusted to the tumor diameter and depth of tumor invasion. Both conventional or hypofractionated radiotherapy schedules were administered to the target skin lesions in the definitive or palliative setting. All patients were closely followed-up until complete remission.

Results: Ten total patients were treated. The mean age was 89 years and all the cases were classified as high risk disease for localization and dimension of the lesions; 8 patients had primary tumours and 2 patients had reccurent lesions after surgery. The pathologic classification of the 10 patients included 9 squamous cell carcinoma and 1 merkel carcinoma. 5 patiens had simptomatic lesions for bleeding and pain. 2 patients were treated with hypofractionated schedule (25 Gy in 5 fractions), 7 patients with moderate hypofractionated schedule (55 Gy in 20 fractions) and 1 patient was treated with conventional schedule (60 Gy in 30 fractions). No severe acute complications were observed after radiation therapy. Only minor complications including radiation dermatitis was treated with supportive care. All patients achieved complete response.

Conclusions: Our experience suggests that radiation therapy in elderly patients with non-melanoma skin cancer is a feasible, safe and effective treatment, improving quality of life of the patients and their caregiver.

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COMPUTED TOMOGRAPHY-BASED RADIOMIC FEATURES AND RESPIRATORY FUNCTION IN PATIENTS TREATED WITH STEREOTACTIC BODY RADIOTHERAPY (SBRT): AN EXPLORATORY ANALYSIS

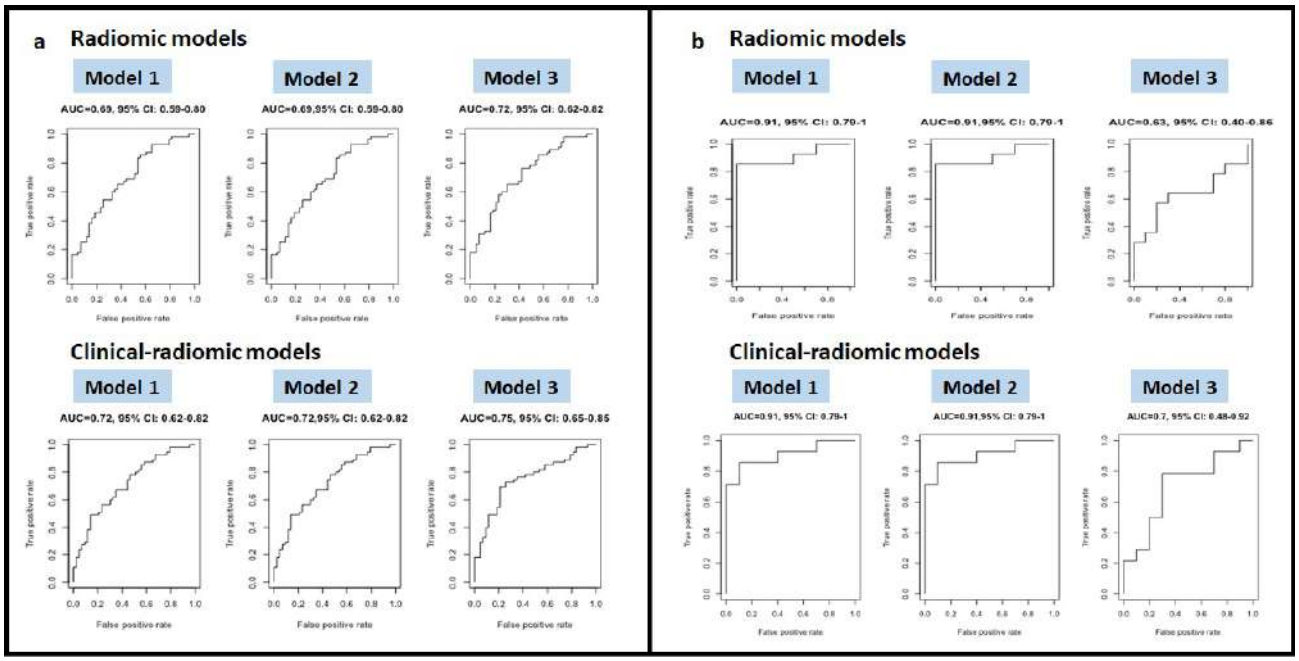
Code: 79

Aims: Radiomics is the extraction of non-invasive and reproducible quantitative imaging features which may yield mineable information for clinical practice implementation. Quantification of lung function through radiomics could play a key role in the NSCLC patients' management. Aim of this study is to test the capability of radiomic features to predict pulmonary function parameters, focusing on the diffusing capacity of lungs for carbon monoxide (DLCO).

Methods: Retrospective data were retrieved from electronical medical records of patients treated with SBRT at the same institution. Inclusion criteria were: 1) diagnosis of early stage NSCLC or oligometastatic NSCLC; 2) availability of 4-dimensional computed tomography (4DCT); 3) availability of baseline spirometry; 4) availability of a written informed consent for the use of clinical data for research purposes. The GTV was segmented on the 4D-CT reconstructed Phase0 and Phase50 and radiomic features were extracted from the lung parenchyma subtracting the lesion/s. Features were clustered by an iterative clustering algorithm to retain only those most associated with baseline and post-treatment DLCO. The logistic LASSO Regression Model calculated a coefficient for each feature. Three models were built to predict DLCO abnormality: the clinical model-containing clinical information; the radiomic model-containing the radiomic score; clinical-radiomic model-containing clinical information and the radiomic score. For each case, the models created were: Model 1 based on the features in Phase0; Model 2 based on the features in Phase50; Model 3 based on the difference between the two phases. AUC was used to compare their performances.

Results: A total of 98 patients met the inclusion criteria. Charlson Comorbidity Index (CCI) scored as the clinical variable most associated with baseline DLCO while the selected features were mainly texture features and similar among the two phases. AUC of the developed radiomic and clinical-radiomic models are reported in **Figure 1**. AUC value for the clinical model was 0.65.

Conclusions: Clinical-radiomic models were the best at predicting both baseline and post-treatment abnormal DLCO. This suggests the potentiality of radiomics in clinics at identifying non-invasive quantitative biomarkers of lung functionality that, together with clinical variables might be used to build predictive models to assist patients' management, follow-up and implement spirometry-derived information.



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FEASIBILITY AND TOLERABILITY OF ADJUVANT RADIOTHERAPY ADMINISTERED WITH SANDWICH CAPECITABINE CHEMOTHERAPY IN A SAMPLE OF 28 BREAST CANCER PATIENTS

Code: 420

Aims: To retrospectively analyze feasibility and toxicity of adjuvant radiotherapy (RT) administered along with alternate capecitabine chemotherapy ("sandwich therapy") in patients who received primary systemic therapy for breast cancer (BC).

Methods: From January 2021 to May 2023 a retrospective cohort of 28 BC patients was analyzed for a total of 29 treatments (one bilateral BC). Our primary endpoint was to evaluate acute and late toxicity with CTCAE 5.0 scale. All patients received primary systemic therapy followed by breast conservative surgery or mastectomy with or without axillary lymph nodal dissection. Clinical characteristics of patients are described in table 1. Six mastectomy patients (21%) underwent surgical reconstruction with a breast expander. All patients received a 40-46 Gy schedule in 15-20 fractions respectively, and in 16 patients an additional simultaneous integrated boost (SIB) of 7.95 Gy in 15 fractions was performed. In most cases, capecitabine was given for four cycles before and four cycles following RT, for an average of 7 cycles (3-8) for each patient. No wash-out time was applied. In terms of acute toxicity we analyzed skin reaction, breast edema, dysphagia/odynophagia and fatigue. As regards late toxicity we examined breast fibrosis, skin hyperpigmentation and telangiectases, capsular prosthesis contracture and arm lymphedema.

Results: Median follow-up time was 19 months (5-34). Seven patients (25%) received RT on breast, 10 (35%) on breast and loco-regional lymph nodes and 12 (42%) on chest wall and loco-regional lymph nodes. Nineteen patients (68%) reported G1-G2 skin toxicity, and only one patient reported G3 erythema. Acute breast edema was observed in 3 patients (10 %). Eight patients (28%) reported low-grade esophageal toxicity (25% G1 and 4% G2) and one patient voluntary interrupted RT without stopping chemotherapy. Only 4 patients (14%) experienced mild fatigue, while no severe fatigue was reported. Only 2 patients (7%) showed G1 fibrosis; no other toxicities were recorded. Arm lymphedema developed in 2 patients (7%) who received extensive nodal irradiation and in one case specific surgery was needed.

Conclusions: In our experience adjuvant breast radiotherapy delivered in an alternate schedule with Capecitabine has proven to be well tolerated with a low grade of acute and late toxicities. Arm lymphedema was a quite frequent side effect (<10%) more likely due to an extensive nodal irradiation rather than chemotherapy association.

Table 1 – Clinical Characteristicts of patients

Stage I-II	Stage IIIA-IIC	Luminal B	Triple Negative
19 pts (68%)	9 (32%)	6 (21%)	23 (82%)

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LOW RADIATION DOSES TO GROSS TUMOR VOLUME AND PERIPHERAL TUMOR TISSUE IN METABOLISM GUIDED LATTICE IRRADIATION BASED ON LATTICE-01 STUDY

Code: 57

Aims: To calculate the gross tumor volume (GTV) and the peripheral tumor tissue (PTT) receiving low radiation doses in patients submitted to "metabolism guided" lattice radiation therapy.

Methods: We reviewed treatment plans developed to treat voluminous masses using "metabolism-guided" Lattice irradiation according to the LATTICE-01 study. All plans aimed to deliver a high dose of spatially fractionated radiation in spherical deposits (vertices, Vs) within the voluminous disease. Vs were placed at the edges of tumor areas with different metabolism on PET examination according to a non-geometric arrangement. From this analysis were excluded the plans which work out the delivery of more 1 fraction to the Vs. Besides, we retrospectively created an external ring structure to include the tumor peripheral tissue by subtracting GTV. The relationships between GTV volumes and PTT with the following dose-volume histograms were evaluated: mean dose, maximum dose (Dmax), minimum dose (Dmin), and percentage of GTV and PTT receiving 0.5, 1, 2, and 3Gy (V1-3).

Results: 56 treatment plans were revised and 51 met the inclusion criteria. The median GTV volumes was 315,9 cc (range = 10,54-2605,9 cc). A median of 1 Vertex was allocated within the GTVs (range 1-9) and were planned to receive a dose of ≥10Gy/1 fraction (median 12Gy, range 10-15Gy). Median V3 percentage was 51.58% (range 2%-100%), median V2 percentage was 67,80% (range 1,60%-100%), median V1 percentage was 83,70% (range 0,80%-100%) and median V0.5 percentage was 88,49% (range 17.60%-100%). Corresponding 0.5, 1, and 2Gy PTT values were: V 0.5 65,21% (range 16-96.25); V1 58,08 (range 10.76-91.7); V2 42.53 (range 4.72-67.87) Dmax 998.8cGy (range 643,9-1415,3 Dmin median 5Gy (range 0-23.3).

Conclusions: A significant portion of GTV receive low doses during metabolism guided lattice irradiation. Lower radiation doses were delivered to PTT. These observations could be useful planning prospective studies on immunotherapy combined with lattice technique.

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PRELIMINARY RESULTS OF A PHASE II TRIAL: SPRINT (SARCOMA PREOPERATIVE RADIATION WITH SIMULTANEOUS INTEGRATED BOOST)

Code: 495

Aims: Neoadjuvant radiotherapy in operable Soft Tissue Sarcoma (STS) patients, aims to downstage tumors and improve resectability, despite increased risk of wound dehiscence. Clear margin resection (R0) may not be achieved in tumors closely situated to critical structures like the neurovascular bundle (NVB), impacting local control. We aim to improve R0 rates by incorporating an IMRT boost to potential areas of suboptimal resection.

Methods: This is a prospective monocentric single-arm Phase II study, enrolling locally advanced STS patients eligible for surgery. Radiotherapy is delivered in 25 daily fractions, to include the MRI-based Gross Tumor Volume (GTV) and the surrounding tissue at risk of microscopic spread (CTV1) with a dose of 50 Gy with SIB (Simultaneous Integrated Boost) intensification to the tumor/dissection plane interface (CTV2) to a dose of 60 Gy. CTV2 is approved by both a Radiation Oncologist and a Surgeon, with a 0.5 cm margin applied to generate PTV1 and PTV2. Concurrent chemotherapy (ChT) is permitted for up to 3 cycles. Primary endpoint is the R0 resection rate. Secondary endpoints include pathologic complete response rate, objective response, overall survival, local and distant progression-free survival, as well as acute and chronic toxicity rates. Pathologic complete response (pCR) and near-complete response (pNCR) are defined as necrosis rates of 100% and 90-99%, respectively. To assess an increase in R0 rate from 81% to 97% assuming ?=80% e ?=0.05, 33 patients will be included. At least 95% of both PTV1 and PTV2 should be covered by 95% of the prescribed dose, with a maximum allowable dose of 107%.

Results: Twelve patients were included, with tumors located in the limbs (10 patients) and in the trunk (2 patients). Mean age was 52.4 years. Concurrent chemotherapy was administered to 2 patients. Mean GTV size was 745.12 cm3. PTV1 and PTV2 achieved a mean coverage of 98% by the prescribed dose. Mean PTV1 and PTV2 Dmax was 61.7 Gy and 63.3 Gy, remaining below the threshold of 107%. Mean Dmax to bone was 57.5 Gy. In 3 patients, the Dmax to the skin corridor exceeded 20 Gy. Although NVB intersected with PTV2 in 8 cases, the Dmax remained below 66 Gy. No Grade ?3 acute skin toxicity was observed. Among twelve patients who underwent surgery, four achieved pCR and eight achieved pNCR. No significant wound complications were documented.

Conclusions: The initial 12 patients met most planning objectives. Preliminary results indicate a safe profile and promising tumor response.

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Table 1. Dose Constraints

Organs at Risk	Primary Objectives
D_{mean} Bone	<37 Gy
D_{max} Bone	<59 Gy
V_{bone} ≥40 Gy	<64%
D_{max} Skin Corridor	20 Gy
D_{max} Neurovascular Bundle	66 Gy (EQD2)
D_{min} GTV	50 Gy

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TOXICITY AND ONCOLOGICAL OUTCOME IN BRCA- CARRIERS RECEIVING RADIOTHERAPY FOR BREAST CANCER: RESULTS AT A MEDIAN FOLLOW-UP OF 5.4 YEARS

Code: 164

Aims: The different pathological aspects of *BRCA*-associated tumors support the hypothesis that *BRCA-carriers* might have a worse breast cancer (BC) prognosis compared to *non-BRCA-carriers.* Study results were inconsistent, with 5y OS ranging from 42% to 100%(1). Moreover, because of BRCA genes are involved in DNA double-strand breaks repair, radiotherapy (RT) may virtually cause higher RT-related toxicity in *BRCA-carriers*. However, clinical data from retrospective studies did not confirm this hypothesis (2). Here we present both clinical and toxicity data of BC *BRCA-carriers* receiving RT at a single Institution.

1)10.1371/journal.pone.0120189
2)10.1016/j.breast.2014.12.003

Methods: Data about BC *BRCA-carriers* receiving RT after surgery for BC were collected retrospectively. Details about tumor, RT treatment, toxicity (according RTOG scale) and oncological outcome were retrieved from clinical reports. In order to achieve a theoretic minimum follow up of 5 years, only consecutive RT-courses before the year 2018 were included. RT was delivered with Tomotherapy Hi-Art System (Tomotherapy Inc., Madison, WI). The prescribed dose was 40.05Gy/15fr. Target volumes included both the whole breast (WB)+/-boost and the chest wall (CW) with axillary levels at the discretion of the radiation oncologist.

Results: Twenty-eight *BRCA-carriers* received RT between 2015 and 2018 for I-III stage BC. Median age was 47y (range:30-78). Target volume were as follows: 7 WB+boost, 1 CW+1-2 axillary levels and 20 CW+supraclavicular nodes. Hormonal therapy, adjuvant chemotherapy and neoadjuvant chemotherapy was administered in 17,13 and 10 patients, respectively. At a median follow up of 5.4y (0.8-8.1y), 25/28 (89%) *BRCA-carriers* had no evidence of disease at the last clinical evaluation, including 2/25 and 1/25 with a contralateral breast and a lung cancer along the follow up, respectively. Acute toxicity (=end of RT) was as follows: G0=3(11%); G1=19(68%); G2=6(21%). Chronic RT-toxicity evaluation (=>6 months after RT) was available for 14/28 patients: at a median follow up of 2y (0.6-7.4y), 3/14(21%) G2 toxicity were present. Among the 18 patients with an implant at the time of RT,14 had a follow up with the plastic surgeon (median=2.8y) with only 2/14(14%) cases of reconstruction failure.

Conclusions: Radiotherapy in *BRCA-carriers* was well tolerated with encouraging oncological outcome of 89% of patients alive at a median follow up of 5.4 years.A larger population and a similar group of *non-BRCA- carriers* are needed to further comparative analysis.

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EVALUATING EFFICACY AND SAFETY OF CONCURRENT NEOADJUVANT CHEMORADIOTHERAPY IN PATIENTS WITH LOCALLY ADVANCED NON-SMALL-CELL LUNG CANCER

Code: 364

Aims: The aim of our study is to evaluate the efficacy and the safety of concurrent neoadjuvant chemoradioterapy (RTCT) followed by surgery in patients affected by locally advanced Non-Small-Cell lung cancer.

Methods: Patients with histologically proven NSCLC, medical/functional operable and deemed candidate to neoadjuvant RTCT by multidisciplinary institutional tumor group were retrospectively evaluated. All pts received concurrent neoadjuvant RTCT followed by surgery. Chemotherapy drugs included platinum compounds, taxanes, gemcitabine and pemetrexed. Before concurrent RTCT, some pts received induction chemotherapy, using platinum compounds and/or taxanes. Data were collected retrospectively and overall survival (OS), progression-free survival (PFS), local control (LC) and metastasis-free survival (MFS) were calculated with Kaplan-Meier analysis. CT response was assessed by RECIST criteria. Acute and late toxicities were assessed for safety using the CTCAE version 5.0 scoring system.

Results: The population study included 97 pts, treated from January 2011 to August 2023, classified according to stage (7 IIB, 38 IIIA, 52 IIIB) and to histology (63 adenocarcinoma, 30 squamous, 4 other histology). 39 pts received induction chemotherapy (40.2%). Median delivered radiotherapy dose was 50 Gy (range: 50-60Gy). Clinical pre-operative partial response was observed in 74 pts (76.3%). All pts underwent R0 surgery: 12,4% pneumonectomy, 11,4% bilobectomy, 70% lobectomy and 6,2% wedge resections. 25 pts (25.7%) experienced a post-operative complication. Pathological downstaging was observed in 60 pts (61.8%). 46,4% of pts had lymph node clearance (N0) and 17,5% had pCR (pT0N0). Overall treatment was well tolerated: G2 pulmonary toxicity was observed in 8 pts (8.2%) and G2 oesophageal toxicity in 24 pts (24.7%). No grade>3 toxicity were recorded. With a median FUP of 38.9 months 2 and 5-year OS was 75.8% and 49.4% with median OS of 59.4 mo. 5y-OS was higher in the group with pCR (59.3% vs 49.5%) but the statistical significance was not reached (p=0.6). The 2 and 5-year PFS was 92.5% and 76.6%. Increased 5-year LC was detected in the group of pts with lymph node clearance after surgery (80% vs 67.2%, p=0.07). Mediastinal lymph node local recurrence occurred in 16 pts (16,5%). The 2 and 5-year MFS was 64.6% and 54.4%.

Conclusions: Concurrent neoadjuvant RTCT followed by surgery is an effective strategy of treatment in Stage III NSCLC with excellent OS and PFS as well as low treatment-related toxicity profile.

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RADIOTHERAPY WITH CONCURRENT CDK4/6 INHIBITORS FOR ELDERLY PATIENTS WITH METASTATIC BREAST CANCER

Code: 362

Aims: Several trials have demonstrated the benefit of CDK4/6 inhibitors plus endocrine therapy in oestrogen receptor-positive (ER+) advanced breast cancer (BC). Retrospective data showed limited toxicities with the combination of radiotherapy with CDK4/6 inhibitors in patients with metastatic breast cancer.
However, there is a lack of information about tolerance of combined treatment in elderly patients. The aim of this study was to evaluate in a retrospective cohort of patients the safety of the combined treatment in elderly patients.

Methods: Patients with histologically proven metastatic or locally advanced BC treated with RT and concurrent CDK4/6 inhibitors were selected. Toxicity was assessed according to the NCI-CTCAE V4.0.
Difference among groups were calculated by means of chi-square test.

Results: 80 patients treated with concurrent CDK4/6 inhibitors and RT to a total of 152 metastatic sites were included in the analysis. The anti-CDK4/6 administered concurrently were Palbociclib in 41.3 %, Ribociclib in 31.2 % and Abemaciclib in 27.7% of patients. Among this patients cohort, 25 patients were older than 70 years old (median 76, range=70-86) and were treated to a total of 46 sites of disease (30.3%). The main results are summarized in Table 1. The majority of radiation treatment were fractionated stereotactic treatments to oligoprogressive/oligorecurrent site of disease (66.4%). 33.6% of treatments were palliative. In the older patients the most common CDK4/6 delivered concurrently was Palbociclib (17 patients, 68%, p=0.013). Overall, the toxicity reported during RT was limited (16.4%). No difference in tolerance was detected between younger and older patients (p=0.470). Grade 3 toxicity was detected in 5 patients in the younger group (9.0%) and in 2 patients in the older group (8.0%).

Conclusions: Radiotherapy given concurrently with anti CDK4/6 seems well tolerated also in older patients showing acceptable toxicity. Patients' age should not be a parameter on the basis of which suspend CDK4/6 inhibitor during RT.

	Whole cohort (n, %)	Age < 70 yrs	Age ≥70 yrs	p
	80 (100.0)	55 (68.8)	25 (16.4)	
Anti CDK4/6 delivered concurrently				0.013
Palbociclib	33 (41.3)	16 (20.0)	17 (21.3)	
Ribociclib	25 (31.2)	21 (26.2)	4 (5.0)	
Abemaciclib	22 (27.5)	18 (22.5)	4 (5.0)	
RT treatments (n)	152 (100.0)	106 (69.7)	46 (30.3)	
Radiotherapy treatments				0.455
SBRT (n, %)	101 (66.4)	68 (44.7)	33(21.7)	
Palliative treatment (n, %)	51 (33.6)	38 (25.0)	13 (8.6)	
RT site				0.853
Bone	124 (81.6)	88 (57.9)	36 (23.7)	
Others	28 (18.4)	18 (11.8)	10 (6.6)	
Overall Toxicity (any grade)				0.470
Yes	25 (16.4)	16 (10.5)	9 (5.9)	
Not	127 (83.6)	90 (59.2)	37 (24.4)	
Toxicity (CTCAE grade)				0.504
grade 1	14	8	6	
grade 2	3	3	0	
grade 3	7	5	2	
grade 4	1	1	0	
Toxicity (type)				
Haematological	17	12	5	
GI	4	2	2	
Other	4	2	2	

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IS BRIDGING RADIOTHERAPY BEFORE CAR-T CELL INFUSION FOR DIFFUSE LARGE B CELL LYMPHOMA EFFICIENT? THE EXPERIENCE OF SAN BORTOLO HOSPITAL (VICENZA). WHAT HAVE WE LEARNED OVER THE PAST 3 YEARS

Code: 470

Aims: Chimeric antigen receptor-modified (CAR) T-cell therapy targeting CD19 has revolutionized the treatment of relapsed or refractory B-cell lymphomas.Radiation therapy (RT) in alternative or concurrent to chemotherapy can be used as a bridging strategy. In this study we updated the results regarding the effectiveness and toxicity of bridging radiation therapy (bRT) after 2 years of CART use.

Methods: We reviewed all the patients treated at our department with CAR-T cell infusion. All data were retrospectively collected. The indications for bridging RT were local and symptom control. We analysed all treatment details, toxicity and disease course. Bridging systemic therapy was defined as either chemo/targeted therapy or steroids administered between leukapheresis and lymphodepleting chemotherapy. bRT was delivered though intensity modulates radiotherapy (IMRT) or three-dimension (3D) techniques.

Results: Between May 2020 and October 2023 47 patients were treated in our department with CAR-T cell therapy. The whole group of patients was characterized by primary refractory diffuse large B cell lymphoma (DLBCL). 26 patients received TISA-CEL and 21 patients ACI-CEL therapy. 17 patients received bRT 2 to 10 Gy/fraction to a median total dose of 24 Gy (range 20-36 Gy). Median follow up was 14 months (range 7-40 months). There was non grade 3 o higher toxicity due to RT. Radiation-related toxicities were all grade 1 and included nausea, vomiting, diarrhoea, abdominal pain, fatigue, and mucositis. Patients with localized disease in the bRT group received radiation to all active sites. At 30 days the objective response rate was 67% with complete response in 42% of cases. At 3 months the odjective response rate was 52% with complete response at 47,5% of the cases. In the RT group the 6 month PFS and OS were of 50% and 54% respectively.

Conclusions: Bridging radiotherapy (with or without concomitant chemotherapy) can be safely administered before CAR-T cell infusion in high-risk lymphoma. Regarding survival outcomes and toxicity of CART, few studies have used bRT for cART. The RC rate ranged from 45% to 83%, and the objective response rate from 80% to 100%. Our results are similar to those reported. Future investigations are needed to prospectively define the optimal RT characteristics (total dose, dose/fraction, timing) to identify patients most likely to benefit in order to maximize efficacy and reduce side effects.

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REPEATED HYPERARC RADIOSURGERY FOR RECURRENT INTRACRANIAL METASTASES AND DOSIMETRIC ANALYSIS OF RECURRENCE PATTERN TO ACCOUNT FOR DIFFUSE DOSE EFFECT ON MICROSCOPICAL DISEASE

Code: 445

Aims: Stereotactic radiosurgery (SRS) is an established non-invasive therapy for multiple brain metastases M(BMs). Mono- isocentric techniques allow the delivery of multiple stereotactic courses, in the event of intracranial failure. Nevertheless, limited data on the effectiveness and toxicity have been reported, as well as details on patterns of failure. The aim of this study is to evaluate the effectiveness and safety of multiple HyperArc courses and patterns of progression in patients affected by BMs with intracranial progression.

Methods: 56 patients were treated for 702 BMs with 197 (range 2-8) HyperArc courses in case of exclusive intracranial progression. The primary end-point was the overall survival (OS), and secondary end-points were intracranial progression-free survival (iPFS), toxicity, local control (LC), neurological death (ND), and WBRT-free survival. Site of progression was evaluated against isodose levels (0, 1, 2, 3, 5, 7, 8, 10, 13, 15, 20, and 24 Gy.).

Results: The 1-year OS was 70%, and the median was 20.8 months (17-36). At the univariate analysis (UVA) BED>51.3Gy and non-melanoma histology significantly correlated with OS. The median time to iPFS was 4.9 months, and the 1-year iPFS was 15%. Globally, 538 new BMs occurred after the first HA cycle in patients with extracranial disease controlled. 96.4% of them occurred within the isodoses range 0-7 Gy as follows: 26.6% (0 Gy), 16.5% (1 Gy),
16.5% (2 Gy), 20.1% (3 Gy), 13.1% (5 Gy), 3.4% (7 Gy) (p=0.00) (figure 1). Clinical toxicity was represented by
headache 4 (7.1%), and radionecrosis 2 (0.28% of treated metastases). One- and 2-year LC was 90% and 79%, respectively. At the UVA BED>70 Gy and non-melanoma histology were significant predictors of higher LC. The 2-year WBRT-free survival was 70%. After a median follow-up of 20 months, 12 patients were deceased by ND (median time 17.4 months).

Conclusions: Intracranial relapses can be safely and effectively treated with repeated HyperArc, with the aim of postponing or avoiding WBRT. Diffuse dose by volumetric RT might reduce microscopic disease also at relatively low levels, potentially acting as a *virtual CTV*. Neurological death is not the most common cause of death in this population, which highlights the impact of extracranial disease on overall survival.

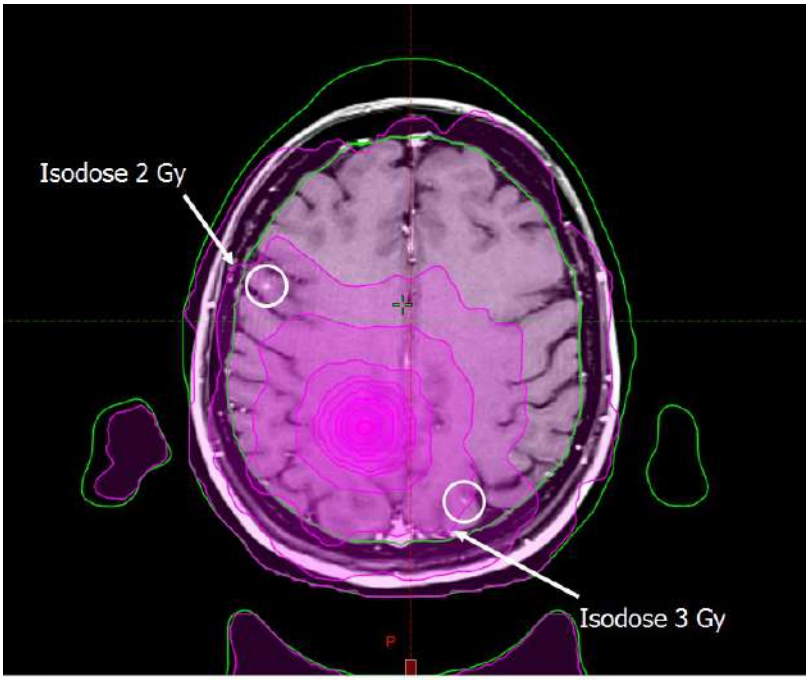

Figure 1. Analysis of pattern of relapse. The site of new BMs occurrence against isodose level from previous SRS was registered by fusing diagnostic MR with the previous HyperArc plan.

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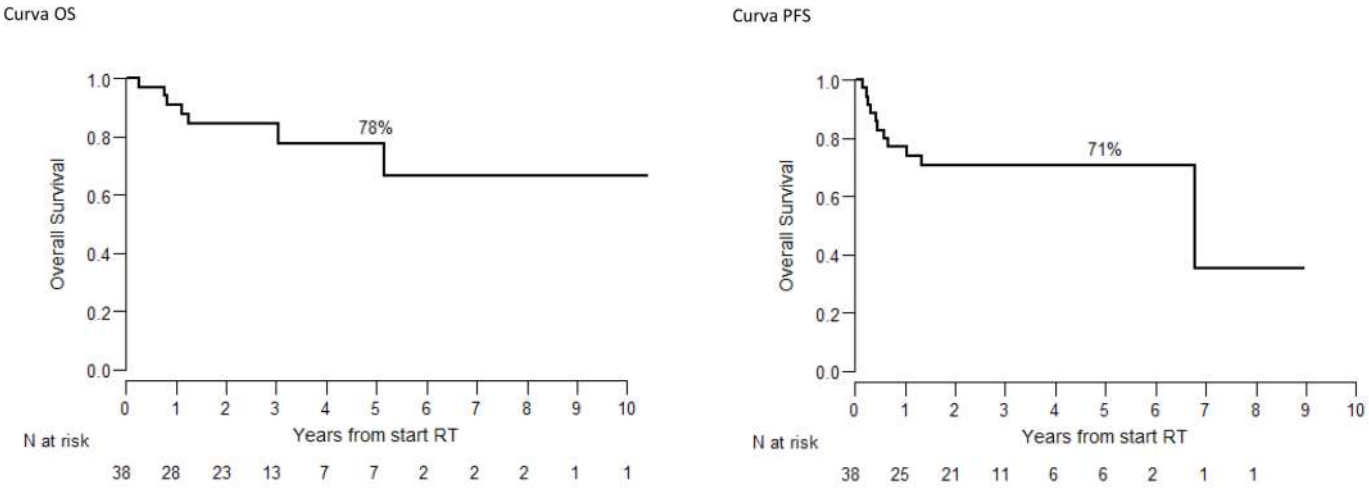
THE ROLE OF RADIOTHERAPY ON SINGLE RESIDUAL PET POSITIVE LESIONS AFTER FRONTLINE CHEMOIMMUNOTHERAPY IN PATIENTS WITH DIFFUSE LARGE B CELL LYMPHOMA: A SINGLE CENTER RETROSPECTIVE ANALYSIS

Code: 266

Aims: Front-line chemoimmunotherapy (CIT) with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) in Diffuse Large B Cell Lymphoma (DLBCL) achieves an 80% complete response (CR) rate. Relapsed or refractory cases often resort to salvage therapies like chimeric antigen receptor-T cells, autologous stem cell transplant, CIT. In cases with a partial response (PR), the impact of radiotherapy (RT) remains underexplored. Despite the absence of randomized trials, recent studies in limited/early stages suggest promising outcomes.

Methods: We included 38 patients(pts) with a diagnosis of DLBCL who performed RT on single residual PET positive lesions after CIT in our center from 2014 to 2024. Median age at diagnosis was 70 years (range 25-85). Disease stage was I-II in 13 pts (34.3%) and III-IV in 25 pts (65.7%). Fifteen patients (39.5%) had a bulky disease at diagnosis. Thirtyfive/38 pts (92.1%) underwent R-CHOP and the remaining 3 pts, other CIT. A RT dose of 30-39.6 Gy was delivered to 12 pts (31.5%) and a dose of 40-50 Gy to 26 pts (68.5%),1.8-2.0 Gy per fraction. Volumetric modulated arc therapy was used in 17(44.7%) pts and 3D-conformal RT in 21(55.3%) pts. Post radiation PET scan was performed in 29 pts (76.3%).

Results: Complete response (CR) was obtained in 17 pts (44.7%), PR in 3 pts (7.9%) and stable disease (SD) in 4 pts (10.5 %). Progressive disease (PD) was observed in 5 pts (13.2%). Among those pts who did not perform a post radiation evaluation, 8/9 (88.9%) did not experience a relapse. Only one patient relapsed, having a disease progression 7 years after RT. At the latest follow up 7 pts (18,4%) were dead, all due to



progressive disease. Among those, only 1 patient (2.6%) had achieved CR after RT, while the other 6 pts (15.8%) achieved PR or no response after RT(p=0.006). Overall, 10 pts (26.3%) had a progressive disease after RT. Five pts (13.2%) had PD at the post radiation PET scan, while 5 pts (13.2%) relapsed later after a SD, PR or CR to RT. All these 10 patients progressed out of radiation field and 8/10 patients had recurrence both in-field and out-field (21.1%). RT dose wasn't related to outcome. At 5 years overall survival (OS) was 78% and progression-free survival (PFS) 71% in the whole population.

Conclusions: Our data confirm the efficacy of RT in DLBCL pts with single residual PET positive lesions after front-line CIT. A CR to RT predicts for better outcome. RT dose was not related to OS and PFS.

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A BIOLOGICAL-DRIVEN APPROACH FOR RADIATION THERAPY PERSONALIZATION IN BREAST CANCER: PRELIMINARY DATA AND RESEARCH PERSPECTIVES

Code: 109

Aims: The clinical scenario in radiotherapy (RT) is increasingly directed toward the evaluation of new hypofractionated protocols in order to increase treatments's effectiveness. Numerous predictive models have been developed and are included in the TPS (Treatment Planning System) software for the elaboration of effective clinical RT plans. All of them are based on the Linear Quadratic (LQ) model, describing the biological response to ionizing radiation according to the alpha (α) and beta (β) parameters. However, in clinical the α/β ratio remains a fixed value for the same organ tumor. We developed a generalized LQ model to calculate the local disease-free survival rate (LSR) and to customize the radiant treatment plan in different BC cell types. The LSR model as a novelty takes into account some radiosensitivity parameters exclusive for each cell lines, in addition to the α/β ratio. The first objective of this study aims to apply the LSR model to different Triple Negative Breast Cancers (TNBCs) cell lines, to address personalized RT plans in terms of dose per fraction and total dose for each BC cell lines and reach an LSR probability close to 100%. The second objective is to assess treatment feasibility for the BC cases that would need higher doses to reach a LSR close to 100%, as in these cases the treatment tolerability for healthy tissues must be considered.

Methods: TNBC cell lines are used as in vitro models for radiobiological characterization and identification of radio- response biomarkers. Preclinical murine models, such as MDA-MB-231 xenografts in the Balb/c nude mice, will be tested to compare the efficacy between standard RT protocol and one LSR calculated. TPS simulation studies will be performed to translate the schedules prescribed by the LSR application to the patients already treated.

Results: Radiobiological parameters such as doubling time, clonogens number, α/β ratio were experimentally calculated. Dose-response curves obtained showed different radiosensitivity. Radio-response biomarkers identification is in progress.

Conclusions: The development of a biological-driven strategy for addressing RT treatment plans to patients based on their tumor radiosensitivity represents a clinical challenge and the final goal of this project.

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THE ROLE OF METASTASIS DIRECTED THERAPY IN THE OLIGOMETASTIC PROSTATE CANCER PATIENT JOURNEY

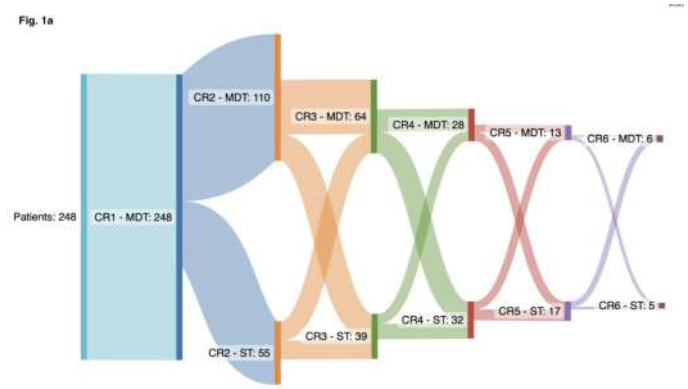
Code: 101

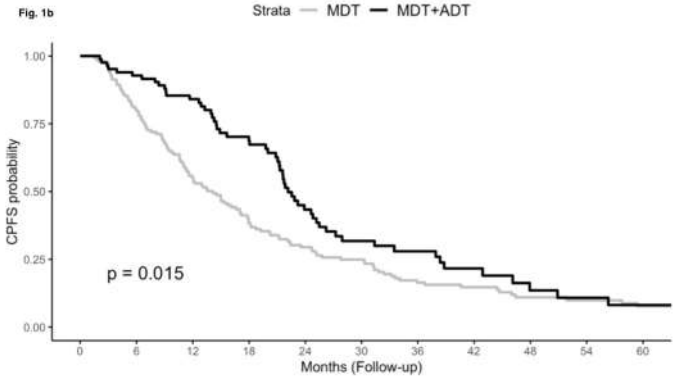
Aims: This research aims to evaluate the trajectories of metachronous hormone-sensitive prostate cancer (omHSPCa) patients, focusing on the influence of various clinical factors on the oncological outcomes - Clinical Progression Free Survival (CPFS) after first MDT treatment, Castration Resistance Free Survival (CRFS) and Free Survival to Polimetastatic state (PMFS)

Methods: The study included patients diagnosed with metachronous omHSPCa, having ≤ 5 metastases, who underwent MDT by SBRT from 2014 to 2022 at the European Institute of Oncology, Milan, Italy. Kruskal- Wallis test, Kaplan-Meier survival curves and log-rank analysis were adopted. Univariate Cox regression analyses was carried out and significant features were included in the multivariate Cox regression. Process mining analysis was performed using the pMineR and pMinShiny libraries.

Results: The study included 248 patients with a median age at primary diagnosis of 64 [IQR 58-68]. Median follow- up was 8.0 years [IQR 5.3-11.9] and the median time to first clinical recurrence from the treatment of the primary tumor was 4.24 years [IQR 2.18–7.44]. A total of 469 MDTs was assessed. Specifically, 54%
(135 patients) underwent more than one course of MDT (Fig.1a).
CPFS median time was 22.1 (95% CI, 21.2-26.2) months for patients receiving concurrent ADT and 14.1 (95% CI, 11.4-17.8) months for those who did not ($p < 0.05$) (Fig.1b).
A total of 60 events was assessed in CRFS analysis, with a median time of 18.7 years. Multivariate Cox analysis identified N1 at primary diagnosis (HR 2.04, 95% CI 1.08-3.86, $p = 0.03$), ISUP4-5 (HR 1.95, 95% CI 1.12-3.38, $p = 0.02$), and ADT usage of ≥ 2 years (HR 1.76, 95% CI 1.03-3.02, $p = 0.04$) as independent CRFS predictors.
PMFS analysis included 72 events with a median time of 17.7 years. Key PMFS predictors included ISUP4-5 (HR 2.34, 95% CI 1.43-3.84, $p <$ 0.01), M1b at first recurrence (HR 1.83, 95% CI 1.14-2.94, $p =$
0.01), 4-5 lesions at first recurrence (HR 5.46, 95% CI 1.57-18.97, $p < 0.01$), MDT not always to all
lesions at imaging (HR 2.70, 95% CI 1.58-4.61, $p < 0.01$).

Conclusions: This study highlights the comprehensive management of omHSPCa, from diagnosis to treatment outcomes. The findings underscore the significance of personalized treatment approaches, the potential benefits of integrating ADT, and the pivotal role of MDT. Additionally, the endpoints analyzed have economic implications. Delaying castration resistance could lead to significant cost savings while enhancing the patient's quality of life.





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EARLY TOXICITY IN ADJUVANT RADIOTHERAPY FOR BREAST CANCER IN COMBINATION WITH PEMBROLIZUMAB: RETROSPECTIVE ANALYSIS OF A MONOCENTRIC COHORT

Code: 584

Aims: After KEYNOTE 522 results, treatments schedule for locally advanced triple negative breast cancer changed with pembrolizumab introdution in neoadjuvant and adjuvant phase. In registrative trial, radiotherapy (RT) was administered after surgery according to clinical practice, with concomitant pembrolizumab administration. No clinical and laboratoristic data were reported in literature about this association. Aim of this study is to report early toxicity data of a monocentric retrospective cohort.

Methods: All the pts who underwent primary sistemic therapy (PST) according KEYNOTE 522 schedule, surgery and adjuvant RT with pembrolizumab were retrospective identified and collected with on-site artifical intelligence-based RWD system called GENERATOR. Data collected were pts characteristics, tumor characteristics, treatments administered characteristics. Toxicity was reported according to CTCAE v5.0 and classified in IT-related, RT-related and RT/IT-related.

Results: From March 2023, 64 pts underwent PST according to KEYNOTE-522 schedule, among them 13 pts underwent also adjuvant radiotherapy with concomitant pembrolizumab administration. Mean age was 53 y (37-78). All the pts presented a ductal infiltrating carcinoma, G3, 12 pts (92%) were basal-like, while 1 pt (8%) was HER2-low TN immunophenotype. 2 pts did not complete epirubicin-cyclophosphamide administration for hemorragic cystitis. About surgery, 3 pts (23%) underwent mastectomy with reconstruction, while 11 pts (77%) underwent conservative surgery. 77% of pts (10 pts) underwent pCR at final hystologic analysis. About RT administration, 3 pts underwent RT on chest wall and II-III-IV level lymph nodes with standard fractionation, 3 pts underwent RT on breast gland and II-III-IV level lymph nodes with standard fractionation, 7 pts underwent RT on breast gland with hypofractionated schedule. Eight pts reported IT toxicities before RT starting (2 artritis G2 with steroids administration, 2 hepatitis G2 and G3 with steroids administration, 4 pts thyroiditis with hormonal administration). During RT, 7 pts reported G1-2 skin erithema and 2 pts reported G1 odinophagia, none of them required steroids. No RT/IT related events were observed.

Conclusions: RT and pembrolizumab concomitant administration has been introduced as treatments of locally advanced TN breast tumor. This study reports real-world data extracted via a system based on text mining and artificial intelligence and did not show a summation effect of RT/IT related toxicity.

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HALFMOON RADIOTHERAPY: RESULTS UPDATE OF A REAL-WORLD MONOCENTRIC EXPERIENCE

Code: 123

Aims: The increasing use of immediate breast reconstruction (IBR) after mastectomy and its interaction with post- mastectomy RT (PMRT) has become a topic of great interest. In fact, in addition to the potential impact of RT on cosmetic outcomes, the reconstructed breast may also affect ideal target coverage and the optimal OARs sparing. Here we report an update of a preliminary experience with implant-sparing RT using the HALFMOON (Helical ALtered Fractionation for iMplant partial OmissiON) technique.

Methods: Breast cancer patients treated with mastectomy, and immediately reconstructed with implants (tissue expander -TE or permanent implant-PI) and receiving Halfmoon RT using TomoTherapy® Hi-Art System in helical modality at the IEO between February 2020 and January 2021 were considered for the analysis. All implants were placed beneath the pectoral muscle. As per our clinical practice, the TE was fully inflated before RT. Contouring was based on ESTRO/ACROP guidelines for PMRT after implant-based IBR. The chest wall CTV consist of the ventral part (between the skin and the implant); in case of adverse tumor factors, the dorsal partial part (between the implant and the rib wall) is added to ventral CTV. Oncological outcomes and data on capsular contracture (CC) of the breast implant according to the Baker classification were collected and reported.

Results: A total of 47 patients were analysed and their baseline characteristics are reported in **Table 1**. For patients reconstructed with TE, median time to TE substitution was 18 months (IQR 15.6-21.2 months).
Considering patients with an IBR with PI only 1 out of 20 required implant substitution after 20 months. Toxicity assessment of CC (RT and/or plastic surgeon FU) was available for 30/47 patients (64%) with a median toxicity FU of 2.8 years (IQR 1.6-3.1 years). Of them, 25 patients reported Baker grade ≥ 2. In 2 patients (4%) PI was removed for a local infection. Data were missing for 1 patient. At a median FU of 3.1 years (IQR 2.6-3.3 years), 44 patients (94%) are alive with no evidence of disease, two (4%) are alive with disease (one regional and one distant recurrence) and one (2%) was lost to FU.

Conclusions: From the reported experience implant sparing RT using Halfmoon technique is technically feasible, with an acceptable rate of CC and encouraging oncological outcomes. A larger cohort and longer FU will likely give clearer indications on this innovative and personalized treatment.

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Table 1. Summary of patients' characteristics

Variable	levels	n (%)
age at surgery (median, IQR)	49 years (44-54.5)	
T stage	*0*	3
	1	14
	2	22
	3	7
	x	1
N stage	*0*	9
	1	13
	2	13
	3	10
	x	2
Available FUs	*Radiotherapy*	27
	Oncology	13
	Senology	14
	Plastic surgery	18
	na	4
Type of reconstruction	*TE*	27
	PI	20

RESULTS OF NEOADJUVANT RADIOTHERAPY IN HIGH-GRADE SOFT TISSUE SARCOMAS OF THE EXTREMITIES: INSIGHTS FROM AN ITALIAN REFERENCE CENTRE

Code: 160

Aims: To assess the outcomes of high-grade soft tissue sarcomas (STS) of the extremities treated with neoadjuvant radio(chemo)therapy in a single-institution series.

Methods: This study involved 102 patients (median age 52 years, range: 16-86) with localized, high-grade STS of the extremities. All cases underwent a multidisciplinary review involving radiation oncologists, orthopaedic surgeons, medical oncologists, radiologists, and pathologists. The median radiation dose was 50 Gy (range 18-50) delivered in 25 fractions. Sixty-eight patients received preoperative chemotherapy, with seven continuing postoperatively. Conservative surgery followed a median of 5 weeks (range 2-14) post- radiotherapy.

Results: Over a median follow-up of 65 months (range 2-207), 40 patients (39.22%) experienced relapse: 2 (1.96%) locally, 36 (35.29%) with distant metastases (median onset 17.08 months, range 2.86-147.25), and 2 (1.96%) with both. The 5-year actuarial rates were: local control (LC) 96.90%, metastasis-free survival (MFS) 70.00%, disease-free survival (DFS) 69.00%, and overall survival (OS) 96.60%. Surgical margins were wide in 74.76% of patients, marginal in 19, and intralesional in 7. Histologic evaluation showed a median tumor necrosis of 80% (range <10%-100%). Log-rank tests indicated statistically significant better 5-year DMFS and DFS in patients with spindle cell histology (p=0.016, p=0.012) and lower median dose (p=0.047, p=0.021), better 5-year LC with wide resection margins (p=0.004), and improved 5-year OS with chemotherapy (p=0.008) (Table 1). None of the significant differences recorded in the multivariate analysis were confirmed in the multivariate analysis (Cox's proportional hazard method).

Conclusions: Neoadjuvant radiotherapy, combined with conservative radical surgery, achieves excellent LC and OS. This underscores the importance of thorough, multidisciplinary evaluation. The extended follow-up period is crucial for timely detection of metastases, which can occur long after treatment.

Table 1: actuarial results and univariate analysis.

Variable	Value	Nr Pz	5 LC	p	5-year-DMFS	p	5-year DFS	p	5-year OS	p
Histology	Spindle cell sarcoma	30	100%	0.387	86.0%	0.016	86.0%	0.012	96.2%	0.445
	Myxoid liposarcoma	34	94.0%		73.3%		70.4%		100%	
	Other	38	97.3%		53.3%		53.3%		93.2%	
Margins	Wide	77	97.2%	0.004	68.9%	0.365	68.9%	0.935	95.5%	0.127
	Marginal	18	100%		62.5%		62.5%		100%	
	Intralesional	7	85.7%		100%		85.7%		100%	
Age	< 52 years	47	95.6%	0.927	66.9%	0.827	64.8%	0.782	100%	0.053
	≥52 years	55	98.1%		72.8%		72.8%		93.4%	
Site	Lower limbs	82	96.1%	0.337	72.7%	0.380	71.5%	0.493	97.3%	0.925
	Upper limbs	20	100%		60.0%		60.0%		91.7%	
Chemotherapy	No	27	95.8%	0.275	68.8%	0.969	68.8%	0.867	95.8%	0.008
	Yes	75	97.3%		70.3%		69.0%		96.9%	
Median dose	<50 Gy	41	97.3%	0.448	80.0%	0.047	77.1%	0.021	97.3%	0.592
	≥50 Gy	61	96.7%		65.6%		63.9%		96.1%	
Boost	No	83	96.2%	0.288	68.3%	0.135	67.1%	0.096	95.7%	0.076
	Yes	19	100.0%		77.9%		77.9%		100.0%	
Necrosis	≥95%	31	93.4%	0.416	66.9%	0.431	63.6%	0.318	96.4%	0.154
	<95%	71	98.5%		71.5%		71.5%		96.8%	
Necrosis	≥90%	41	95.0%	0.741	66.3%	0.451	63.9%	0.387	97.3%	0.489
	<90%	61	98.3%		72.6%		72.6%		96.2%	
T	T1-T2	33	93.9%	0.080	72.3%	0.547	69.3%	0.926	100.0%	0.762
	T3-T4	79	98.3%		68.7%		68.7%		94.9%	

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LATTICE RADIATION THERAPY EFFICACY AND SAFETY: A RETROSPECTIVE STUDY

Code: 217

Aims: Lattice Radiation Therapy (LRT) is an innovative irradiation technique developed to improve large neoplastic lesions response, when SBRT[CP1] is excluded due to target dimensions. LRT aims delivering ablative doses with a toxicity similar to a conventional palliative RT[CP2] , thanks to an inhomogeneous target irradiation, where areas of high and low doses alternate as peaks and valleys. The LITE SABR M1 study highlighted the short-term safety of LRT, however, no data is currently available about its efficacy. The purpose of this study is to evaluate LRT efficacy and toxicity for palliative patients affected by large neoplastic lesions [CP3] (d>4.5cm).

Methods: We retrospectively evaluated 20 consecutive metastatic palliative patients above 18 years of age, who had undergone LRT in our institution. The treatment was 5 LRT fractions for a total dose of 20Gy prescribed to the entire lesion, with several simultaneous integrated boosts up to 66.70Gy. The primary endpoint was the Objective Response Rate (ORR) evaluated at the 6-month CT (RECIST 1.1 criteria). The secondary endpoints were the 6-month median lesions reduction, and the 6-month evolution of patients' antalgic response and performance status (ECOG PS). Treatment toxicity was recorded (CTCAE v5.0).

Results: Median patients' age was 70 years (range 18-85) with 10 males and 10 females. Median ECOG PS was 2 (range 0-3), with a median NRS of 6 (range 0-10[CP1] [CP2]), with 85% of patients under antalgic therapy. Lesions were located in the thorax (40%), abdomen-pelvis (15%), abdomen (5%), and extremities (25%). Median GTV and PTV dimension was 560.4cc (range 168.3-3838.3cc) and 873.75cc (251.7-4320.3cc), respectively. Median vertices number was 8 (range 4-17) and median beam on time was 5 min (range 3-16). Patients alive at 3 and 6 months were 14 and 10, respectively, with an ORR of 79% (95%CI: 49-95%) and 80% (95%CI: 44-97%) at 3 and 6-month CT, respectively. Median lesion reduction was 54% (range 6-74%) and 71% (14-71%) at 3 and 6 months, respectively. At 3 and 6 months, 6 out of 14 and in 3 out of 10 patients reported a partial antalgic response, while there was a complete antalgic response in 8 out of 14 and 7 out of 10 patients, at 3 and 6 months, respectively. All patients had an improvement in performance status. No >G3 toxicity was recorded during the 6-month follow up period.

Conclusions: According to our data, LRT resulted safe and effective option for palliative patients affected by large cancer.

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FIRST RESULTS OF A PHASE II TRIAL OF HYPOFRACTIONATED ADJUVANT RADIOTHERAPY FOR EARLY-STAGE BREAST CANCER WITH VOLUMETRIC MODULATED ARC THERAPY AND HIGH DOSE SIMULTANEOUS INTEGRATED BOOST (DEBORATRIAL)

Code: 269

Aims: DEBORA trial is a phase II trial enrolling early stage breast cancer patients <50 years of age with at least one additional risk factor treated with breast conserving therapy and radiotherapy with high dose simultaneous integrated boost (total dose to tumor bed 52.5/3.5 Gy per fraction). Primary endpoint is the 4 year rate of fibrosis. Here we report the interim analysis on the first 50 patients enrolled with regard to acute toxicity. Also late toxicity was reported for patients with at least one year of follow-up.

Methods: Patients aged < 50 yr with histologically proven breast cancer who underwent conservative surgery with at least 3 inserted clips on tumor bed and at least one of the following histopathologic additional risk for local recurrence: T>2 cm, N1 disease; unfavourable biology, lymphovascular invasion; close margins (≤4 mm) were considered eligible for the trial. Patients were treated with hypofractionated RT to whole breast to a total dose of 40.05 Gy in 15 fractions (2.67 Gy/die) and a simoultaneous integrated tumor bed dose of 52.5 Gy (3.5 gy/die). VMAT planning was used. Acute Toxicity and Breast fibrosis were evaluated by means of Common Terminology Criteria for Adverse Events (CTCAE) v. 5 scale at baseline and each year during follow-up.

Results: Between May 2020 and July 2023, 50 consecutive patients, all with an age lower or equal to 50 years old (48;32-50) were enrolled. Additional risk factor in the patients population are listed in Table 1. Most of the patients enrolled had as additional risk factor surgical margin < 4 mm (40.0%). Among patients with unfavourable biology (13, 26%), 11 (22%) patients presented with luminal B tumors, 2 patients (4.0%) with triple negative tumors. Median follow-up time was 21 months (range: 4-42 months). 36 (72%) patients had a follow-up longer than one year. All the patients completed treatment to the prescribed dose. All patients were evaluable for acute toxicity. No patients experienced grade ≥2 acute and subacute toxicity. Table 2 and 3 summarize results on toxicity. In regard to late effects, breast fibrosis was beterten in 22,2%

Conclusions: Toxicity was deemed acceptable in the first 50 patients enrolled. Longer follow-up and completion of enrollment is awaited to confirm the results, expecially in regart to late toxicity.

Table 1. Patients' population additional risk factors.

Risk factors	Tot: 50 Pts (100%)
T>2cm	13, 26.0%
N+	11, 22.0 %
Unfavorable Hystology	13, 26.0%
LVI	6, 12.0 %
Close Margins (≤4 mm)	20, 40.0%

Abbreviations: N+= Positive Nodal Status; Unfavorable histology= Triple Negative/Luminal B; LVI= Lymphovascular Invasion

Table 2. Summary of acute and subacute effect, absolute and relative numbers classified by CTCAE v 5.0

	Acute toxicity (during RT)			Subacute toxicity (3 months after RT)		
	1	2	3	1	2	3
Skin Dermatitis	N= 21 (42%)	N=0 (0.0%)	N=0 (0.0%)	N=17 (34%)	N=0 (0.0%)	N=0 (0.0%)
Breast Edema	N=1 (2.0%)	N=0 (0.0%)	N=0 (0.0%)	N=11 (22%)	N=0 (0.0%)	N=0 (0.0%)
Breast pain	N=0 (0.0%)	N=0 (0.0%)	N=0 (0.0%)	N=3 (6%)	N=0 (0.0%)	N=0 (0.0%)

Table 3. Summary of late effects (3 months), absolute and relative numbers classified by CTCAE v 5.0

	1	2	3
Skin Dermatitis	N=3 (8,3%)	N=0 (0.0%)	N=0 (0.0%)
Breast Edema	N=1 (2,78%)	N=0 (0.0%)	N=0 (0.0%)
Breast pain	N=3 (8,3%)	N=0 (0.0%)	N=0 (0.0%)
Fibrosis	N=8 (22,22%)	N=0 (0.0%)	N=0 (0.0%)
Pneumonitis	N=0 (0.0%)	N=0 (0.0%)	N=0 (0.0%)
Cardiac disease	N=0 (0.0%)	N=0 (0.0%)	N=0 (0.0%)

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MOLECULAR BIOMARKERS AND GLOBAL LONGITUDINAL STRAIN AS POTENTIAL EARLY PREDICTORS OF POST-TREATMENT CARDIAC TOXICITY IN PATIENTS AFFECTED BY LYMPHOMA WITH MEDIASTINAL SITE: A PILOT STUDY

Code: 136

Aims: To detect molecular and instrumental markers of early onset cardiac damage in patients (pts) with mediastinal lymphoma receiving chemotherapy (CT) and radiation therapy (RT) directed to mediastinum.

Methods: Between March and December 2023, we admitted 7 pts with mediastinal B-cell lymphoma (PMBCL) and 3 with Hodgkin lymphoma (HL) with a mediastinal involvement. All pts had bulky disease, underwent CT according to their pathology (fig1), and were radiated to the mediastinum with IMRT technique (30Gy for 9 pts and 36Gy for 1 patient). The protocol consists of molecular and instrumental evaluations at baseline (T0), 48h after CT (T1), 48h after RT (T2), and thereafter every 3 months (T3). Peripheral whole blood molecular biomarkers include: B-type natriuretic peptide (BNP), high sensibility Troponin (T-HS) and cardiac specific micro-RNAs (miRNA) (miR-1, miR-133, miR-145, miR-208, miR-499), which are measured with real time PCR. Instrumental evaluations include: Cardiac Computed Tomography Angiography (CCTA) and Cardiac Magnetic Resonance Imaging (MRI) at T0, and echocardiogram (ETG) with 2-dimension global longitudinal strain (2D-GLS) at each time-point. CCTA and cardiac MRI are fused with CT RT-planning to perform cardiac segmentation (whole heart (WH), chambers, arteries, valves, and interventricular septum (SIV) were identified).

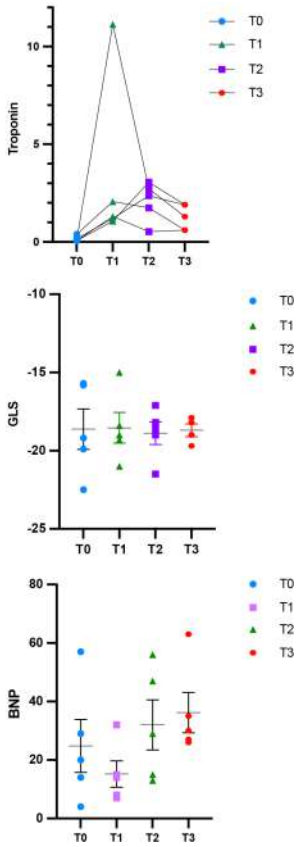
Results: So far, 5 pts completed the evaluation pipeline, the rest is currently under treatment. Measurement of miRNAs is in progress. After CT, of the 5 pts only one had a 2D-GLS reduction>15% (T0: -22; T1: -15). ETG revealed slight reduction in SIV kinetics: preventive cardiac therapy with beta-blocker was prescribed. After RT, another patient experienced a reduction of 2D-GLS >15% (GLS T1 -21 vs GLS T2 -17). ETG showed mid-basal SIV hypokinesia; preventive dual cardiac therapy was prescribed. In this patient mean dose (DM) of WH and ISV were respectively 5.94 and 2.02 Gy. In all pts, DM received by WH, left ventricular (LV), SIV and lateral wall of the LV were respectively 5.12, 2.4, 2.27 and 1.74 Gy (other dosimetric parameters in Fig1). At T3, ETG showed an upturn of GLS parameters in both pts described above (first patient: GLS after CT, T1 -15 vs T3 -18.2: second patient: GLS after RT, T2 -17.01 vs -19.00). The trend of GLS and molecular parameters in all pts are reported in Fig1.

Conclusions: Molecular and instrumental markers seem a promising tool to detect early cardiotoxicity in asymptomatic lymphoma pts in order to set an early therapeutic approach.

Figure1

DEMOGRAPHICS FEATURES	NO. PATIENTS (10)
Median age (range)	35 (20-48)
Gender	
Female	9 (90%)
Male	1 (10%)
Histopathology	
PMBCL	7 (70%)
HL	3 (30%)
Site	
Mediastinum	7 (70%)
Mediastinum + supraclavicular fossa (FSV)	2 (20%)
Mediastinum + FSV + axilla	1 (10%)
Cardiovascular involvement at diagnosis	
Cardiac tamponade	1 (10%)
Pericardial effusion	6 (60%)
Superior Vena Cava Syndrome	3 (30%)
None	3 (30%)
Mediastinal bulky volume cm3	
> 500	7 (70%)
< 500	3 (30%)
Chemotherapy schedule	
12 R-VACOP-B cycles	7 (70%)
4 ABVD cycles	3 (30%)

DOSIMETRIC EVALUATION (five pts)	
Heart	
Dmean	5,12 Gy
V25	8,6%
Left Ventricle	
Dmean	2,4Gy
Dmax	18,16 Gy
Septum	
Dmean	2,47 Gy
Dmax	9,81 Gy
Lateral wall	
Dmean	1,74 Gy
Dmax	4,56 Gy
Left Atrium	
Dmean	9,18 Gy
Dmax	24,11 Gy
Right ventricle	
Dmean	3,83 Gy
Dmax	23,38 Gy
Right Atrium	
Dmean	7,43 Gy
Dmax	22,1 Gy
Left main trunk	
Dmean	14,4 Gy
Dmax	21,6 Gy
Right coronary artery	
Dmean	7,4 Gy
0,03 cm3 volume	22 Gy
Left anterior descending artery	
Dmean	5,4 Gy
0,03 cm3 volume	14,5 Gy
Circumflex coronary artery	
Dmean	3,3 Gy
0,03 cm3 volume	9,5 Gy
Sum Coronary artery	
Dmean	6,97 Gy
Valve tricuspid	
Dmean	4,57 Gy
Valve aortic	
Dmean	8,91 Gy
Valve mitral	
Dmean	6,97 Gy
PTV	
Volume	260,15 cm3
95%	96,24%



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PRELIMINARY ANALYSIS OF A MULTICENTER RETROSPECTIVE STUDY ASSESSING CONCURRENT ADMINISTRATION OF RADIOTHERAPY AND NEWLY APPROVED SYSTEMIC TREATMENTS IN METASTATIC BREAST CANCER PATIENTS

Code: 442

Aims: up to date only a few studies have been published regarding potential interactions between radiotherapy (RT) and newly approved systemic treatments (NAST) against metastatic breast cancer (mBC), mainly represented by small retrospective case series. The objective of this retrospective multi-centric analysis is to gather evidence from real-world clinical data of mBC patients, with the objective to partially fill this gap.

Methods: Patients that received RT concomitantly (less then 5 half lives from last administration) with NAST between 01 January 2006 and 28 February 2021 were enrolled. Primary outcomes were safety of combination treatment and percentage of RT suspension. Toxicities were graded using CTCAE version
5.0. In this preliminary analysis we report data from the first 5 Institutions that participated in the study.

Results: characteristics of the 168 enrolled patients are summarized in Table 1; 89.3% of patients already received CHT before current NAST, with a median of 2 previous lines (range 0-7, 50.6% 1-2 lines, >2 38.7%).
Considering the 286 treated lesions, the proportion of concurrent NAST was as follows: eribulin 38 (13.3%), trastuzumab+pertuzumab 57 (19.9%), trastuzumab 69 (24.1%), pertuzumab 10 (3.5%), trastuzumab emtansine 8 (2.8%), bevacizumab 26 (9.1%), everolimus 24 (8.4%), caelyx 21 (7.3%), myocet 5 (1.7%), nab-paclitaxel 15 (5.2%), lapatinib 13 (4.5%). Most commonly treated sites were spine (36%), brain (28%), pelvis (10.8%), extremities 30 (10.5%) and lymphnodes (5.9%).
Median total dose was 27 Gy (30 Gy for 119 lesions, 20 Gy for 84, 27 Gy for 28 lesions); median dose per fraction was 4 Gy (3 Gy for 119 lesions, 4 Gy for 78, 9 Gy for 29). Most used technique was 3DCRT (71% of lesions).
Considering the 193 RT courses (multiple lesions were often treated in the same course) the following toxicities were reported during treatment: pain increase G1 7.2%, pharyngodynia G1 4.1% G2 1.5% G3 0.5%, Esophagitis G1 5.2% G2 0.5% G3 1%, Dermatitis G1 4.1% G2 0.5%, Nausea/vomit G1 16.5% G2 0.5%, fatigue G1 19.1% G2 1% G3 0.5%, neurologic toxicity G1 6.7% G2 1%, diarrhea G1 4.1% G2 0.5% G3 0.5%, other toxicities G1 5.2% G2 0.5% G3 1.5%. Definitive and temporary suspension due to toxicity were both reported for 1% of the courses.

Conclusions: in this preliminary analysis, rates of toxicity G>2 and treatment suspension were extremely low for concurrent administration of NAST and RT. Results regarding larger series and sub-acute and chronic toxicities are awaited.

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BREAST IRRADIATA (ITALIAN REPOSITORY OF RADIOTHERAPY dATA) PROSPECTIVE PROJECT: PRELIMINARY RESULTS

Code: 601

Aims: The Breast IRRADIATA (Italian Repository of RADIotherapy dATA) project represents a collaborative nationwide initiative supported by the Italian Society of Radiotherapy and Clinical Oncology (AIRO) and the Italian League Against Cancer (LILT). The project aims to establish a national registry and delineate care patterns within Italy regarding breast cancer, focused on radiotherapy. A dedicated web-based tool for data collection was developed and subjected to a pilot test. Based on the outcomes of the feasibility study, a prospective data collection was launched in April/2023. This report presents the preliminary findings of the Breast IRRADIATA project.

Methods: Participation in the study was open to all Italian Cancer Centers through the AIRO website and weekly newsletter, with ongoing enrollment. The Breast IRRADIATA tool template comprises two parts: the first for de-identified patient demographics and data pertaining to disease diagnosis and treatments, and the second for follow-up data. In total, 35 items organized into 6 folders based on areas of interest are included. Each patient in the dataset is identified using a unique alphanumeric code. Clinicians involved have access to their respective patients' entered data and can export them to an Excel file for statistical analysis. Additionally, all other data in the database are accessible to participating institutions in a de-identified format.

Results: Currently, 41 Italian Cancer Centers have expressed their willingness to participate, with 17 having obtained necessary approvals from relevant ethics committees and proceeding with data entering. The remaining 24 centers are working to obtain the green light. 509 patients have been entered into the dataset. The most of them presented with early stage hormonal sensitive breast cancer and underwent conservative surgery, adjuvant hypofractionated RT and hormone therapy. The median age is 63 years.

Conclusions: The evolving landscape of treating high-prevalence diseases, such as BC, emphasizes patient-centered medicine, evidence-based care, and real-world evidence derived from real-world data. In line with this, Breast IRRADIATA serves as a valuable tool to assess current patterns of RT care in Italy. The encouraging preliminary results of IRRADIATA advocate for its wider application nationwide.

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A DEEP LEARNING MODEL TO PREDICT PATHOLOGICAL COMPLETE RESPONSE IN NSCLC PATIENTS UNDERGOING NEOADJUVANT CHEMORADIATION

Code: 431

Aims: About 20-30% of newly diagnosed lung cancer cases can undergo surgery with curative intent. Moreover many patients undergoing surgery have an high risk of recurrence (25%-70%) following surgery. For this reason neoadjuvant treatments are employed in order to improve patients' outcome. Among these patients undergoing preoperative treatments, pathologic complete response (pCR) may halve a potential prognostic role and be a surrogate endpoint for local control and survival. The aim of this study was to develop a deep learning (DL) model to predict pCR in NSCLC undergoing preoperative chemoradiation (p-CRT).

Methods: NSCLC patients (II-III TNM stage) included in a prospective database, receiving surgery after neoadjuvant chemoradiotherapy were selected for this analysis. CT scans acquired before p-CRT were utilized to build a DL model to predict pCR. Two densenet169 convolutional neural networks were trained on two different regions of interest of the CT scans, one corresponding to the lungs and the other including the primary tumor only region of the CT scan. This dual approach aimed to analyse the contributions of different views of the same CT scan to the final pCR prediction.

Results: The study includes 65 NSCLC patients (II-IIIA/B TNM stage) receiving surgery after neoadjuvant chemoradiotherapy. pCR was achieved in 23.08% of patients. The accuracy and the area under the curve (AUC) of the DL model to predict pCR were 0.60±0.08 and 0.35±0.18 respectively, in the lesion view, and
0.69±0.12 and 0.63±0.14 respectively, in the lungs view (Fig.1). Integrating both views increased the total accuracy by 18.84% with respect to the lungs view (Fig. 2), by achieving an accuracy value of 0.82.

Conclusions: both views are informative for the final pCR prediction and integrating different views enables the achievement of more accurate pCR prediction. These findings underscore the value of multiple views in developing DL model to predict pCR.

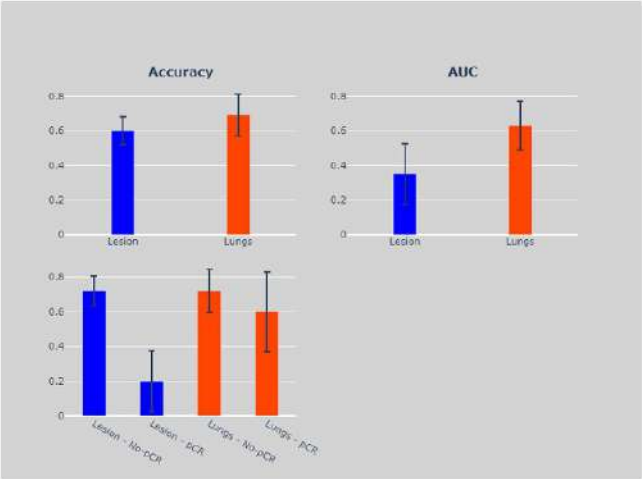

Fig 1. This figure shows the accuracy and AUC values of the two implemented approaches: lesion and lungs view. The top section on the left side of the figure shows the overall accuracy, while the bottom section provides the accuracy for the two predicted classes: the absence of a complete pathological response (no-pCR), and the presence of a complete pathological response (pCR).

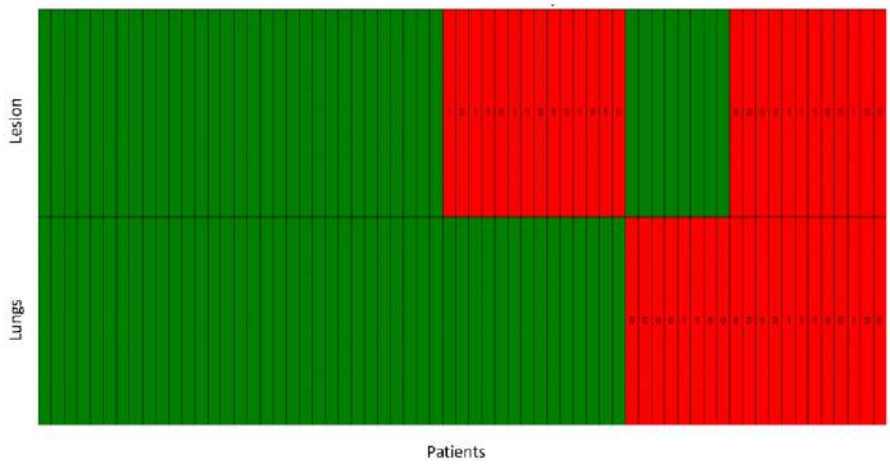

Fig 2. This figure shows the patients' classification heatmap for the two implemented approaches: lesion and lungs views. The green blocks represent patients correctly predicted by the network, while the red ones represent those inaccurately predicted by the network.

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NON-PERSISTENT NANO-ARCHITECTURES ENHANCE CONCURRENT CHEMORADIOTHERAPY IN AN IMMUNOCOMPETENT ORTHOTOPIC MODEL OF HPV+ HEAD/NECK CARCINOMA (HNSCC)

Code: 238

Aims: Cisplatin-based chemoradiotherapy (CRT) is the standard treatment for HPV+ HNSCC but often results in severe and prolonged side effects affecting the patients' quality of life. In this context, the progressive application of metal nanoparticles (NPs) as radiosensitizers emerges as a promising strategy in preclinical exploration. In the present study, a novel type of NAs (NAs-Cluster-CisPt) encapsulating gold clusters of about 1 nm and cisplatin has been designed. In this study, we investigated the radiosensitizing effects of NAs-Cluster and NAs-Cluster-CisPt in an orthotopic murine model of HNSCC.

Methods: The HNSCC model was obtained by grafting HPV16 E7-expressing TC-1/Luc cells at the submucosal site of the inner lip in C57BL/6 mice. The treatment protocol combined local tumor irradiation with intratumoral administration of NAs-Cluster, NAs-Cluster-CisPt, free CisPt, or PBS.The amount of gold and/or platinum for the tested treatments was fixed at, 5 and 1.4 μg, respectively, by following the previous *in vitro* assays. A single high dose of radiation (8 Gy) was administered, consistent with previous investigations. The tumor growth was measured and recorded every three days using In Vivo Imaging System (IVIS).

Results: In mice, combined therapy led to significantly smaller tumor burdens compared to monomodal therapies (RT, NAs, or free CisPt). The NAs-Cluster-CisPt/RT combination demonstrated substantial reductions in tumor signal ($p < 0.01$, one-way ANOVA) and a notable increase in survival ($p < 0.0001$) compared to control groups. Remarkably, 25% of mice treated with NAs-Cluster-CisPt/RT achieved complete tumor clearance throughout the 60-day observation period. Mechanistically, increased DNA damage, as indicated by γH2AX staining, was observed with the NAs-Cluster-CisPt/RT combination, suggesting an amplified DNA damage response contributing to its efficacy. Metal persistence assessment using ICP-MS in the liver and spleen 20 days and 6 months post-treatment confirmed the favorable excretion trend of NAs, with negligible metal amounts found in these organs, highlighting efficient renal excretion of cluster-sized gold NPs.

Conclusions: Our findings highlight the potential of combining NAs-Cluster-CisPt with RT. This approach has the dual benefit of minimizing the use of cisplatin in concurrent treatments and enhancing outcomes by elevating tumor sensitivity to radiation while preserving healthy tissue.

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COLLABORATION BETWEEN RADIOLOGISTS AND RADIATION ONCOLOGISTS IN TARGETING NON-MELANOMA SKIN CANCER BY HIGH-FREQUENCY ULTRASOUND

Code: 347

Aims: Non-melanoma skin cancer (NMSC), a common tumor affecting individuals primarily in their 70s, is escalating in frequency, possibly due to increased sun exposure. This study investigates the impact of High-Frequency Ultrasound (HFUS) in delineating Gross Tumor Volume (GTV) and Clinical Target Volume (CTV) for patients undergoing radiotherapy (RT) for skin cancers.

Methods: 30 patients, diagnosed with NMSC or cutaneous lymphoma, were enrolled between July 2022 and July 2023. A multidisciplinary evaluation, including joint consultations and HFUS assessment, was conducted. The GTV was determined using HFUS, and margins were added to create the CTV. RT was administered with two fractionation schemes tailored to patient needs: 55 Gy in 20 fractions (total of 4 weeks) and 60 Gy in 10 fractions (2 per week for a total of 5 weeks).

Results: HFUS significantly contributed to accurate visualization of the tumor extent. In cases of adjuvant radiotherapy for positive margins, HFUS detected residual macroscopic disease, leading to dose adjustments. Treatment field expansion was required in 8 patients to include subcutaneous tumor portions detectable only by ultrasonography. HFUS facilitated treatment flexibility, enabling 3 patients to switch from photon to electron beam therapy. Aone-yearfollow-uprevealeda100%localcontrolrate.

Conclusions: The study supports the relevance of HFUS in radiotherapy treatment planning for NMSC, emphasizing its role in accurately defining treatment fields and improving patient outcomes. Despite study limitations related to a small sample size, the consistent evidence from various studies advocates for further exploration of HFUS in radiotherapy planning. The integration of HFUS into clinical practice, in collaboration with radiation oncologists, radiologists, and dermatologists, is recommended to enhance personalized and effective management of skin cancers, ultimately optimizing therapeutic outcomes and patients' quality of life.

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LOCAL CONTROL AND BRONCHIAL TOXICITY OF STEREOTACTIC ABLATIVE RADIOTHERAPY (SABR) FOR CENTRAL AND ULTRA-CENTRAL LUNG TUMORS

Code: 557

Aims: To analyze disease control and bronchial toxicity of Stereotactic Ablative Radiotherapy (SABR) in central and ultra-central primary and oligometastatic lung tumors.

Methods: Central and ultra-central tumors treated at our Institution with SABR were retrospectively analyzed. Tumor centrality was defined according to the IASLC definition. According to Tekatli et al. tumors were further sub-divided in Group A (<1 cm from the trachea/main bronchi), B (>1 cm from the trachea/main bronchi, but <1 cm from the intermediate/lobar bronchi), or C (≥1 cm from proximal bronchial tree, but ≤2 cm from mediastinum). Local control, incidence and grade of clinical/radiological bronchial toxicity were evaluated.

Results: Between 2018-2022, 57 patients accounting for 60 lung lesions (53.3% early-stage lung cancer and 46.7% lung metastases), including 13 (21.7%) ultra-central and 47 (78.3%) central tumors, received SABR. Median iGTV and PTV were 7.7 (IQR 4.6-17.8) and 33.1 (IQR 18.5-52.2) cc, respectively. The prescribed SABR dose ranged from 35 Gy to 70 Gy over 5 to 15 fractions, with a median BED10 of 96 Gy (IQR 72-105 Gy) and 72 Gy (IQR 70.3-97 Gy) to the iGTV and PTV, respectively. A higher median BED10 was administered for Group B and C lesions versus Group A lesions (100 Gy and 96 Gy vs 59.5 Gy; p = 0.05). Median estimated follow-up was 16 months (95%CI 11.8-23). One-, 2-, and 3-year LC rates were 95.7% (95%CI 84.0-98.9), 86.2% (95%CI 64.8-95.0), and 78.4% (95%CI 51.3-91.5), respectively. Median OS and PFS were 47.4 months (95%CI 24.2-77.1) and 26.7 months (95%CI 13.3-NE), respectively. After SABR, 31 cases (54.4%) of G1-2 adverse events were recorded, while no G3-4 toxicity occurred. One patient (1.8%) died of post-acute pneumonitis (G5) 15 weeks after SABR. Radiological bronchial damage occurred in 14 (23.3%) cases as lobar, segmental, and sub-segmental stenosis in 2 (3.3%), 9 (15%), and 3 (5%), respectively. One- and 2-year radiological bronchial event free survival were 79.9% (95%CI 68.8-92.7) and 66.2% (95%CI 52.1-84.1), respectively. All lobar stenosis occurred for Group A (p = 0.002). No other variables correlated to incidence or type of bronchial toxicity.

Conclusions: Although it remains a challenging clinical scenario, SABR represents an effective and safe treatment for central and ultra-central lung tumors. Despite the lower administered dose, all radiological lobar stenosis occurred for lesions located <1 cm from the trachea/main bronchi.

Table 1. Patients and treatment characteristics

Patients, n		57
Treated lesions, n		60
Sex, n (%)	Female	19 (33.3)
	Male	38 (66.7)
Age, median (IQR)		74 (69-78)
Performance status (ECOG)	0	25 (43.9)
	1	25 (43.9)
	2	7 (12.2)
Comorbidities at baseline, n (%)	Pulmonary	19 (33.3)
	Cardio-vascular	16 (28.1)
Tumor histology, n (%)	Primary, non-metastatic NSCLC	32 (53.3)
	Metastatic disease	28 (46.7)
	NSCLC	15 (53.5)
	Colorectal	2 (7.1)
	SCLC	1 (3.6)
	Melanoma	1 (3.6)
	Breast	1 (3.6)
	Renal Cell Carcinoma	1 (3.6)
	Sarcoma	1 (3.6)
	Others	6 (21.4)
Lung, n (%)	Left	32 (53.3)
	Right	28 (46.7)
Lobe, n (%)	Superior	32 (53.3)
	Inferior	24 (40.0)
	Middle	4 (6.7)
Lesion diameter, cm, median (IQR)		3.1 (2.5-4.1)
iGTV, cc, median (IQR)		7.7 (4.6-17.8)
PTV, cc, median (IQR)		33.1 (18.5-52.2)
GTV within 2 cm of, n (%)	Main bronchus	11 (18.3)
	Lobar bronchus	37 (61.7)
	Trachea	1 (1.7)
	Heart	18 (30.0)
	Esophagus	9 (15.0)
	Great vessels	26 (43.3)
Lesion location, n (%)	Central	47 (78.3)
	Ultra-central	13 (21.7)
Tekatli group , n (%)	A	5 (8.3)
	B	14 (23.3)
	C	41 (68.3)
Prescribed dose, Gy, median (range)		50 (35-70)
Fractions number, n, median (range)		8 (5-15)
Prescription modality, n (%)	Homogeneous	25 (41.7)
	iGTV BED_{10}, Gy, median (IQR)	72 (72-100)
	PTV BED_{10}, Gy, median (IQR)	72 (72-100)
	Inhomogeneous	35 (58.3)
	iGTV BED_{10}, Gy, median (IQR)	105 (96-115.5)
	PTV BED_{10}, Gy, median (IQR)	72 (72-100)
Most frequent fractionation schemes, n (%)	40-55 Gy/5 fractions	29 (48.3)
	50-64 Gy/8-10 fractions	16 (26.7)

IQR: interquartile range; NSCLC: non-small cell lung cancer; SCLC: small cell lung cancer; RCC: renal cell carcinoma; GTV: gross tumor volume; PTV: planning target volume; Gy: gray; BED: biological effective dose.

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LONG-TERM RESULTS OF IMAGE-GUIDED MODERATELY HYPOFRACTIONATED RADIOTHERAPY FOR LOCALIZED PROSTATE CANCER: A MULTICENTRIC RETROSPECTIVE STUDY (IPOPROMISE)

Code: 498

Aims: Long-term results on the outcome and toxicity of moderate hypofractionation for localized prostate cancer (PCa) based on cutting-edge techniques are lacking. This study aims to present real-world results of a large multicentric series with a long follow-up.

Methods: retrospective analysis of 1325 PCa patients treated with moderate hypofractionated radiotherapy using cutting-edge techniques and daily volumetric image-guided checks between 2007 and 2020 in 16 Centers. For survival endpoints, we used Kaplan-Meier survival curves and fitted univariate and multivariable Cox's proportional hazards regression models to study the association between the clinical variables and each survival type.

Results: The 15-year values of cancer-specific survival (CSS) and biochemical relapse-free survival (b-RFS) were 98.5% (95%CI 97.3%-99.6%) and 85.5% (95%CI 81.9%-89.4%), respectively. The multivariate analysis showed that baseline PSA, Gleason score, and the use of androgen deprivation therapy were significant variables for all the outcomes. Acute gastrointestinal (GI) and genitourinary (GU) toxicities of grade ≥ 2 were 7.0% and 16.98%, respectively. the 15-year late grade ≥ 2 GI and GU toxicities were 5% (95%CI, 4%-6%) and 6% (95%CI, 4%-8%), respectively.

Conclusions: the real-world results of this multicentric study on hypofractionated radiotherapy for localized PCa demonstrated excellent b-RFS and CSS rates at 15 years, and very low rates of ≥ G3 late GU and GI toxicity.

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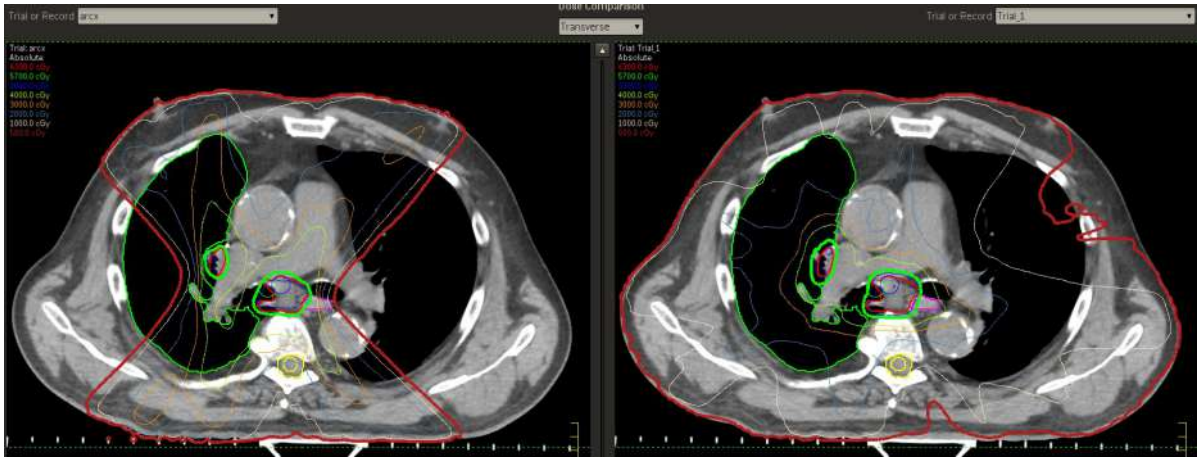
A DOSIMETRIC ANALYSIS OF RADIATION-INDUCED- PNEUMONITIS AFTER A CURATIVE RADIOCHEMOTHERAPY USING X SHAPE FIELDS INTENSITY MODULATED RADIATION THERAPY FOR NON-SMALL CELL LUNG CANCER PATIENTS

Code: 181

Aims: To evaluate radiation-induced pneumonitis (RIP) onset using an "institutional defined" intensity-modulated technique in non-small cell lung cancer patients treated with chemo-radiation therapy.

Methods: In April 2014 we start to treat NSCLC patients using intensity-modulated techniques. To avoid direct and/or outgoing irradiation of healthy lung tissue as much as possible, the therapeutic beams are arranged in a very narrow X shape (both in the case of step-shoot IMRT and VMAT). See Figure 1.
By analyzing the dose-volume histogram (DVH) of various treatment plans, the V1, V2, V3, V4, V5, V6, V8, V10, V13, V20, V25, V30 and mean dose of the ipsilateral, contralateral, and joined lungs were compared. All radiation-induced pneumonitis events were collected.

Results: From April 2014 to May 2023, 150 patients were evaluated. In 7/150 (4.6%) patients a symptomatic RIP was observed. Comparing all 150 treatment plans with plans in patients with RIP the following values were detected:



1. Ipsilateral lung (median value in %): V1 79 vs 83.09; V2 66.82 vs 71.62; V3 59.59 vs 64.84; V4 54.15 vs 59.95; V5 50.09 vs 56.35; V6 46.99 vs 53.63; V8 42.45 vs 49.83; V10 39.11 vs 47.10; V13 35.16 vs 43.78; V20 27.69 vs 37.96; V25 22.52 vs 33.97; V30 17.67 vs 30.24. Median lung dose, 13.22Gy vs 19.08Gy.
2. Contralateral lung (median value in %): V1 40.77 vs 57.56; V2 28.78 vs 42.17; V3 22.43 vs 33.81; V4 17.79 vs 26.12; V5 14.82 vs 21.35; V6 12.76 vs 18.33; V8 10.08 vs 14.27; V10 8.32 vs 11.17; V13 6.61 vs 8.32; V20 4.35 vs 5.28; V25 3.37 vs 4.15; V30 2.59 vs 3.09. Median lung dose, 3.64Gy vs 4.42Gy.
3. Joined lungs (median value in %): V1 57.62 vs 68.35; V2 45.17 vs 54.79; V3 37.78 vs 47.23; V4 32.81 vs 41.08; V5 29.29 vs 37.04; V6 26.84 vs 34.27; V8 23.44 vs 30.82; V10 20.09 vs 27.78; V13 18.38 vs 24.82; V20 13.95 vs 20.51; V25 10.75 vs 18.03; V30 8.51 vs 15.72. Median lung dose, 7.45Gy vs 11.24Gy.

Conclusions: Analyzing the collected data, it seems to be necessary to optimize the constrains, stressing the planning system to obtain for "joined lungs" a V1<60%, V5<30%, V10<20%, V20<14%, V30<8.5% and a mean lung dose less than 8Gy.

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ARE THERE HIGH-RISK SUBGROUPS FOR LOCOREGIONAL FAILURE IN EARLY- STAGE BREAST CANCER PATIENTS WHO RECEIVED MASTECTOMY WITHOUT ADJUVANT RADIATION THERAPY?

Code: 471

Aims: The purpose of this retrospectively study was to determine whether exist a significant independent association between prognostic factors and clinical outcomes in early-stage breast cancer (BC) patients (pts) treated with mastectomy and adjuvant systemic therapy without post-mastectomy radiation therapy (PMRT).

Methods: Two hundred and six pts treated between December 2009 and December 2018 with mastectomy were retrospectively reviewed. Tumors were classified by intrinsic molecular subtype and prognostic factors. The Kaplan-Meier method was used to estimate outcomes. Univariate analysis for prognostic factors was performed with the long-rank test and Cox proportional hazards regression was used to estimate hazard ratios (HR) to evaluate the association between factors and survival. P-values less than 0,05 were deemed statistically significance.

		Local Recurrence			Disease Free Survival			Metastasis Free Survival		
Variable	**Classifications**	**HR**	**95%CI**	**p-value**	**HR**	**95%CI**	**p-value**	**HR**	**95%CI**	**p-value**
Age, years	≤50vs>50	3.65	0.3-40	0.25	0.69	0.1-2.5	0.58	0.55	0.1-2.6	0.46
Tumor size	T2 vs T1	0.03	0-266	0.33	2.1	0.6-6.3	0.22	**3.72**	**0.9-13**	**0.03**
N	N+ vs N-	0.81	0.7-9	0.86	1.6	0.5-5.2	0.35	3.42	0.8-13	0.06
1-3 pos axillary nodes	1-3 vs 0	0.98	0.8-10	0.99	1.5	0.5-4.9	0.43	2.82	0.7-10	0.10
Grade	G3 vs G1-2	1.12	0.1-12	0.93	0.83	0.2-3.0	0.78	0.98	0.2-3	0.98
LVI	Pos vs neg	2.96	0.2-33	0.35	1.7	0.4-6.3	0.41	1.85	0.4-7.3	0.40
ER	Neg vs pos	2.56	0.2-28	0.42	1.8	0.4-6.8	0.35	1.59	0.3-7.7	0.55
TN	Yes vs no	4.83	0.4-54	0.15	**3.5**	**0.9-13**	**0.04**	3.01	0.6-14	0.14
Ki67	≥30 vs <30	1.11	0.1-12	0.92	0.72	0.1-2.6	0.62	0.62	0.1-3.0	0.55
	≥15 vs <15	1.30	0.1-14	0.82	1.33	0.4-4.4	0.63	1.05	0.2-3.7	0.93
CHT	Yes vs no	0.49	0.4-5.5	0.55	0.59	0.1-2.0	0.40	0.50	0.1-1.9	0.31

Table : Univariate analysis of survival by explicative variables

Results: Median age at mastectomy was 60 years (IQR 49-75) and median follow-up was 86.5 months (IQR 66.6-119.7). Median Ki67 was 20% (IQR 10-35; dst 21.63). Seventy-six (36,8%) pts were pN1, 59 (28,6%) 1-3 positive axillary nodes, 55 (26,6%) grade 3, 38 (18,4%) lymphovascular invasion (LVI), 28 (13,5%) ER negative and 63 (30,5%) T2. Seventy-seven (37,3%) underwent adjuvant systemic therapy with chemotherapy. Local recurrence (LR) at 5 and 10 years was 99.1% and 95.3%. Disease-free survival (DFS) at 1 and 5 years was 99.5% and 97.5% respectively. Metastasis-free survival (MFS) at 1 and 10 years was 99.5% and 94.1% respectively. Only 3 (1,4%) pts had a local recurrence and 10 (2,5%) developed metastases. Overall survival (OS) at 2 and 5 years was 99.5% and 97.5% respectively. At uni- variate analysis (table1), DFS was associated with triple negative status with a p-value of 0.04 and MFS with tumor size (p-value: 0.03). No statistically significant emerged in pts with 1-3 positive axillary nodes.

Conclusions: The use of PMRT to improve survival outcomes in early-stage breast cancer with high-risk recurrence factors is controversial. We showed that in early-stage BC pts treated with mastectomy and adjuvant systemic therapy the rate of LR and MFS were exceptionally high. We confirmed the prognostic rule of TN status in term of DFS. PMRT for T1-2 and 1-3 positive axillary lymph nodes must be reconsidered according to the prognostic factors and the decision has to be individually.

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VARIATIONS OF CYTOKINE CONCENTRATION IN OLIGOMETASTATIC NON- SMALL CELL LUNG CANCER TREATED WITH STEREOTACTIC RADIOTHERAPY

Code: 74

Aims: The oligometastatic stage occurs in about 50% of Non-Small Cell Lung Cancer (NSCLC) patients due to the introduction of Immunotherapy (IO) and Target Therapy with Tyrosine Kinase Inhibitors (TKI).
Stereotactic Radiotherapy (SRT), is an effective treatment in this stage, assuring high local control rates. SRT, even as a local treatment, can have systemic effects due to abscopal effect, involving cytokines (CKs).

Methods: This prospective multicenter pilot study analyzes plasma concentrations of CKs (IFN-γ, IL-1, IL-2, IL-4, IL-6, IL- 10, IL-12, IL-17, TNF-α) in oligometastatic NSCLC patients undergoing SRT on all lesions.
The involved centers were the Radiotherapy Department at Spedali Civili and University of Brescia and the Radiotherapy Complex at the University Hospital of Modena. Blood samples were collected before and one month after SRT. CKs concentrations were analyzed with Luminex Immunoassay.

Results: Data from 19 patients (pts), median age 68, with oligometastatic NSCLC were retrieved. 11 had oligoprogressive disease. Target mutations were present in 12 pts. 6 pts were receiving TKI and 6 were undergoing IO during SRT. SRT targeted lesions of lung (35%), brain (25%), bones (15%), liver and adrenal gland (25%).
Variations of the median CKs concentrations within different pts' subgroups were analyzed. Oligoprogressive pts showed smaller variations of both inflammatory (ProInf) and anti-inflammatory (AntInf) CKs compared to metachronous oligometastatic pts. The same behaviour was noted confronting pts with metastases to Brain & Bones to Lung & Liver localizations. Higher ProInf CKs levels and lower AntInf CKs concetrations were observed in pts receiving IO during SRT. The same variations were noted in Oncogene-Addicted patients compared to Wild-Type patients.
Five-year Overall Survival was 70.1% with a median Progression-Free Survival of 11 months.

Conclusions: This study explores cytokine variations in oligometastatic NSCLC patients undergoing SRT, aiming to identify biomarkers predicting response and survival. Results align with literature, but the exploratory nature and
sample size limit definitive conclusions, suggesting the need for numerical expansion and further molecule selection in future phases.

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CORRELATION BETWEEN IRRADIATED LUNG VOLUMES AND ACUTE RADIATION PNEUMONITIS IN MESOTHELIOMA PATIENTS UNDERGOING ADJUVANT RADIOTHERAPY FOLLOWING PLEURECTOMY/DECORTICATION

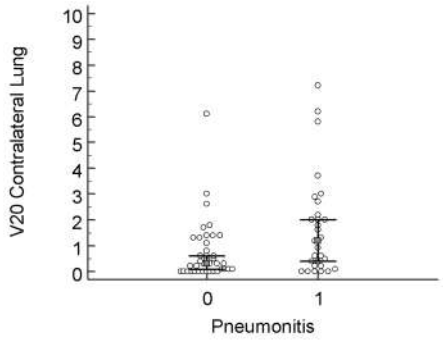
Code: 437

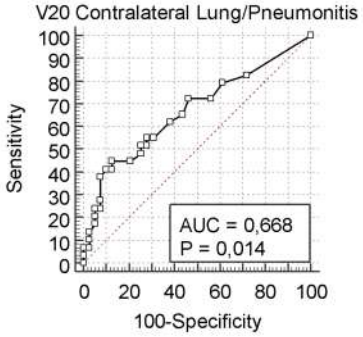
Aims: Our study explores the link between irradiated lung volumes and acute radiation pneumonitis in pleurectomy/decortication-treated mesothelioma patients. Excluding emphysematous lung parts, we evaluate functional lung volume's role in predicting radiation toxicity.

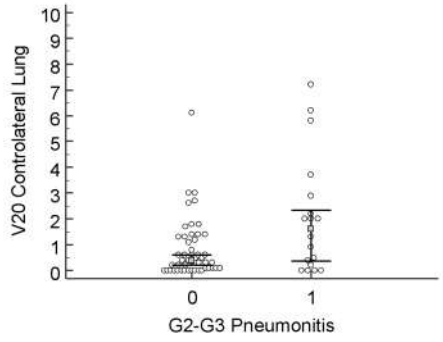
Methods: We collected data from a cohort of non-metastatic mesothelioma patients treated from April 2013 to February 2022 with adjuvant radiotherapy (RT) following pleurectomy/decortication.Clinical and dosimetric parameters to contralateral lung (V20, V5, Mean Lung Dose, MLD) recorded. Functional Contralateral Lung (FLC) parameters calculated by excluding areas below CT threshold of -860 HU. Differences between median dose parameters and FCL counterparts assessed using Wilcoxon test.
Statistical correlation between acute toxicity and dose parameters tested. Parameters with significant correlation underwent Kruskal-Wallis test, ROC curves, and Youden index (J) calculation for predictive accuracy comparison.

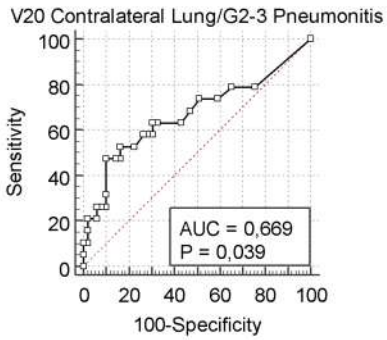
Results: Data from 68 patients were collected. Median age was 65 (range 37-78) years. R0 resection was achieved in 85% (n=58) of patients. Adjuvant chemotherapy, platinum-pemetrexed, was given to 96% (n=65). RT, conventionally fractionated at 44 Gy, with a boost in 88% (n=60) to a median dose of 50.6 Gy (range 50.6-59.4). Median V20, V5, MLD: 0.5% (95%CI 0.3-1.1%), 55% (95%CI 48.7-57.7%), 6.25 (95%CI
6.0-6.50), respectively. Median FLC_V20, FLC_V5, FLC_MLD: 0.46% (95%CI 0.17-0.88%), 56.7% (95%CI 49.9-59.5%), 6.35 (95%CI 6.03-6.75). Median V20 (p=0.016), V5 (p<0.001), MLD (p=0.012) significantly differed from functional counterparts. Acute pneumonitis observed in 29 patients (42%), Grade 2-3 toxicity in 19 (28%) cases. Correlation between pneumonitis and dose parameters only for V20 (0.3 vs 1.2, p=0.017) and FLC_V20 (0.2 vs 1, p=0.028). ROC curve favored V20 (AUC: 0.668) over FLC_V20 (AUC: 0.655). No difference between V20 and FLC_V20 in pairwise comparison (p=0.6). Youden-J >1.4: Sensitivity 44.8%, Specificity 87.1%. For G2-3 pneumonitis, significant correlation only with V20 (0.4 vs 1.6, p=0.03). At ROC curve analysis, AUC was 0.67. Youden-J >1.8: Sensitivity 47.3%, Specificity 89.8%.

Conclusions: A correlation between V20 to the contralateral lung and acute pneumonitis incidence was observed in mesothelioma patients undergoing adjuvant RT. However, predictive performance remained modest (AUC <0.7). FLC_V20 did not improve acute pneumonitis prediction. Further research is warranted to refine predictive models for improved patient outcomes.









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CARDIOIMAGING IN PATIENTS WITH STAGE III LUNG CANCER UNDERGOING CHEMORADIOTHERAPY: PRELIMINARY RESULTS OF A PROSPECTIVE SINGLE- CENTER TRIAL (CARE-RT)

Code: 294

Aims: In our prospective, single-center trial, we aim to assess both acute and delayed cardiac complications using advanced cardiac imaging techniques (CardiacCT and CardiacMRI) in patients diagnosed with locally advanced non-small cell lung cancer (NSCLC) who are undergoing radical radiation therapy (RT).

Methods: We prospectively enrolled consecutive patients with stage III NSCLC eligible for radical RT in this trial. Prior to the commencement of their treatment and during follow-up, they underwent a cardiology evaluation, cardiac-MRI, and cardiac-CT. We collected personal information, comorbidities, related treatments, disease characteristics, timing and types of oncological therapies, as well as cardiological parameters obtained from clinical assessments, CT, and MRI. This preliminary analysis aims to describe the baseline characteristics of the patients included in our study.

Results: Between November 2022 and December 2023, we enrolled 18 patients, consisting of 14 males (77.8%) and four females (22.2%), all of whom received concurrent or sequential chemo-radiotherapy. Eight patients (44.4%) were former smokers, while ten (55.6%) were active smokers. Concerning comorbidities, four patients (22.2%) had previously undergone cardiac surgery, and fourteen (77.8%) were taking medication for hypertension, with six (33.3%) also receiving treatment for diabetes. Despite these conditions, all patients were in good clinical condition with a PS-ECOG score of 0-1. Cardiologically, ten patients (55.6%) showed no symptoms, yet when assessed with cardiac-CT imaging using the Coronary Artery Disease Reporting and Data System (CAD-RADS), none received a score of 0. Six patients (33.3%) were scored as 1, four (22.2%) were scored as 3, and six (33.3%) were scored as 4. Cardiac-MRI revealed severe cardiac function impairment in four patients. Notably, a discrepancy between clinical cardiac examination and cardiac imaging was observed in six out of 14 patients, with two patients (11.1%) undergoing percutaneous transluminal coronary angioplasty (PTCA) after completing their oncological treatment.

Conclusions: Our initial study findings suggest that cardiac imaging holds clinical significance in evaluating patients with stage III lung cancer eligible for aggressive treatments. It can help identify cardiac risks even in clinically asymptomatic patients, potentially aiding in the prevention of adverse cardiac conditions.

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DOSE TO CARDIAC SUBSTRUCTURES IN PATIENTS WITH STAGE III NSCLC TREATED WITH DEFINITIVE CHEMORADIO-IMMUNOTHERAPY: A RETROSPECTIVE MONOCENTRIC ANALYSIS OF ACUTE AND LATE TOXICITY

Code: 183

Aims: Since concurrent chemoradiotherapy (cCRT) followed by immunotherapy (IT) maintenance became the standard of care for unresectable LA-NSCLC, OS has increased considerably. Based on the results of RTOG 0617, a reduction of cardiac dose might further improve survival and therefore dose to the heart and more recently to individual cardiac subregions has become of major interest. The aim of our study is to evaluate RT dose to cardiac substructures (CS) and observed cardiac toxicity in a real-world cohort.

Methods: We retrospectively analyzed 45 pts consecutively treated with cCRT or exclusive RT between 2018 and 2022 affected by IIIA-IIIC NSCLC (TNM 8th edition). All pts were considered unresectable and received curative RT doses, in line with current ESMO guidelines (60-66 Gy in 30-33 fraction), using Volumetric Modulated Arc Therapy (VMAT) or Tomotherapy. After anonymization of pts' treatment plan, CS were manually delineated by two junior radiation oncologists and revised by a senior physician, based on a commonly used cardiac atlas (left anterior descending artery (LAD), sinoatrial node (SAN), atrioventricular node (AVN) and heart base). RT doses to CS were then calculated and analyzed.

Results: Forty-five pts with a median age of 71 years (range 45-85) were evaluated (28 male (62.2%) and 17 female (37.8%)). Median follow up was 25.2 months. In four pts, adaptive replanning had to be performed due to anatomy modifications during RT. Recorded median whole heart (WH) mean doses in the full cohort was 7.98 Gy (range 0.06-22.5 Gy). Overall toxicity was low with only 6 pts experiencing grade>=3 acute toxicity, 5 hematological and 1 cardiac. In 6 pts cardiac conditions were observed after RT that were not reported before treatment (Table 1). In these pts, median and mean WH mean dose were 8.6 Gy (range 1.9-14.11 Gy) and 8.05 Gy, while median and mean max dose to SAN, AVN and V10 to heart base were 31.5Gy/31.3 Gy, 5.5 Gy/6.5 Gy and 84%/69%, respectively, thus not significantly different from the total cohort. No other late side effects >= grade 3 were observed.

Conclusions: In line with the secondary analysis of RTOG0617, heart exposure achieved with modern RT techniques (IMRT/VMAT) seem to result in low RT related cardiac toxicity when standard RT doses are used and even in pts treated with IT. Larger NSCLC cohorts and more robust prospective studies are needed to clarify the role of CS radiation doses in this setting, particularly in new attempts to escalate RT dose.

ID PTS	Previous Heart Conditions	WH Dmean (Gy)	WH V5 (%)	WH V30 (%)	SAN Dmax (Gy)	SAN Dmean (Gy)	AVN Dmax (Gy)	AVN Dmean (Gy)	heart base V10 (%)	Heart Base V40 (%)	LAD V15 (%)	Acute Cardiac Toxicity (CTCAE 5.0 grade)	Late Cardiac Toxicity (CTCAE 5.0 grade)
2		14,11	74,5	8,86	42,6	30,3	21,37	12,89	95	8,62	5,97	None	Aortic Valve Disease (G1) Myocardial Infarction (G3) Right Bundle Branch Block (G1)
28		10,57	32,71	15,13	55,21	27,75	5,49	4,45	92,24	29,5	27,5	Atrial Flutter (G3)	Heart Failure (G1)
34	Chronic Ischemic Heart Disease (G3)	5,41	17,5	5,81	16,04	7,54	3	2,35	50,1	14,5	8,81	None	Atrial Fibrillation (G3) Pericarditis (G2) Sinus Bradycardia (G1) Conduct disorder (G1) Atrioventricular Block (G1)
35	Carotid artery stenosis (G1) Sinus bradycardia (G1) Supraventricular extrasystoles (G1)	7,68	33,84	5,81	31,46	17,51	2,2	1,61	84	5,5	41,22	None	Tricuspid Valve Disease (G1) Mitral Valve Disease (G1)
44	Carotid artery stenosis (G1) Hypetension (G1)	1,9	6	0,3	1,88	1,61	1,37	1,16	8,76	0,36	0	None	Mitral Valve Disease (G1)
51	Atrial Fibrillation (G1)	8,62	36,25	7,49	40,77	8,88	5,49	3,29	86,06	13	14,23	None	Atrial Fibrillation (G2)
	Whole Cohort Mean Cardiac Dosimetric Value	8,69	43,92	6,94	25,27	15,69	13,08	10,61	61,57	10,52	15,12	-	

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LOW DOSE RADIOTHERAPY IN PRIMARY INDOLENT CUTANEOUS B-CELL LYMPHOMA

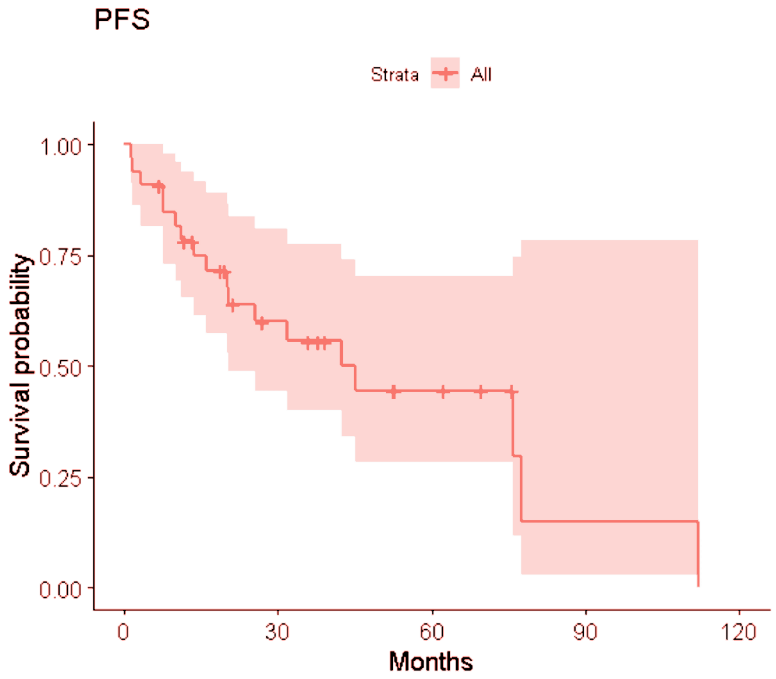
Code: 401

Aims: Primary indolent cutaneous B cell lymphomas (PCBCL) represent approximately 20% of all primary cutaneous lymphoma with a predominant skin location and a rare extracutaneous involvement at diagnosis. Radiotherapy (RT) has a recognized therapeutic effect in the treatment of PCBCL and recent evidence suggest an ultra-low dose schedule as initial therapeutic approach for some sensitive anatomic sites. So in this observational multicentric retrospective study we aimed to evaluate the low-dose RT (LDRT) efficacy in terms of local control in patients affected by PCBCL.

Methods: We retrospectively reviewed 33 patients with 35 (20 first diagnosis and 15 recurrences) cutaneous lesions treated in 2 radiation oncology centers between 2010 and 2021 (19 Marginal zone lymphoma (PCMZL) lesions, 13 Follicole center lymphoma (PCFCL) lesions and 1 chronic lymphatic leukaemia (LLC)). All lesions were treated with low-dose RT (4 Gy, 2Gyx2 fractions). Fefteen lesions (42%) were treated with orthovolt (Roentgen), 18 lesions (51%) were treated with electrons and 2 lesions (7%) were treated with photons (3D-CRT).

Results: The median age was 64 (range 32 - 86) years and the median follow up of 33 (range 1-129) months. The overall progression free survival (PFS) at 12, 24, 38 and 50 months after LDRT was 78% (95%CI: 65.4-93.9), 64% (95%CI: 48.9-83.8), 55% (95%CI: 40.0-77.6) and 44% (95%CI: 28.3-70.2), respectively with a local control rate of 100%. 3 patients experienced G1 acute toxicity (erythema) and 2 patients experienced G1 late toxicity according to CTCAE v5.0. There were no cases of grade ≥ 3 acute or late toxicity.

Conclusions: Our analysis highlighted the potential efficacy of low-dose radiotherapy in the management of PCBCL in terms of local control with a good toxicity profile. Thus, low-dose radiotherapy could be considered as a therapeutic option for indolent PCBCL.



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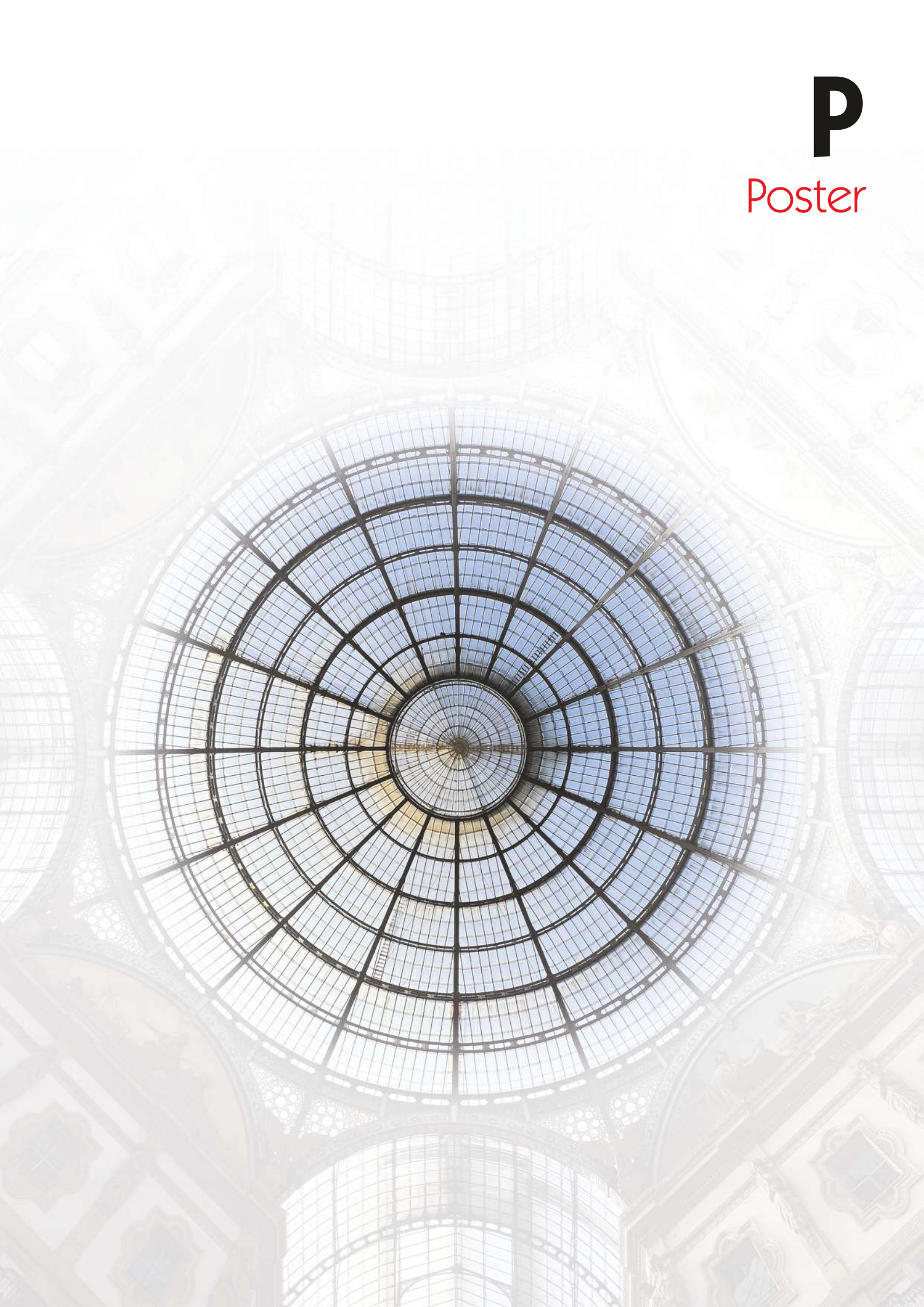

STEREOTACTIC BODY RADIOTHERAPY FOR LOCALLY ADVANCED AND METASTATIC PANCREATIC CANCER

Code: 571

Aims: Pancreatic cancer is one of the most malignant tumors of the digestive tract with poor prognosis. 5-years survival rate was less than 10%, due to drug and radiation resistance. Stereotactic radiation therapy (SBRT), in combination with chemotherapy, was an alternative treatment for patient with inoperable pancreatic tumors (locally advanced and metastatic disease). We analyzed the SBRT results in terms of OS and toxicity.

Methods: 48 pts were enrolled into this study (22 F and 26 M) from November 2011 to January 2024, the median age at the diagnosis was 66 years (range 31-90). Histological type was in 41/48 pts Adenocarcinoma, 1/48 was NET and 6/48 was not submitted biopsy. Inclusion criteria were: inoperable judged by the surgeon, UICC stage T2-4N0-2M1, tumor visualized on CT-scan, WHO/ECOG performance status 0-2. Mean CTV volume was 79.1cc (range 8.0-258.9cc).
All 48 pts were treated on the primitive pancreatic lesion with different schedule: 37.5% of pts with 36 Gy (isodose of 70%) in 3 fr, 27.1% of pts with 33 Gy (isodose of 80%) in 5 fr, 27.1% of pts with 30 Gy (isodose of 70%) in 3 fr, and 8.3% of pts with 37.5 Gy (isodose of 67%) in 3 fr.
The CTV delineation was performed on CT-PET fusion in 41.7% of pts. The VMAT treatment was delivered by 6MV Linac. CBCT was employed to control patient set-up before each fraction. Toxicity was recorded according to CTCAE v.4.02 and radiological response was described according to RECIST criteria.

Results: We analyzed the SBRT results in terms of OS and toxicity for oligometastatic patients With median follow up of 18 months (range 2-47 months), 5 patients (10.42%) are still alive and out of these, 1 pts is NED. OS is 91.7%, 87.5%, 60.4% at 3,6 and 12 month respectively.
No acute and late toxicity was observed all pts. Betametasone and Ondansetron were administered to all pts after every treatment fraction.

Conclusions: In our experience, SBRT appears as a safe and effective treatment modality for pts with locally advanced or metastatic pancreatic carcinoma without adverse events.

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TREATING NODAL METASTASIS WITH PALLIATIVE INTENT: STEREOTACTIC BODY RADIOTHERAPY (SBRT) TO POSITIVE CHOLINE PET / CT LYMPH NODES FOR OLIGOMETASTASIZED PROSTATE CANCER (PCA) PATIENTS

Code: 94

Aims: The purpose of this study is to evaluate the feasibility and toxicity of based stereotactic body radiotherapy (SBRT) for oligometastatic prostate cancer (PCa) patients.

Methods: In this study, oligometastasized PCa patients with nodal (≤ 3 lesions) were treated using SBRT in association with androgen-deprivation therapy. All patients were studied with Choline PET/CT before RT. The prescribed SBRT to pathologic lymph nodes was 8 Gray (Gy), delivered in three fraction to have a better control of organ motion (bowel above all) and normalized so that the 80% isodose covers 100% of the PTV.

Results: Between January 2019 and December 2023, 170 oligometastasized PCa patients with nodal metastasis were treated stereotactic on positive choline PET / CT lymph nodes. At a median follow-up of 4 (1-10) months, no toxicity was observed and a reduction in the volume of irradiated lymph nodes in 60% of patients. Only 5%of the disease progressed, while the remaining lymph node volume was stationary. All patients were re- evaluated with PET/CT.

Conclusions: SBRT to positive choline PET / CT lymph nodes for oligometastic prostate cancer is a feasible treatment modality with minimal toxicity. Further studies with a longer follow-up are needed to better evaluate late toxicity and local control.

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EFFECTIVENESS OF RADIOTHERAPY ON DELAYING THERAPEUTIC SWITCH IN PRIMARY OR SECONDARY IMMUNE REFRACTORY OLIGO PROGRESSIVE PATIENTS: PRELIMINARY RESULTS FROM A SINGLE CENTRE STUDY

Code: 99

Aims: To investigate whether radiotherapy could provide clinical benefits to patients with metastatic oligoprogressive solid tumors who have acquired (AR) or innate (IR) resistance to Immune checkpoint inhibitors (ICIs).

Methods: Patients with oligoprogressive disease treated at our Institute from January 2019 to … 2023 were retrospectively identified. Patients were stratified by drug resistance (AR vs IR) according to the time of resistance development. Time to switch (TTS)and Time to resistance (TTR) were the primary outcomes. Secondary outcomes included: post-radiotherapy first progression free survival (prf-PFS), Local Control (LC), Overall Survival (OS), and treatment related-toxicities.

Results: 40 patients (28 with acquired resistance and 12 with innate resistance) met the inclusion criteria. Concomitant radiotherapy was offered as a local treatment approach with a median total dose of 30 Gy (range 18-63.8Gy) in 5 fractions (range 1-12) for external beam radiotherapy and a median total dose of 30 Gy (range 18-50Gy) in 3 fractions (range 1-5) for stereotactic radiotherapy. Lattice radiotherapy was administered in six patients with a total median dose of 15 Gy in a single fraction to the vertices, followed by a median total dose of 30 Gy to the clinical target volume.
The median TTS in patients with acquired and innate resistance was not reached (NR) and 19,5 months respectively. At the time of this analysis, 46,42% of patients with acquired resistance and 58,3% of patients with innate resistance had switched systemic therapy. The median time to acquire resistance from the start of immunotherapy was 12 months in patients with acquired resistance vs 3 months in patients with innate resistance. The median OS was not reached for both groups. Namely, only three patients succumbed to disease progression. Overall, six patients suffered a local relapse within 12 months after completion of radiotherapy. Regardless of the radiation dose, we did not observe any acute or late treatment-related toxicity ≥ G3.

Conclusions: Our preliminary results seem to confirm that the integration of radiotherapy and ICIs may allow the continuation of systemic therapy beyond disease progression with a subsequent benefit in terms of clinical outcomes even in patients with innate resistance.

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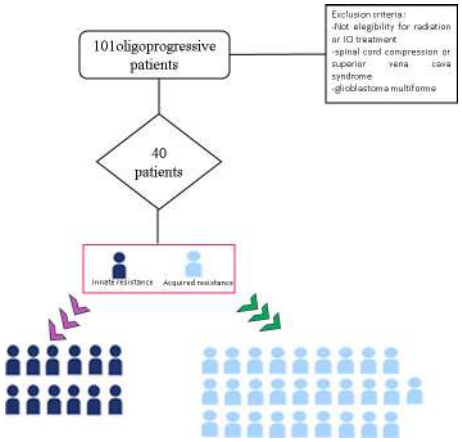

MACHINE LEARNING-AIDED AUTOMATABLE REPLANNING TOOL TO ENHANCE DELIVERABILITY IN MODULATED RADIOTHERAPY PLANS

Code: 70

Aims: The over-modulation of RT plans can substantially hinder their deliverability. The gamma passing rate (GPR) is a standard indicator for identifying plans with suboptimal deliverability. Recently, in our centre a machine learning (ML) model was trained on a large dataset of over 15,000 arcs, aiming to predict the GPR using a 3%/1 mm criteria. The aim of this study was to investigate whether an automatable replanning process, supported by our ML model, can effectively enhance the deliverability of plans.

Methods: The ML model was tested on the latest 2,507 patients treated with volumetric modulated arc therapy in our center during 2022-2023. From the cohort of 100 patients with the lowest mean predicted GPR, ten patients of which eight Head&Neck, were chosen. These plans were re-optimized from scratch with the same dose volume objectives as the original plans using two automatable approaches: (i) limiting the Monitor Units to 70% of the total original count (MUlimit), (ii) utilizing the Aperture Shape Controller (ASC) tool of the Eclipse TPS. The re-optimized plans were compared with the original ones in terms of modulation complexity score (MCS), predicted GPR(3%,1mm), patient-specific QA (PSQA) GPR(3%,1mm), and DVH points. The Wilcoxon signed-rank test was used for statistical analysis ($p<0.05$ significant).

Results: We analysed 102 arcs from 30 treatment plans of the 10 selected patients (see Figure 1). The re-optimized plans displayed a significant reduction in complexity, with a median increase in MCS from 0.17 to 0.21 (MUlimit) and to 0.19 (ASC). The predicted GPR significantly improved from 93.3% to 94.4% (MUlimit) and to 95.0% (ASC). The PSQA improved, with an increase in median value from 99.3% to 99.7% (MUlimit) and to 99.5% (ASC). Plan constraints were respected with no significant differences between the three groups. However, we observed a median increase of 3% (MUlimit) and 2% (ASC) in dose to OARs, and of 3% (MUlimit) and 1% (ASC) to the body, with a reduction of 2% in dose to the PTV and CTV.

Conclusions: This study highlighted the feasibility of employing an automatable ML-based tool for the replanning of patients at risk of poor deliverability. The replanning process, focusing on specific parameters with MUlimit and ASC, effectively produced plans with improved deliverability while maintaining consistent quality. This approach holds the potential to enhance the quality of care delivered to patients undergoing radiotherapy.

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STEREOTACTIC BODY RADIOTHERAPY (SBRT) IN HIGH-RISK LOCALIZED PROSTATE CANCER (HRPCa): A MONO-INSTITUTIONAL EXPERIENCE

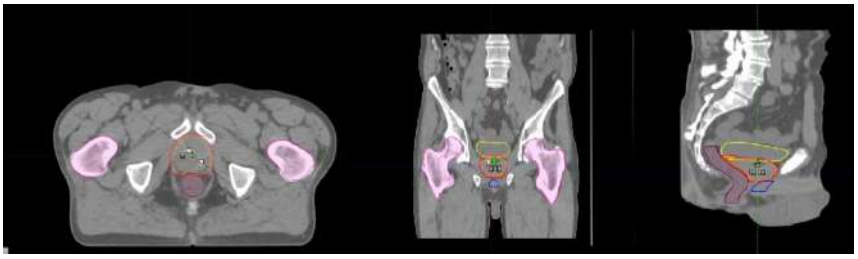
Code: 525

Aims: To report oncological outcomes and toxicities from a series of high-risk prostate cancer (HRPCa) treated with stereotactic body radiotherapy (SBRT).

Methods: We retrospectively analysed a series of HRPCa patients treated from June 2013 and July 2021 with SBRT, consisting of 42 Gy/7 fx or 36,25 Gy/5 fx to prostate and seminal vesicles. The inclusion criteria were histologically verified prostate cancer, NCCN risk classification HR- or very HR and a minimum follow- up of 24 months. Daily cone beam CT and fiducial markers image-guidance were used. Oncological endpoints were: biochemical recurrence-free survival (BRFS), metastasis-free survival (MFS), local control (LC) and cancer specific survival (CSS). Biochemical recurrence was defined according to Phoenix criteria (nadir +2 ng/mL). Survival analysis was performed using the Kaplan-Meier method and the log rank test was applied to compare the effect of the individual variables (iPSA, ISUP, T stage, NCCN risk classification, staging with/without pelvic MRI or PET-CT) on different outcomes. Acute and late genitourinary (GU) and gastrointestinal (GI) toxicities were graded using the Common Terminology Criteria for Adverse Events, version 5.0.

Results: Median follow-up was 54 months (IQR, 40-66). Thirty (60%) and 20 (40%) patients were classified as HR and very high-risk (VHR) group, respectively. Thirty-five (70%) of patients received androgen deprivation therapy (ADT) for a median duration of 12 months (range 6-24). The 5-year CSS was 97,8%. Ten (20%) patients developed biochemical recurrence after a median time of 15 months (IQR, 12–29). Five-years BRFS was 77%. Only higher ISUP grade groups were related to worst BRFS (p.value 0,038). All those 10 patients had loco-regional lymph nodal progression and 4 (8%) of them had local failure and thus received salvage ADT. Six (12%) patients developed distant metastasis after a median time of 30 months (IQR 17-49). Five- year MFS was 82%. Clinical cT3a-b were associated to worst MFS (p.value 0.044). No acute G3-4 toxicities were reported. Only one late G3 GU toxicity was reported (dysuria).

Conclusions: This analysis shows there is a cohort of HRPCa patients who may benefit from local SBRT with ADT without lymph nodal elective irradiation. SBRT delivered to prostate and seminal vesicles in 5-7 fx represents a safe treatment for clinically localized HRPCa.



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MANAGEMENT AND OUTCOMES OF PATIENTS WITH BRAIN METASTASIS FROM OESOPHAGAL CANCER: A SINGLE CENTRE STUDY

Code: 277

Aims: To report the management and survival outcome of oesophagal cancer patients (pts) with brain metastases (BM) treated with a multimodality approach in a single centre.

Methods: Data from a prospectively maintained institutional database were analyzed for pts with oesophagal adenocarcinoma or squamous cell carcinoma who underwent surgical resection and subsequently developed BM. Treatment modalities included surgical resection, stereotactic radiosurgery (SRS), whole brain radiotherapy (WBRT), and combinations of these. Survival rates were calculated from the time of BM diagnosis. Data for overall survival were considered complete at the time of ascertainment of patient death or were censored on 31 May 2023. Survival curves were estimated using the Kaplan-Meier method, and differences between groups were tested using the log-rank test.

Results: From January 2006 to December 2022, 572 patients underwent curative surgery in our institution, and 34 (5.9%) developed BM. BM patients were 91.2% male, with a median age of 61 (47-78) years. The majority of pts presented with a locally advanced oesophagal disease; none had BM at diagnosis. The tumour histology was adenocarcinoma in 79.4% of cases. Fifteen (44.1%) patients presented with synchronous BM (time to onset <6 months from diagnosis), while 19 of them (55.9%) received the diagnosis of BM more than 180 days after esophagectomy. In 22 patients (64.7%), the BM was single; in 10 patients (29.4%), it was multiple; for two patients data was not available. Pts and BM characteristics are summarized in Table 1. Twenty-three pts were treated with a local approach: 9 pts surgery alone, 5 pts surgery + SRS, 4 pts surgery + WBRT, 5 pts SRS. Eleven pts had a palliative approach with 7 WBRT, one chemotherapy and three best supportive care. With a median follow-up of 8.9 months (range 0-90) from BM diagnosis, five patients (14.7%) are still alive. Twenty-nine patients died with a median survival of 7.5 months from BM diagnosis. The median overall survival in the locally treated pts group was 29.2 months (CI 95% 21.2 - 37.9), whereas in patients with a palliative approach, the median OS was 5.6 months (CI 95% 1.3 - 10.9) ($p < 0.001$).

Conclusions: In pts with BM from oesophagal cancer, a local therapy approach, including SRT or surgery with SRT, showed significantly improved overall survival compared to WBRT or chemotherapy. Further prospective studies are warranted to validate these findings and guide treatment decisions.

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		N=34 (%)
Sex	Male	31 (91.2)
Age	Years (median; min-max)	61 (47-78)
Karnfosky PS score at BM diagnosis	(median; min-max)	80 (50-100)
Esophageal tumor location	Cervical	2 (5.9)
	Thorax	7 (20.6)
	EGJ	25 (73.5)
Histology	Squamous cell carcinoma	7 (20.6)
	Adenocarcinoma	27 (79.4)
Clinical stage	II	1 (2.9)
	III	17 (50.0)
	IVa	11 (32.4)
	IVb	5 (14.7)
Neoadjuvant therapy	Chemo-radio therapy	24 (70.6)
	Chemotherapy	10 (29.4)
Response to neoadjuvant therapy	Stable disease	11 (32.4)
	Partial response	23 (67.6)
Pathological complete response	ypT0N0	15 (44.1)
Time surgery-metastasis	(days, median; min-max)	177 (33-1881)
Timing of BM diagnosis	Synchronous (<180 days)	15 (44.1)
	Metachronous (>180 days)	19 (55.9)
Number	Single	22 (64.7)
	Multiple	10 (29.4)
	Missing	2 (5.9)
Main symptom at diagnosis	Vertigo	7 (20.6)
	Confusion	7 (20.6)
	Paresis	7 (20.6)
	Other	4 (11.7)
	Asymptomatic	9 (26.5)

Table 1. Pts and BM characteristics.

HAEMATOLOGICAL ACUTE TOXICITY AND LONG-TERM OUTCOME OF THREE DIFFERENT CRANIOSPINAL IRRADIATION SCHEDULES USING HELICAL TOMOTHERAPY IN ADULTS: A MONOCENTRIC RESTROSPECTIVE STUDY

Code: 609

Aims: To describe haematological acute toxicity, overall survival (OS) and freedom form progression (FFP) in adult patients (pts) treated with helical Tomotherapy craniospinal irradiation (HT-CSI).

Methods: From 2006 to 2024, 89 pts (age 2-59 years, median 20) were treated with HT-CSI. Among that cohort, we considered for the analysis adult pts with a previous diagnosis of medulloblastoma (n=37). For the analysis we found three different schedules of HT-CSI dose (changes were made based on the progressively newer clinical and technical improvements): 36 Gy (1.8 Gy/fr), 32.4 Gy (1.8 Gy/fr) and 35.2 Gy (1.6 Gy/fr). Acute side effects were recorded according to the CTCAE 4.0. For the analysis we considered pts without neoadjuvant/concomitant chemotherapy (CT), or, in case of neoadjuvant CT, we considered only pts in complete haematological recovery before HT-CSI.

Results: 36 Gy HT-CSI: 72% grade (G) >3 leukopenia; 28% G>3 neutropenia; 29% G>3 thrombocytopenia.
32.4 Gy HT-CSI: 44% G >3 leukopenia; 11% G>3 neutropenia; 17% G>3 thrombocytopenia.
35.2 Gy HT-CSI: 42% G >3 leukopenia; 17% G >3neutropenia; 42% G>3 thrombocytopenia.
Values of Hb were not considered for the analysis because not significantly low.
30 months OS was 83.9% (SE 7.5%) and FFP was 69.5% (SE 10.6%) among the three groups

Conclusions: HT-CSI acute toxicity was in line with Literature. We registered lower haematological toxicities with the 32.4 Gy (1.8 Gy/fr) schedule. Further efforts to correlate dosimetric and toxicity data are needed.

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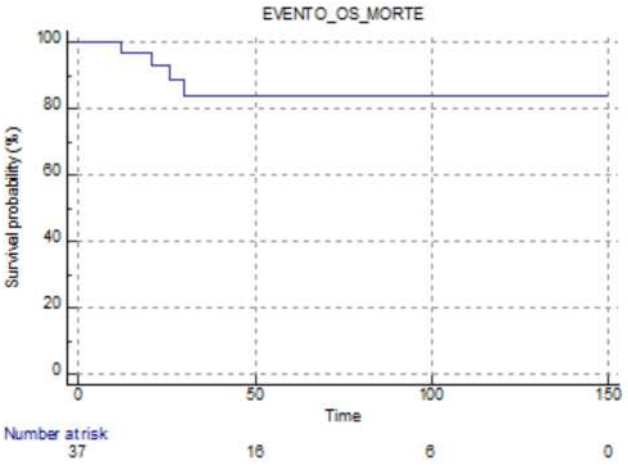
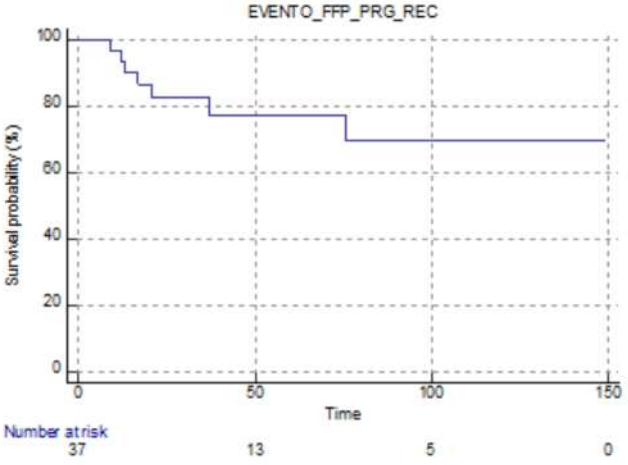




MANAGEMENT OF RADIOTHERAPY IN A PATIENT WITH LEADLESS VENTRICULAR PACEMAKER: A CASE REPORT

Code: 224

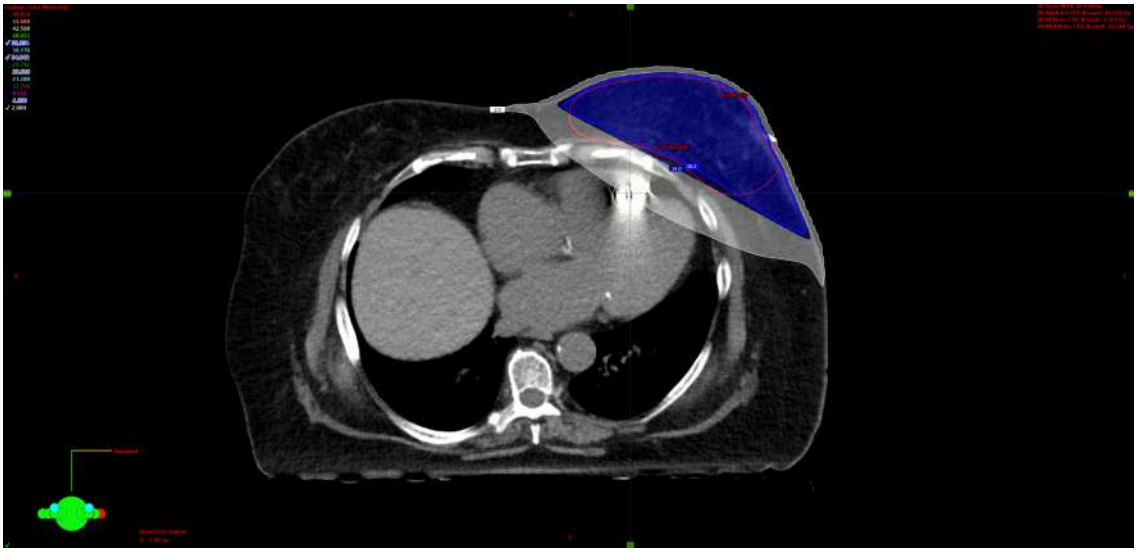
Aims: Cardiac pacemakers (PM) are one of the most frequently implanted medical devices in Italy. Radiation therapy (RT) poses a risk of altering PM function. Most PMs are subcutaneous on the upper chest, but some have leadless pacemakers in the heart. We report a case of RT for left breast cancer in a patient with a Micra AV leadless ventricular PM.

Methods: An 80-year-old woman, with an intracardiac pacemaker, presented with stage IIB (pT2pN1a) luminal A left breast invasive carcinoma post quadrantectomy and axillary lymphadenectomy. Left breast radiotherapy (RT) involved 42.56 Gy in 16 fractions to the whole breast, followed by a 10 Gy boost in 4 fractions to the surgical cavity. Supine positioning was employed during simulation, with a tailored treatment plan to minimize pacemaker radiation exposure. Classical 3D Intensity-Modulated Radiation Therapy (IMRT) was utilized, carefully positioning the isocenter and collimator rotation to close primary collimators on the patient's chest wall. The isocenter unchanged throughout treatment, even during the boost phase. Weekly monitoring for pacemaker malfunction, supervised by the electrophysiologist, aimed to address potential electromagnetic interference risks. Careful planning balanced effective tumor treatment with minimizing risks to the pacemaker. Prioritizing

patient safety, the customized radiotherapy plan, and continuous pacemaker monitoring ensured a comprehensive and individualized approach to her care.

Results: Despite lower treatment coverage (90% dose for 84% treated volume) than standard methods, our focus on shielding the pacemaker near the target area was paramount. Scientific literature advises limiting the maximum pacemaker surface dose to 2 Gy during radiotherapy. Recent studies and the pacemaker manual suggest no functional differences with doses up to 5 Gy for beams under 10 MV. The patient's pacemaker received a maximum of 4.5 Gy and an average of 2.5 Gy, in contrast to a standard plan resulting in a 34 Gy and 9 Gy, respectively.

Conclusions: The patient tolerated radiotherapy well, without acute symptoms or pacemaker issues. The monitoring of the pacemaker during the treatment didn't detect any alterations in its functioning that could compromise the ongoing therapeutic course. The integrated management of radiotherapy and the cardiac device in this case underscores the importance of meticulous planning to ensure effective and safe treatment. However, long-term monitoring for potential chronic toxicity is currently unavailable.



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FALLBACK PLANNING IN PROTON THERAPY: VALIDATION OF THE DOSE MIMICKING ALGORITHM

Code: 213

Aims: In case of a failure of the proton accelerator, patients (pts) would have to interrupt their proton therapy (PT) treatment and wait for restoration, with a subsequent reduction in therapeutic efficacy. Fallback (FB) planning, available in Raystation TPS v.12A, is a tool used to automatically generate a dose-mimicking photon plan from a proton plan. However, FB becomes more tricky when it is used to switch from PT to photon radiation therapy (RT). The purpose of this work is to test and validate FB planning as an algorithm able to provide a suitable photon plan as backup.

Methods: Ten (5 head&neck, 3 prostate, 2 breast cancer) pts treated with RT were retrospectively selected. For the purpose of the study (Figure 1), for each patient, an Intensity-modulated PT (IMPT) plan was developed with Monte Carlo calculation algorithm and prescribing the dose to the Clinical Target Volume (CTV). Then, FB plans were automatically generated with Collapse Cone Convolution (CCC) algorithm, using different protocols (different beam energies, accelerator, treatment techniques, and system geometry). For each patient, the best automatically-generated FB plan was manually re-optimized to ensure adequate PTV coverage, obtaining a semi-automatically generated plan. To assess the deliverability of FB plans, gamma analysis was used for quality assurance (QA) measurements. Finally, these semi-automatically generated plans were compared with fully-manual developed photon plans.

Results: Each FB plan was generate in approximately 10 – 15 minutes, depending on the complexity of the original PT plan. Totally, 20, 18, and 8 best automatically-generated FB plans were chosen for the head-neck, prostate, and breast districts, respectively. Re-optimisation of FB plan was necessary to ensure PTV coverage. FB plans were found to be adequate at the QA analysis. The low sample size prevented statistical tests, however, photon manual plans and the semi-automatically plans (FB re-optimised) were comparable.

Conclusions: Currently, FB system does not allow the generation of fully-automatically generated backup plans from proton-to-photon transition without subsequent re-optimisation. However, despite this limitation, it is hoped that shortly FB via dose mimicking will ensure continuity of treatment and optimal therapeutic efficacy, even in the event of prolonged technical problems of the proton accelerator.

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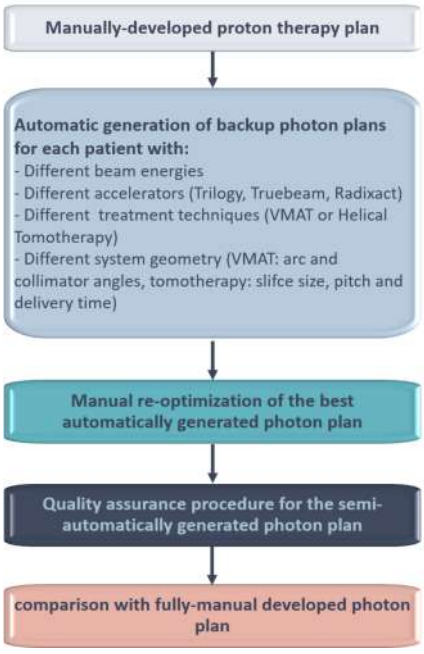
Figure 1 Workflow of the study.
List of abbreviations: VMAT (Volumetric Modulated Arc Therapy).



IN THE DEEP-INSPIRATION BREATH-HOLD TECHNIQUE ERA, IS THERE STILL A ROLE FOR FREE-BREATHING TREATMENT? THE EXPERIENCE OF AN ITALIAN CENTER IN LEFT BREAST CANCER: EMPIRICAL CRITERIA TO GUIDE THE CLINICIAN

Code: 168

Aims: Adjuvant treatment of left breast cancer can induce late cardiac complications. The use of deep inspiration breath-hold (DIBH) compared with free breathing (FB) technique may reduce the absorbed dose by heart and left anterior descending artery (LAD).
The study aims to quantify the role of FB treatment in an Italian center.
In the decision-making process, in addition to clinical exclusion criteria (age > 70 years/life expectancy, compliance, comorbidity, previous RT on the chest wall), criteria linked to the expected benefit of DIBH treatment in terms of dose saving to organs at risk were empirically identified.

Methods: Patients not fulfill inclusion clinical criteria were referred to FB treatment. 70 patients were selected for evaluation for DIBH treatment from July 2022 to January 2024. Computed tomography (CT) scans in FB and DIBH were performed for all patients with Sentinel. Intrafractional 3D position monitoring of the patients surface in DIBH was performed using Catalyst HD 3D surface scanning system. 3D treatment planning was performed using standard tangential treatment fields (6-10 MV). The total dose delivered was 40.05 Gy in 15 fractions plus final (6 Gy) or concomitant boost (7.95 Gy). The dose constraints used for the evaluation of the plans refer to those used in the START B study.
When both plans meet the constraints, we introduce empirical criteria to select the patient who could have the maximum benefit from DIBH: If the DIBH plan reduces one or both threshold constraint values by 2 Gy the DIBH treatment is performed; when the dosimetric gap is less than 2 Gy the treatment plan is performed in FB unless the patient has cardiac pathology or in case of retreatment.

Results: 70 patients were evaluated for treatment in DIBH. 14 (20%) did not reach the expected threshold of 2 Gy and were therefore referred for treatment in FB. All patients, DIBH and FB, completed treatment without reporting significant complications.

Conclusions: in our experience, only 20% of patients who underwent CT in DIBH finally underwent treatment in FB. In addition to the "conventional" exclusion criteria, the addition of empirical criteria linked to the expected benefit of the DIBH treatment made it possible to limit the breath-hold treatment to 80% of eligible patients with consequent savings in terms of treatment time and complexity as well as reduction of waiting lists. Prospective studies and long-term follow-up are needed to evaluate the clinical outcomes of applying the above criteria.

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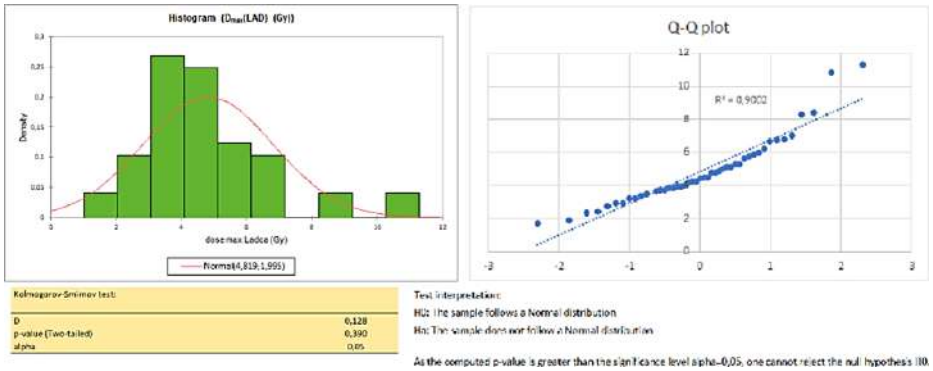
OPTIMIZE TREATMENT PLANS WITH CONTROLLED BREATHING TECHNIQUE IN PATIENTS AFFECTED BY LEFT BREAST CANCER WITH LOWER REFERENCE DOSIMETRIC LEVELS OF ORGANS AT RISK

Code: 454

Aims: The use of deep inspiration breath-hold (DIBH) compared with free breathing (FB) technique reduces the absorbed dose by heart and particularly by left anterior descending artery (LAD).
The dose constraints of the organs at risk have been established by studies about plans delivered in FB technique. Therefore in the majority of plans performed in DIBH technique the constraints are higher than the obtained values. For this reason, our study aims to identify more restrictive dosimetric reference values to optimize treatment plans.

Methods: 70 patients were selected for evaluation for DIBH treatment from July 2022 to January 2024. Computed tomography (CT) scans in FB and DIBH were performed with Sentinel for all patients. Intrafractional 3D position monitoring of the patients surface in DIBH was performed using Catalyst HD 3D surface scanning system. Three-dimensional treatment planning was performed using standard tangential treatment fields (6-10MV). For 47 patient total dose delivered was 40.05 Gy in 15 fractions plus final (6 Gy) or concomitant boost (7.95 Gy). Dose constraints used for the evaluation of the plans refer to the START B study (D_{max}(LAD)<16Gy $D_{2\%}$(heart)$_{optimal}$<40%).
Treatment plans were optimized with both techniques (FB and DIBH) trying to favor target coverage ($V_{95\%}$(PTV)=94.9% in both groups) keeping the dose at organs at risk as low as possible.



Results: The DIBH plans allowed a notable dose reduction delivered to the heart and LAD. In particular D_{max}(LAD) was 4.8 Gy ($p<0.0001$) in DIBH group and 12Gy ($p<0.0001$) in FB group. $D_{2\%}$(heart) was 3.4% ($p<0.0001$) in DIBH group and 7.9% ($p<0.0001$) in FB group. The average dose to the heart was essentially the same for both groups (0.9 Gy ($p<0.0001$)).
The data obtained for D_{max}(LAD) and $D_{2\%}$(heart) can be described by a normal distribution (Kolmogorov- Smirnov test: p-value 0,39). This distribution was used to define the dosimetric reference levels for plan optimization for these parameters, and in particular as the average value of the distribution plus one standard deviation ($D_{max}(LAD)_{optimal}<7$Gy $D_{2\%}(heart)_{optimal}<5.5\%$). Mandatory constraints defined by the study START B were maintained.

Conclusions: The retrospective analysis of the dosimetric values for OAR obtained by our center using the DIBH technique permits to identify more restrictive dosimetric reference levels than traditional ones leading us to optimize the treatment plans in clinical practice.

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SBRT FOR LOCAL ABLATION OF LIVER METASTASIS

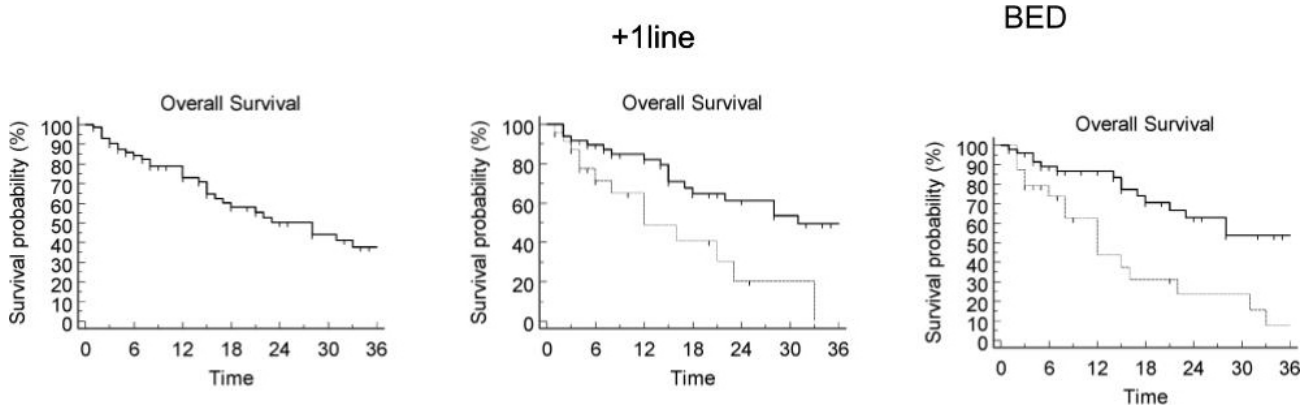
Code: 578

Aims: Stereotactic Body Radiation Therapy (SBRT) has been applied to local management of liver metastases, both in oligometastatic (OM) and oligoprogressive (OP) setting. However, no selection criteria and dose requirements have been clearly elucidated. The aim of our study is to assess the clinical predictor of improved outcome in liver metastases treated with SBRT.

Methods: Data from a retrospective cohort of patients treated with liver SBRT from Jan 2019 to Jul 2023, for whom clincal follow-up was available, were collected. SBRT was delivered either with fiducial-based real-time tumor tracking (RTTT) using a robotic arm treatment platform or with VMAT, with abdominal compression for respiratory motion mitigation. Local control (LC) and Progression Free Survival (PFS) were calculated for each treatment and Overall Survival (OS) for each patient. Univariate and multivariate statistics was performed, using the log rank test and Cox analysis respectively.

Results: Seventy-three patients, (median age 66 years, range 41-83), with 81 metastases, 32 in OM and 49 in OP setting, were identified. Second or further lines of chemotherapy (2L-CHT) were prescribed in 27/81 cases. SBRT was delivered with RRTT and VMAT in 25 and 56 cases respectively, with 3 or 5 fractions for a total dose of 30-60 Gy. Median BED was 112.5 Gy (59.5-180), with 54 lesions receiving a BED > 100Gy. Median OS, LC and PFS were 28 months (95%CI 16-37), 30 months (95%CI 21-41) and 8 months (95%CI 6-10) respectively, while OS, LC and PFS were 79%, 74% and 32% at 1 year and 50%, 57% and 21% at 2 years, respectively. Only BED>100 Gy was correlated with improved LC (41 vs 21 months, p 0.041, HR 0,47 95%CI 0.19 - 1.1). At univariate analysis, PFS was associated with BED >100 Gy (p0.0002, HR 0,4 95%CI 0.2-0.75) and prior 2L-CHT (p0.00014 HR 0,4 95%CI 0.2-0.75), both independently correlated at multivariate analysis (p 0.008 and p 0,0048 respectively). Improved OS was correlated with BED >100 Gy (p 0,001, HR 0,35 95%CI 0.16-0.78), while poorer OS with 2L-CHT (31 vs 12 months, p 0.0301, HR 2.4 95%CI 1.1 -5.9). Both BED>100 and 2L-CHT were independent at multivariate analysis (p 0.01 and p 0,037 respectively). No differences were found in terms of treatment outcome for other variables.

Conclusions: Liver SBRT resulted in long disease control and PFS, with encouraging survival rates both in OP and OM setting, particularly if a BED>100Gy or in lightly pre-treated patients. No difference was found in terms of outcome between treatment techniques.



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GLIOBLASTOMA AND INTERNAL CAROTID ARTERY CALCIUM SCORE: A POSSIBLE NOVEL PROGNOSTIC PARTNERSHIP? THE FINAL RESULTS OF A MONOCENTRIC RETROSPECTIVE STUDY

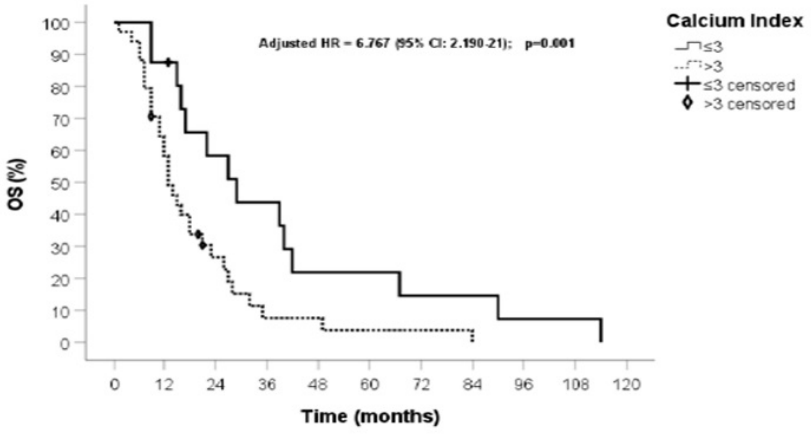
Code: 193

Aims: Clinical evidence suggests an association between comorbidities and outcome in patients with glioblastoma (GBM). We hypothesized that internal carotid artery (ICA) calcium score could represent a promising prognostic biomarker in patients diagnosed with GBM

Methods: As preliminary step of the present study, we validated the use of ICA calcium score as surrogate marker of coronary calcium score in 32 patients with lung cancer (A statistically significant correlation was found between ICA and coronary Agatston scores ($p<0.05$)). Subsequently, we assessed the impact of the ICA calcium score on overall survival (OS) in GBM patients treated with radio-chemotherapy. The continuous calcium score variable was transformed in quartiles and successively in two categories (≤ 3, >3) where 3 represents the 25th percentile. OS curve was calculated by the Kaplan-Meier method and the log-rank test was used to evaluate the differences between curves (fig.1).

Results: 196 patients with GBM were identified from the Radiotherapy Department's dataset (146 patients (74.5%) were excluded due to ICA proximity to the bony skull base, hindering an accurate quantification of ICA wall calcifications). Fifty patients (28 male, 22 female) were eligible for the final analysis. At univariate analysis, methyl-guanine-methyltransferase gene (MGMT) promoter methylation (P=0.048), gross total tumor resection (p=0.017), and calcium score (P=0.011) were significant prognostic predictors in patients with GBM. These three variables also maintained statistical significance in the multivariate analysis (Tab. 1).

Conclusions: Based on our results, the ICA calcium score could be a promising prognostic biomarker in GBM patients.



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TRIMODAL THERAPY APPROACH: A VALID ALTERNATIVE THERAPY FOR VERY HIGH GRADE NON MUSCLE-INVASIVE BLADDER CANCER

Code: 292

Aims: According to current guidelines, radical cystectomy is indicated for h igh grade and very high grade non muscle-invasive bladder cancer (NMIB C) unresponsive to BCG therapy. Many patients decline this major surge ry especially for worsening of quality of life or because unfit to sur gery. Actually, there are not alternative therapy. In our multidiscipl inary team (MDT), in according with oncologist and urologist we propos e a trimodal therapy approach.

Methods: From 2020 to 2023 we selected 7 patients with a pT1G3 bladder cancer (BC) unresponsive to BCG therapy. The mean time to recurrence after BCG therapy was 4 months. All patients refused the early cystectomy and underwent a multidisciplinary team (MDT) evaluation. The trimodal approach was proposed as an alternative therapy. The follow-up was based on cystoscopies and TC/ MRI. The average time of the follow-up was 10.7 months (2-21).

Results: The mean age was 76.5 years (73-84). The Charlson Comorbility Index was 5.5 (5-6). All patients were no metastatic, and before radiotherapy and chemotherapy, they underwent cystoscopy to confirm cT0 in the bladder. The chemotherapy of 3 of them was based on Cisplatin (for 1 patient 6 sessions, each session of 80 mg; for 3 patients 5 sessions, each session of 60 mg), for the last patient was based on Gemcitabine (5 sessions, each of 180 mg). The radiotherapy consists of external beam radiation therapy whit VMAT technique, the total dose for 2 of the patients was 60 Gy (divided in 30 fractions each of 2 Gy), for 3 patient was 55 Gy (divided in 20 fractions each of 2.75 Gy) and for 2 patient was 52.25 Gy (divided in 19 fractions each of 2.75 Gy). The last one didn't receive the last fraction of radiotherapy because he had a worsening of his clinical conditions not related to his bladder history of tumor. After the MDT decision, the patients begin the trimodal approach in 4.15 months (0.5-8.8). The duration of the treatment based on chemo- and radiotherapy for all the patients was 30 days. No severe side effects were observed and all patients had a good quality of life. The follow-up was based on cystoscopies every three months and imaging (TC/MRI) every 6 months. Currently no recurrence or progression was reported.

Conclusions: According to guideline a cystectomy sparing approach should not be offered in the patients with NMIBC BCG failure or unresponsive. However, the trimodal approach could be a valid alternative to cystectomy in patients who refuse surgery.

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LEFT BREAST IRRADIATION WITH DIBH: TECHNICAL FEASIBILITY AND TREATMENT TOLERANCE ASSESSED ACCORDING TO PROMS

Code: 411

Aims: To retrospectively evaluate protocol's implementation, feasibility and patient reported outcomes measures (PROMs) of deep inspiration breath hold (DIBH) using a cone-beam CT for left-sided breast cancer irradiation

Methods: From July 2021 to October 2022 fifty-five patients (pts) underwent adjuvant left breast/chest wall DIBH with (40%) or without (60%) loco-regional lymph nodes irradiation. Average patients' age was 52 years (31-79). Forty-two (76%) pts received breast conservative surgery followed by whole breast irradiation, 12 (29%) with concomitant lymph nodes irradiation. In thirteen (24%) pts chest wall irradiation was delivered and 10 (76%) pts with concomitant lymph nodes. Total dose ranged from 40.05 to 46Gy in 15-20 fractions (fx). A 7.95 Gy simultaneous integrated boost was added in pts treated with 15 fx. RT was delivered through volumetric modulated arc therapy with remotely technician's vocal instructions without any visual coaching. We retrospectively analysed average delivery treatment time for each pts and we explored specific PROMs, obtained through a questionnaire administered at the end of treatment.

Results: The average delivered treatment time for all patients was 10 minutes with a great variability in time interval (range 2-41). We observed that for the first 13 patients' the median treatment time was longer than 20 minutes, maybe also due to a slower technicians' learning curve implementation, although there has been a reduction in delivered treatment. Among all patients a progressive minutes reduction was registered for 16 pts (9%) after the first three sessions, while a floating trend has been noted for 8 pts (5%) and a worsening one for 2 pts (1%). For the majority of pts (29pts-16%) the treatment time was quite regular and constant. Fortythree pts (24%) did not report any treatment-related anxiety or stress during or after RT but 14 pts were concerned about the impact of DIBH on the therapy's success.
Eleven pts (6%) reported a moderate dyspnea or fatigue at the end of treatment. Thirty-seven pts (20%) declared they would benefit from visual coaching, whereas 39 (22%) did not reported any benefit from potential written instructions or tutorial videos.

Conclusions: This recent update of a sample of all the breast cancer patients treated with DIBH at our department confirms that is a feasible and well tolerated treatment. Maybe a visual coaching system could be useful to reduce treatment delivery time and to minimize the detected patient discomfort

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STEREOTACTIC RADIOTHERAPY FOR BRAIN METASTASES FROM BREAST CANCER: SINGLE INSTITUTION ANALYSIS OF TOXICITY AND LOCAL CONTROL

Code: 105

Aims: Stereotactic radiotherapy (SRT) has an increasing role in the multimodal management of patients (pts) with metastases from solid tumors. We report our experience in the treatment of brain metastasis from breast cancer.

Methods: From 01/2018 to 07/2023, 60 SRTs were delivered to 293 brain metastases (BM) of 38 breast cancer pts. Molecular subtypes of primary tumor were: luminal (A&B) 34%, triple negative 11%, HER2+ 55%. SRT was delivered to a median of 3 concomitant lesions (1-46). At the time of the treatment, the state of systemic desease was oligometastatic in 55% and plurimetastatic in 45% of cases. Robotic SRT was delivered with the following schedules: 19-24 Gy in single fraction, 24-30 Gy in 3 fractions, 30-35 Gy in 5 fractions, prescribed to a median isodose of 79.5 (50-80) %. Median BED was 60 (43.2-81.6) Gy. In 8 cases, more than 10 lesions were simultaneously treated, with cumulative median PTV of 22.2 (10.7-33) cc. Nine pts were previously treated with SRT to the same target and 2 pts with WBRT. Acute and late toxicity were registered according to CTCAE v.5 scale. Clinical outcomes were evaluated by MRI.

Results: Median follow-up was 13 (2.5-70) months. SRT was well tolerated, with 20% of grade (G)1 acute toxicity (headache, nausea, dizziness). Late toxicity (headache, dissiness, radionecrosis) was 10% G1 and 18.3% G2. Radionecrosis occurred in 10 cases (16.6%) after a median time of 12 (2.5-40.8) months from SRT. Six out of 10 pts (60%) were symptomatic; all of them were treated with concomitant anti-HER2 therapy and 4 pts underwent reirradiation. Among pts treated for >10 lesions, only one patient relapsed in field, and 4 pts had intracranial progression. In this group, toxicity was not significant, with the exception of one patient, who had symptomatic radionecrosis. Local relapse free survival at 6, 12 and 18 months was 94.7%, 89.6% and 82.6%, respectively (figure 1).

Conclusions: SRT can achieve good local control with acceptable toxicity. Careful selection and management of patients is essential to reduce complications such as radionecrosis.

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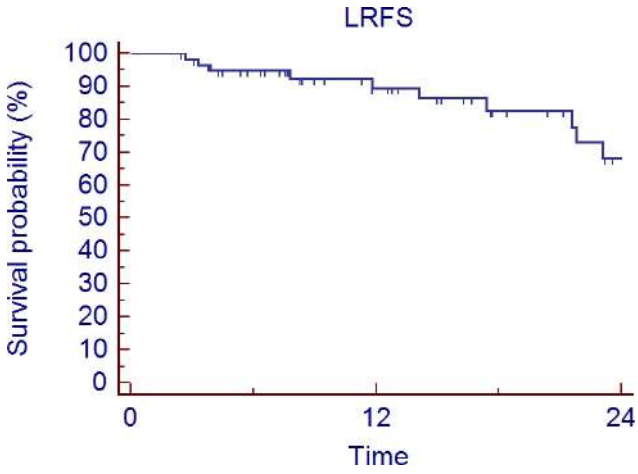

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ADJUVANT EXTERNAL-BEAM PELVIC RADIATION (EBRT) FOLLOWED BY VAGINAL BRACHYTHERAPY (VB) BOOST IN ENDOMETRIAL CARCINOMA (EC). AN UPDATE

Code: 403

Aims: To analyze the impact on local control and toxicity of adjuvant VB boost to EBRT in EC considering age, stage, histology, grade, risk group, lower uterine segment involvement (LUS), cervical stromal infiltration (CSI) andlymphvascular space invasion (LVSI).

Methods: One hundred and eighteen EC patients (pts) were treated from 2012 to 2019 with postoperative EBRT and VB+/- chemotherapy (CT). The median age was 63 years (41-83 years). All pts underwent primary surgery, 75 with and 43 without lymphadenectomy. 50,8%pts received CT. FIGO stage I was 37,3%, stage II 39,8% and stage III 22,9%. Endometrioid and high risk hystology were 83,9% and 16,1% respectively.
The tumor grade was 54,2% G1-G2 and 45,7% G3. LUS was present in 48,3% of tumors, CSI in 49,2% and LVSI in 42,4%. The risk stratification was: intermediate risk 16,1%, high-intermediate risk 50%, and high risk 33,9%. All pts received EBRT: 45,8% with IMRT and 54,2% with 3 DCRT. The median dose was 45 Gy (range 43.2-50.4 Gy) in 25-28 fr. All pts riceived high dose rate VB. The upper half of vagina was treated with10-15 Gy in 2-3fr.

Results: The median follow-up was 77 months (14-104 months). The 6,5 years OS, DSS, DFS, and LC were 87,9%, 89%, 79,9%, 89%, rispectively. At univariate analysis histology, grade, and risk group were significantly correlated with OS, DSS, DFS, and LC, ($p< 0.05$). The multivariate analysis based on the stratified Cox regression, suggested that histology, FIGO stage, and CSI were significantly correlated with OS; grade, and LA were correlated with DFS; while grade and CT were correlated with DSS; histology, risk group, and LA with LC. Tumor relapsed in 16/118 pts (13,6%). The median time to recurrence was 28 months (1-87 m). Local recurrences (1 vagina, 1 central pelvis) were in 3 (2,54%) pts, distant (1 both pelvis, 1 both vagina, 3 both lymph node, 5 other sites) in 10 (8,5%), retroperitoneal lymphnodal in 3 (2,5%) (1 para-aortic, 1 para-aortic and pelvic, 1 para-aortic and vagina).

Conclusions: Our patients cohort impact on the traditional adverse features (histology, grade, risk groups) impact OS, DSS, DFS, and LC. Furthermore, our study population experienced a high local control rate of 89% at median follow-up. Distant failure was 8,5%. However, the role of a VB boost needs further investigation to understand the incremental benefit beyond pelvic RT.

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ANALYSIS OF EARLY AND LATE SIDE EFFECTS IN PATIENTS AFFECTED BY ENDOMETRIAL CARCINOMA AND TREATED WITH ADJUVANT EXTERNAL-BEAM PELVIC RADIATION (EBRT) FOLLOWED BY VAGINAL BRACHYTHERAPY (VB) BOOST

Code: 406

Aims: Aim of the study was to report the early and late toxicities of adjuvant EBRT and VB boost in Endometrial cancer (EC)

Methods: One hundred and eighteen EC patients (pts) were treated from 2012 to 2019 with postoperative EBRT and VB+/- chemotherapy (CT). The median age was 63 years (41-83 years). All pts underwent primary surgery, 75 with and 43 without lymphadenectomy. 50,8% received CT. FIGO stage I was 37,3%, stage II 39,8% and stage III 22,9%. Endometrioid and high risk hystology were 83,9% and 16,1% respectively.
The tumor grade was 54,2% G1-G2 and 45,7% G3. Lower uterine segment involvement (LUS) was present in 48,3% of tumors, cervical stromal infiltration (CSI) in 49,2% and lymphvascular space invasion (LVSI) in 42,4%. The risk stratification was: intermediate risk 16,1%, high-intermediate risk 50%, and high risk 33,9%. All pts received EBRT: 45,8% with IMRT and 54,2% with 3 DCRT. The median dose was 45 Gy (range 43.2-50.4 Gy) in 25-28 fr. All pts received high dose rate VB. The upper half of vagina was treated with 10-15 Gy in 2-3fr. Early and late toxicities was graded according to CTCAE 5.0 scale.

Results: The median follow-up was 77 months (14-104 months). The side effects comparison between 3D-CRT vs IMRT for EBRT was made with Chi square test or Fisher's exact test. Early G1-G2 gastrointestinal (GI) toxicities were globally 34,74% (41/118 pts) : 48,4% (31/64 pts) in 3D-CRT group and 18,52% (10/54 pts) in IMRT group, $p<0.0001$. Early G1-G2 genitourinary (GU) toxicities were globally 41,52% (49/118 pts): 43,75% (28/64 pts) in 3D-CRT group and 38,89% (21/54 pts) in IMRT group, $p=0.5$. Overall late GI and GU toxicities were 12,71% (15/118 pts): 17,18% (11/64 pts) in 3D-CRT group and 7,4% (4/54 pts) in IMRT group, $p=0.05$. There was only 1 late urinary incontinence G3 in 3D-CRT group. Early VB side effects were found in 11/118 pts (9,32%); while late complications were found in 30/118 pts (25,4%): 12 vaginal stenosis (10,16%), 4 (3,38%) vaginal dryness, and 14 (11,86%) vaginal atrophy. No G3-G4 vaginal side effect was found for VB.

Conclusions: In our series, acute GI effects and lare toxicity are significantly greater in the 3D-CRT group than in IMRT group. Acute GU toxicities do not appear to be affected by the radiation technique used. The treatment is very well tolerated for late side effects, that were mainly grade G1-G2, while no G3-G4 late vaginal toxicities were reported, in line with current data of literature.

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A DEEP LEARNING-BASED TOOL FOR AUTO- SEGMENTATION FOR BRAIN METASTASES RADIOSURGERY

Code: 330

Aims: A comprehensive evaluation of a deep learning (DL)-based commercial tool for CT auto-segmentation has been performed. The geometric, time-based, and clinical qualitative evaluation (QE) focused on contouring of the brain, brainstem, optic chiasm, optic nerves, eyes, lens, and cochlea.

Methods: A mono-institutional consecutive series of 20 brain SRS patients (21 Gy/1 fraction, December 2022-September 2023) was retrospectively selected.To allow manual delineation, a post-contrast T1-weighted volumetric magnetic resonance imaging scan was registered on the planning CT. Both image sets were acquired with a maximum slice thickness of 1 mm. CT images were retrieved and structure sets were DL auto-segmented (AS) and compared to manual Ground-Truth (mGT). AS duration and correction times needed by a radiation oncologist (RO) to validate AS have been registered. MR images and image co- registration were maintained as in mGT and made available for AS validation to avoid bias. A QE was performed with 5 degrees of scoring (good, minor differences, edits required, moderate edits, gross error). Tests of DL-performance (20 AS vs 20 mGT) were conducted using Dice Similarity Coefficient (DSC) and Hausdorff Distance (HD). As DSC and HD depend on structure size, contours were also compared using the Distance-to-Agreement Portion DAP_{2mm}, which is the percentage of AS within 2 mm of mGT.

Organ	DSC	HD [mm]	DAP_{2mm} [%]
Brain	0.99 [0.98 – 0.99]	20.75 [14.23 – 30.24]	66.25 [30.30 – 89.70]
Brainstem	0.87 [0.60 – 0.98]	10.10 [7.37 – 45.67]	70.55 [9.90 -86.30]
Optic chiasm	0.11 [0.00 – 0.35]	11.87 [5.52 – 20.92]	34.70 [0.00 – 51.60]
Right optical nerve	0.67 [0.54 – 0.76]	7.91 [2.72 – 19.21]	73.10 [41.50 – 94.70]
Left optical nerve	0.65 [0.51 – 0.73]	7.85 [3.40 – 20.01]	66.15 [47.90 – 91.80]
Right eye	0.93 [0.90 – 0.95]	5.64 [4.05 – 7.84]	91.25 [81.70 – 97.20]
Left eye	0.94 [0.90 -0.95]	5.17 [2.27 – 6.80]	91.30 [74.80 – 99.80]
Right lens	0.77 [0.37 – 0.89]	1.68 [0.90 – 2.91]	100.00 [83.10 – 100.00]
Left lens	0.75 [0.51 – 0.89]	1.98 [1.35 – 3.01]	100.00 [86.40 – 100.00]
Right cochlea	0.58 [0.33 – 0.72]	2.04 [0.85 – 3.20]	98.30 [88.90 – 100.00]
Left cochlea	0.55 [0.25 – 0.77]	2.08 [1.41 – 3.01]	98.40 [84.90 – 100.00]

Figure 1 – Geometric performances of DL-based automated contouring compared with the manual Ground-Truth. *Abbreviations: DSC Dice Similarity Coefficient; HD Hausdorff Distance; DAP_{2mm} Distance-to-Agreement Portion.*

Results: Median estimated mGT duration is 30 minutes. The median AS and manual correction time per structure set was 0.8 [0.6 – 1.5] min and 8.9 [6.9 – 14.9] min, respectively. The median DSC, HD, and DAP_{2mm} are reported in **Figure 1**, along with their ranges. For the eyes and lens, QE showed a good agreement, but some minor differences were necessary in the brain and cochlea contouring. Brainstem and optic nerves resulted in needing edits and moderate edits in the majority of cases. According to the lowest DSC values registered, 19/20 optic chiasms received the worst evaluation.

Conclusions: The CT-based DL-tool could reduce manual operations duration by one third and provide a clinical advantage in the delineation of the brain, the brainstem and the eyes. For all small structures but the optical chiasm, DAP_{2mm} confirmed QE results by finding most AS in the mGT surroundings. A low DAP_{2mm} for the optical chiasm demonstrated that MRI images are necessary to correctly delineate it. Future studies will include other ROs' QE in a larger cohort.

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MULTIMODALITY THERAPY FOR HIGH-RISK SOFT TISSUE SARCOMAS OF THE TRUNK AND LIMBS: EVALUATION OF TOXICITY, EFFICACY AND LONG-TERM OUTCOMES OF HYPERTHERMIA IN COMBINATION WITH PREOPERATIVE RADIOTHERAPY AND CHEMOTHERAPY

Code: 251

Aims: The aim of the study was to analyse the toxicity and efficacy of adding hyperthermia (HT) to radiotherapy (RT) and chemotherapy (CT) in patients with high-risk soft tissue sarcomas (STS) localised to the trunk and limbs.

Methods: We retrospectively reviewed patients with STS treated with HT combined with RT and/or CT. The treatment plan for each patients was decided by a multidisciplinary team. All patients underwent RT combined with HT according to quality and safety assurance guidelines. Radiotherapy was administered preoperatively using the VMAT technique with a total dose of 50 Gy in 2 Gy fractions. All patients eligible for surgery underwent wide resection and regular follow-up after treatment.

Results: Twenty-four patients (14 men and 10 women; mean age 62.5 years, range: 34-87) with STS were included in this study. The mean size of the treated tumours was 9.2 cm (range 2-20). The most common histology was undifferentiated pleomorphic sarcoma (8 patients, 33.3%). Eight patients (33.4%) received upfront concurrent chemoradiation and HT and 10 (41.6%) received RT and HT alone. Overall, the treatment was well tolerated and 22/24 (91.6%) patients completed the planned course of treatment. Only two cases of grade 3 toxicity (limb edema) were reported with RT. The objective response rate (partial response or stable disease) was 95.8% (23/24 patients). Twenty-three patients (95.8%) underwent surgery after completion of treatment and all achieved negative surgical margins except for two patients (8.2%) who had microscopic R1 margin involvement. Complete pathological response was achieved in 7 of 23 patients (30.4%). Two patients experienced local progression, four patients experienced distant progression and two patients experienced both local and distant progression. With a median follow-up of 18 months (range, 4.5-46.3), median disease-free survival (DFS) was 18.5 months and 3-year DFS was 44%. The 3-year overall survival (OS), local progression-free survival (LPFS) and metastasis-free survival (MFS) rates were 77%, 78% and 71%, respectively (median not reached).

Conclusions: In our experience, the integration of HT, RT and CT was feasible in patients with STS of the trunk and extremities, achieving good local control. However, a larger number of patients and a longer follow-up are needed to understand the best way to synergize these therapies.

Characteristics	No. of patients	%
Sex		
Male	14	58.4
Female	10	41.6
Age at Diagnosis (years)		
Mean	62.5	
Range	34-87	
Site		
Lower extremity	2	8.3
Upper extremity	15	62.5
Trunk	7	29.2
Grade according to French system		
Intermediate	7	29.2
High	88	70.8
Tumour size (cm)[§]		
Median	9.2	
Range	2-20	
Histological subtype		
UPS	8	33.3
Liposarcoma	3	12.5
Synovial sarcoma	2	8.3
Leiomyosarcoma	1	4.1
Fibrosarcoma	1	4.1
Myxofibrosarcoma	3	12.5
Epithelioid sarcoma	1	4.1
Other	5	20.8

Characteristics	No. of patients	%
Treatments	**No. of patients**	**%**
CT→ RTCT+HT	2	8.5
CT→ RT+HT	4	17
RTCT+HT	8	34
RT+HT	10	40.5

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CERVICAL CANCER RADIOTHERAPY; HIGH DOSE OF VOLUMETRIC MODULATED ARC THERAPY (VMAT) PLUS BRACHYTHERAPY AND RISK OF FISTULA

Code: 236

Aims: Locally Advanced Cervical Cancer (LACC) in recent years local control has been improved but unfortunately around 40% of patients still experience disease recurrence, improved selection of patients for whom treatment intensification is justified1. Gynaecology Study Group (AIRO) reported evidence emerged that high-tech external beam radiotherapy seemed no better than image-guided brachytherapy for delivering a boost in LACC2; sometimes BT fails in distant areas or large masses.

Methods: VMAT was delivered with 6 MeV linear accelerator photons. PTV on pelvis 45 Gy/25 fr. 1.8 Gy die+ SIB on cervix and/or nodal PET positive 54-60 Gy/ 25 fr. 2,16-2.4 Gy x day. The VMAT is followed by the BT (1-3 sessions of 7 Gy per day/week). The superior ability of MRI to distinguish between diseased tissue and normal tissue is used to fusion with CT for CTV delineation and dose OaR according to Embrace study3. Six patients (pts) were treated between 2018 and 2023. The median age was 53 (range 35-71).

Results: All patients are currently NED (no evidence of disease). One patient relapsed at the lumboaortic node level and underwent adjuvant chemotherapy. All in full response locally. No degree of acute toxicity
>G2 was found. In terms of late toxicity profile one G4 event was recorded (fistula bladder-rectal). This patient was previous surgery on rectal and the addition of bevacizumab to chemotherapy. K.S.Tewari4 reported that the addition of bevacizumab to chemotherapy was associated with increased overall survival (17.0 months vs. 13.3 months), but also associated with an increased risk of GI fistula of grade 3 or higher (3% vs. 0%)4. In Cheng study5, patients with >110 Gy of a total maximal proximal rectal biologic effective dose presented with a significantly increased frequency of G2 or greater rectal complications.
The maximum effective rectal biological dose was at 2 cc of 110 Gy. Therefore, it is likely that the development of rectovaginal fistula in our patient was associated with these 3 factors: dose limit, previous surgery and use of bevacizumab. Other adverse events were reported as grade 1 or 2 genitourinary late toxicity (hematuria).

Conclusions: We think that combining the potential of high-dose VMAT with the proven successes of BT can provide benefits in those patients who have a large mass, positive lymph nodes and/or difficult to reach with BT but attention at risk of fistula. These are preliminary data that need further confirmation.

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A MULTI-INSTITUTIONAL ANALYSIS OF PATTERNS OF RECURRENCE AND TREATMENT RESPONSE

Code: 38

Aims: The management of multifocal glioblastoma (mGBM) is not standardized and there are no guidelines to define target delineation for radiotherapy treatment (RT). This study analyzed margins around the Gross Tumour Volume (GTV) to create a Clinical Target Volume (CTV), comparing response parameters and modalities of recurrence.

Methods: One-hundred and three mGBM patients were retrospectively analyzed. Selection criteria included patients with mGBM and a clinical target volume (CTV) margin of 2 (GTV + 2.0 cm) or 1 cm (GTV + 1.0 cm). All patients received daily concomitant temozolomide (75 mg./m2) with RT. A total dose of 56-59.4 Gy in 2/1.8 Gy fractions was delivered 4 to 8 weeks after surgery. Overall survival (OS) and progression-free survival (PFS) were calculated from the date of surgery until diagnosis of progression of disease by MRI. Progression patterns were classified as marginal, in-field, or distant, comparing site of progression with dose distribution in RT plan.

Results: The mean OS in mGBM CTV1 group was 11.2 months (95% CI 10.3 to 12.1), compared to 9.2 months in mGBM CTV2 group (95% CI 9 to 11.3). The mean progression-free survival (PFS) in mGBM CTV1 group was 8.3 months (95% CI 7.3 to 9.3), compared to 7.3 months in mGBM CTV2 group (95% CI 6.4 to 8.1). No statistically significant difference was observed between the two groups in terms of both OS and PFS time distribution. When adjusted to a multivariate COX risk model, our analysis showed that EGFR amplification was negative prognostic factors for both OS and PFS

Conclusions: In mGBM, the use of a 1 cm CTV expansion seems feasible as it does not significantly affect oncological outcomes and progression outcome.

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RADIOTHERAPY RELEVANT INTERRUPTIONS DURING CURATIVE RADIOTHERAPY FOR PROSTATE CANCER ARE ASSOCIATED WITH POORER BIOCHEMICAL AND DISTANT CONTROL OUTCOME: A POSSIBLE ROLE FOR CANCER STEM CELLS

Code: 56

Aims: To investigate the effects of radiotherapy (RT) relevant interruptions (RRI), single (sRRI) or multiple (mRRI), determining prolonged overall treatment time (OTT) in prostate cancer (PCa) patients.

Methods: Retrospectively review 221 PCa patients treated between March 2013 and April 2021 with curative-intent RT, 60-80 Gy (median dose 69.44 Gy), combined or not with androgen deprivation therapy. The association of sRRI, mRRI with Biochemical Failure-Free Survival (BFFS), Distant Recurrence-Free Survival (DRFS) and Overall Survival (OS) was assessed through the Kaplan–Meier method and adjusted for relevant prognostic factors using three multivariable Cox regression proportional hazard models.
Hormone sensitive 22Rv1 and LNCaP PCa cell lines were used in vitro.

Results: Patients who underwent unexpected RRIs (56.1%: 37.1% sRRI and 62.9% mRRI), determining a median OTT prolongation of 7 days, more frequently experienced biochemical failure (BF), distant relapse (DR), without no difference in OS. Multivariable analysis shows that RRIs were associated with higher hazards of BF (mRRI, aHR: 2.44, 95% CI: 1.42–4.20, p = 0.001; mRRIs, aHR: 2.89, 95% CI: 1.55–5.40, p = 0.001) and DR (sRRI, aHR: 9.35, 95% CI: 1.84–47.42, p = 0.007; mRRI, aHR: 8.42, 95% CI: 1.55–45.64, p = 0.014), with no significant differences between sRRI and mRRI on both outcomes. RRIs in vitro induced epithelial-mesenchymal transition (EMT) activation and cancer stem cells (CSCs) enrichment, Determining radioresistance.

Conclusions: RRIs were associated with lower BFFS and DRFS, and in vitro capable of EMT-mediated selection of CSCs, known to be the cause of radioresistance and metastatic progression.

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ANALYSIS OF SURVIVAL OUCOMES AND PROGNOSTIC FACTORS IN ORAL CANCER PATIENTS UNDERGOING POSTOPERATIVE (CHEMO)RADIOTHERAPY AFTER SURGERY: A RETROSPECTIVE STUDY

Code: 36

Aims: Oral cavity cancer (OCC) is the most common type in head and neck district. The primary treatment is surgery followed by postoperative radiotherapy (PORT) with/out concurrent chemotherapy in patients with high risk of locoregional recurrence. The aim of our study was to evaluate survival outcomes and prognostic factors in this adjuvant setting.

Methods: A retrospective analysis of overall survival (OS), disease-free survival (DFS), locoregional control (LRC) and treatment-related toxicity was perfomed. The multivariate analysis was assessed to identify factors influencing survival outcomes.

Results: 99 OCC patients treated with PORT between 2013-2022 were included in the analysis. Most of them were male (n=60). The median age was 64 years (19-81). The tongue was the subsite most affected of tumor (n=57). Histology showed a squamous cell carcinoma for all population. The median time from surgery to start of PORT was 9 weeks (4-18). The median dose was 66 Gy (48-66) in daily fraction of 2 Gy. The 39% of sample received concurrent platinum-based chemotherapy due to high adverse features (positive margins and/or extranodal extension). The median follow-up was 29,3 months (4-101). At time of analysis, 71.7% of patients was alive. The 1-, 3- and 5-year OS rates were 86%, 74% and 66%, respectively. Grade
3 (HR 2.460) and age >64 years (HR 2.829) were significantly associated with worse OS. The 1-, 3- and 5-year DFS rates were 75%, 66% and 50%, respectively. The perineural invasion (HR 1.979), higher
performance status (PS) (HR 2.103) and pathological nodal staging (HR 2.004) significantly influenced the DFS. Locoregional failures were observed in 22% of patients. The 1-, 3- and 5-year locoregional control (LRC) rates were 83%, 82% and 68%, respectively. The LRC was longer in patients receiving concurrent chemotherapy (HR 0.332); conversely it was worse in patients with higher pathological nodal staging (HR 2.466). The most common side effect (SE) was grade 1-2 acute mucositis (n=82) followed by grade 1-2 dysphagia (n=46). Grade 1-2 dry mouth and dysgeusia were the most frequent late SEs. Two patients, both smokers and drinkers, had osteoradionecrosis 19-27 months after PORT (1 received chemotherapy), with a median dose of 60 Gy**.**

Conclusions: PORT after surgery achieved long survival with acceptable toxicity in OCC patients. Pathological nodal staging, perineural invasion, PS and the use of chemotherapy influenced disease control. Older patients and those with higher grading showed shorter OS.

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TREATMENT OF ELDERLY PATIENTS WITH INOPERABLE PRIMARY HEAD AND NECK CANCER, AN UPDATE OF OUR EXPERIENCE

Code: 378

Aims: For elderly patients with head and neck cancer, conventional local therapies, such as surgery and external beam radiotherapy ± chemotherapy, can significantly impact quality of life. Stereotactic body radiotherapy (SBRT) could be a curative strategy for medical-inoperable head and neck cancer.

Methods: Twentytwo elderly patients with primary head and neck cancer, with locally advanced disease without neck involvement, treated with SBRT from 2019 to 2023 were retrospectively reviewed. Patients were discussed on a case-by-case basis by the Multidisciplinary Committee on Head and Neck Cancer and evaluated with morphological and functional imaging and considered unsuitable for surgery and / or standard radiotherapy +/- chemotherapy due to multiple comorbidities, life expectancy and poor performance scores. SBRT consisted of 40 Gy in five delivered in daily fractions. All patients were initially evaluated at the start of treatment and at 1-month follow-up visit after SBRT, and subsequently for routine follow-up visits every 3 months.

Results: The mean age was 82 (range 72-96 years), 12 males and 10 females. The primary sites were oral cavity in 11 patients, oropharynx in 6 patients and parotid glands in 5 patients. 45.5% were AJCC stage III, 36.5% stage IVA, 18% stage IVB. The mean follow up was 12 months (range 1-24 months). Odynophagia was assessed with the numerical rating scale (NRS), an analgesic drug therapy was administered according to the NRS value, maximum value reported before therapy, at 1-month follow-up visit and at last FUP visit were NRS 8 (in 4 cases; 18%), NRS 7 (in 3 patients; 14%), NRS 6 (in 5 patients; 23%) and NRS 5 (in 7 patients; 31%), NRS 4 (in 3 patients, 14%) respectively, allowing pain therapy dose reduction. There was only one severe (G3) dysphagia case before RT that required feeding tube placement for nutritional support using percutaneous endoscopic gastrostomy (PEG) tube, moderate (G2) dysphagia reported before therapy, at 1-month follow-up visit and at last FUP visit was present in 12, 7 and 4 patients respectively. 55% percent had an objective response and 30% had stable disease, with overall survival of 12 months.

Conclusions: In our experience, in elderly unresectable HNSCC patients, due to multiple comorbidities, life expectancy and poor performance scores, treated with a radiation shortened course using SBRT may offer an effective alternative to standard treatments, with encouraging survival and relatively low toxicity.

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ARE MRI AND PET-CT RELIABLE FOR POST CT-RT RE-STAGING IN LOCALLY ADVANCED CERVICAL CANCER? A CASE REPORT

Code: 517

Aims: Cervical cancer ranks as the fourth most prevalent cancer in women globally and holds the same position as the fourth leading cause of cancer-related mortality. Platinum-based chemoradiotherapy (CT-RT), coupled with brachytherapy, stands as the current standard treatment for Locally Advanced Cervical Cancer (LACC), with optional adjuvant surgery. In patients with LACC, there is still a high reported locoregional recurrence rate after CT-RT. Therefore, timely detection of locoregional residual disease is important for patients to be treated with salvage surgery.

Methods: In this abstract, we present the case of a 52-year-old woman with 50 in KPS, diagnosed with LACC. Staging revealed a 57x30x68 mm exocervical lesion with parametrial infiltration. PET- CT indicated involvement of para-aortic, pelvic, and inguinal lymph nodes, leading to the decision for chemoradiotherapy. Prior to treatment, the patient experienced sepsis and severe anemia that required hospitalization, once blood values were normalized, we started a systemic treatment with weekly cisplatin with reduced dose for four cycles together with a whole-pelvis external beam radiotherapy (EBRT) with VMAT technique to a total dose of 45 Gy in 25 fractions. Due to the patient's KPS, PET-avid

lymph nodes were not boosted. Six weeks post- chemoradiotherapy, according to worldwide practice, an MRI was performed with detection of suspected residual disease, as a consequence, we used PET-CT to clarify these findings. PET- CT reported reduced uptake in the uterine cervix and para-aortic lymph nodes, with weak uptake (SUVmax 4.26) in some pelvic lymph nodes. Given the uncertain persistence of pelvic disease, the multi-disciplinary team recommended surgical re-staging.

Results: The patient underwent laparoscopic radical hysterectomy, bilateral salpingo-oophorectomy, pelvic lymphadenectomy, and resection of the upper two-thirds of the vagina. Histological examination revealed isolated tumor cells in the cervical wall and a single pelvic lymph node. Considering the radicality of the surgery and negative histological findings, the patient started the follow-up and currently maintains a good KPS (90) with no evidence of recurrence.

Conclusions: In conclusion, even if literature reports a specificity of 95% and 96% respectively for MRI and PET-CT, this case highlights the need to explore additional re-staging techniques to avoid a major surgery in false positive cases.

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BREAST CANCER PATIENTS TREATED WITH VOLUMETRIC MODULATED ARC THERAPY (VMAT) FOR IRRADIATION OF THE INTERNAL MAMMARY CHAIN: DOSIMETRIC AND TOXICITY DATA

Code: 574

Aims: To analyze dosimetric and safety data on internal mammary chain (IMC) irradiation in a contemporary cohort of breast cancer patients.

Methods: Patients affected by breast cancer treated in our institution with postoperative radiotherapy including regional nodal irradiation with IMC from 2018 to 2023 were included in this analysis. The prescription dose was 50 gy in 25 fraction or 40.05 Gy in 15 fraction. Dosimetry data (CTV/PTV coverage, contralateral breast dose, heart dose, ipsilateral lung dose and esophageal dose) were recorded for each patient. Toxicity was assessed according to the CTCAE 5.0 scale.

Results: Sixty-eight patients, aged between 34-79 years, were analysed. Patients characteristics are listed in Table 1. The majority of patients (n=60, 88.2%) were treated with conventional fractionation (50 Gy in 25 fractions), while 8 patients were treated with an a hypofractionated regimen (o40.05 Gy in 15 fractions). An additional nodal boost of 10 Gy in 5 fraction was delivered to the sovraclavicular area (n=4, 5.9%) and/or CMI area (n=4, 5.9%). Dosimetric data are listed in table 2. Consolidative systemic treatment after primary systemic therapy (PST) with either capecitabine or TDM1 was administered in 3 (4.4%), 2 (2.9%) respectively. Two (2.9%) patients received Abemaciclib after adjuvant

Table n.1: Dosimetric data

Variables	Left Breast+CMI+SCLN		Right Breast+CMI+SCLN	
	Mean	Std Deviation	Mean	Std Deviation
Volume (%) of the CTV CMI covered by 95% D	99,06	0,36	98,58	1,03
Volume (%) of the CTV SCLN covered by 95% D	99,60	0,24	99,54	0,15
Volume (%) of the CTV BREAST covered by 95% D	98,05	0,35	98,06	0,26
Volume (%) of the PTV CMI covered by 95% D	96,51	0,64	96,40	0,38
Volume (%) of the PTV SCLN covered by 95% D	97,67	0,41	97,07	0,24
Volume (%) of the PTV BREAST covered by 95% D	97,14	0,50	97,22	0,33
Mean Dose Ipsilateral Lung (Gy)	11,48	0,55	11,60	0,46
Mean Dose Heart (Gy)	4,46	0,23	4,53	0,14
Volume (%) of the Heart covered by 25.00 Gy	0,20	0,06	0,36	0,19
Maximum Dose LAD (Gy)	15,34	0,59	7,14	0,61
Mean Dose LAD (Gy)	8,06	0,46	4,40	0,42
Mean Dose Controlateral Lung (Gy)	3,85	0,38	4,17	0,18
Mean Dose Controlateral Breast (Gy)	3,46	0,24	3,33	0,16
Mean Dose Thyroid (Gy)	18,38	2,32	28,59	2,21
Volume (%) of the esophagus covered by 25.00 Gy	9,29	1,83	7,86	1,52
Volume (cc) of the esophagus covered by 35.00 Gy	0,72	0,22	0,40	0,15
Maximum Dose Humer (Gy)	38,21	3,95	33,37	1,48

Table n.2: Patients characteristics

Total= 68 (100%)	N (%)
Age	
Median (years)	54
Range (years)	34-79
Molecular Subtype	
Luminal B	40 (58.8)
Her 2+	17 (25.0)
Triple Negative	11 (16.2)
Side	
Right	42 (61.8)
Left	26 (38.2)
Primary Systemic Therapy	
Yes	46 (67.6)
Not	22 (32.4)
Adjuvant Systemic Therapy	
Yes	35 (51.5)
Not	33 (48.5)
Breast Surgery	
BCS	29 (42.6)
Mastectomy	39 (56.4)
Axillary Surgery	
Sentinel Node Biopsy	9 (13.2)
Lymphadenectomy	59 (86.8)

systemic treatment. None developed grade ≥ 3 toxicity. Grade 1 and 2 skin toxicity were observed in 13 (19.1%) and 10 (14.7%) patients, while grade 1 and 2 esophageal toxicity was experienced in 2 (2.9%) and 3 (4.4%) patients. Four patients (5.8%) experienced prothesis complications.
Ten patients (14.7%) progressed: 3 (4.4%) developed loco-regional recurrence alone (median timeto recurrence=30 months), 3 (4.4%) distant failure, while 4 (5.8%) showed both local and systemic progression.

Conclusions: Both dosimetric and toxicity data of this cohort of patients treated with comprehensive RNI with VMAT technique and intensified systemic treatment appear encouraging. Evaluation in a larger cohort of patients is needed.

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EFFICACY AND TOXICITY OF POSTOPERATIVE PORT RADIOTHERAPY IN NSCLC PATIENTS: A SINGLE-CENTRE EXPERIENCE

Code: 591

Aims: The role of postoperative radiotherapy (PORT) remains controversial, as randomized trials failed to prove any benefit in terms of overall survival, notwithstanding the reduction of local relapse rate. The aim of our study is to evaluate efficacy and toxicity of PORT for patients affected by Non-Small-Cell lung (NSCLC) cancer treated with modern radiation therapy techniques.

Methods: All patiens (pts) with stage III NSCLC undergoing surgery and PORT were included in this retrospective analysis. Data on histology, lymphonode status, resection margins, radiotherapy treatment were recorded for each patient. Overall survival (OS) at 2 and 5 years, progression-free survival (PFS) at 2 and 5 years, local control (LC) were calculated with Kaplan-Meier analysis. Acute and late toxicity were assessed according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE).

Results: Our cohort consists of 72 pts, 47 males (65%) and 25 females (35%), with a median age at diagnosis of 66.6 years-old (range 39-86), enrolled from June 2005 to December 2022. Patients' characteristics are listed in Table 1. No Grade 4 acute or late toxicities were detected. Only 1 patient (1.4%) presented acute cardiac toxicity G3 (acute coronary syndrome). Nine (12.6%) presented late cardiac toxicity: five pts G1 (rhythm alterations); four G2 (atrial permanent fibrillation). Symptomatic pneumonitis was recorded 17 pts (23.6%). Four patients (5.5%) developed G3 pulmonary toxicity (pneumonitis) in acute requiring hospitalization. Late pulmonary toxicity (G2-G3) was observed in 11 pts (15.2%): Three pneumoniae G2, 6 fibrosis G2 and 2 fibrosis G3. Fourteen (19.4%) pts presented acute oesophageal toxicity (8 G1; 6 G2) and no late toxicity were detected. With a median fup of 47 months, .2 years PFS was 72.9% and 59.9% at 5 years. 2 years OS was 90.2% and 70.3% at 5 years. Local Recurrence occurred in 19 pts (26.4%).

Table 1 : Characteristics of population	
Age 66.6 years-old (range 39-86)	66.6 years-old (range 39-86)
Sex	
male	47 (65%)
female	25 (35%)
Histology	
Adenocarcinoma	57 (79.1%)
Squamous	14 (19.4%)
Large cells carcinoma	1 (1.5%)
Resection Margin	
R0	52 (72%)
R1	20 (28/%)
Dose	MEAN DOSE 49,6 Gy RANGE 14.4-60 Gy
Chemotherapy	
concurrent	20 (28%)
sequential	34 (47%)
Radiotherapy alone	18 (25%)

Conclusions: Post-operative Radiotherapy allows encouraging rate of local control and may improve clinical outcomes in carefully selected patients using modern techniques in order to limit cardio-pulmonary toxicity.

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DEFINITIVE CHEMORADIATION FOR NON-METASTATIC ANAL CANCER: A TEN- YEAR RETROSPECTIVE STUDY OF CLINICAL RESPONSE, SURVIVAL, AND TOXICITIES USING IMRT AND VMAT TECHNIQUES

Code: 209

Aims: This retrospective study evaluates the clinical response, survival outcomes, colostomy-free survival (CFS), and toxicities in non-metastatic anal cancer patients undergoing definitive chemoradiation.

Methods: The study included patients treated between December 2007 and June 2023 and focused on patients with histologically confirmed stage I to stage III anal cancer. Enrolled patients received radiotherapy using intensity-modulated radiation therapy (IMRT) or volumetric modulated arc therapy (VMAT). A radiation dose of 45 Gy (1.8 Gy/fraction) was administered to the pelvic lymph nodes, with a boost of 10 to 14.4 Gy for advanced tumours and involved lymph nodes. Concomitant chemotherapy with mitomycin-C-and 5FU or capecitabine was admnistered to eligible patients. Data analysis was performed using the Statistical Package for Social Sciences, version 27 (SPSS Inc., Chicago, IL, USA) for colostomy-free survival (CFS), overall survival (OS), progression-free survival (PFS), local control (LC), and metastasis-free survival (MFS). Toxicity was assessed using the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 5.0.

Results: The cohort consisted of 90 patients (23 men, 67 women) with a median age of 64 years (range 32 - 89 years). The median follow-up was 50.57 months (range 4.63-194.33 months). At 6 months after chemoradiation, a clinical complete response was observed in 68.8% of patients. At the time of the last evaluation, 67 patients (74.4%) were alive with no evidence of disease. The 3-year, 5-year, and 10-year survival rates for PFS, LC, MFS, OS, and CFS were reported (Table 1). Local recurrence occurred in 2.2% of cases, with subsequent distant metastases observed in these patients. Acute toxicities were detected in 87.7% of patients, including haematological, gastrointestinal, cutaneous, and urinary toxicities. Grade 3 or higher late toxicities occurred in 13.3% of patients, and included fistula, proctitis, and rectorrhagia reported (Table 2).

Survival rates	3-years	5-years	10-years
PFS	88%	82%	79%
LC	97%	95%	92%
MFS	89%	83%	80%
OS	85%	79%	61%
CFS	100%	98%	95%

Table 1

Late toxixity (N=24/90)	G0	G1	G2	G3	G4
fistula	0	0	0	5	0
proctitis	0	0	2	5	1
faecal incontinence	0	6	4	0	0
rectorrhagia	0	0	0	1	0

Table 2

Conclusions: This long-term analysis confirms the efficacy of chemoradiation in patients with non-metastatic anal cancer, using IMRT and VMAT techniques. The treatment demonstrated favourable clinical outcomes in terms of OS, PFS, and CFS, with a manageable toxicity profile.

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CERENKOV AND RADIOLUMINESCENCE DOSIMETRY FOR FLASH RADIOTHERAPY: PRELIMINARY RESULTS

Code: 203

Aims: The FLASH effect in external beam radiotherapy (EBRT) can improve and change dramatically how cancer patients will be treated in the coming years. This, to some extent, revolutionary approach requires the development of new adequate and accurate dosimetric tools.
The main goal our work is to develop two dimensional optical based methods for FLASH real time dosimetry using Cerenkov and radioluminescence light.

Methods: The measurements were performed using the Electron Flash (EF) source installed at the CPFR of Pisa. The EF source can deliver dose in the Flash and conventional regimes by modifying the temporal parameters of the beam indipendently in the following range: Pulse duration from 0.5 to 4 microseconds (step of 0.1), dose-per-pulse up to 25 Gy, frequency from 1 up to 249 Hz, average dose-rate up to 6000 Gy/s, Energy of 7 and 9 MeV. Dose linearity was evaluated by changing the dose per pulse from 0.18 up to 11.5 Gy (pulse duration 4 microsec). Dose rate independence was evaluated using the following settings dose per pulse = 4.16 Gy with a pulse frequency from 1 up to 100 Hz. In this case the average dose rate was ranging from: 4 Gy/s (conv) up to 400 Gy/s (Flash).
Cerenkov optical imaging was acquired using a CMOS detector placed 2m away from a plexiglass Cerenkov radiator at 90 degrees from the beam axis. The production of Cerenkov light was also evaluated in tissue using an ex vivo slab of chicken breast in order to mimic real time dose delivery.

Results: We found a good linearity with r^2=0.9993 between the measured Cerenkov light with respect to the dose per pulse. The Cerenkov signal showed no dependence from the dose rate, the maximum difference was less the 1.5% in the range 4 to 400 Gy/s.
The Cerenkov radiation measured at the surface of a chicken breast slab show a linearity with r^2=0.9992 for a dose per pulse ranging from 0.18 to 11.5 Gy.

Conclusions: These preliminary results show that Cerenkov and radioluminescence imaging can be alternative optical approaches for real time dosimetry for FLASH radiotherapy.

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ASSESSMENT OF DAILY CBCT MATCHES IN HEAD AND NECK CANCER PATIENTS UNDERGOING VMAT: IMPLICATIONS FOR REPLANNING AND IMMOBILIZATION

Code: 127

Aims: Radiotherapy is pivotal in managing head and neck (H&N) cancer. This study aims to assess displacements of daily cone-beam computed tomography (CBCT) matches in squamous cell carcinoma patients (pharynx, larynx, and oral cavity) undergoing VMAT. The primary objective is to evaluate the feasibility of treatment replanning and its impact on patient positioning.

Methods: Thirty-one H&N prospective patients received treatment through a simultaneous integrated boost (SIB – 2.2, 2.0, and 1.8 Gy/fractions) technique over 30 sessions (ClinicalTrials.gov ID: NCT05081531). Initial CT simulation (sCT) and, after 15 fractions, a second CT for replanning (rCT) were performed. CBCT displacement data were compared between sCT and rCT groups using the Mann-Whitney test for unpaired data. A qualitative analysis, using a five-point scale, assessed CBCT and CT image agreement at the start (sCT_first), conclusion (sCT_last) of the first phase, and at the first replanning CT series (rCT_first). The Wilcoxon signed-rank test for paired data was applied to compare these evaluations. Median and interquartile ranges (Q1 and Q3) were used to statistically summarize the data.

Results: A total of 935 CBCT scans were analysed. No significant differences in online CBCT shifts were observed between sCT (3.5 mm, [2.5-4.7] mm) and rCT (3.6 mm, [2.6-4.9] mm). Significant variation was noted between sCT_first and sCT_last for all the considered evaluations. The maximum differences were found for target66Gy (4 [2-4] vs. 5 [5-5]), target54Gy (4 [3-5] vs. 5 [5-5]), and parotids (4 [2-5] vs. 5 [5-5]). No significant differences were observed between sCT_first and rCT_first (see figure 1). The overall visual analysis revealed that 19% of patients achieved optimal image match quality in the sCT_last, suggesting that rCT scans could be removed in selected cases. Moreover, 29% of patients exhibited an optimal immobilization mask during the final treatment session, suggesting that the creation of a new immobilization system during the rCT acquisition might be unnecessary.

Conclusions: Statistical analysis highlights advantages of replanning and new immobilization masks during treatment. A clinical decision tree based on image shifts and quality could optimize efficiency, reducing treatment times and costs.

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HYPOFRACTIONATED EXTERNAL BEAM RADIOTHERAPY IN GERIATRIC CANCERS: A GOOD BALANCE FOR PATIENTS AND PHYSICIANS

Code: 243

Aims: Due to demographic changes in our country with a growing aging of the resident population, decision-making process with radiotherapy for elderly cancer is a big challenge. Economic matters, frailty due to comorbidity, care giver availability and distance from RT unit influence the choice to treat patients (pts) with radiotherapy (RT) or not. Hypo-fractionated radiotherapy (Hypo RT) is a good balance to offer in geriatric cancers. Herein our experience**.**

Methods: Data on 80 elderly pts (30 females and 50 males) treated with hypo-RT from January 2022 to December 2023 were collected. The mean age was 83 years (range 75- 90). Almost of them lived more than 100 km from our RT Unit. The most relevant cancer treated types were rectal (15 pts), prostate (21 pts), breast (15 pts) glioblastoma (8 pts), bladder (11 pts) non-melanoma skin cancer (10 pts). Hypo-RT was delivered in adjuvant or exclusive setting according to cancers and pts characteristics.

Results: In rectal cancer 25 Gy in 5 fractions (frs) were delivered to 13 pts; 5 frs-SIB with a dose of 30 Gy to tumor was delivered to 2 pts. Complete pathological response and down-staging were recorded in 6 pts and 7 pts, respectively. SIB pts had clinical complete response and they refused surgery. In prostate cancer 37.5 Gy in 5 fractions was delivered; hormone-therapy was added in 12 pts. In breast cancer 10 pts received adjuvant whole breast-RT with 26 Gy in 5 frs; 5 pts unfit for surgery received 30 Gy in 5 weekly-frs on tumor and hormone-therapy. Six pts with glioblastoma were treated with 34 Gy in 10 frs; 2 pts received SIB-RT with 40 Gy to tumor; all pts received concomitant Temozolamide. In bladder cancer, a schedule of 6 Gy for 6 weekly frs was applied. In skin cancers' adjuvant setting, we used a schedule of 45 Gy in 15 frs; a case of extramammary Paget's disease was treated with 51 Gy in 17 frs. All pts completed RT without acute and late severe toxicities. Treatments were effective and safe.

Conclusions: Hypo-fractionated regimens gave good results in terms of efficacy and compliance among elderly patients and their caregivers. Moreover, Hypo-RT give many advantages with a reduction in socioeconomic burden for the patients. Next, we will create a geriatric tumor-board.

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HYPOFRATIONATED RADIOTHERAPY AND CONCURRENT WEEKLY CISPLATIN IN GIANT NON MELANOMA SKIN CANCER (NMSCs) OF THE SCALP: A CASE REPORT

Code: 242

Aims: Non melanoma skin cancers (NMSCs) with a diameter of ≥ 5cm are considered giant, and exhibit features that fulfil the criteria for high-risk aggressive squamous cell carcinoma (SCC). These tumors are usually localized to the scalp and shows usually invasive features like extensive tissue ulceration or periosteum invasion. Thus, they are not suitable for surgery. Hypo-fractionated radiotherapy and concurrent chemotherapy was a good option when surgery is excluded.

Methods: A 70 years old man went to our observation showing of an ulcerated skin mass on the right frontal region of the scalp. Biopsy showed a diagnosis of squamous cell carcinoma of the scalp. After a first resection R1 on the deep margin, the tumor quickly relapsed with aggressive features not suitable for another surgery. Lesion was 6 cm large and 2 cm thick with a necrotic and ulcerated core. On CT-scan, the external periosteum appeared focally involved. Brachytherapy and electron beam were excluded. External Beam Radiotherapy (EBRT) with a customized cap bolus was applied; hypo-fractionated radiotherapy with concurrent weekly cisplatin were prescribed.

Results: EBRT with a 5 mm bolus covering the mass and the surrounding scalp was applied. Seven IMRT 6 MV photon beams were delivered. A hypo-fractionated schedule of 62.2 Gy in 18 fractions was chosen which is EQD2 =80 Gy for BED 10. Concomitant weekly 30 mg/m2 cisplatin was also delivered for 5 weeks.
During the treatment the mass progressively shrinked and smothed-out. A complete resolution was recorded 2 months after the end of radiotherapy. Erythema and desquamation on the surrounding scalp were the most important acute side effects. After 6 months-follow-up the patient was NED (non-evidence of disease) and no late toxicities was recorded.

Conclusions: Hypo-fractionated radiotherapy with concurrent weekly-cisplatin was a good option in case of inoperable giant NMSCs of the scalp. The treatment was effective and well tolerated, however a long-term follow-up is required.

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DOES RADIOTHERAPY A VALID OPTION OF TREATMENT IN HEPATOCARCINOMA?

Code: 302

Aims: Radiotherapy (RT) is an option treatment in patients (pts) with hepatocarcinoma (HCC) (NCCN Guidelines version 2.2023) we report our monoistitutional experience in term of toxicity and outcomes in pts with HCC treated with RT.

Methods: From February 2009 to Dicember 2023, twenty pts (14 males, 6 females) with radiological, hystological and/or biological diagnosis of HCC were treated whith locoregional RT in our istitution with helicoidal IMRT (Tomotherapy) or Stereotactic RT (Cyberknife), Simulation consisted in c-e CT scan with fiducials implantation or 4DCT scan.

Results: Median age of pts was 74 years (43-87), 70% were child A5, 30% were Child A6. Twelve pts were previously treated: surgery (5 pts), other locoregional treatments (7 pts). We treated 4 pts with R1, 5 pts with multiple lesions, 11 pts with a single lesion. Median volume of liver was 1262 cc (788- 1714 cc).
Median GTV/ITV was 33 cc (4- 275 cc), median PTV was 173 cc (17- 412 cc); Median volume of liver out PTV was 1016 cc (516 - 1672 cc). Median delivered dose was 50 Gy (42.5 Gy- 62.5 Gy). Median BED was 70 Gy (57-151 Gy). Median EQD2 was 61.2 Gy (48-126 Gy). Median number of fractions (frs) was: 15 (3-30). Median dose of fr: 3 Gy (2 -18 Gy).
Toxicity: No acute toxicity occured, only one pt had a late Rild after six months from the end of RT, he died 15 days after for sepsis; he was eithy-one years old with cirrosis in HCV and portal hypertention, treated with interferone and ribavirine without benefit, Child A5, diabetic and had diverticolosis, he previously underwent surgery and subsequently 3 TACE, RT was delivered concurrently in 3 lesions located in the dome of liver and recieved 50 Gy in 5 frs.
Outcomes: at a median first radiological control of 3 months (m) from the start of RT (1.5- 12.4), 5/19 pts (26%) had a PR, 11/19 (58%) had SD and 3/19 (16%) had PD. At a median follow up of 28 m (1.6-115 m), 25% pts are still alive.

Conclusions: Locoregional RT is feasible in pts with HCC, not only in pts escluded from surgery and/or other ablation treatment but also in pts previously treated. The profile of toxicity is acceptable if the status and volume of liver (entier and out PTV) are sufficient. BED? to 85 Gy allows better results in term of outcomes. RT can be considered a valid treatment in selected pts, it can be used not only as ultra palliative treatment but also as bridge waiting for surgery or transplantation allowing good response even if lower dose are delivered.

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HEMOSTATIC EFFECTS OF PALLIATIVE RADIOTHERAPY FOR BLEEDING IN UNRESECTABLE GASTRIC CANCER

Code: 306

Aims: To report our experience in patients (pts) with unresectable gastric cancer treated for bleeding with hemostatic palliative radiotherapy (RT).

Methods: Seventeen pts with unresectable gastric cancer presenting bleeding requiring blood transfusions were treated with hemostatic palliative RT and analyzed retrospectively in our institution. The comparison between the hemoglobine (Hb) level at the start of RT, post RT and at the first control after RT was evaluated. Blood transfusion free survival (BTFS) and overall survival (OS) were calculated from the start of RT. Symptoms before and after RT were evaluated.

Results: From May 2017 to June 2023, 12 males and 5 females with unresectable bleeding gastric cancer received RT with a palliative intent. Median age of pts was 72 years (57-89), RT was delivered with helical Tomotherapy : 8 pts and VMAT: 9 pts. Median Hb level at the first RT consultation was 8.2 g/dL (5.3- 10.9), 82% of pts received blood transfusions before the start of RT, median bags of blood was 7 (1-14). Twenty-three % of pts presented dysphagia and abdominal pain before RT. Clinical target volume (CTV) was defined on CT scan with or without c-e and when possible on CT/PET scan (4/17). In 14/17 pts we included all the stomach, CTV was defined as only the bleeding portion of stomach in 3 pts.
Median CTV was 513 cc (87- 957), median planning target volume (PTV) was 912 cc (290-2023). Median RT dose was 36 Gy (30-45). Median number of fractions (frs) was 12 (10-25), Median dose per fr was 2 Gy (1.8-3). Median Hb level at the half and the end of RT was respectively 9.7 g/dL (7.3-12.2) and 9.7 g/dL (7.6-12.5). Eighty-eight % of pts (15/17) had an increase of Hb level. At a median follow up of 27 days (6-930), 77% of pts (10/13) had a stable level of Hb. Twenty-three % pts (4/17) needed blood transfusions after RT. Median time to BTFS was 4.3 months (2.7- 19). The median OS was 2.9 months (0.2- 31) and only one pt is still alive. He previously received 40 Gy in 20 frs on all the stomach, he maintained Hb level > 8 g/dL for 19 monthes and subsequently when Hb level decreased after repeated blood transfusions, we planned another RT delivering 20 Gy in 5 frs to the portion of stomach defined by PET positive. No toxicity occurred 2 weeks after RT. Among symptomatic pts before RT only 17% of them had persistent symptoms after RT.

Conclusions: Palliative RT is an effective treatment for hemostasis in unresectable gastric cancer, it allows a good control of Hb level and acceptable BTFS.

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HIGHLIGHTS ON LATE ONSET OF CHECKPOINT INHIBITOR RELATED PNEUMONITIS (CIP) AND DISEASE CONTROL AFTER EBRT: A CASE REPORT OF CIP AFTER 12 MONTHS FROM CESSATION OF ATEZOLIZUMAB

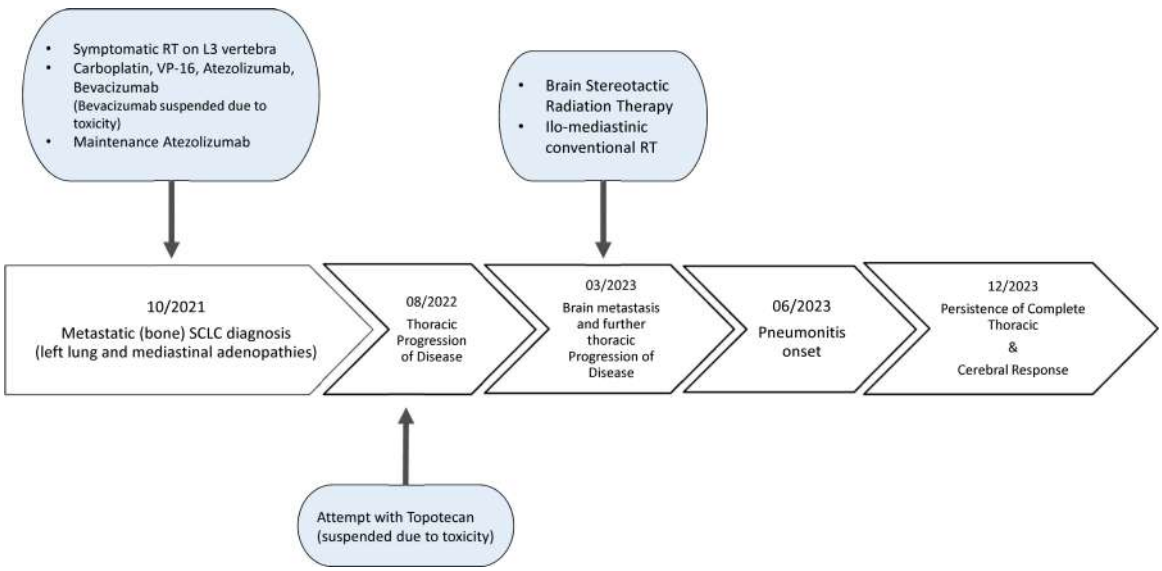
Code: 257

Aims: Immune checkpoint inhibitors have revolutionized cancer therapy, with a generally favorable toxicity profile. Long-term toxicity reports are often incomplete due to the expedited approval of drugs for significant impacts on overall survival (OS), potentially underestimating late-onset toxicity.
Individuals with pre-existing autoimmune conditions are likely more susceptible to immune-related side effects. We present the case of a patient affected by lung microcytoma with both, loco-regional and distant (cerebral) progression, referred for radiation treatment evaluation. The patient's therapeutic history is summarized on the table.

Methods: In February 2023, a 71-year-old patient with metastatic microcytoma underwent brain MRI and CT restaging. Three repetitive brain lesions were confirmed, along with extracranial staging revealing pulmonary progression. Radiotherapy was proposed for brain, lung, and mediastinal sites due to poor systemic therapy tolerance, excellent previous response to bone metastases-directed radiation, good Performance status and absence of other feasible systemic treatments. The patient also had the following comorbidities: hypertension and non-specific interstitial lung disease.

Results: Radiation treatment on the brain and thoracic targets ended in May 2023 with good tolerance. In July, due to persistent cough, dyspnea, and low-grade fever, the patient was hospitalized for bilateral pneumonitis, responsive to corticosteroid therapy. Insulin therapy was initiated for steroid-induced diabetes. Disease restaging showed a complete thoracic and cerebral response.
The diagnosis was CIP triggered by the recent radiotherapy treatment. The patient continued with clinical check-ups. After 6 months, a good radiological response of the CIP pattern was found at CT scanning.
Clinically the patient reported fatigue and limitations in daily activity. The restaging exam reported some subcentimetric paraesophageal lymph nodes and the millimetric increase of a known adrenal nodulation.

Conclusions: Whether the therapeutic gain from immune checkpoint inhibitors outweighs or not long-term side effects, needs further investigation, especially given the introduction of these drugs in increasingly early therapeutic lines. However despite metastatic microcytoma, the patient, without further systemic therapy for 13 months, shows no brain disease and minimal residual extracranial disease.



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ANALYSIS OF HISTOPATHOLOGICAL FEATURES OF RESPONDER AND NON-RESPONDER TO II-LINE REGORAFENIB IN GLIOBLASTOMA MULTIFORME

Code: 211

Aims: Preliminary analysis of histopathological phenotypes and molecular alterations dissimilarities between responders and non-responders to II-line Regorafenib in recurrent Glioblastoma Multiforme (GBM).

Methods: We retrospective analyzed molecular data of 8 patients who received Regorafenib for recurrent disease between 2022-2023. At the time of diagnosis, all pts have been treated with radio-chemotherapy, according to the Stupp protocol. Response to treatment, in the context of our Multidisciplinary Tumor Board (MTB), has been evaluated by serial contrast-enhanced magnetic resonances. If necessary, addition of perfusion and spectroscopy-studies as well as PET-18F-DOPA scan were performed in order to assess the response. Once progression was established, II-line Regorafenib was administered.

Results: 8 pts received II-line Regorafenib due to progressive disease; 2 out of 8 achieved a radiological response to treatment, as well as clinical improvement; in one case, also a clear reduction of cerebral blood volume (CBV) was achieved. All 8 pts presented the following features: non-methylated MGMT, wild-type IDH1-2, wild-type BRAF, non codeleted 1p-19q, EGFR amplification, chromosome 10 deletion as well as chromosome 7 amplification. On the contrary, the 2 pts with radiological response presented TERT promoter 124C/T mutation, while the 6 non responder pts had Mouse Double Minute (MDM) 2 and 4-amplification as well as positivity for Glial fibrillary acidic protein (GFAP).

Conclusions: Despite the retrospective nature of our analysis as well as the small number of patients, what we found is that the 2 responders to II-line Regorafenib presented TERT Promoter 124C/T mutation while the 6 non- responders had MDM 2/4 amplification and positive GFAP.

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DESCRIPTIVE ADHERENCE TO THERAPY ANALYSIS OF GYNAECOLOGICAL GERIATRIC PATIENTS TREATED WITH ENDOVAGINAL BRACHYTHERAPY IN ORDINARY RECOVERY REGIMEN (ORR)

Code: 480

Aims: To evaluate the adherence to therapies in gynecological geriatric patients submitted to endovaginal brachytherapy treated in ORR.

Methods: From January 2020 to December 2023, we retrospectively evaluated all geriatric patients with histological diagnosis of gynecological cancer, KPS≥60, and treated with endovaginal brachytherapy in ordinary recovery regimen.

Results: In the period of observation, 90 geriatric patients with endometrial cancer were hospitalized and submitted to postoperative endovaginal brachytherapy in our department. According to Italian Society of Gerontology and Geriatrics (SIGG) criteria, patients were allocated into two groups: elderly (≥65age) and very elderly (≥75age) patients. Of these, 62/90 patients were elderly and 28/90 were very elderly. Median Charlson Comorbidity Index Score (CCIs) was 5 (range 2-8pt) in elderly and 6 (range 2-9) in very elderly. A median Karnofsky Performance Status (KPS) of 70 was observed (range 50-90). All patients subscribed an anonymous patients' satisfaction questionnaire at the time of ORR: they had to assign a score (scr) from 0 to 10 for each question.
98% of the patients in both groups were satisfied by the treatment in ORR and assigned a >5 scr, and showed an improving in the therapy's adherence compared to 177 patients treated in ambulatory regimen. No physical discomfort and psychological distress have been recorded in patients treated during ORR.

Conclusions: Our results confirmed that the brachytherapy treatment delivery during ORR in elderly and very elderly patients could improve the adherence to therapy reducing treatment-related discomfort and psychological distress.

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ABLATIVE STEREOTACTIC RADIOTHERAPY (SABR) TREATMENT FOR PULMONARY LESIONS WITH REAL- TIME TUMOR TRACKING USING HELICOIDAL THOMOTHERAPY WITH SYNCHRONY RADIXACT SYSTEM: FEASIBILITY AND TOLERABILITY

Code: 402

Aims: To evaluate feasibility and tolerability of stereotactic ablative radiotherapy (SABR) in free breathing real time tumor tracking treatment with Helical Tomotherapy delivery (Synchrony on Radixact® System) in patients(pts) with primary or secondary lungs lesions.

Methods: We retrospectively analysed all pts that underwent SBRT with Synchrony from December 2020 to December 2023. Inclusion criteria were: primary and secondary lungs lesions, central or peripheral lesions located with a minimum distance not less than 2cm to the bronchial tree and to the chest wall. Exclusion criteria was poor compliance.
Primary endpoint was toxicities(tox) evaluation, secondary endpoints was local control.
Acute, subacute and late tox were evaluated according CTCAE scale and radiological pneumonitis according to the “CT-based radiological appearance scale of radiation-induced lung injury”.

Results: A total of 24pts were enrolled for 29 lesions treated, 4 of them were excluded to treatment due to technical problems. Median follow-up was 16.5 months (range 3-30).
Clinical characteristics of patients enrolled are shown in table 1.
The total dose delivered was 28Gy/1fx for 22 lesions and 45, 50 and 60Gy in 3, 5, 6fx for 3 lesions respectively. Eleven pts (44%) received exclusive Radiotherapy (RT) and 14pts RT concomitant with chemotherapy, immunotherapy or target therapy.

As acute and subacute tox, 6 pts (24%) reported G1-G2 dyspnea without substantial worsening at the subsequent follow up other than 1pt with a worsening symptom at the following visits.
Severe (G3) subacute radiological pulmonary tox was found in 3pts (12%), with a stable trend in 1pt and in improvement in subsequent follow-up in the other 2pts. G1-G2 lungs tox was found in 8 pts (32%) with persistence in 5pts, improving in 2pts, worsening in 1pt. No late tox was found in 14pts. All pts were re-staged with CT scans performed within one month after treatment and 11pts were also staged with PET scans. 2 years local control was 77%; 2 years MFS was 38%. At the last follow up 1pt was alive without disease, 6pts were in stable disease (SD), 3pts were alive with local complete response but distant progression (PD),6pts remained in local SD with distant PD, 1pt evolved in target lesion PD, 5pts presented both a local and distant PD, 3pts were lost to the follow up.

Table 1. Clinical characteristics of patients enrolled.		
Median age (y)	75 y (range 43-89)	
Male sex (%)	65.5% (19 pts)	
Primitive histology (%)	Melanoma	34.5% (10pts)
	CRC	20.7% (6pts)
	HCC	6.9% (2pts)
	NSCLC	24.2% (7pts)
	Breast	3.4% (1pts)
	Sarcoma	6.9% (2pts)
	Urothelial	3.4% (1pts)
Metastases (%)	86.2% (25)	
Typed lesions (%)	10.3% (3)	
Median Dmax lesions (mm)	17.5 mm (range 3-42)	
Median cc GTV	3.8 cc (range 0.1-3.8)	
Median cc healthy lung	1628.5 cc (range 956.5-3583)	
Median estimated Beam on	500.48 (range 388.9-627.3)	
Basal images (%)	TC	38% (11pts)
	TC+PET	62% (18pts)
Esclusive SABR (%)	44% (11pts)	
Systemic therapy (%)	Chemotherapy	8% (2pts)
	Immunotherapy	20% (5pts)
	Target Therapy	28% (7pts)
Follow up images (%)	TC	44% (11pts)
	PET	4% (1pts)
	TC+PET	40% (10pts)
	No radiological data	12% (3pts)
Median FUP (m)	16.5 m (range 3-30)	

Conclusions: In our experience lungs SABR with Synchrony Radixact® System is a safe and well tolerated treatment with a low incidence of acute and late toxicities and an overall good treatment response.

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MODERATELY HYPOFRACTIONATED RADIOTHERAPY FOR LARGE OR CENTRALLY LOCATED NEOPLASTIC LUNG LESIONS, TREATED WITH RADICAL INTENT

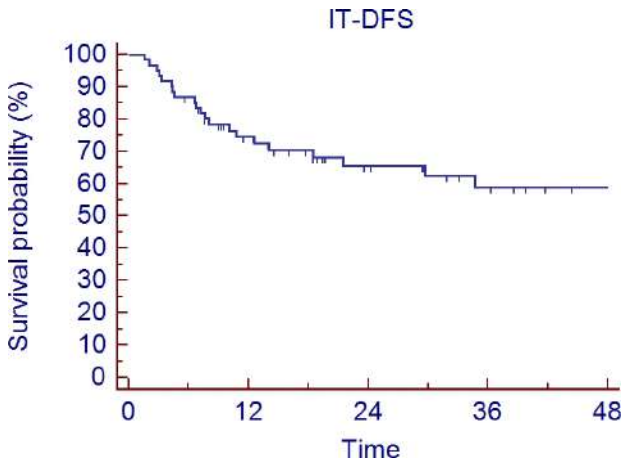
Code: 260

Aims: To report the clinical outocomes from a monoinstitutional cohort of patients, with large or centrally located neoplastic lung disease (both primary tumors and metastases), treated with moderately hypofractionated radiotherapy (MHRT) with radical intent.

Methods: Between December 2006 and April 2023, a total of 61 patients with neoplastic lung disease, comprising 44 cases of primary lung cancer and 17 instances of metastases, were enrolled. All of them were deemed too large or centrally located to be suitable for stereotactic body radiotherapy. Therefore they were treated with MHRT, by administering 48 Gy-60 Gy in 12-15 fractions (4 Gy per fraction), with radical intent. Among them, 15 underwent lung surgery as first treatment at diagnosis, and 23 received systemic therapy before radiotherapy.

Results: Median follow-up was 30.4 months. Median number of lesions included in the PTV was 1 (1-4), and were localized in lung paren chyma (49), mediastinal lymph nodes (1) or both (10). Median total PTV was 120.10 cc (9.20-697.30). Forty patients died during follow up, 28 of them from cancer. Median Overall survival (OS) calculated from the end of RT was 36.3 months (range: 2.3-130.8); 1-yr OS was 85%. Acute toxicity was mild, with only one patient experiencing G3 dyspnea requiring treatment interruption. Late toxicity was either absent or mild in 49 patients, although 5 cases of radiation pneumonitis were documented in frail individuals. The remaining patients exhibited G2 chronic dyspnea. Out of the total, 15, 19, 16 and 10 patients achieved complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD), respectively. One patient died before follow up. Among the study population, 32 patients experienced a progressive disease, with 21 exhibiting intra-thoracic relapse and 15 developing one or more distant metastases. Intra-thoracic disease-free survival (DFS) was 74% after 12 months and decreased to 59% after 36 months, irrespective of whether it was the primary tumor or metastasis (Fig.1). The 12-month metastasis-free survival (MFS) rate was 74.5%, and remained stable at 67.2% after 24 months and beyond.

Conclusions: MHRT with 4 Gy per fraction, for 12-15 fractions, for large or centrally located neoplastic lung lesions demonstrated promising local and distant disease control, for both primary lung cancer and metastases. The toxicity was acceptable, and occurred especially in frail patients.



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LOCAL CONTROL AFTER RADIOTHERAPY IN PATIENTS WITH WHO GRADE II AND III MENINGIOMAS: A SINGLE CENTRE EXPERIENCE

Code: 115

Aims: Meningiomas are the most common primary tumors of the central nervous system. In patients with WHO grade I meningiomas no adjuvant therapy is recommended after resection. In case of WHO grade III meningiomas, adjuvant fractionated radiotherapy(RT) is generally recommended, regardless of the extent of surgical resection. For atypical meningiomas (WHO grade II) optimal postoperative management has not been clearly defined yet.

Methods: We retrospectively reviewed Grade II-III meningioma patients treated in our Institute from 2017 until 2023 after surgery. The residual tumor evaluation was assessed by a post-operative MRI. The follow up was continued with contrast brain MRI.

Results: To date 7 patients received RT course with intensity-modulated radiotherapy (IMRT) after surgery. The median age was 70.3 years. One patient was a WHO grade III meningioma at histological examination (14.3%) and six patients were WHO grade II meningioma (87.7%). Three patients had previously undergone surgery: two patients had a grade I meningioma that progressed to grade II and one patient had a recurrence of grade III meningioma. Median follow up was 9.5 months (one patient has not yet had a follow-up MRI). Four patients (57.1%) had residual disease on post-operative MRI. One patient presented neurological symptoms due to the localization of the residual disease, which completely regressed after radiotherapy. All patients received a dose of 60 Gy in 30 fractions on the surgical cord and on any residual. No patient discontinued treatment due to adverse events. Two patients presented stable disease after radiation treatment, the remaining four showed absence of disease after RT.

Conclusions: RT resulted in improvement of clinical and radiological response. RT should be offered after surgical resection in adjuvant setting to increase progression-free survival as well as overall survival.

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IMAGE-GUIDED SBRT ON DETECTABLE PROSTATE BED RECURRENCE AFTER PROSTATECTOMY IN RT-NAÏVE PATIENTS: A REAL-WORLD REPORT

Code: 129

Aims: The aim of the present study is to evaluate the efficacy and safety of SBRT on the detectable prostate bed recurrence in RT-naïve prostate cancer patients.

Methods: Men who underwent SBRT to macroscopic bed recurrence after prostatectomy were retrospectively considered. Patients were treated based on mpMRI or choline/PSMA PET. Toxicities were collected according to the CTCAE scale. Biochemical recurrence-free survival (bRFS), was defined as the time from the end of RT to BCR or last contact at follow-up; Clinical Recurrence free survival (cRFS), was defined as the end of fine RT to CR or last contact at follow-up.

Results: A total of 86 patients, with a median age at recurrence of 71 years, were included in the analysis. Median time to biochemical relapse (BCR) after RP was 46 months (IQR 22 – 94) with a median PSA at restaging of 1.04 ng/ml. Forty-six patients (53%) were staged with both mpMRI and choline/PSMA PET, while ten (12%) and 30 (35%) were treated based on PET and MRI only, respectively. At a median follow-up of
17.9 months (range 3.9 – 99.2 months), only one late G≥2 GI toxicity was observed. With a median BCR follow-up of 14 months, 29 (34%) patients experienced a BCR with a median PSA at recurrence of 1.66 ng/ml and median survival free from the event of 40.1 months. Median time to BCR was 17.9 months. Twenty-seven (26%) patients had CR with a median CR follow-up of 16.27 months and a median time to CR of 23.0 months. bRFS at 1- was 88% and 66%, respectively while cRFS at 1- and 2-year was 92% and 82%, respectively. Regarding local relapses (n = 15), seven were in the field of treatment, while 8 of them were outfield

Conclusions: These preliminary data showed that targeting macroscopic bed recurrence with SBRT is safe and effective. Additional data and longer follow-ups will provide a clearer indication on the right way to treat these patients and on the more appropriate staging methodology for this cohort of patients.

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INCIDENCE OF NODAL INVOLVEMENT OF IX LEVEL IN HEAD & NECK CANCER

Code: 376

Aims: Bucco-facial nodes are at risk of harboring metastases from cancers of the skin of the face, the nose, the maxillary sinus, and the buccal mucosa. Incidence of IX involvement is unknown, probably below 10%. This multicentric work aims to elucidate the incidence of metastases to level IX nodes and to compile a pictorial review.

Methods: Bucco-facial nodes are at risk of harboring metastases from cancers of the skin of the face, the nose, the maxillary sinus, and the buccal mucosa. Incidence of IX involvement is unknown, probably below 10%. This multicentric work aims to elucidate the incidence of metastases to level IX nodes and to compile a pictorial review.

Results: We reviewed records (TC, RMN, PET) of 76 patients. The subsite distribution was: 20 nasal vestibule, 16 retromolar trigone, 15 cheek mucosa, 13 nasal cavity, 6 maxillary sinus, 1 ethmoid sinus, 1 gingiva, [and 4 alveolar ridge.] Level IX positivity was identified in 4 out of 76 patients 5.2%; 2 detected via clinical imaging as early loco-regional recurrence post-surgery (2 retromolar trigone stage pT3 pN3b, and pT4 pN3b), and 2 through histopathological reports in patients without preoperative imaging evidence (1 retromolar trigone, pT4a pN1 and 1 cheek mucosa pT2 pN2b). 2/4 patients died for rapid progressive disease.

Conclusions: Incidence of bucco-facial involvement was rare in cases. The risk of IX level involvement resulted high (18.7%) for retromolar trigone and cheek tumors, but probably this reflected more the advanced stage of disease than a specific risk for these sub-sites. Prognosis significance is unclear.

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ADRENAL STEREOTACTIC BODY RADIATION THERAPY (SBRT) IN PATIENTS WITH ADVANCED NON-SMALL CELL LUNG CANCER: PRELIMINARY MONOCENTER ANALYSIS

Code: 505

Aims: Lung cancer remains the leading cause of death in the world. The majority of patients is diagnosed at advanced stage. Despite treatment improvements, patients frequently experienced disease progression. Stereotactic body radiation therapy (SBRT) is recognized as an optimal therapeutic strategy to treat oligoprogressive sites in order to delay as far as possible the treatment line change.
The adrenal gland is a common site for metastasis or oligoprogressive localization of non-small cell lung cancer.
This monocenter analysis, aims to demonstrate the safety of adrenal SBRT, without clinical impact on organ function.

Methods: Between December 2021 and December 2023 11 patients (12 lesions) affected by advanced non-small cell lung cancer underwent SBRT targeting the adrenal gland as an oligo progression site. All patients received 35 Gy in 5 fractions (isodose 80%).
Baseline features were as follows: median age of 61 years (58-83); 7 patients (pts) were male, 7 pts were adenocarcinoma. All patients were non-oncogene driven and received systemic treatment according to PD-L1 status.

Results: Most patients underwent SBRT concomitant with systemic therapies: three pts with chemotherapy (2 Gemcitabine, 1 Docetaxel), two pts with chemo-immunotherapy (Pemetrexed plus Pembrolizumab), three patients with monotherapy anti-PD-L1 (1 Durvalumab and 2 Pembrolizumab) and finally two patients were treated with exclusive SBRT.
Adrenal function was measured as alteration of ACTH and cortisol serum level at four time points: at baseline (before SBRT) and after one, three and six month respectively.
Only one patient developed hypocorticoadrenalism and was treated with steroids, other patients showed elevated ACTH serum level without accompanying symptoms.

Conclusions: Adrenal SBRT with or without concomitant systemic treatment, proved to be safe and well-tolerated by patients affected by advanced non-small cell lung cancer. Further analysis with longer follow-up are needed to confirm this preliminary report.

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TRANSURETHRAL RESECTION BEFORE RADIOTHERAPY FOR PROSTATE CANCER: RESULTS ON 398 PATIENTS

Code: 342

Aims: To determine the genitourinary (GU) toxicity and outcomes in prostate cancer patients treated with radiotherapy who have undergone to transurethral resection.

Methods: In this single-center retrospective study, were collected data about prostate cancer patients, treated with moderately hypo-fractionated external-beam radiotherapy or with stereotactic treatment. All patients were screened by self-administered IPSS questionnaires and underwent to uroflowmetry (UFM) before radiation treatment. UFM recorded the amount of urine emitted in the unit of time, the urination time, the maximum flow, and the average flow. Those patients with low UFM value and high IPSS score were evaluated for transurethral

resection of the prostate (TURP). Data on acute and late toxicity along with progressive disease were analyzed and compared with other patients who underwent to radiation treatment without TURP at the same time. Acute and late GU toxicity were scored using Common Terminology for Common Adverse Events (CTCAE v 5.0).

Results: Between 2014 and 2023, 398 patients were treated at our institution. The median age was 74 years (range:46-85 years), mean follow-up 33 months. Ninety patients (23%) underwent resection. Acute toxicity was recorded in 46% of patients who underwent resection and 54% of the other cohort. Grade 1 toxicity was predominant in both groups (88% vs 84%), G2 only in 10% vs 16% one's, while one patient for each group experienced a G3 toxicity (urinary retention). No Grade 4 urinary toxicities were observed in both groups. For late toxicity only grade 1 GU toxicity was recorded between the two groups: dysuria (27% vs 38%) and increased urinary frequency (39% vs 42%) were the most reported symptoms.
Progression free survival was 86% at 5 years and 83% at 8 years for both patients receiving or not resection. In multivariate analysis a statistically significant impact in PD was recorded for ADT use (0.24, 95%CI 0.08 to 0.72; p=0.011), Gleason score (1.8, 95% CI 1.193 to 2.865; p=0.006) and iPSA (2.17, 95% CI 1.296 to 3.653; p=0.003).

Conclusions: No significant difference was observed between the groups with or without resection, neither in terms of toxicity GU, acute and late, nor in terms of PD. This underlines the feasibility of TURP before RT without any harmful correlated event.

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PREVIOUS RADIOTHERAPY INCREASES THE EFFICACY OF CEMIPLIMAB IN THE TREATMENT OF SQUAMOUS CELL CARCINOMA SKIN CANCER: A RETROSPECTIVE ANALYSIS

Code: 365

Aims: Cemiplimab, an anti-pd1 drug that have recently received approval for locally advanced or metastatic squamous cell carcinoma unfit for radical therapies (ie surgery or radiotherapy) is used in real life from several months with good results. Despite that, it is unclear which patients may benefit more from this therapy. Aim of the study is the retrospective analysis of a cohort of consecutive patients treated with cemiplimab to correlate clinical variables to the outcomes.

Methods: A retrospective single-institution analysis involved 45 patients treated with cemiplimab for locally advanced or metastatic cSCC. Clinical variables, including prior treatments, demographics, and time intervals, were collected. Progression-Free Survival (PFS) and Overall Survival (OS) were calculated, and statistical analyses assessed the impact of previous radiotherapy on outcomes.

Results: The analyzed cohort, predominantly male (73.3%) with a median age of 77 months, exhibited varied cSCC localizations. PFS showed a median not reached and a mean of 21.3 months; 40% experienced disease progression. OS demonstrated a median not reached and a mean of 25.3 months, with 26.7% mortality.
Univariate and multivariate analyses revealed significant correlations only between PFS and previous radiotherapy (p: 0.043, p-value: 0.046, respectively).

Conclusions: This study unveils a significant association between previous radiotherapy and improved PFS in cemiplimab-treated advanced cSCC. While confirming preclinical and clinical synergies of radiotherapy and immunotherapy, our findings emphasize the potential of combining radiotherapy with cemiplimab. Further exploration of this combination approach is warranted, recognizing baseline differences in patients who received or did not receive previous radiotherapy. These results offer valuable insights into optimizing treatment strategies for advanced cSCC.

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PHOTOBIOMODULATION IN HEAD AND NECK CANCER PATIENTS UNDERGOING CRT: ROLE IN TOXICITIES PREVENTION

Code: 40

Aims: To evaluate the beneficial effect of photobiomodulation therapy (PBMT) in the prevention of toxicities induced by chemoradiotherapy (CRT) in head and neck cancer (HNC) patients (pts)

Toxicities	T2			T3			T4		
	pbm<10	pbm≥10	P-value (OR; CI95%)	pbm<10	pbm≥10	P-value (OR; CI95%)	pbm<10	pbm≥10	P-value (OR; CI95%)
Oral mucositis N of PBM sequences Yes /no (continuous) G0-1/2-3 (continuous) <10 vs ≥10 Yes/no G0-1/2-3	 28/5 16/17	 34/13 27/20	 0.535(0.95;0.82-1.10) 0.459(0.95;0.84-1.07) 0.264 0.429	 10/23 31/2	 17/30 43/4	 0.112(1.095;0.97-1.22) 0.831(0.98;0.81-1.18) 0.585 0.682	 0/33 33/0	 0/47 47/0	
Radiodermitis N of PBM sequences Yes /no (continuous) G0-1/2-3 (continuous) <10 vs ≥10 Yes/no G0-1/2-3	 31/2 25/8	 46/1 31/16	 0.185(1.27;0.89-1.82) 0.732(1.03;0.89-1.16) 0.362 0.346	 9/24 33/0	 18/29 47/0	 0.306(0.94;0.84-1.05) No tox G2 0.305 No tox G2	 4/29 33/0	 11/36 47/0	 0.661(1.03;0.88-1.21) No tox G2 0.203 No tox G2
Dysphagia N of PBM sequences Yes /no (continuous) G0-1/2-3 (continuous) <10 vs ≥10 Yes/no G0-1/2-3	 32/1 7/26	 47/0 15/32	 0.555(1.19;0.66-2.11) 0.432(0.94;0.82-1.02) 0.230 0.291	 22/11 23/10	 28/19 36/11	 0.916(1.00;091-1.10) 0.500(0.96;0.85-1.08) 0.519 0.490	 13/20 31/2	 5/42 47/0	 **0.032(0.84;0.71-0.98)** 0.307(0.80;0.52-1.22) **0.020** 0.087
Xerostomia N of PBM sequences Yes /no (continuous) G0-1/2-3 (continuous) <10 vs ≥10 Yes/no G0-1/2-3	 1/32 33/0	 4/43 46/1	 0.251(1.16;0.89-1.52) 0.451(1.26;0.68-2.34) 0.319 0.399	 17/16 27/6	 30/17 31/16	 0.816(0.98;0.90-1.08) 0.277(1.05;0.95-1.16) 0.271 0.118	 20/13 30/3	 27/20 45/2	 0.932(1.00;0.88-1.13) 0.720(0.95;0.74-1.22) 0.777 0.379
Trismus N of PBM sequences Yes /no (continuous) G0-1/2-3 (continuous) <10 vs ≥10 Yes/no G0-1/2-3	 3/30 32/1	 3/44 45/2	 0.487(0.92;0.72-1.16) 0.687(0.93;0.67-1.29) 0.651 0.776	 4/29 32/1	 3/44 46/1	 0.087(1.11;0.98-1.26) 0.098(1.29;0.95-1.76) 0.371 0.799	 4/29 33/0	 3/44 47/0	 **0.047(0.77;0.60-0.99)** 0.371

Toxicity in T2, T3, T4 in two groups. N: number. PBM: photobiomodulation. G: toxicity grade. T2: at end of treatment. T3: at 3 months to end treatment. T4: last follow up. OR: odds ratio. CI: confidence interval

Methods: Between May 2021 and May 2023 we retrospectively analyzed 80 pts with HNC treated with CRT in adjuvant or definitive intent and concomitant PBMT with two devices: ATP38 and CareMin650.
The median number of session was 10 (IQR,7-13 sessions) and the population was divided into two groups: group A (PBMT<10 sessions) 33 pts (41.25%), group B (PBMT≥10 sessions) 47 pts (58.75%).
The main toxicities were assessed according to the CTCAE v5.0 at the half of PBMT (T1), at the end of it (T2), at 3 months (T3) and at the last medical record (T4).
It was considered also the weight loss between T2 and T0 (starting time of CRT) and T4-T0.
The chi-square test for ordinal variables was used to evaluate the association between PBMT sessions and toxicity; logistic regression for continuous variables; the Kaplan–Meier method for survival analysis.
Analysis of dependent variable "weight" was performed with a repeated-measures 2-way ANOVA with time and sessions of PBMT

Results: The median age was 59 years (IQR,53-64 years), most common primary tumor was squamous carcinoma (91.2%), the median follow-up was 15 months (IQR11.2-18.7 months).
The weight loss (T2-T0) was significantly with a p-value <0.01.
The table shows the analyses of toxicity at T2, T3 and T4 between PBMT sessions.
In the analyses of oral pain at T2 continue variables show significantly with a p-value of 0.047 in the yes/no toxicities category. Group B developed significantly fewer ≥G2 toxicities compared to Group A with a p-value<0.01.
In T4 continue variables show a significantly in dysphagia and trismus with a p-value of 0.032 (OR0.84;95CI:0.71-0.98) and 0.047 (OR0.77;95CI:0.60-0.99) respectively, in the yes/no toxicities category. In the analyses of dysphagia at T4, Group B developed significantly fewer ≥G2 toxicities compared to Group A with a p-value of 0.020.
The local control (LC), metastasis free survival (MFS), disease-free survival (DFS) and overall survival (OS) at 6, 12 and 15 months were, respectively: 96.3%, 93.3% and 87.6% (LC), 95%, 91.3% and 89.3%
(MFS), 92.5%, 89.6% and 82% (DFS), 98.8%, 98.8% and 97% (OS)

Conclusions: This study evidence that PBMT has an important role in decreasing the incidence and the severity of sides effects induced by chemoradiotherapy in HNC patients while preserving an excellent oncological outcome profile

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ENHANCING THERAPEUTIC PRECISION: MR-GUIDED STEREOTACTIC RADIOTHERAPY FOR OLIGOMETASTATIC PERITONEAL CARCINOMATOSIS

Code: 231

Aims: Historically, peritoneal carcinomatosis (PC) has been associated with a poor prognosis. Currently, in selected cases of oligometastatic setting, it may benefit from a combination of systemic treatments and locoregional therapies, such as stereotactic radiotherapy (SBRT). Magnetic resonance-guided stereotactic radiotherapy (MRgSBRT) allows online adaptation (OA) for optimizing daily dose distribution based on the patient's anatomy, in order to enhance treatment precision and to minimize toxicities. This single- institution study evaluates the feasibility and efficacy of MRgSBRT in a case series of patients with PC.

Methods: The clinical and dosimetric data of PC patients who were treated with MRgSBRT were collected. The primary objectives were to define 1-year local recurrence-free survival (LRFS), progression-free survival (PFS) and overall survival (OS) rates. Complete response (CR) and partial response (PR) were defined as objective response rate (ORR). The achievement of ORR and stable disease (SD) were defined as clinical benefit (CB). The CTCAE 5.0 scale was used to assess acute and late toxicities.

Results: From July 2019 to December 2023, 33 consecutive oligometastatic PC patients, accounting for a total of 47 lesions, were treated by MRgSBRT. Patients and treatment characteristics are summarized in Table 1**.** Of the 11 (33.3%) patients with multiple PC nodules, all but one received radiation simultaneously in the same treatment fractions. The median PTV dose was 35 (2-50) Gy in 5 (2-5) fractions. Out of a total of 212 treatment fractions, 169 (79.7%) were delivered using an OA protocol. CR, PR and SD were observed in 26 (55.3%), 9 (19.1%) and 7(14.9%) lesions, respectively, resulting in a CB rate of 89.4%. With a median follow-up of 9 months (range: 1-51), the 1-year LRFS, PFS and OS rate were 84%, 25% and 100%, respectively. ADP-ribose polymerase (PARP) inhibitors were administered after MRgSBRT in 10 (29.4%) patients. This was shown to have a positive effect on PFS (P=0.0282). The LRFS was beneficially influenced by the histology of ovarian cancer in 30 (63.8%) lesions (P=0.0045), as was the achievement of a BED≥80 in 20 (42.6%) lesions (P=0.0055). Overall, no acute or chronic toxicity has been reported.

Conclusions: This study demonstrates the efficacy and safety of MRgSBRT in patients with PC, also in combination with PARP inhibitors, allowing dose escalation and OARs-sparing. The treatment was well tolerated, and any grade toxicities were reported.

	N. (%)
Patients	34 (100)
Lesions	47 (100)
Age, years	
Median (range)	54 (39-86)
Gender	
Male	4 (11.8)
Female	30 (88.2)
ECOG Performance Status	
0	28 (82.4)
1	6 (17.6)
Primary tumor	
Ovarian	30 (63.8)
Cervical	1 (2.1)
Endometrial	4 (8.5)
Colorectal	9 (19.2)
Other	3 (6.4)
Metachronous lesions (>6 months)	
No	2 (4.3)
Yes	45 (95.7)
PTV	
Median, range (cc)	7.4 (1.8- 45.3)
Total dose, Gy	
Median (range)	35 (10-50)
Dmean $BED_{\alpha/\beta 10}$, Gy	
Median (range)	75.7 (14.8-128.5)
Dose/fraction, Gy	
Median (range)	7(5-10)
Prescription isodose	
Dmean	12 (25.5)
80% isodose	35 (74.5)
Gating	
Breath-hold inspiration	24 (51.1)
Free-breathing	23 (48.9)
Treatment after MRgSBRT	
Surgery	3 (8.8)
Chemotherapy	18 (52.9)
Target therapy	10 (29.4)
RT/SBRT	10 (29.4)

Table 1. Patients and treatments characteristics

ECOG: Eastern Cooperative Oncology Group; PTV: planning target volume; BED: biologically effective dose with $\alpha/\beta = 10$ Gy; MRgSBRT: magnetic resonance guided stereotactic body radiation therapy; RT: radiation therapy; SBRT: stereotactic body radiation therapy.

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RETROSPECTIVE MONOINSTITUTIONAL ANALYSIS OF OVERALL SURVIVAL IN OROPHARYNGEAL CANCERS (STAGE III) ACCORDING TO AGE AND GENDER

Code: 130

Aims: We have previously demonstrated, according to literature, that p16 status is one of the strongest predictive factor for overall survival (OS) and cancer-specific survival (CSS) in patients (pts) treated with radical radio-chemotherapy (RT-CT) for oropharyngeal squamous cell cancer (OSCC) stage III. In the updated casistic, we evaluated OS stratified by age at diagnosis (≥65 and <65 years) and gender, and we examined the incidence of cancer-related death versus other causes.

Methods: We retrospectively analyzed 99 pts, consecutively treated from September 2013 to December 2023 in our Institute, with OSCC stage III according to TNM 8th edition, adjusting TNM 7th for pts diagnosed before 2018. 79 were males, and 20 were females. All pts were treated using Volumetric Modulated Arch Therapy with Image-Guided Radiation Therapy. The dose prescription was 70 Gy in 35 fractions to the high-risk volume, 60-54 Gy to intermediate and low-risk volumes, respectively. Concomitant CT with cisplatin/3 week was prescribed in 25 pts, CT/week in 74 pts.

Results: The median age was 62.6 (56.6-68.5) years (y). 32/99 pts (22 males 10 females) were p16 -. There were no statistically significant differences in age between p16 positive (+) and p16 - pts. Overall survival, estimated by Kaplan Meier method, was 73.5% and 61.4% at 3 and 6 years, respectively. Results of analysis stratified by age under and over 65 y indicate that at 6 years, in pts <65 y, the p16+ group has a statistically significant better OS of 80.9% [95% CI 61.2-91.3], compared to the p16- group (46.7% [18.7-70.8], p=0.004). Similarly in pts ≥65 y, OS remains higher in the p16+ group compared to p16- (49.9% [24.1-71.3], vs 18.7% [0.9-55.4], p=0.076). [Fig.1] No statistically significant differences for OS related to gender were demonstrated in the stratified analysis. [Fig 2] In a multivariate sex-corrected Cox regression model, p16 positivity (HR=0.36 [0.17-0.77]) and age ≥65 (HR=2.45[1.2-5.0]) were found independently associated with OS. Analysis of cause-specific mortality showed that cumulative incidence function of cancer-related death rises more rapidly than other causes' death function and remains higher during the first 6 y from RT-CT. [Fig 3]

Conclusions: In our experience, p16 status but also age are independent risk factors for OS. According to NCCN guidelines, pts ≥65 y should be evaluated by comprehensive geriatric assessment (CGA), for example G8, to estimate life expectancy and treatment compliance.

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Fig.1 KM curves for OS by p16 positivity stratified by age (<65 and ≥65)

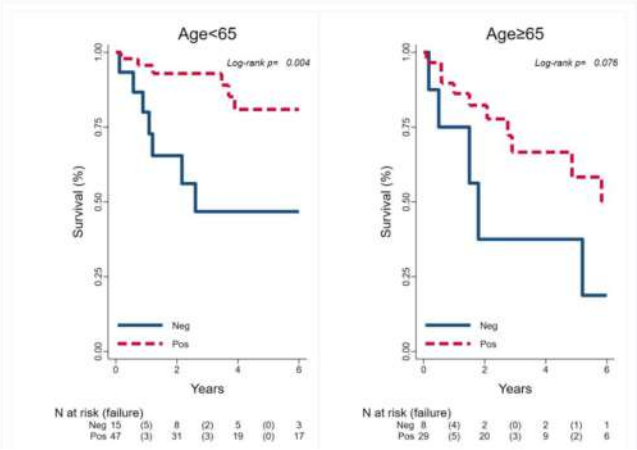

Fig.2 Multivariate Cox regression models for OS. HR and corresponding 95% confidence intervals (CI).

Model A

	HR	[95% Conf. Interval]		p
age≥65	2.20	1.08	4.50	0.030
sex	0.51	0.18	1.46	0.209

Model B

	HR	[95% Conf. Interval]		p
age≥65	2.45	1.20	5.03	0.014
sex	0.66	0.22	1.94	0.449
p16 pos	0.36	0.17	0.77	0.008

FIRST PILOT WORLDWIDE ADAPTIVE TREATMENT WITH COMPREHENSIVE MOTION MANAGEMENT WITH 1.5T MR-LINAC

Code: 313

Aims: 1.5T MR-linac improves target volume and adjacent OARs visualization, ensuring high precision in radiation treatment delivery. Daily MR-imaging allows on-table adapted planning and real-time intra- fraction imaging without additional exposure to radiation.
We aim to report the first pilot worldwide adaptive treatment with true tracking and automatic gating by means of high-field MR-Linac. This implementation allows to compensate for any respiratory and/or accidental movements of the target during RT delivery.

Methods: On 25th September 2023, we treated a 60-year-old female affected by liver oligometastasis from high grade serous ovarian carcinoma. For treatment simulation we used a 3D T2-navigated MR sequence in full exhale. On this sequence we contoured the target and the organs-at-risk. The PTV from GTV were 5 mm in all directions except 10 mm caudally. A 12-fields IMRT plan was prepared and daily adapted with adapt- to-shape workflow during every fraction. The treatment dose was 50 Gy in 5 daily fractions. The treatment was delivered in free-breathing modality.
Comprehensive Motion Management (CMM) was set to deliver the treatment when at least 95% of the GTV overlapped with the PTV. We collected details and times of all treatment phases.

Results: The median on-table time was 36 minutes. The median daily 3D T2-navigated sequence acquisition lasted 10 minutes, the registration between daily sequence and reference sequence lasted 2 minutes, the daily target and OARs contour definition lasted 1 to 3 minutes, since no target shape correction was provided. The daily plan adaptation lasted between 5 and 7 minutes. The median delivery time was 15 minutes with a median beam-on time of 6 minutes (range 5-8 minutes) and a median gating efficiency of 33%
(30-38%). No drift corrections were needed. The patient performed all the sessions without any clinical problems.

Conclusions: MR-guided radiation adaptive treatment using comprehensive motion management has been successfully implemented into clinical routine. This approach has proven CMM clinically feasible. The data reported support an optimal profile of tolerability of daily on-table adaptive radiation therapy with true tracking and automatic gating delivery in acceptable time slots compatible with Online Adaptive Workflow.

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FIRST CLINICAL APPLICATION OF COMPREHENSIVE MOTION MANAGEMENT ON PROSTATE SBRT USING 1.5T MR-LINAC

Code: 309

Aims: High-field MR-linac allows improved soft-tissue visualization of the tumour and the surroundings tissues. Furthermore, daily MR-imaging allows on-table adapted planning and real-time intra-fraction imaging without additional exposure to radiation. The recent implementation of Comprehensive Motion Management (CMM) guarantees more precise radiation treatments by interrupting the delivery when the target moves outside the defined position and enables radiation oncologist to perform target drift corrections. We report our first clinical experience on prostate adaptive SBRT with true tracking and automatic gating with high-field MR-Linac.

Methods: Between 26th September and 13rd October 2023, we treated 5 male patients affected by low-to-favourable intermediate prostate cancer. For treatment simulation we used a T2-weighted MR sequence that lasts 2 minutes. On this sequence we contour the target and the organs-at-risk. The GTV-to-PTV margins were 5 mm in all directions and 3 mm posteriorly. A 16-fields IMRT plan was prepared and daily adapted with adapt-to-shape workflow during every fraction. The 5-fraction delivered total dose was 35 Gy in low risk and 36.25 Gy in intermediate risk. The motion management was set to deliver the treatment when 100% of the GTV was contained within the PTV. We collected details and times of all treatment phases.

Results: The median on-table time was 34 minutes. The daily 3D T2-weighted sequence acquisition lasted 2 minutes, the registration between daily sequence and reference sequence lasted 1 minute, the daily target and OARs contour definition lasted 4 to 5 minutes and the daily plan adaptation lasted between 7 and 9 minutes. The median delivery time was 17 minutes (range 15-20 minutes) with a median beam-on time of 14 minutes (range 13.5-17 minutes) and a median gating efficiency of 85% (range 82%-91%). Among the 25 delivered fractions only one drift corrections was needed and the baseline shift replanning lasted 1 minute. The patients performed all the sessions without any clinical issue.

Conclusions: Daily-adaptive MR-guided SBRT to the prostate using Comprehensive Motion Management has been successfully implemented into clinical routine. The whole process is safe and completely automated even in the case on in-treatment corrections and baseline shift replanning. CMM could allow now a safe reduction of the treatment margins with a guided workflow to manage real tracking and gating.

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AN UPDATE OF MICROSTYLE STUDY: A RANDOMIZED CONTROLLED TRIAL ON LIFESTYLE AND INTERACTION WITH MICROBIOTA IN PROSTATE CANCER PATIENTS UNDERGOING RADIOTHERAPY

Code: 287

Aims: To report preliminary data from MICROSTYLE study, a RCT for prostate cancer (PCa) patients (pts) undergoing RT designed to investigate whether changes towards a healthy lifestyle are able to modify microbiome, improve quality of life and decrease the side effects of RT.

Methods: According to the study protocol 300 PCa pts undergoing adjuvant/salvage or curative RT will be recruited in two Italian Cancer Centers. Participants will be randomized in two arms: Intervention Group (IG) and Control Group (CG); the IG will receive personalized counseling on diet and exercise to improve overall lifestyle and to reduce eventual RT-related toxicities and a steps counter to monitor and increase physical activity. The CG will receive baseline general advice. The primary outcome will be assessed after 6 months by measuring the change in healthy lifestyle adherence (HLA) score between groups. As secondary outcomes, the change from baseline in fasting serum metabolic and inflammatory
biomarkers will be monitored. Intestinal microbiome composition will be evaluated trough fecal samples analyses. According to the cross-over design, the CG will cross to the IG after 6 months.

Results: Recruitment started on October 2021 and to date, 287 pts have been enrolled (139 allocated to IG and 148 to CG) with a median age at recruitment of 71 years. Baseline characteristics of pts are reported in Figure 1a. One-hundred and ninety pts completed the RT course with no grade (G) ?3 gastrointestinal (GI) acute toxicities reported and only 2 genitourinary (GU) G?3 acute toxicities observed among both arms. The HLA score resulted significantly higher at 6 months (data available for 47 pts) with respect to baseline (median HLA 4.4 vs 4.8, $p < .0001$, Figure 1b). When stratifying pts according to BMI at baseline, pts with a BMI ? 30 had a greater increase in HLA at 6 months. While, when stratified by age, pts aged 66-75 resulted the ones with a major change in HLA score (Figure 1c). At 12-month FU (data available for 27 pts) all pts are alive with no evidence of disease and only one GI ?G3 late toxicity was reported.

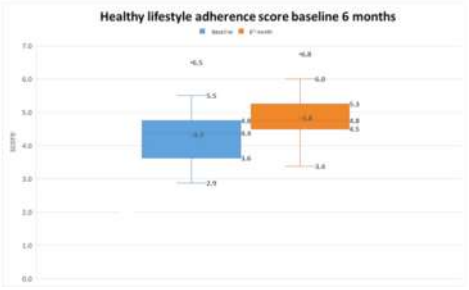
Conclusions: This innovative RCT proposes a lifestyle intervention during RT: dietary and physical activity counselling, as well ad monitoring changes in microbiome and serum biomarkers. The promotion of healthy behavior will be started before initiation of standard care, to achieve long lasting impacts, control side effects, coping with feelings of anxiety and depression and improve the effectiveness of RT.

Figure 1. Summary of patients baseline characteristics and treatment (a); HLA score at baseline and at 6 months (b); change in HLA score according to BMI and age at recruitment (c).

a)

Variable	N.	ALL, n (%) 198	IG, n (%) 94	CG, n (%) 104
ISUP group	1	29 (14.6)	16 (17)	13 (12.5)
	2	55 (27.8)	30 (31.9)	25 (24)
	3	47 (23.7)	20 (21.3)	27 (26)
	4	25 (12.6)	11 (11.7)	14 (13.5)
	5	16 (8.1)	9 (9.6)	7 (6.7)
	missing	26 (13.1)	8 (8.5)	18 (17.3)
Smoking habits	Smoker	31 (15.7)	16 (17)	15 (14.4)
	Former smoker	86 (43.4)	41 (43.6)	45 (43.3)
	Never smoker	72 (36.4)	34 (36.2)	38 (36.5)
	missing	9 (4.5)	3 (3.2)	6 (5.8)
PSA (ng/ml)	Median (IQR)	1.08 (4.82)	1.12 (4.97)	0.94 (4.72)
BMI (kg/m²)	Median (IQR)	27.9 (5.7)	28.5 (5.6)	27.6 (5.9)
WHR	Median (IQR)	1 (0.1)	1 (0.1)	1 (0.1)
Heart rate (bpm)	Median (IQR)	73 (16)	73 (14.3)	72 (17.5)
Glycemia (mg/dl)	Median (IQR)	97 (19.5)	98 (20)	95 (19)
Triglyceride (mg/dl)	Median (IQR)	102 (62)	104 (61)	99 (67)
Total cholesterol (mg/dl)	Median (IQR)	189 (46)	186 (38)	196 (47)
HDL cholesterol (mg/dl)	Median (IQR)	51 (15)	49 (14.0)	52 (14)
LDL cholesterol (mg/dl)	Median (IQR)	113 (34.5)	105 (38)	124 (50)
RT treatment		ALL, n (%)	IG, n (%)	CG, n (%)
Curative treatment		109 (55.1)	54 (57.4)	55 (52.9)
Adjuvant/salvage RT		41 (20.7)	25 (26.6)	16 (15.4)
ADT		68 (34.3)	35 (37.2)	33 (31.7)

b)



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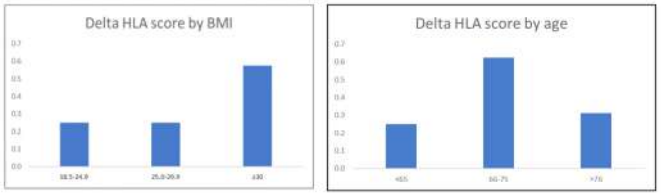
c)



List of abbreviations: ***BMI:*** *body mass index;* ***HLA:*** *healty lifestyle adherence;* ***ISUP:*** *international society of urological pathology;* ***PSA:*** *prostate specific antigen;* ***WHR:*** *Waist to Hip Ratio.*

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SERUM CYTOKINES MODULATION BY PELVIC RADIOTHERAPY WITH HYPOFRACTIONATED SIMULTANEOUS INTEGRATED BOOST IN PROSTATE CANCER

Code: 29

Aims: Our study aims to monitor the trend of 10 serum cytokines over time in prostate cancer patients undergoing pelvic irradiation with a hypofractionated simultaneous integrated boost. We analyzed whether there was a correlation between cytokine levels and genitourinary (GU) and gastrointestinal (GI) toxicity.

Methods: Thirty-eight prostate cancer patients were prospectively enrolled in our study (Table 1). All enrolled patients were treated according to our Institutional guidelines. In particular, 17 patients underwent definitive moderately hypofractionated RT (66-69 Gy/25-27 fractions) and 21 patients underwent post- operative moderately hypofractionated RT (66-70 Gy/25-28 fractions). Both groups were treated by VMAT. Target volumes were: prostate + seminal vesicles + pelvis for definitive RT; prostate bed + pelvis for post-operative RT. Patients received a daily dose of 180 cGy to the pelvis and simultaneously a boost of 250-270 cGy to the prostate/prostate bed. Peripheral blood was collected before RT, at the end of RT, at FUP time of 3, 6 and 12 months after the end of RT. Serum samples were tested to quantify 10 human cytokines (IFN-α, IFN-β, IFN-γ, IL-1β, IL-2, IL-6, IL-8, IL-10, TNF-α, TGF-β1).

Results: After a median FUP time of 30.5 months, only 2 patients experienced biochemical relapse (5.2%). Fourteen patients (36.8%) developed grade 1 acute GU toxicity and 7 (18.4%) grade 2. As regards acute GI toxicity, 26.3% of patients had grade 1 and 31.6% grade 2 toxicity. The prevalence of grade 1 and 2 GU late toxicity at last FUP was 34.2% and 15.2%, and for grade 1 and 2 GI toxicity was 31.6% and 15.8% respectively. Considering the entire group of patients, the circulating concentrations of IFN-α, IL-2 and IFN-β displayed significant variations during the 5 time points. In particular, we found reduction of IFN-α values for all time points, reduction of IL-2 until the FUP 3 months and a slight subsequent increase, IFN-β clear reduction in value at FUP time points of 6 and 12 months. As regards the treatment, basal serum concentration of IFN-γ was significantly lower in definitive group respect to the post- operative one. No correlation between late GI or GU toxicity and the cytokines concentrations was found.

Conclusions: Our preliminary data found significant variations of the levels of cytokine IL-2, IFN-α and IFN-β. Furthermore, we found a significant difference in IFN-γ levels between patients with or without prostate, in agreement with what has been reported in literature.

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EVALUATION OF LATE TOXICITY AND OUTCOME IN PROSTATE CANCER PATIENTS UNDERGOING POST-OPERATIVE HYPOFRACTIONATED RADIOTHERAPY

Code: 146

Aims: The optimal hypofractionated schedule of post-prostatectomy radiotherapy (RT) remains to be established. We evaluated treatment outcomes and toxicity of post-prostatectomy hypofractionated RT (adjuvant and salvage) in seventy-one patients treated with volumetric modulated arc therapy (VMAT).

Methods: Seventy-one prostate cancer patients were enrolled in this retrospective single center study; 36 (50.7%) underwent adjuvant RT and 35 (49.3%) salvage RT (Table 1). The dose prescription for prostate bed planning target volume was 6750 cGy in 25-27 fractions (dose per fraction range: 250-270 cGy). In patients planned to undergo also pelvic lymph nodes RT (63.4%), a simultaneous dose of 180 cGy was administered to the pelvis.

Results: With a median follow up of 45 months (range 21-91), we had 10 biochemical relapse (14.1%) and 7 metastasis (9.9%) (3 bone and 4 lymph node). Hormone therapy was administered in 43.6% of patients. Four patients died, resulting in 3-years overall survival rate of 92.2%. Thirty-six (50.7%) patients experienced acute G1 and 5 (7%) patients acute G2 gastrointestinal (GI) toxicity. As regards acute genitourinary (GU) toxicity, 25 (35.2%) patients experienced G1 events and we did not record any G2 events. Late GI toxicity was: 14.1% G1 and 2.8% G2. Late GU toxicity (incontinence, hematuria,
retention) was: 31% G1 and 5.6% G2. In particular, 28 patients (39.4%) reported urinary incontinence post- RT, of these: 10 (14.1%) already had it before RT, 15 (21.1%) had new onset and in 3 patients (4.2%)
there was post-operative incontinence worsening.

Conclusions: Our experience has highlighted that hypofractionated RT is feasible and well tolerated in post- prostatectomy setting, but further studies on larger series are needed to better define late GU toxicity rate.

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Table 1. Patients' characteristics

Variable	Median (range) or number of patients (%)
Age	70 (51 – 88)
Gleason score	7 (5 – 9)
pT2	21 (29.6)
pT3	49 (69)
pT4	1 (1.4)
pNx	23 (32.4)
pN0	41 (57.7)
pN1	7 (9.9)
R1	38 (53.5)
Adjuvant RT	36 (50.7)
Salvage RT	35 (49.3)
Prostate bed irradiation	26 (36.6)
Prostate bed + pelvic lymph node irradiation	45 (63.4)
Hormone therapy	31 (43.6)
Follow-up in months	45 (21 – 91)

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AI-BASED ONLINE ADAPTIVE RADIOTHERAPY IN PROSTATE CANCER TREATMENT: CONSIDERATIONS ON ACTIVITIES TIME AND DOSIMETRIC BENEFITS

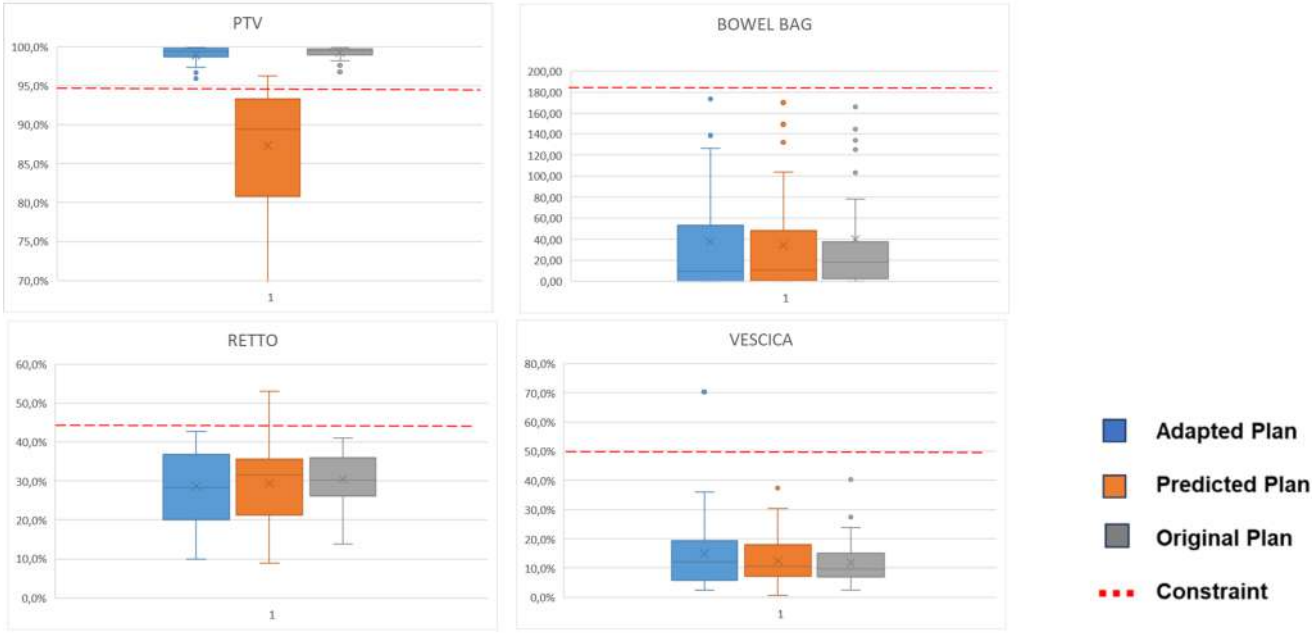
Code: 324

Aims: Recent advancements in Radiotherapy (RT) technology have led to the development of online adaptive RT (oART), a novel clinical procedure that aims to online address the anatomical variations encountered during each RT treatment fraction. Integrating Artificial Intelligence (AI) into the online adaptive procedure automates key manual tasks, such as contouring and planning, speeding up the process and standardizing treatment while reducing user-dependency. The aim of this study is to investigate the dosimetric advantage of implementing AI-driven oART in the context of prostate cancer.

Methods: A total of 31 prostate cancer patients treated from August 2021 to January 2024 were analysed. Patients received an oART treatment on an AI-based Linac (Varian Ethos), with 67.5 Gy administered in 25 fractions. CTV included prostate and seminal vesicles, with a 5 mm expansion for PTV in all directions except to 8 mm in caudal. Daily CBCT were acquired each day of therapy, organs at risk (rectum, bladder, bowel) were automatically segmented by the AI-system, while target volumes were manually delineated.
Two treatment plans were generated: a predicted one, obtained calculating the fluence of the original plan on the daily patient anatomy, and an adapted one, obtained through a complete fluence reoptimisation.
Daily DVH indicators for PTV (V95%), bladder (V65Gy), bowel (V45Gy), and rectum (V50Gy) were analysed for each treatment fraction and the values obtained in the predicted and adapted plans were compared using the Wilcoxon Mann Whitney test. Total treatment session time, defined as the time between the CBCT acquisition and end of treatment delivery, was also recorded.

Results: Figure 1 reports the box-plot analysis related to the DVH indicators above mentioned, separately for the predicted, adapted and the original plan. Performing oART treatment led to a significant gain in terms of target coverage (+11.9% in PTV V95%, 98.7% with adaptive versus 86.8% in predicted plan, p-value <0,001), while no significant difference was observed for the OARs DVH indicators (p>0.1 for all cases). The mean total treatment session time was 18±5 minutes. According to CTCAE v5, no toxicity ≥ G2 were recorded.

Conclusions: This study demonstrates that online adaptive RT in prostate cancer results in a significant improvement in target coverage with no significant difference in OARs. Further studies correlating dosimetric advantages with clinical outcomes are underway.



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HYPOFRACTIONATED STEREOTACTIC ABLATIVE RADIOTHERAPY (SABR) FOR HEPATOCELLULAR CARCINOMA (HCC) IN WESTERN LIGURIA

Code: 607

Aims: To present our initial experience in the treatment of patients (pts) affected with HCC by SABR.

Methods: Since august 2020, 16 treatments in 15 pts affected with recurrent or newly diagnosed, MRI or histologically confirmed HCC, have been treated in the San Paolo hospital of Savona. Median age has been 82 years (range 52 – 86); each pts has been discussed in multidisciplinary liver cancers dedicated Disease Management Team (DMT), referred to RT department and evaluated by the radiation oncologist on MRI/CT images or by simulation CT for eventual needing of CT or US guided fiducial marker placement; if the markers were implanted, after 3-7 day a new simulation CT has been performed and the patient planned for SABR; all pts were classified as Child-Pugh A5 to B6 before SABR; 13 pts received liver directed SABR on single (11) or multiple (3) lesions, 2 pts were treated on solitary regional lymph node recurrencies; 40 Gy in 5 fractions every other day has been prescribed in all liver SABR and 30 Gy in 5 fractions, due to ileal and duodenal tolerance in one Lymph node directed SABR.

Results: Median follow-up is 370 days (range 1 to 790), 14 patients were followed up in RT department and re-discussed in DMT, 1 pts was lost to follow up; 5 patiens obtained (4 liver and 1 lymph node) a complete and 6 (all liver) a partial remission of the disease; 1 had a progressive disease at the first CT after SABR and died at 78 y.o. 6 months after SABR; 3 more pts died, 2 at 80 and 87 y.o. for causes not related to the principal diagnosis or therapy, the last at 88 y.o. for liver insufficiency after more than 2 years from SABR. Other 2 pts developed temporary liver insufficiency 2 months after SABR; no other toxicity more except fatigue G1 has been recorded.

Conclusions: HCC SABR is feasible and remain a valid option in pts with limited disease, not addressed to more invasive local therapies due to age, comorbidities or who relapsed after them. DMT evaluation is mandatory to personalize and chose the proper approach for each pts and optimize the results.

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PRECLINICAL MONTE CARLO TREATMENT PLANNING SYSTEM FOR X-RAY MINIBEAM RADIOTHERAPY

Code: 190

Aims: Minibeam Radiation Therapy (MBRT) is a promising approach to improve the therapeutic index by splitting the radiation field into multiple narrow high dose regions (peaks) separated by low dose regions (valleys). The objective of this study is to present the development of a preclinical TPS for X-ray MBRT using Monte Carlo (MC) simulations performed with Topas (Tool for Particle Simulation). By simulating the minibeam irradiation process, this work investigates the relevant parameters, such as peak- to-valley dose ratio (PVDR), beam full width at half maximum (FWHM) and peak-to-peak distance, in the real scenario of mice irradiation.

Methods: The MC simulations are based on a small animal irradiator (SmART, PXI) available at the Preclinical Imaging Facility of the San Raffaele Scientific Institute. This irradiator has an X-ray source of 225 kV, 13 mA and the size of the aperture is set to 14.4x14.4 mm. A 40x40 mm lead collimator with a thickness of 5 mm is inserted at the exit to generate minibeams: this collimator consists of 0.5 mm thick slits spaced by 0.5 mm of air, resulting in minibeams with an expected peak-to-peak distance of 1 mm. A calibrated Cone Beam Computed Tomography (CBCT) of a mouse with a subcutaneous tumour is imported in the MC simulation. The mouse is positioned to ensure that the tumour is centrally located within the radiation beam at 2.5 mm from the collimator. The dose is scored in the tumour region using voxel sizes of 0.1x0.1x0.1 mm. In total, 1E11 primary histories are simulated using the Research Cluster of the San Raffaele Hospital.

Results: At the end of the simulation, it is obtained a dose DICOM file showing the axial, coronal and sagittal MBRT dose distribution and the dose profile at the centre of the tumour. The peak-to-peak distance is equal to 1.03±0.01 mm, in good agreement with the simulated collimator geometry.
Subsequently, the variation of PVDR and beam FWHM at different depths within the tumour area is computed. These are obtained by averaging the values of the three central peaks. The beam FWHM is stable with a 5% variation across the tumour. The PVDR shows, as expected, an exponential decay from 27 down to 17 as we move away from the collimator.

Conclusions: This study is focused on the development of a prototypal preclinical TPS for small animals MBRT using X-ray. This toolbox enables dose calculations for preclinical in vivo MBRT treatments and facilitates the exploration and comparison of different irradiation geometries.

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ULTRAHYPOFRACTIONATED (UHF) RADIOTHERAPY IN BREAST CANCER: UPDATE TO 36 MONTHS

Code: 606

Aims: Monitoring local disease control and toxicity in patients (pt) with early-stage breast cancer (EBC) undergoing breast- conserving surgery (BCS) and adjuvant weekly ultrahypofractionated radiotherapy.

Methods: From June 2020 to October 23, we recruited 168 women ?50 years old, with EBC, undergoing BCS (pT12(?3 cm) pN0), G1-2 and negative margins. The prescribed dose was 28.5 Gy in once weekly fractions over 5 weeks. The primary end-point was local tumor control, acute and chronic toxicity (tox) end esthetic outcomes. Secondary end points were impact on quality of life (QoL) and on waiting list.
After a CTscan, a whole breast irradiation 3Dplanning was performed using opposite tangent with fields in fields, with 6 MV photons, and subfields to improve dose homogeneity. Skin tox was assessed with the RTOG score. In order to evaluate aesthetic outcomes, two photos were taken for each pt (antero-lateral and antero-medial), at the beginning, at the end of the treatment, and then at 3, 6, 12, 24, 36 months (mo) follow up.

Results: We enrolled 168 pt with mean age of 64 years (range 50-84). The median follow-up was 16 mo (range 3-36). The most common tox were acute erythema, edema, late breast fibrosis and shrinkage. With the limit of the short follow- up, no one pt developed recurrence and only five had significant esthetic changes with moderate fibrosis and breast shrinkage a 12, 24 e 36 mo. Acute tox evaluated was not greater than G2, with 146(86,91%), 156(92.86%) pt respectively G0-1 at end radiotherapy and 3 mo later.

Similarly, chronic tox evaluated was not greater than G2 with 140(94.6%), 107(92.25%), 64(91.44%), 27(84.4%) pt respectively G0-1 at 6, 12, 24 and 36 mo.
All pt showed a high level of satisfaction and among all pt who experienced acute o chronic tox G2, this impacted QoL respectively only in 4(18,2%) and 5(25%) cases and with low entity.

Conclusions: Once weekly UHF radiotherapy is a feasible alternative in the adjuvant management of EBC. It is well tolerated and particularly appreciated by pt, has a low acute and chronic tox and good cosmetic outcomes. Finally, it significantly reduces the waiting lists.

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ELDERLY PATIENTS WITH NON MELANOMA SKIN CANCERS (NMSC) TREATED BY CONTACT HIGH DOSE RATE BRACHYTHERAPY (CHDR BRT) AND INTERSTITIAL HIGH DOSE RATE BRACHYTHERAPY (IHDR BRT)

Code: 608

Aims: Non Melanoma skin cancers (NMSC) are the most common human malignancy in the world with increasing incidence in recent years. In this study shows the data concerning elderly patients affected by NMSC treated with high dose rate interstitial and contact brachytherapy (contact High Dose Rate Brachytherapy, cHDR – BRT, interstitial High Dose Rate Brachytherapy, iHDR- BRT).

Methods: Patients with NMSCs enrolled in the study underwent cHDR BRT or iHDR – BRT.
Applicators were used: Freiburg Flap or silicone mold in the cHDR BRT, flexible catheters and needles for the iHDR – BRT. The source used is I'192 with remote afterloading.

Results: From May 2021 to December 2023, 37 patients aged between 60 and 98 years were treated : 27 with cHDR BRT, 5 with iHDR – BRT, 3 with iHDR – BRT plus cHDR BRT 16 patients with primary BRT, 12 patients with adjuvant BRT and 7 patients with palliative/cytoreductive BRT, for a total of 40 lesions, with the following histological types: basal cell carcinoma, squamous cell carcinoma, pleomorphic sarcoma, Merkel cell carcinoma. The fractionation schemes used were the following: 45/40 Gy in 9/8 fractions, 35/30 Gy in 7/6 fractions, 50 Gy in 10 fractions bid.Three patients had acute G3 toxicity with resolution within three months. Thirtyfour patients are currently in the absence of local recurrence. Four patients died of causes unrelated to the oncological disease in the absence of local recurrence.

Conclusions: cHDR BRT and or plus iHDR- BRT is a safe and effective therapeutic option well tolerated for elderly patients with NMSC with good results in terms of toxicity and local control disease.

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EVALUATION OF RESPIRATORY MOTION IN LUNG CANCER SBRT USING 4D CBCT WITH NO EXTERNAL SURROGATES

Code: 85

Aims: The study aimed to compare the use of 4DCT scans with external surrogates to determine respiratory motion against the use of 4D-CBCT, which directly assesses internal anatomy and diaphragm motion without surrogates, in lung Stereotactic Body Radiation Therapy (SBRT).

Methods: A cohort of 6 lung SBRT patients underwent 4DCT simulation using a tension belt to generate breathing traces. 4DCT scans without contrast media, with 2 mm-thick slices and selected pitch values based on patients' breathing rates, were acquired. A retrospective phase-binning reconstruction in 10 phases defined Internal Target Volume (ITV) as the envelope of Gross Tumor Volumes (GTVs) delineated on each breathing phase, with the Planning Target Volume (PTV) defined as ITV with a 5-mm isotropic expansion. VMAT 6 MV-FFF single-isocenter SBRT plans were optimized for the Versa HD linac. During the first treatment session, a 4D CBCT scan using Elekta Symmetry protocol was acquired for dual registration image matching. An experienced Radiation Oncologist (RO) evaluated positioning deviation in the spinal region (clipbox registration), followed by mask registration to correct motion deviation around the ITV. Clipbox and mask data were analyzed to evaluate baseline shifts. Quantitative evaluation of target definition and volume differences employed a MIM-automated workflow on both 4DCT and 4D CBCT images, checked by the same RO. ITV volume differences and relative centroid position variations (ΔCP) between the two methods were recorded and analyzed.

Results: Results from 6 lung SBRT patients treated between September 2023 and October 2023 showed nearly negligible baseline shifts for upper lobe lesions, with a maximum of 1.9 mm, while a C-C shift of 11.2 mm was observed for a diaphragmatic tumor. Mean ITV volume delineated in 4DCT scans was 9.8 [1.2; 34.7] cm^3, while on 4D CBCT it was 11.9 [1.5; 38.6] cm^3, representing a mean 20.6 [-2.2; 56.0] % increase.
Only one patient exhibited reduced ITV delineation in 4D CBCT, while the diaphragmatic lesion's ITV increased by 56.0% at CBCT contouring. Mean L-L ΔCP was < 1 mm, A-P ΔCP was 1.6 mm, and C-C ΔCP was 2.1 mm, with a maximum of 9.5 mm for the diaphragmatic lesion.

Conclusions: In conclusion, these preliminary results suggest that 4D CBCT could offer a more accurate motion assessment than conventional surrogate-based 4DCT in lung SBRT. However, limitations such as poor CBCT image quality and a small dataset warrant further studies for confirmation.

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RT HYPOFRACTIONATION ON PROSTATE WITH SUPPLEMENT BASED OF GABA AND LEMON BALM FOR RELAXATION

Code: 128

Aims: Prostate cancer survivors experience physical side effects related to treatment and cancer that can impair emotional well-being for years after treatment, various fears about their health, anxiety, and frequent insomnia are common and often require treatment. We used a supplement based on GABA (SBGA) and lemon balm, used for relaxation and to normalize mood, during RT.

Methods: October 2022 to September 2023, 49 pts. prostate cancer pts. were enrolled in the following prospective study: RT on prostate scheduling 2.7 up to 70.2 Gy while simultaneously using supplement based on GABA (SBGA) and lemon balm useful for relaxation and normal mood. Before taking the supplements, pts. underwent clinical psychological interview to evaluate both the impact of disease on each of them and the degree of motivation for treatment. During interview, various fears emerged regarding their health status, states of anxiety and frequent insomnia. Study involved taking supplement three times a day from five days before centering CT scan and then throughout entire period of radiotherapy treatment.

Results: 49 patients, 8 (16.3%) were excluded because three were already taking antidepressant therapy and 5 because they refused (mandatory informed consent), 12 patients (24.4%) took SBGA only in days preceding Centering TC while 29 pts. (59.1%) continued to take it until end of treatment (TSBG). For this reason pts. were divided into two groups: 12 pts. who have undergone centering-CT therapy; 29 points who followed therapy for entire treatment. After a month from taking supplement at end of RT, pts. underwent administration of following tests:

- STAY-Y1-State Anxiety (assessing current state of anxiety); Range 40-50: mild, 51-60: moderate, > 60 severe form
- Zung Self-Rating Depression Scale (SDS) (assessing state of depression and level of severity); Range 25-49 normal range, 50-59 mildly depressed, 60-69 moderately, >70 severely depressed
- Pittsburgh Sleep Quality Index (PSQI) (evaluating sleep quality). Scores >5 Bad sleep, <5 Good sleep, >60 Severe

	12 Patients SGBA	29 TSGBA
Mild anxiety	58.30 %	89.65 %
Moderate/severe form of anxiety	41.60 %	10.35 %
Depression Scale (normal range)	83.40 %	93.10 %
Depression Scale (mildly range)	16.6 %	6.89 %
Bad Sleep (*)	83.30 %	55.17 %
Good sleep	16.6 %	44.82%

FRACTIONATED RADIOSURGERY FOR OPTIC NERVE SHEATH MENINGIOMAS: RESULTS FROM A SINGLE- ARM, PROSPECTIVE TRIAL

Code: 304

Aims: Optic nerve sheath meningiomas (ONSM) are rare benign neoplasms affecting the meninges surrounding the optic nerve. Despite their typically slow growth, the gradual compression of the pial vasculature often results in optic nerve dysfunction and irreversible visual loss. Available approaches for ONSM are observation, surgery, and radiotherapy by means of both conventional and radiosurgical approaches. The aim of this study was to evaluate the efficacy and safety of fractionated radiosurgery (fSRS) for ONSM, in terms of local control and toxicity, with a particular emphasis on preserving visual function.

Methods: The current study is an exploratory, single-arm prospective trial on patients diagnosed with ONSM treated by fSRS. Inclusion criteria were diagnosis of ONSM, visual impairment at presentation, radiological or visual dysfunction progression during the observation period. The histological diagnosis was not mandatory. The primary endpoint of the study was to assess the impact of fSRS on preserving visual function. This evaluation relied on the analysis of both visual acuity and visual field before and after treatment, over a minimum follow-up period of 5 years. The secondary endpoint focused on evaluating the efficacy of fSRS in terms of local control.

Results: Fifty patients diagnosed with ONSM underwent hSRS between February 2011 and February 2019. The mean age at the time of treatment was 50 years (range 19-78). Each patient received a dose of 25 Gy delivered in 5 fractions over 5 consecutive days, prescribed to the 77-91% isodose line (median 82%). The mean treatment volume was 2.57 cc (range 0.49-16.42 cc). The mean dose to chiasma and omolateral optic nerve, were 4.7Gy (range 1.5-11.6) Gy and 22.8Gy (range 8.3-28.5) respectively; while the maximum point doses were 15.4 Gy (2.3-26.6) and 28.6 Gy (20.1-32.5), respectively. After a mean follow-up of 74 months (range 3-142 months), 1 patient experienced a deterioration in visual function, 3 patients showed improvement, and 41 maintained stable visual function, including both visual acuity and visual field. No cases of radiation-induced retinopathies were observed. None of the treated meningiomas exhibited radiological progression during the follow-up period.

Conclusions: The results of the present trial show that fSRS delivering 25Gy in 5 fractions is a safe and effective treatment for ONSM patients. A longer follow-up and a larger population are needed to confirm these data.

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FRACTIONATED RADIOSURGERY FOR RESIDUAL/ RECURRENT NON SECRETING PITUITARY ADENOMAS: PRELIMINARY RESULTS OF A PROSPECTIVE STUDY

Code: 296

Aims: Single-session radiosurgery (SRS) can represent a viable option for patients with residual and recurrent non-functioning adenomas. Fractionated radiosurgery (fSRS) may be useful for larger adenomas or those located near to the optic pathways. However, due to the absence of long-term tumor control data, the suitability of this treatment schedule has to be confirmed. The aim of this study is to examine the safety and efficacy of fRS in this setting.

Methods: We carried-out this monocentric prospective exploratory study, focusing on patients with residual/recurrent non-functioning pituitary adenomas. Patients fulfilling the inclusion criteria (no prior cranial irradiation, absence of pregnancy, no contraindications for MRI or CT scans, and the ability to provide informed consent) were enrolled and treated with fSRS using CyberKnife technology (Accuray). The primary end-point of the study was to assess early and delayed toxicity concerning cranial nerves and post-treatment pituitary function. Secondary end-points were late toxicities, local control, and evaluation of patients' quality of life (QoL).

Results: From September 2020 to September 2023, 21 patients underwent fSRS for pituitary adenomas. All patients received a total dose of 25 Gy delivered in 5 fractions over 5 consecutive days. At the time of treatment, the average age was 52 years (range 20-74 years, median 55 years). The treated lesions had a mean volume of 10 cc (range 0.5-33 cc, median 6 cc). The maximum point dose to the chiasm varied from 6 to 32 Gy. The mean value of the maxiumum and the mean doses to the pituitary gland, when identifiable, were 24 Gy (range 14-31 Gy) and 19 Gy (range 6-28 Gy), respectively. Following a mean follow-up of 32 months (range 6-36 months), 1 patient experienced transient dysphagia and dysphonia, which was successfully treated with low-dose oral dexamethasone, and 4 patients required minor adjustments in their substitutive hormonal therapy. Overall, visual function remained stable, and none of the treated tumors showed progression during the follow-up period.

Conclusions: The current study suggests the safety of fSRS, as well as its efficacy in the short term. A long term follow-up is needed to confirm our results.

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PATTERN OF CARE FOR THE USE OF SRT FOR OLIGOMETASTATIC PATIENTS: THE CAMPANIA OLIGO-RT PROJECT

Code: 452

Aims: The landscape of cancer care has evolved significantly with the recent redefinition of oligometastatic disease, presenting a potential avenue for achieving prolonged disease control or even cure in a subset of metastatic patients through radiotherapy or surgery. In light of this, the AIRO Campania Regional society conducted a retrospective evaluation of patients who underwent stereotactic RT (SRT) in this context, aiming to elucidate key issues and disseminate knowledge regarding this approach.

Methods: Clinical and technical parameters of radiotherapy were analyzed for oligometastatic patients undergoing SRT between January 2019 and April 2022, and between May 2022 and December 2023. Additionally, toxicity, follow-up, regional control, distant metastasis, and overall survival were assessed.

Results: In timeshift 1, the majority of patients were referred for RT by Medical Oncologists, followed by multidisciplinary tumor boards and other specialists. In timeshift 2, there was a slight improvement in referral patterns, with 45 patients referred by Medical Oncologists, 52 by the MTB, and 13 by other specialists. SRT was predominantly directed to the brain, lung, bone, nodes, liver, or other areas. The majority of patients received systemic therapy during SRT, with a median prescription dose of 27 Gy (mean 29 +/- 10.4 Gy) and a median number of 5 fractions (mean 5 +/- 1.2, range 1-8 fx). Acute and subacute toxicity attributed to SRT were graded as G0 in 321 patients (73.6%), G1 in 97 patients (22.2%), G2 in 15 patients (3.4%), and G3 in 3 patients (0.6%). However, only a limited percentage of patients had a follow-up period exceeding 6 months after SRT, with a mean overall survival of 45 +/- 3.6 months (median not reached). Between the two time intervals, there was an increase in patients referred from the MTB and an increase in stereotactic ablative radiotherapy (SABR) for bone metastases, possibly due to emerging literature.

Conclusions: The findings of this project affirm the increasing utilization of SRT for oligometastatic patients, demonstrating a favorable safety and efficacy profile. However, enhanced communication within MTBs is warranted to extend this strategy to a larger patient population. Additionally, long-term follow-up of radiotherapy patients is crucial for comprehensively understanding late toxicity profiles and proposing salvage strategies upon disease recurrence.

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PROGNOSTIC FACTOR IN STEREOTACTIC RADIOTHERAPY FOR LIVER OLIGOMETASTASES

Code: 259

Aims: A large pooled real-world analysis of liver metastases treated by stereotactic radiotherapy (SBRT) was carried out.

Methods: Clinical and dosimetric data of patients who underwent stereotactic radiotherapy for liver metastases were used for an univariate (UVA) and multivariate analysis (MVA) in order to identify prognostic factor for Local Control (LC), Distant Metastases Free Survival (DMFS), Disease-Free Survival (DFS), Overall Survival (OS), and the Next Systemic Therapy Free Survival (NEST-FS) rates.

Results: Data of 113 patients (M/F: 49/64), accounting for a total of 150 hepatic lesions, that were treated between March 2006 and February 2023 in two Italian Institution were evaluated. More details on patient and lesion characteristics are reported in Table 1. Actuarial LC, DMFS, DFS, OS, and NEST-FS at one year were 75.8%, 37.7%, 34.9%, 78.7%, and 59.4% respectively; while actuarial LC, DMFS, DFS, OS, and NEST-FS at two years were 52.1%, 24.9%, 21.9%, 51.3%, and 36.8% respectively. In UVA for LC, complete response (CR), synchronous oligometastases, and favorable histology were statistically significant positive prognostic factors, as was the absence of treatment interruption. However, only the first three factors were confirmed at MVA. The UVA identified only synchronous oligometastases and favorable histology as statistically significant positive prognostic factors for DMFS and DFS, which was confirmed by the MVA. For OS, UVA demonstrated that CR, synchronous oligometastases, and favorable histology were statistically significant positive prognostic factors, all of which were confirmed in the MVA. For NEST-FS, UVA demonstrated that both CR and synchronous oligometastases were statistically significant positive prognostic factors. Avoiding treatment interruption was also found to be a positive prognostic factor. However, only the first two variables were confirmed in the MVA.

Conclusions: Stereotactic treatment for liver metastases seems to be a safe and promising treatment option, however individual patient characteristics, tumor biology, and treatment specifics should always be considered in clinical decision-making.

Patients	
113	
Lesions	
150	
Comorbidities	
Cardiopathy	40
Polmunary	4
Diabetes	11
Liver	2
Kidney	4
Other Tumour	4
Histology	
Colorectal	55
Breast	25
Lung	9
Ovary	11
Pancreas	21
H&N	4
Melanoma	9
Other	16
Oligometastases Status*	
Synchronus Oligometastatic Disease	16
Metacronus Oligorecurrence	15
Metacronus Oligoprogression	15
Repeat Oligorecurrence	15
Repeat Oligopersistence	8
Repeat Oligoprogression	19
Induced Oligorecurrence	6
Induced Oligopersistence	10
Induce Oligoprogression	46

* ESTRO/EORTC consensus on oligometastases classification

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POSTOPERATIVE RADIATION THERAPY IN THYMOMAS: ONCOLOGICAL AND TOXICITY OUTCOMES FROM A SINGLE INSTITUTION EXPERIENCE

Code: 532

Aims: Thymomas are rare mediastinal tumors, therefore recommendations on postoperative radiotherapy (PORT) are based mainly on retrospective data and its added benefit on oncological outcomes is still debated. Here, we evaluated oncological and toxicity outcomes from a single institution experience of patients treated with PORT after surgical resection of localized thymomas.

Methods: Patients who underwent surgical resection for thymomas and indicated for PORT were selected from medical records. Clinical data were extrapolated to evaluate overall survival (OS), progression-free survival (PFS) and radiation-related adverse events (AE). Data on radiation treatment delivered were also collected. Clinical, pathological and treatment characteristics were tested to evaluate correlation with PFS or toxicity.

Results: Twenty-eight patients diagnosed and treated from 2010 to 2022 were included in the present analysis. Median age at diagnosis was 60 years (range 27 – 80), 17 patients were male and 11 were female. After surgical resection, according to TNM 8th edition were considered: 12 patients with stage II disease, 11 stage III, 5 stage IV. Eighteen cases were reported as R0 resections, 7 R1 and 2 R2. Histological subtypes, when identified, were as follows: 1 AB; 6 B2; 17 B3. Median prescribed RT dose was 50 Gy (range 50 – 66) in 25 daily fractions (range 25 – 33). PORT was delivered with 3DCRT in 9 cases, VMAT in 12 cases, Thomotherapy in 7 cases. Most common acute toxicity reported was dysphagia (n=11), followed by cough (4), GERD (2), nausea (1), dyspnea (1), fatigue (1). All reported AEs were G1 but 2 cases of dysphagia and 1 case of dispnea were G2. No late toxicities were reported. At a median follow-up of 61.5 months, PFS rate was 71,4% with 8 PD, all local recurrences. Only 1 patient died due to progressive disease, with others alive with controlled disease. At UVA only higher pathological stage of disease resulted significant for words PFS, none of the other clinical, pathological or RT related variables tested resulted significant for PFS or AEs rates.

Conclusions: PORT is feasible and its favorable efficacy and toxicity profile is maintained with modern RT-techniques. Our rates of local control, considering the high-risk population selected, accounting also for selection bias due to small numbers and retrospective nature, confirm the need for local postoperative therapies in selected patients and further studies are needed to better understand high-risk factors besides pathological staging.

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RETROSPECTIVE ANALYSIS OF QUANTIB PROSTATE BENEFIT FOR MP-MRI DIAGNOSIS AND THERAPY ON RADIOTHERAPY PLANS FOR PROSTATE CANCER PATIENTS: A SINGLE CENTER EXPERIENCE

Code: 468

Aims: The aim of this retrospective analysis is to assess the benefit for diagnosis on mpRMI and for therapy, especially for coverage evaluation on RT plans after MRI revision of intraprostatic lesions detected by Quantib®Prostate system, version 2.1.1. (Quantib B.V. Rotterdam, The Netherlands).

Methods: We evaluated 15 patients treated with moderate hypofractionated RT or SBRT (70 Gy/28 fr, 60 Gy/20 fr, or 36.25 Gy/5 fr) with intermediate-to- very high-risk prostate cancer. The patients treated with 60 Gy/20 fr or with SBRT were managed with intraprostatic fiducials. All patients were staged with pre-RT MRI. The Quantib Prostate artificial intelligence is an FDA and CE-approved MRI viewing and reporting platform based on deep learning, so it can help the Radiologist in identification of intraprostatic target lesions suspected as disease. This system

Table 1.

Prescription Dose	Number of patients	D95% coverage	D98% coverage
70 Gy/28 fr	12	58.7 Gy min - 70.7 Gy max	57.9 Gy min - 70.7 Gy max
60 Gy/20 fr	1	59.3 Gy	59.3 Gy
36.25 Gy/5 fr	2	36.6 Gy min - 39.6 Gy max	36.7 Gy min - 39.5 Gy max

was not available at our hospital at the time of diagnosis for most patients. It was decided to review these MRI with this system, then to evaluate the coverage of these lesions on the previous RT plan. Contouring was performed without MRI fusion for moderate hypofractionated RT and with fusion-imaging for SBRT. The Radiologist carried out the analysis without consider the report previously produced to avoid bias for 13 patients. In 2 patients Quantib was used at MRI diagnosis.

Results: A total of 26 lesions were identified in 15 patients. In two cases Quantib failed to detect the lesions previously identified: these were in the transitional zone, where Quantib has the greatest difficulty in detection. However, the remaining lesions were anatomically related to those previously identified and there was almost a complete congruence in most patients. We also appreciated the benefit of Quantib in contouring capsular peripheral lesions. The coverage of intraprostatic lesions was optimal in all prescriptions (Table 1).

Conclusions: The analysis shows how this system can help the identification of intraprostatic target lesions on MRI. The difficulty noticed in detecting TZ lesions is to be related to this version of software, because it mostly uses DWI to consider an area at risk and the most important MRI sequence for the TZ evaluation is the T2-weighted scan. The review of RT plans confirms optimal coverage of target volumes therefore Quantib, at this time, could be useful to plan simultaneous integrated boost with higher accuracy in non-transitional intraprostatic lesion. These are preliminary results and a more detailed analysis is necessary.

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PET/CT-BASED RADIOMIC SIGNATURE PREDICTS EARLY PROGRESSION OF LOCALLY ADVANCED PANCREATIC CANCER

Code: 372

Aims: The aim of the study is to investigate the value of radiomic features derived from pre-treatment 18F-FDG PET/CT images of the primary tumour for predicting early progression in patients with locally advanced pancreatic cancer (LAPC).

Methods: Of one hundred and four patients with histologically proven LAPC treated with initial chemotherapy followed by curative chemoradiotherapy (CRT) at our institution between July 2013 and May 2021, a secondary analysis with baseline 18F-FDG PET/CT was performed in fifty-seven patients. Clinical factors such as semiquantitative PET parameters including standardized uptake value (SUV), metabolic tumour volume (MTV) and total lesion glycolysis (TLG) were also reported. Early progression (EP) was defined in time as progression at the first assessment, 3 months after the start of treatment. EP was assessed by CT scan, resulting in a dichotomous label of progression. A 3D volume of interest (VOI) was placed over the primary tumour. Lesions were manually delineated. Three families of hand-crafted features were extracted from the VOIs of each patient's images, from both CT and PET acquisitions, quantifying grey intensity and tissue texture. The final dataset was then constructed by adding clinical data from each patient. The prediction pipeline consisted of a feature selection phase followed by a sequence of two cascading decision trees, where the second uses the predictions of the first as additional features for sample prediction and optimising the binarization threshold for classification in the training phase, to be applied later in the testing phase. The whole system follows a tenfold cross-validation approach. The quality of the proposed model was assessed using receiver operating characteristics (ROC) and area under the ROC curve (AUC).

Results: Figure 1 shows the final performance. To the best of our knowledge, this is the first study on the feasibility and hypothesis generation of a radiomic strategy to predict early progression in LAPC and our data suggest that a specific signature can be identified (AUC 0.83; prediction accuracy 80.7%).

Conclusions: This model, based on pre-treatment clinical and PET/CT radiomic features, can predict early progression in LAPC patients. It could be a promising non-invasive pre-treatment approach to help clinicians assess the risk of early progression in patients individually, thus enabling personalised treatment and better clinical outcomes. The external validation dataset is currently being identified.

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HYDROGEL SPACER REDUCES RECTAL DOSE DURING VOLUMETRIC MODULATED ARC RADIOTHERAPY FOR PROSTATE CANCER: A MONO-INSTITUTIONAL DOSIMETRIC ANALYSIS

Code: 518

Aims: Radiation toxicity remains a significant challenge in prostate cancer radiotherapy (RT), due to the proximity of the rectum and other structures to the prostate. Injecting SpaceOAR hydrogel (OAR = organs at risk) prior to prostate RT can reduce the radiation dose to the rectum, thereby improving rectal side effects. Aim of this study is to evaluate the association between SpaceOAR and radiation dosing and toxicity vs no spacer in moderately hypofractionated treatments of prostate cancer.

Methods: We evaluated dosimetric data to OARs during moderately hypofractionated RT for low and intermediate risk prostate cancer. Patients were divided in the group with the spacer and the group without the spacer. Both groups included patients with similar pretreatment characteristics. Primary endpoint was the evaluation of rectal dosimetry in each group; we used V30, V57, V60 and mean rectal dose. Secondary endpoint was the evaluation of acute and late rectal toxicity, according to the CTCAE toxicity scale. Data were analyzed with Wilkoxon Mann-Whitney test. Both groups received RT in 20 fractions of 3Gy. All treatments were planned with volumetric modulated arc radiotherapy (V-MAT).

Results: We evaluated 18 patients with spacer and 20 patients without spacer, treated between 2020 and 2023 at our department. The presence of a spacer reduced all dosimetric parameters, with a statistically significant advantage in V30 (19.5% vs 32.6%, $p<0.001$), V57 (5.0% vs 12.4%, $p<0.001$), V60 (2.2% vs 4.5%, $p<0.001$) and mean rectal dose (1781 cGy vs 2294 cGy, $p=0.005$) in spacer group and no-spacer group respectively. No significant difference was found in acute and late rectal toxicity, with a mean follow-up of 11 and 6 months in spacer group and no-spacer group respectively.

Conclusions: Our experience confirmed that spacer hydrogel significantly improves rectal dosimetry. The clinical impact of this dosimetric gain in terms of acute and late toxicity must be evaluated in a larger sample with a longer follow up.

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PHASE II TRIAL OF MULTIFRACTION RADIOSURGERY IN GLIOBLASTOMA PATIENTS: PRELIMINARY RESULTS

Code: 73

Aims: Glioblastoma (GBM) is the most common primary brain tumor, with survival rates still among the lowest, especially for patients who have not undergone complete resection surgery.
In this preliminary analysis, we aim to evaluate the safety and effectiveness of a multifraction radiosurgery (SRS), a radiotherapy regimen that is different from the standard, in patients with a primary diagnosis of glioblastoma and post-surgical residual tumor.

Methods: From January 2021 to July 2023, 12 adult patients were enrolled. The main inclusion criteria were subtotal resection with a tumor volume ≤60 cc (approximately 5 cm maximum diameter) and a maximum PTV of 150 cm^3.
Target was defined on volumetric MRI as follows: GTV consisted of the tumor resection cavity and residual enhancing tumor; CTV was defined by adding a 3-5 mm margin to the GTV; PTV was the same as the CTV. Patients received fractionated radiosurgery treatment delivering 30 Gy (6 Gy/fx) in 5 fractions over 5 consecutive days, followed by adjuvant temozolomide. Tretment was delivered with CyberKnife (Accuray) technology.
Follow-up consisted of physical examination, MRI, and EORTC-C30 and HADS questionnaire after 45-60 days and then every 2 months. FET-PET and advanced MRI sequences were integrated at progression (PD) in selected cases.

Results: The median follow-up was 10 months (range 4-33). PD occurred in 10 patients (7 marginal, 2 outfield, and 1 both). Median PFS was 5.5 months (range 1-17). At 6 months, the PFS rate was 50%. At time of analysis, 4 patients were alive at 35, 25, 11, and 6 months, 2 without signs of progression. The OS rate at 12 months was 66.7%.
Events possibly or definitely related to radiation treatment were reported in 7 patients (58.3%): 5 (41.7%) were acute (within 4 months) (2 grade 1, 2 grade 2, 1 grade 3 according to CTCAEv5), and 2 were late (16.7%, both grade 2). Of these, 4 had regression of the symptoms, and 3 had stabilization. Radiation necrosis was registered in 3 patients (25%): 1 asymptomatic and 2 regressed with bevacizumab.

Conclusions: Current literature does not clearly define the role of SRS in GBM. Our study proposes an SRS protocol in a particularly disadvantaged GBM subpopulation: those patients with post-surgical residual disease and IDH-wild type status. Preliminary results appear promising in terms of PFS and OS with an acceptable level of toxicity risk. Exploring integration with advanced imaging techniques will be analyzed.

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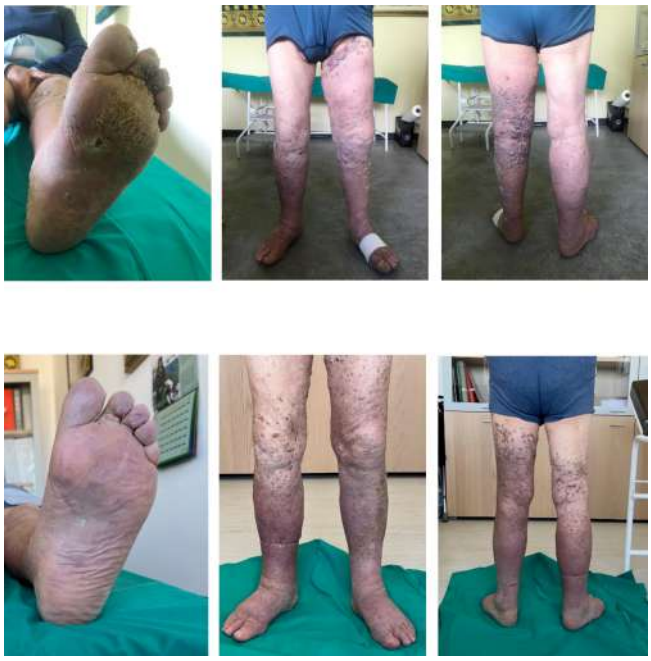
ROLE OF PALLIATIVE RADIATION THERAPY IN NON-HIV ASSOCIATED KAPOSI'S SARCOMA - COMPLETE RESPONSE TO RADIATION: A CASE REPORT

Code: 426

Aims: Kaposi's sarcoma (KS) is a rare adult lymphatic endothelial cell neoplasm caused by human herpes virus 8. Although it commonly affects human immunodefiency virus (HIV) positive patients (pts), there have been some HIV negative cases reported. HIV-negative Kaposi's sarcoma (HNKS) usually presents on the skin of lower extremities and it has an indolent nature. KS is considered a radiosensitive tumor and excellent palliation of symptoms can be achived by radiation therapy (RT) with more than 90% response and 70% complete remission. Optimal radiation dose is uncertain. Good palliative results and local control were demonstrated with doses higher than 20Gy. The choice of treatment modalities is based on the extent and distribution of cutaneous disease and depth of lesions.

Methods: A 80 years old man with a long history of NHKS was treated three times in our RT Departement since 2021. He presented with painful widespread dermatosis with maculopapular, nodular, violaceous lesions on his legs and ulcerated lesions on his left foot. These cutaneous lesions were associated with edema and limited ambulation.
RT was delivered prescribing a total dose of 30Gy in 10 fractions to left foot, left knee and right leg, respectively.
Planned target volume was defined from the skin surface to a costant depht of 1cm.
Given the complex shape, the multifocal left foot lesions were treated dipping of the extremity in the water using an acryl box in order to improve dose homogeneity and reproducibility of alignment.
Volumetric modulated arc therapy was preferred to treat the very extensive lesions of left knee and right leg in order to ensure an adequate target coverage and high bone sparing. Each tratment was performed with 6MV photon beams and 0.5cm bolus application.



Results: The median follow-up was 25 months (range 12-31). Complete response was observed to left foot 10 months after RT and it remained tumor free-status at the last follow-up. Partial response was recorded to lower extremities.
Symptoms relief was achieved in all cases with improved mobility and complete disappearance of pain.
No grade 3 or 4 acute skin toxicity was reported. Late toxicity was limited to grade 1 and consisted of skin hyperpigmentation and dry desquamation.
No in-field progression was reported.

Conclusions: RT is an effective and useful treatment modality to improve the quality of life in pts with NHKS, often representing the optimal local therapy for palliation of pain, bleeding or edema. RT is well tolerated with minimal toxicity.

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RETROSPECTIVE MONOCENTRIC STUDY OF STEREOTACTIC BODY RADIATION THERAPY IN THE MANAGEMENT OF HEPATOCELLULAR CARCINOMA

Code: 410

Aims: The role of Stereotactic Body Radiation Therapy (SBRT) is growing in the management of hepatocellular carcinoma (HCC), mainly due to recent advances in imaging technology and radiation delivery. SBRT is the treatment of choice for HCC patients (pts) not eligible for other locoregional treatment modalities due to factors such as comorbidities and frailty. The aim of this retrospective analysis was to evaluate the efficacy and safety of SBRT in pts treated at our institution.

Methods: Twenty-four pts with HCC were treated between June 2021 and June 2023. Seventeen were males and 7 females with a median age of 78.5 years (range 61-89 years). In 17 pts 1 lesion was treated while in 7 pts 2 lesions were treated concomitantly or sequentially, for a total of 31 lesions treated. The volume of GTV ranged from 0.968 cm3 to 13.167 cm3 with a median volume of 5.32 cm3. Radiation prescription dose

ranged from 37.5 Gy to 50 Gy (median 40.87 Gy) in 3 to 7 fractions. Prior to treatment pts underwent a CT simulation with intravenous contrast using abdominal compression. SBRT was delivered with VMAT technique and use of Cone Beam CT with online correction for all fractions.

Results: The median follow-up for current analysis was 15 months (range 6-30 months). After treatment all pts were planned for restaging with CT or MRI at 3-4 months. Eight pts had evidence of extrahepatic progression before or at restaging. Out of the 26 lesions treated and restaged, 15 showed a complete response, 8 showed a partial response, 2 were stable and one progressed locally. The 2-year overall survival rate was 70%. The treatment was well tolerated by all pts and no significant acute or late adverse effects were observed.

Conclusions: Stereotactic body radiation therapy is a safe, effective and non-invasive treatment option for patients with HCC who are not eligible for other loco-regional treatment modalities. The 2-year survival rate of 70% in our series is encouraging since the majority of pts had advanced age and/or significant comorbidities precluding surgery or other relatively invasive treatment options.

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LYMPH-NODAL OLIGOMETASTASES FROM PROSTATE CANCER: DIFFERENT OUTCOMES AND PATTERN OF RELAPSE BETWEEN PELVIC AND PARA-AORTIC DISEASE

Code: 323

Aims: Lymph-nodal metastases from prostate cancer (PC) are differently treated according to their site: pelvic are locoregional lymph-nodes, instead positive lymph-nodes above aortic bifurcation are considered as distant metastases. Aim of the study was the evaluation of differences between oligometastatic para-aortic disease and pelvic disease. We report the retrospective data of a cohort of PC patients who received SBRT for lymph-nodal pelvic or para-aortic metastases

Methods: Inclusion criteria were: diagnosis of oligometastatic para-aortic or pelvic lymph-nodes from PC; primary tumor previously treated with radical intent; no extra-nodal disease. Patients with de novo metastatic disease were excluded. All lymph-nodes were treated with SBRT and diagnosed through PET (PSMA or choline). The two cohorts were compared for survival analyses; pattern of recurrence was evaluated too. A propensity score matching (PSM) was applied to create comparable cohorts. Primary end point of the study was the progression-free survival (PFS) between the two cohorts. Secondary end-points were biochemical relapse-free survival (BRFS), androgen deprivation therapy-free survival (ADTFS), polymetastatic disease-free survival (PMFS), local progression-free survival (LPFSC) and pattern of relapse.

Results: Between 2012 and 2022, 240 lymph-nodes in 164 patients were in three different radiotherapy institutions. 127 patients had a pelvic disease and 37 had a para-aortic disease. Median follow up was 37. Median RT dose was 35 Gy in 5 fractions. Median PFS was 20 and 11 months respectively in pelvic and para-aortic group (p=0.07). No statistically significant differences for ADTFS or PMFS were detected. The cumulative 5-years LPFS was 90.5%. Patients treated on pelvic disease recur to the pelvis again in 51.8% cases, while those treated on para-aortic nodes in 12.9% cases (p=0.0006). The absolute rate of subsequent distant metastases was not significantly different between para aortic and pelvic lymph nodes (38,7% versus 26%; p=0.07). At PSM, no statistically significant differences for all the study end-points were detected.

Conclusions: Patients affected by para-aortic disease might have PFS comparable to pelvic disease at the matched analysis. Local control in our cohort is high in both para aortic and pelvic lymph nodes. The results of the present study further support the use of SBRT also to para aortic metastases with the aim to delay ADT start, or eventually prolong its duration.

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ONLINE ADAPTIVE SALVAGE RADIOTHERAPY WITH INTEGRATED PET PSMA-GUIDED DOSE ESCALATION BOOST AFTER RADICAL PROSTATECTOMY: ACUTE TOXICITY ANALYSIS

Code: 530

Aims: After radical prostatectomy, if there is a biochemical recurrence (PSA > 0.20 ng/ml), standard salvage radiotherapy to the entire prostate bed is required. The integration of cone-beam computed tomography (CBCT) provides a way to adapt to daily anatomical variations in organs at risk (OAR), like the bladder and rectum. This adaptive approach holds promise for optimizing OAR sparing, facilitating dose escalation, and implementing hypofractionation treatments.
The aim of this study is to describe the use of online adaptive techniques for the delivery of salvage radiotherapy.

Methods: The first four patients with macroscopic recurrence in the prostate bed, validated through PET PSMA imaging, treated at our Institute were selected. The radiotherapy field includes the prostate bed with 66 Gy in 33 fractions and a simultaneous integrated boost to the PET PSMA lesions with 72.6Gy), delivered with a Varian ETHOS linac with 6 MV-FFF energy. The CTV to PTV margins were set at 7 mm and 5 mm posteriorly for the prostate bed and 3 mm for the PTV boost.
The adaptive workflow includes CBCT scans, focusing on delineating OAR and target structures. The attending physician ensures rigid transfer and modifies all the contours as necessary. Manual adjustments to boost targets precede automated software reoptimization of the treatment plan, which is performed in real-time. No patients received hormonal therapy despite high PSA levels.

Results: The cumulative doses delivered to the target, rectum, and bladder were analyzed for the adapted plans. The targets received a dose comparable to the planned one, with significant reductions in V45 Gy and V60 Gy for the rectum (-23.2% and -71.2%, respectively) and the bladder V65 Gy (-38.9%). Clinical toxicity was minimal, with genitourinary acute toxicity was G1 in two patients and G0 in the other two. Gastrointestinal symptoms were absent (G0), even in patients with boosted lesions near the rectum.

Conclusions: Online adaptive techniques have shown feasibility and promising outcomes in sparing organs at risk and minimizing toxicity in salvage radiotherapy. Further studies with larger cohorts are needed to validate and refine adaptive strategies for enhanced efficacy. This approach has the potential to personalize post-prostatectomy biochemical recurrence management.

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Patient	Age	Gleason Score	Histological Exam	PSA at biochemical recurrence	Hormonal therapy
1	73	8 (4+4)	pT3b pN1	0.61 ng/ml	no
2	67	7 (3+4)	pT2 pNx	5.81 ng/ml	no
3	61	8 (5+3)	pT3b pN0	3.06 ng/ml	no
4	72	7 (3+4)	pT3 pN0	0.28 ng/ml	no

RADIOTHERAPY DOSE INTENSIFICATION CONCOMITANT TO CAPECITABINE AFTER INDUCTION CHEMOTHERAPY FOR LOCALLY ADVANCED PANCREATIC ADENOCARCINOMA: EARLY RESULTS

Code: 261

Aims: We previously showed that the delivery of 44.25 Gy in 15 fractions (frs) concomitant to capecitabine (CAPE) after induction chemotherapy (CHT) for locally advanced pancreatic cancer (LAPC) was feasible and effective with acceptable toxicity. Recent studies suggest that the delivery of biological effective dose (BED) ≥ 100 Gy improves local control; however the optimal "safe" dose remains unknown. Within an Institutional trial aimed at safely escalating the dose within the 15 frs context, we herein report our early results referred to a cohort of LAPC patients (pts) receiving 50 Gy in 15 frs concomitant to CAPE.

Methods: Consecutive pts with unresectable LAPC after induction CHT were considered. All pts underwent 4D simulation contrast-enhanced computed tomography (4D-CT) and FDG-PET/CT. Primary tumor was defined as GTV, contoured at least on four 4D-CT series and merged to create ITV. PET positive volumes were merged with ITV and isotropically expanded of 0.5 cm to generate PTV1. CTV was defined as the portion of pancreas containing the lesion (head, body or tail). PTV2 was defined as CTV plus margins of 1.0 cm in axial e 1.5 cm in cranial-caudal directions, respectively. Duodenum and stomach were contoured on 4D-CT and expanded of 3 mm to create their corresponding PRVs. A dose of 44.25 Gy in 15 frs was prescribed to the overlap between PTV1 and PRVs, 50 Gy to the remaining PTV1 and 37.5 Gy to PTV2. Constraints derived by a published analysis on 254 pts treated at 44.25 Gy were for stomach: D0.03cc<45, V44<2cc; for duodenum: D0.03cc<47Gy, V44<9cc). Concomitant CHT was CAPE 1250 mg/day.

Results: From May 2021 and August 2023, 22 pts were treated. Median follow-up was 19.73 months. Median number of induction CHT cycles was 6. All pts completed RT-CHT. No pts experienced ≥G3 GI acute toxicity, 1 pt had G3 lymphopenia. No late toxicity occurred. Two pts did not receive induction CHT and 2 pts were lost, thus 18 pts were evaluable. Twelve pts had a progressive disease, 4 of them local only, 7 distant only and 1 both local+distant. 13 patients died. Median PFS and OS, calculated from the start of induction CHT, were 13.87 and 21.83 months, respectively. Median LPFS was not reached; local control at 1 and 2 years was 80% and 63%.

Conclusions: The current regimen of hypofractionated RT is feasible with an acceptable rate of toxicity, providing PFS and OS rates comparable to a standard schedule. Furthermore, local control is encouraging. The study is ongoing.

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CYTOKINES ANALYSIS IN METASTATIC BULKY TUMOUR TREATED WITH LATTICE RADIOTHERAPY TECHNIQUE: PRELIMINARY RESULTS OF PROSPECTIVE MULTICENTRIC STUDY

Code: 465

Aims: To evaluate radiation-induced cytokines in patients submitted to palliative "metabolism guide" LATTICE irradiation.

Methods: Patients with histologically proven metastatic disease with bulky masses were included. Inclusion criteria were age >18 years, >5 cm solid lesions (bulky disease), availability of 18F-FDG CT/PET, and life expectancy >70% at 30 days (Risk Group PaP score); patients with clinical diagnosis of superior vena cava syndrome, extradural spinal compression, and severe bleeding were excluded. The radiation treatment provided for a median irradiation dose of 15 Gy in a single fraction to "Vertex" (Vs) and hypofractionated radiation therapy to GTV with at least 20 Gy in 4 fractions. Blood samples (Two EDTA of 6 mL BD Vacutainer®) are collected at pre-establishing time points: Time 0 (T0, before Vs treatment), Time 1, (T1, 24 h after Vs treatment) and Time 2, (T2, at the end of the treatment). 22 cytokines from plasma are assessed: IL-2, IL-4, IL-6, IL-10, IL-12, IL-13, IL-15, CCL-2, IFN-γ, TNF-α, TGF-β and VEGF (Figure 1).

Results: Up-to-date five patients (3 male and 2 female), were recruited. All patients had contrast-enhanced CT and 18F- PET/CT. At the T0 5/5 patients showed high blood cytokines levels: VEGF, CCL-2, IL6, IL10, IL15, TNFα, TGFβ and IL4. At the T1, 24h after Vs treatment, IL10 and IL15 had a relative increase. At T2, 5/5 patients showed high level of INF, IL12, IL13, TGF-β and IL2 (Figure2).

Conclusions: These preliminary results confirm that LATTICE technique stimulates cytokines secretion. More accurate results could emerge by increasing the data.

Figure 1 shows a summary schema for the trial.

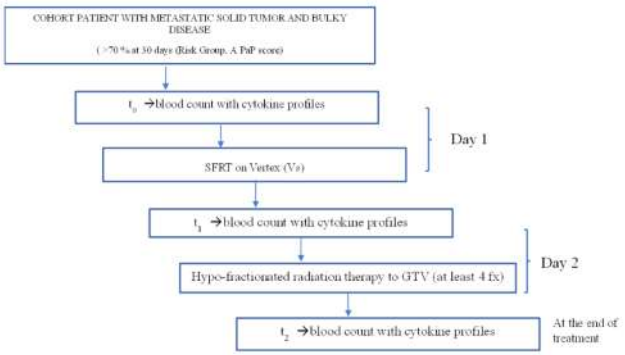

Figure 2

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MAGNETIC RESONANCE-GUIDED STEREOTACTIC BODY RADIOTHERAPY (MRGSBRT) FOR NODAL RECURRENCE IN OLIGOMETASTATIC SETTING: A RETROSPECTIVE SINGLE-INSTITUTION STUDY

Code: 145

Aims: Oligometastatic disease (OMD) is a clinical condition were patients (pts) have a limited number of metastases. Ability of MRgSBRT to deliver high doses to metastatic site with minimal damage to the surrounding tissue makes it a promising treatment option for pts with OMD. This retrospective single- institution study aimed to evaluate the feasibility and clinical benefit (CB) of MRgSBRT for nodal recurrence in OMD.

Methods: We collected data from pts underwent MRgSBRT for oligometastatic nodal recurrence at our institution. The primary objectives were to determine the 1-year progression-free survival (PFS) and local progression- free survival (LPFS) and 3-years overall survival (OS) rate. The objective response rate (ORR) included complete response (CR) and partial response (PR). We defined clinical benefit (CB) as the achievement of ORR and stable disease (SD). Additionally, we assessed toxicities according to the CTCAE v.5.0 scale.

Results: Between July 2017 and May 2022, 88 pts received MRgSBRT, 30 pts having more than one lesion, 5 of them have subsequently undergone to MRgSBRT for another nodal recurrence. Therefore, a total of 130 metastatic lesions were treated. Table 1 summarize patient characteristic. According to Guckenberger's OMD classification [1,2], 25 pts were metachronous OMD, 55 pts were repeat OMD and 8 induced OMD. Features of lesions and treatment details were reported in Table 2. Mean prescribed dose (dmean) to PTV was 40 Gy (25-60) in 4-8 fraction, with Biologically equivalent dose (BEDa/b10) dmean of 85 (range 37-136). CR and PR as well as SD were observed in 80 (61,5%), 28 (21,5%) and 11 (8%) of lesions, respectively, with an overall CB rate of 87,5% and an ORR of 75%. At a median follow up of 24 months (range 2-51) OS rates at 1, 2 and 3-years were 100%, 98% and 95%, respectively. The 1-year PFS rate was 48%. The 1-year and 2-year LPFS was 95% and 93%, respectively. A significant association between biologically equivalent dose (BED) > 70 and better OS was observed ($p < 0.01$). The prognostic factors associated with a worse outcome were ovarian cancer ($p = 0.02$). No acute or late toxicities were reported.

Table 1. Patients charateristic

patients charateristic	
	N (%)
All	88
Age at the cancer diagnosis	
Median (range)	62 (37-84)
Age at MRgSBRT	
Median (range)	66 (38-88)
Gender	
Male	32 (36%)
Female	56 (64%)
Eastern Cooperative Oncology Group performance status	
0	65 (74%)
1	21 (23,7%)
2	2 (2,3%)
Primary diagnosis	
ovary cancer	40 (46%)
uterine cancer	10 (11%)
prostate cancer	20 (23%)
colorectal cancer	5 (6%)
pancreas cancer	1 (1,2%)
breast cancer	2 (2,3%)
lung cancer	3 (3,5%)
other	7 (8%)
Hystotipe	
Adenocarcinoma	32 (36%)
Squamos carcinoma	7 (8%)
other	49 (56%)
Guckenberger OMD classification	
synchronus oligometastatic disease	0
metacronus oligorecurrence	23 (26%)
metacronus oligoprogression	2 (2,3%)
Repeat oligorecurrence	25 (28%)
Repeat oligopersistant	7 (8%)
repeat oligoprogression	23 (26%)
Induced oligorecurrence	6 (7%)
induced oligopersistance	1 (1,2%)
induce oligoprogression	1 (1,2%)
N. patients undergoing chemotherapy before MRgSBRT	
yes	60 (68%)
no	28 (32%)
N. patients undergoing chemotherapy after MRgSBRT	
yes	47 (53%)
no	36 (41%)
NA	5 (6%)
N. patients undergoing target therapy or immunotherapy after MRgSBRT	
yes	17 (19%)
no	67 (76%)
NA	4 (5%)
N. patients undergoing radiotherapy after MRgSBRT	
yes	35 (40%)
no	49 (55%)
NA	4 (5%)

Table 2. Features of lesions and treatment details (N=130).
*Calculated on the number of patients (N=88)

Features of lesions and treatment details (N=130)	
Anatomical district	
Thorax	17 (13%)
Abdomen	74 (57%)
Pelvis	38 (30%)
N° of pts bearing *	
1 lesion	58 (66%)
2 lesion	21 (24%)
3 lesion	6 (7%)
4 lesion	1 (1%)
5 lesion	2 (2%)
N° of pts underwent second MRgSBRT	5 (6%)
PTV (cc)	
Median, range	9,5 (1,2-66)
Total Dose, Gy	
Median, range	40 (25-60)
N° of fraction	
Median, range	5 (4-8)
Dose/fraction Gy	
Median, range	8 (5-10)
Dose normalizzation	
80% isodoses	92 (71%)
target mean	38 (29%)
BED $\alpha/\beta 10$	
Median, range	85 (37-136)
Adaptive treatment	
yes	76 (59%)
no	53 (41%)
Breathing control	
FB	74 (57%)
BHI	56 (43%)

Conclusions: MRgSBRT for nodal metastasis represents a viable treatment option in various oligometastatic settings and for variety of primary diagnoses. Tolerance is good, reporting no toxicity levels and experiencing a satisfying CB. Further prospective studies are needed to confirm these results and to assess the long-term survival and quality of life of patients.

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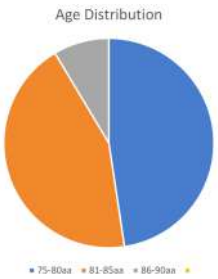
GERIATRIC ONCOLOGY OF HEAD AND NECK AND LUNG CANCER: ELDERLY PATIENTS MAY RECEIVE RADICAL TREATMENTS? OUR EXPERIENCE

Code: 464

Aims: The primary aim is to choose the best tolerated external beam radiation treatment option in older adults with locally lung and/or head and neck advanced cancer. Aging is associated with physiological changes and comorbid illnesses, which may affect an individual's tolerance to radiation. An increase in acute effects or a lowered functional tolerance has been reported in older patients (pts).

Methods: From January to December 2023 we evaluated 105 pts, older than 75 years, affected by lung and/or head and neck advanced cancer. To select candidates for radical treatments, we choose to use G8 score. It consists of seven items from the Mini Nutritional Assessment (MNA) questionnaire and age. G8 allowed us to stratify elderly patients as a function of the physiological status. Patients were stratified according to their baseline G8 score: <11 as 'vulnerable', 11-14 as 'intermediate', and >14 as 'fit'. In treated pts G8 questionnaires were collected also at 4-6 weeks, and at 2-3 months post-treatment.



Results: 51% of pts were 'vulnerable', 37% were 'intermediate', and 12% were 'fit' at baseline. Pts with score >14 underwent radical treatment as younger adults, patients with score < 11 underwent palliative treatment or supportive care. In 'intermediate' pts a more comprehensive evaluation is needed. They underwent geriatric evaluation with nutritional and social support for 1 month before registered another G8 score, in order to try to modify the baseline score. The 30% of intermediate pts had score increment up to 'fit', the 70% decreased to 'vulnerable' score during the interval time. For patients that underwent active treatment, radical or palliative, weekly CTCAE (ver 5) toxicity score was collected.

Conclusions: In 'fit' pts median score toxicity didn't differ from younger pts. In 'vulnerable' pts toxicity was as expected by palliative radiation therapy regimen. G8 geriatric assessment is a useful score in clinical practice, to decide treatment protocol for elderly patients with advanced head and neck and or lung cancer.

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ENHANCING PANCREATIC CANCER CARE IN THE ELDERLY: ASSESSING THE EFFICACY AND SAFETY OF STEREOTACTIC BODY RADIOTHERAPY

Code: 219

Aims: Patients with pancreatic cancer have a poor prognosis, and the disease is often diagnosed in elderly patients who may not be candidates for surgery or chemoradiation approach due to their comorbidities.
Stereotactic body radiotherapy (SBRT) is a novel approach in the treatment of pancreatic cancer and our study aims to evaluate its efficacy and its safety in elderly patients.

Methods: SBRT was administered according to three schedules using the VMAT technique: 30 Gy in 5 fractions, 35 Gy in 5 fractions and 45 Gy in 5 fractions according to the tolerance of the adjacent normal tissues. Data were collected retrospectively and the statistical analysis was performed for overall survival (OS), progression-free survival (PFS), local progression-free survival (LPFS) and metastasis-free survival (MFS). Local control was the primary endpoint and it was assessed by CT scan or 18F-FDG PET-CT scan. In addition, to assess the safety, acute and late toxicities were assessed for safety using the CTCAE version
5.0 scoring system.

Results: The population study consisted of 26 patients (9 men and 17 women) enrolled between July 2018 and May 2023, with a median age of 77 years (range 58 - 90 years). Pancreatic disease was defined as resectable or borderline resectable in 20 patients (77%) and unresectable in six cases (23%). Fifteen patients (57.8%) were unfit for surgery due to comorbidities and five patients (19.2%) refused surgery.
In the population, 20 patients (77%) were treated with 30 Gy in 5 fractions (600 cGy/die), 5 patients
(19.2%) with 35 Gy in 5 fractions (700 cGy/die) and one patient (3.8%) with 45 Gy in 5 fractions (900 cGy/die).
Median follow-up was 11.4 months (range 0.5 – 25.6 months). Among the 26 patients, the median PFS was 26.1 months.
The one-year and two -year PFS rates were 79% and 60%, respectively. The median LPFS was 33.3 months, with one-year and 2-year LPFS of 86% and 70%, respectively. The median MFS was 29.6 months, and one-year and two-year MFS rates were 85% and 79%, respectively. The median OS was 30 months, with one-year and two-year OS rates of 78% and 57%, respectively.
There were no acute toxicities with SBRT, while late toxicities were observed in only 2 patients (7.7%), including one pancreatic fistula (grade 3) and one duodenal stenosis (grade 3).

Conclusions: In our experience, SBRT is an effective and safe therapeutic approach in elderly patients with pancreatic cancer, with an impressive local control rate and no significant toxicities.

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VOLUME CHANGES DURING IRRADIATION OF HPV-RELATED OROPHARYNGEAL CANCER

Code: 577

Aims: Our study aims to describe changes in volumes of interest including PTV High Dose, parotid glands, masticatory, paravertebral and sternocleidomastoid muscles in patients affected by HPV-related squamous cell oropharyngeal cancers (OPC).

Methods: Patients with histologically proven HPV-related squamous cell OPC were included in the study.

All pts received radiotherapy treatment in both adjuvant and radical setting, using VMAT technique and acquiring daily positioning Cone-Beam-CT (CBCT). Median delivered radiotherapy dose was 66 Gy [50-70 Gy].
Most of pts received concurrent chemotherapy with platinum compounds, according to stage and risks factors.
The contouring, according to international guidelines, was performed for masticatory muscles (masseter and pterygoid) on the first CT slice showing the bilateral mandibular notches; and for paravertebral and sternocleidomastoid muscles on the first CT slice identifying the entire vertebral arch of C3.
Radiological volumes of PTV-High Dose, parotids and muscles were collected on simulation CT and on last CBCT. Weight was recorded at the beginning and end of treatment.
Data were collected retrospectively and the statistical analysis was performed for variation in PTV, parotids and muscles volume.
Acute toxicities were assessed for safety using CTCAE scale (version 4.03).
Clinical response was assessed using CT/PET-CT according to RECIST/PERCIST criteria.

Results: The population study included 27 pts with a median age of 64 years [53-86y], treated from August 2020 to September 2023.
18 pts (66.7%) were treated with radical intent while 9 pts (33.3%) received adjuvant treatment. 22 pts (81.5%) received concurrent chemotherapy.
With a median FUP of 12 mo. we experience only 1 Local Recurrence and 1 pt had a systemic progression. 21 pts (77.7%) reached Complete Response and 4 pts (14.8%) had a Partial Response.
G2 and G3 toxicities were respectively observed in 4 pts (14.8%) and they consisted of odynophagia, dysphagia and oral mucositis
Median weight loss among pts is 5 Kg and mean differences between volumes of interest are shown in Table 1.

Conclusions: During radiotherapy for HPV-related squamous cell oropharyngeal cancers targets and OARs change significantly in volume. Individualised treatment resulting in plan adaptations could result in a clinically useful volume reduction.

Differences	Mean	95% Confidence Interval	p-value
PTV	7.79	[2.87 - 12.7]	0.003
Parotid Glands	10.56	[6.17 - 14.9]	0.000
Masticatory Muscles	1.17	[0.89 - 1.44]	0.000
Paravertebral and sternocleidomastoid muscles	4.34	[3.11 - 5.56]	0.000

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PROSTATE STEREOTACTIC BODY RADIOTHERAPY (SBRT) DELIVERED WITH 1.5T MR-LINAC OR CYBERKNIFE IN PATIENTS AFFECTED BY LOCALIZED PROSTATE CANCER: A PROPENSITY SCORE MATCHING ANALYSIS

Code: 444

Aims: To compare acute and late toxicity of prostate cancer (PCa) stereotactic body radiotherapy (SBRT) delivered by daily-adaptive MR-guided radiotherapy (MRgRT) with 1.5T MR-linac or robotic SBRT with CyberKnife (CK).

Methods: This is a multi-institutional analysis of 238 PCa patients treated with 5 fractions SBRT with the following doses: 35 Gy and 36.25 Gy delivered to low/favorable intermediate, and unfavorable intermediate/high risk, respectively. 120 (55.5%) patients were treated with MRgRT and 118 (49.5%) with CK at two Institutions. The primary end-point was acute toxicity comparison (minimum required follow-up 6 months). Toxicity assessment was measured by CTCAE v5.0 scale. Secondary end-point was late toxicity. A PSM analysis was performed by matching patients 1:1 by the following characteristics: prostate volume (threshold 50 cc), IPSS before SBRT (threshold 7), and total treatment dose (35 Gy versus 36.25 Gy).

Results: The population after PSM was represented by 150 individuals. The median prostate volume was 50 cc (range 20-113.5). The PTV margin was 5 mm in all directions and 3 mm posteriorly in both groups. In the CK, the median maximal dose administered to the CTV was 44.3 Gy (range 42.6-46.7), compared to 38.7 Gy in MRgRT. Globally, acute G1, G2, and G3 genitourinary (GU) toxicity occurred in 49.3%, 12%, and 2.7% cases, respectively. Acute G1, and G2 gastrointestinal (GI) toxicity occurred in 18%, and 6%, cases, respectively.
In the univariate analysis, MRgRT patients had a significantly lower acute GU toxicity (G1: 37.3% versus 61.3%, G2: 10.7% versus 13.3%; p=0.007), while G3 toxicity was 2.7% in both groups. Acute GI toxicity did not differ significantly (p=0.28). Late GU toxicity was significantly lower in MRgRT patients (G1 18.7% versus 50%, G2: 9.3% versus 10.6%, G3 2.7% versus 0%; p=0.000). There was no difference in late GI toxicity (p=0.39).
In the multivariate analysis (MVA), treatment technique was the only factor associated with acute (OR 2.645, 95%CI 1.099-6.365; p=0.02) and late (OR 4.578. 95%CI 2.063-10.162; p=0.000) GU toxicity. No factors were associated with acute and late GI toxicity in the MVA.

Conclusions: MRgRT using homogenous planning might be associated with lower moderate genitourinary toxicity. However, no significant differences in high-grade acute and late GU and GI toxicities were reported in both groups. Both techniques, prostate SBRT with 1.5TMR-linac or the CK, exhibit a satisfactory late toxicity profile with rare severe adverse events.

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FIRST CLINICAL APPLICATION OF COMPREHENSIVE MOTION MANAGEMENT ON PROSTATE RADIOTHERAPY USING HIGH-FIELD MR-LINAC

Code: 527

Aims: High-field MR-linac allows improved soft-tissue visualization of the tumour and the surroundings tissues. Furthermore, daily MR-imaging allows on-table adapted planning and real-time intra-fraction imaging without additional exposure to radiation. The recent implementation of Comprehensive Motion Management (CMM) guarantees more precise radiation treatments by interrupting the delivery when the target moves outside the defined position and enables radiation oncologist to perform target drift corrections. We report our first clinical experience on prostate adaptive RT with true tracking and automatic gating with high-field MR-Linac.

Methods: from September 2024, we treated 40 male patients affected by low-to-unfavorable intermediate prostate cancer. Patients were simulated with a T2-w MR that was used for contouring the target and the organs-at- risk. The GTV-to-PTV margins were 5 mm in all directions and 3 mm posteriorly. A 16-fields IMRT plan was prepared and daily adapted with adapt-to-shape workflow during every fraction. Patients were treated with SBRT (30 cases) with a dose of 35 Gy for low-risk and 36.25 for intermediate-risk, and hypofractionated RT with 60 Gy in 20 fractions. The motion management was set to deliver the treatment when 100% of the GTV was contained within the PTV. We collected details and times of all treatment phases.

Results: globally 350 treatment fractions were administered. The median on-table time was 34 minutes. The median delivery time was 17 minutes (range 15-20 minutes) with a median beam-on time of 14 minutes (range 13.5-17 minutes) and a median gating efficiency of 85% (range 82%-91%). Among the 350 delivered fractions only 4 drift corrections was needed and the baseline shift replanning lasted 1 minute. The patients performed all the sessions without any clinical issue.

Conclusions: daily-adaptive MR-guided SBRT to the prostate using Comprehensive Motion Management has been successfully implemented into clinical routine. The whole process is safe and completely automated even in the case on in-treatment corrections and baseline shift replanning. CMM could allow now a safe reduction of the treatment margins with a guided workflow to manage real tracking and gating.

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DELAYED CONTRAST MRI, PERFUSION MRI, AND 11CMETCTPET, TO ASSESS RESPONCE IN RADIATION THERAPY TREATED BRAIN TUMORS

Code: 215

Aims: Treatment effects (TE), in irradiated primary or metastatic brain tumors, are recorded in up to 25-30% of cases. Perfusion MRI is the most methodology used to distinguish TE from tumor progression (TP). More recently delayed contrast MRI, that through contrast clearance analysis (CCA) allows to calculate high resolution maps called “treatment response assessment maps” (TRAMs) would seem overcome limitation of perfusion MRI. We prospectively evaluated patients with doubtful framework between TE and TP aiming to assess ability of CCA in differentiate these two conditions in a cohort of treated brain tumor patients.

Methods: TRAMs were calculated through CCA by subtracting ceT1MRI images acquired 5 minutes after contrast injection from images acquired at least 60-105 minutes after. Diagnosis of TP was based on presence of contrast clearance (CC) region in blue, and TE on contrast accumulation (CA) region in red. Data of CCA were compared to perfusion MRI. TRAMs were generated and at last the calculation of effective volume of viable tumor tissue (CC region) and treatment-induced tissue changes within each lesion (CA region) have been calculated.

Results: From February 2021 and December 2023, 110 patients, for 184 delayed-contrast-MRI, underwent CCA and perfusion-MRI. Among these 27 underwent 11CMETPET, and 36 received surgical resection. Thirty- two were treated for newly diagnosed or recurrent glioma, and 78 for BMs. Significantly increased rCBV value in CC regions compared to CA was observed (p=0.01). Patients with TP showed significantly greater CC that subjects with stable disease or partial response 33% vs 78% (p=0.01). TRAMs metric were in agreement with perfusion results.

Greater accuracy of TRAMs compared to perfusion-MRI in discriminate TE from TP 81% vs 69% has been observed. 11CMETPET observations were in agreement with perfusion MRI and TRAMs in 85% of cases while histopathological confirmed according to imaging has been recorded in all patients underwent surgical resection. This observation confirmed the need of the histology data to validate CCA tool.

Conclusions: In our experience CCA tool compared to perfusion MRI had greater accuracy in discriminating true TP from TE, and can be of improvement in patient management. The employ of CTPET using amino acid tracers needs further investigations. Finally, to validate CCA tool, the histopathological confirm is advisable, and should be carried out in all patients.

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PARTIAL CHEST WALL REIRRADIATION FOR SKIN RECURRENCE OF LEFT BREAST CANCER: A CASE REPORT

Code: 389

Aims: Approximately one-third of all breast cancer (BC) patients experience local recurrence (LR) of their tumor after initial treatment. At present, the standard surgical approach for the treatment of LR BC is mastectomy. Reirradiation (RI) may be a component of locoregional therapy for isolated LR, with curative or palliative purposes. We report our experience with a BC partial RI and we report the associated toxicity and clinical outcomes.

Methods: A 52 years old woman with invasive ductal carcinoma (CDI)of the left breast performed in 2018 quadrantectomy with left axillary lymphadenectomy (pT1cN2a ER80%, PgR80%, ki67 36%, Her2 0). Adjuvant chemotherapy (CT) with EC for 4 cycles+Taxol for 12 cycles was performed. Between December 2018 and January 2019 radiotherapy (RT) on left breast with tangential fields of photons (6/15 MV) at a total dose of 50 Gy with conventional fractionation and with an electron boost of 10 Gy was performed and a total dose of 46 Gy were delivered at supra/infraclavicular nodes. Hormonal therapy with Exemestane and LHRH Analog was somministrated until May 2021 when a recurrence appeared on surgical scar (biopsy: CDI G3, triple negative). A CT with CMF (6 cycles) from August 2021 to January 2022 was performed. In March 2022 PET scan showed persistence of the skin nodules. In April 2022 the patient underwent simple mastectomy (Histology: multiple focus of CDI G3, triple negative, PDL1< 1%). In May 2022 started of CT with Eribuline.

Results: The patient was referred to our radiation department in Barletta in August 2022 for new appearance of skin nodules on the medial part of left chest wall (LCW). From September 2022 to October 2022 a RI of the skin nodules was delivered at the total dose of 50 Gy with 9 MeV electrons. Dose constraints to heart and left lung were respected. During treatment, acute dermatite G1(according to CTCAE v 4.0 scale) was reported, while no grade 3 or 4 toxicity was observed. After irradiation, patient started therapy with sacituzumab and govitecan. In March 2022 there was a clinical complete response on the LCW, confirmed by PET scan. At last follow up in November 2023, there were no skin nodules on the LCW, but patient showed progression disease with appearance of bone and nodal metastases.

Conclusions: By our experience, BC RI is feasible, with acceptable morbidity, permitting a long local control of skin disease and allowing to continue systemic therapies.

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SALVAGE RE-TREATMENT OR LOCAL RECURRENCE OF PROSTATIC CARCINOMA AFTER PRIOR IRRADIATION: A SINGLE CENTER CLINICAL EXPERIENCE

Code: 86

Aims: We evaluated the efficacy and safety of stereotactic body radiation therapy (SBRT) retreatment after an initial treatment course of radiotherapy (RT) for patients (pts) with biochemical failure and evidence of local recurrence in prostate cancer (PC).

Methods: From May 2019 to May 2023, 18 pts with evidence of clinical/radiological local relapse in the prostate or prostatic bed and no distant metastasis were retreated with SBRT. Local relapses were assessed with pelvic multiparametric MRI or PSMA/choline PET in 44% and 56% of pts, respectively. The precedent radiotherapy was delivered in 14 pts as adjuvant/salvage RT and 4 pts as radical treatment RT. At recurrence, median prostate-specific antigen (PSA) was 1.02 ng/mL (range, 0.15-1.9) in the 11 patients treated with postoperative RT and 3.5 ng/ml (range, 2.3-5.4) in patients treated radically. An androgen deprivation therapy was administered in 8 pts at the time of SBRT. The median time interval between the two treatments was five years (range 1-8). The median SBRT dose was 36 Gy (range, 25-36) in 5 consecutive fractions (range 5-6). Salvage SBRT was delivered using volumetric arc therapy (VMAT) and image-guided radiotherapy (IGRT) (Elekta Versa HD™).

Results: After a mean follow-up of 19.5 months (range, 1-24 mo), no patients had gastrointestinal and genitourinary toxicity early and/or late ≥ G3. The median age at salvage SBRT was 79 years (range,
71-87), median post-salvage SBRT PSA was 0.1 ng/mL (range, 0.0-1.1) in the adjuvant/salvage RT group and 2.75 ng ml (range, 1.8-4.2) in the radical treatment RT group. Five pts had a clinical relapse: 3 lymph nodes and two bone metastases, all outside the radiotherapy target. These patients underwent a second course of SBRT, and there is no radiological evidence of disease.

Conclusions: Our experience shows that salvage SBRT is an effective and safe treatment option, despite the small sample examined, allowing good control disease without severe toxicity.

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ELDERLY PATIENTS WITH GLIOBLASTOMA: MANAGEMENT OF SAFETY AND QUALITY OF LIFE

Code: 84

Aims: Glioblastoma is characterized by a poor prognosis in the elderly, with a median survival of less than two years. Survival increases when chemotherapy is added to radiation therapy among patients 70 years.

Methods: We analyzed the tolerance profile and quality of life of elderly patients treated in our center with glioblastoma treated with hypofractionated radiotherapy and concomitant temozolomide. The patients received either radiotherapy alone or radiotherapy with concurrent and adjuvant temozolomide.

Results: Fourteen pts were analyzed from January 2020 to December 2023 (M/F: 8/6). The mean age is 75.4 years (65-87). Ten pts operated totally or sub-totally, and 8 pts had MGMT promoter methylation. Eight pts received hypofractionation radiotherapy (40 Gy in 15 fractions) alone, and eight pts received hypofractionation radiotherapy with concurrent and adjuvant temozolomide. Overall survival was higher in patients who received temozolomide in addition to radiotherapy (21 months vs 15 months), as was progression-free survival (6 months vs 3.8 months). Quality of life was comparable in patients who received radiotherapy alone and those who received combined treatment and was analyzed using the EORTC QLQ-C30 questionnaires for cancer in general and the EORTC QLQ-BN2 questionnaire specific for brain tumors. In 8 pts, it was necessary to activate psychological support for the patient and caregivers. Hematological toxicity was found in 9 pts taking temozolomide and cortisone but was acceptable.

Conclusions: In our experience with elderly patients with glioblastoma, adding temozolomide to short-term radiotherapy confirmed an increase in overall survival compared to radiotherapy alone with acceptable safety profiles and tolerance

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LIGHT QUALITY MODULATES THE ANTIOXIDANT PROPERTIES OF MICROTOM FRUITS: A PILOT STUDY TESTING THE RADIOPROTECTIVE EFFECT ON HUMAN CELLS

Code: 341

Aims: This study explored whether two light-quality regimes, that is fluorescent white (FL) and red-blue (RB), further increased the concentration of antioxidant compounds in tomato fruits and tested in vitro their radioprotective properties on normal human cells exposed to ionizing radiation (IR) in the form of 6MV photons as used in cancer radiotherapy (RT).

Methods: In this work, immortalized normal breast epithelial MCF10A cells were used. To evaluate the putative radioprotective properties of tomato fruits grown under RB and FL light conditions, extracts were obtained and tested at two final concentrations, 100 (g mL^{-1}) and 200 (g mL^{-1}). The cells were incubated for 24 h before radiation exposure with the tomato extracts and then irradiated by the Synergy Agility LINAC (ELEKTA) at Istituto Nazionale Tumori IRCCS Fondazione G. Pascale. Doses used were: 0, 0.5, 2 and 4 Gy. IR-induced genotoxic damage was assessed using the Cytokinesis-Block Micronucleus (CBMN) assay. In cythochalasin B-induced binucleated cells: DAPI-stained micronuclei (MN), originated from lagging chromosomes or chromosome fragments failing to be incorporated into either of the two daughter nuclei were scored at a Zeiss epifluorescence microscope. As photons act prevalently by generating DNA-damaging reactive oxygen species (ROS), the levels of (ROS) were also evaluated using the CellRox kit run on an Attune NxT acousting focussing flow cytometer.

Results: As for MN frequency, the FL extract appeared to exert a radioprotective action at the higher concentration (200 μg ml^{-1}) at all photon doses, but to a lesser extent than the RB one. Conversely, at the lower concentration (100 μg ml^{-1}), the FL extract manifested radioprotection

only at the highest dose, that is 4 Gy. On the other hand, RB exerted significant radioprotection at both concentrations at all radiation doses. As for the ROS assay, the concentration used was 200 μg ml^{-1}. Both extracts seem to protect cells from IR-induced elevationof oxidative stress, with RB exhibiting particularly notable protection.

Conclusions: Light growth conditions affect the level of antioxidant phenols in tomato fruits, which in turn lead to significant radioprotection in normal cells. In particular, RB tomato plants have an overall increased antioxidant capacity compared to the FL condition.

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DOSIMETRIC COMPARISON AMONG VMAT, CYBERKNIFE AND RADIXACT FOR THE LOCALIZED PROSTATE CANCER

Code: 337

Aims: One of the most important techniques to treat the localized prostate cancer in SBRT regime is the CyberKnife, nevertheless this accelerator is not widely spread throughout the national territory. This study aims to compare if SBRT is achievable by means of VMAT-FFF and Radixact. Such objective was pursued by comparing the dose distribution, OARs sparing and beam on time.

Methods: To this study CT images of patients treated in our Institute were selected. CyberKnife tracks fiducials implanted inside the prostatic gland that are imaged during the dose delivery, therefore the prostate can be followed with high accuracy. A similar tracking method is possible by Radixact, thus on the same CT images Radixact treatment plans were computed. Finally, SBRT was simulated with a classic LINAC in VMAT-FFF mode. With FFF modality a steepest dose gradient is achievable. VMAT-FFF patients' group were imaged with an ultrasound probe (Clarity) in position: such device allows to reduce the PTV expansion. Treatment plans were computed with the following prescription 36.25 Gy in 5 fractions, moreover, to compare the different modalities, plans have been normalized to reach the same coverage.

Results: For the comparison, dose values coming from plans computed with the same technique were averaged. The V_{5Gy} and V_{10Gy} result smaller with Radixact and VMAT-FFF with respect to CyberKnife, this is due to the different dose delivery modality: cylindrical geometry vs a star-shape dose distribution. Such peculiarity is also able to explain the dose differences in the bowel and the rectum. An important difference is evidenced for the dose delivered to the penile bulb: the VMAT-FFF delivers the highest one, this is due to the presence of the probe that pushes the bulb close to the prostate. The conformity index is statistically higher for CyberKnife, whereas Radixact shows the lowest homogeneity index, and the gradient index is comparable for the three techniques. The beam on time for the VMAT- FFF plans was the lowest one.

Conclusions: The SBRT represents an important and effective treatment chance for the localized prostate cancer. SBRT is commonly performed with the CyberKnife but as evidenced in this work, if there are not some specific indications due to anatomical patient's condition, SBRT is realizable also by Radixact and VMAT-FFF. Thus, SBRT can be applied also in smaller centers which are equipped with classic LINAC.

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IMPACT ON SURVIVAL OF THE PET-CT RESPONSE AFTER RADICAL RADIOTHERAPY TREATMENT IN CERVICAL CANCER

Code: 166

Aims: Locally advanced cervical cancer is typically treated with chemo-radiotherapy (CRT), a regimen known to enhance local control and survival rates. In the management of locally advanced cervical cancer, 18F- fluorodeoxyglucose (FDG) positron emission tomography – computed tomography (PET/CT) has become integral in the initial assessment of disease extent. With additional insights from FDG-PET, adjustments to radiation treatment volumes can be made, allowing for the safe delivery of higher doses to FDG-positive lymph nodes. This study aims to assess the role of FDG-PET/CT in predicting the response to radiotherapy treatment.

Methods: We evaluated 41 patients eligible for curative radiotherapy (RT) for cervical carcinoma, from October 2015 to March 2023. Among them, 19 received Volumetric Modulated Arc Therapy, 16 underwent Tomotherapy, 4 were treated with 3D conformal RT, and 2 underwent Intensity-Modulated Radiation Therapy. All patients underwent pre-treatment Positron Emission Tomography with integrated CT (PET- CT) using [18F]-FDG, and a similar PET-CT was conducted post-treatment, using the same equipment throughout. FDG-PET was utilized to assess treatment response three months after completing CRT. The data were analyzed using Kaplan-Meier estimation to calculate the probability of long-term overall survival.

Results: Analysis of SUV values derived from pre and post PET-CT revealed a complete response (RC) in 20 patients, a partial response (RP) in 17 patients, and disease progression (PD) in 4 patients. Kaplan-Meier analysis of the collected data showed that, for cases of RC with normalization of tumor uptake in the first PET post-RT, overall survival at 12, 36, and 60 months was 100.0%, 92.3%, and 79.1%, respectively. For
cases of RP, overall survival at 12, 36, and 60 months was 92.3%, 71.2%, and 44.5%, respectively. In instances of PD, overall survival at 12 months was 75.0%.

Conclusions: The integration of PET-CT into the radiotherapy treatment is beneficial for evaluating response, proving to be a valuable tool in predicting long-term survival outcomes. Our data suggest that the PET-CT response evaluated a few months after the conclusion of radiotherapy treatment is a valid indicator of tumor regression. An early complete response, observed at the first follow-up examination, has a positive impact on overall survival.

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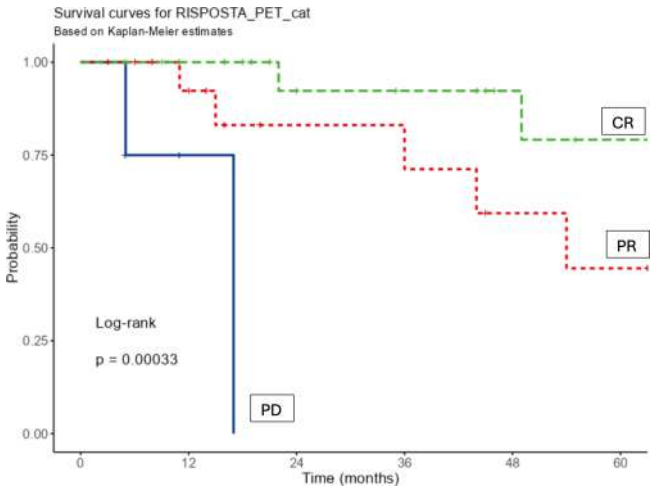

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PALLIATIVE RADIOTHERAPY FOR PANCREATIC CANCER

Code: 137

Aims: Pancreatic cancer, often considered untreatable, is frequently accompanied by significant abdominal pain and symptoms.
This study aims to characterize the symptomatic impact on pancreatic cancer patients undergoing palliative radiotherapy, along with their symptomatic responses.

Methods: A retrospective review was conducted on patients diagnosed with pancreatic adenocarcinoma and referred to our hospital between 2013 and 2022. A descriptive statistics analysis was implemented.

Results: 68 patients were identified, of which 25 received palliative treatment. Among them, 12 were male and 13 were female, with a median age of 67 years (range 51-83). Most patients had intermediate health status (ECOG score 2), had received one line of chemotherapy or none, and were in pain. The most common radiotherapy prescription was 30 Gy in 10 fractions, with 2 patients receiving only palliative stereotactic radiotherapy (36 Gy in 6 fractions) and two patients receiving SBRT as early salvage treatment. Pain decreased on average by three points from baseline to eight weeks, leading to a reduction in opioid intake, with a significant decrease in pain occurring within the first three weeks.Treatment toxicity was graded as 1-2 in 47% of cases, with only one case of grade 3 toxicity.
The median survival was 12 months (range 1-54).
Tumor size, radiation therapy dose, and previous chemotherapy did not predict symptomatic response or prolonged survival.

Conclusions: In this cohort examining palliative radiotherapy in pancreatic adenocarcinoma, radiotherapy effectively decreased pain and was generally well tolerated. Further research on the efficacy and optimal prescriptions for palliative radiotherapy in this population is needed.

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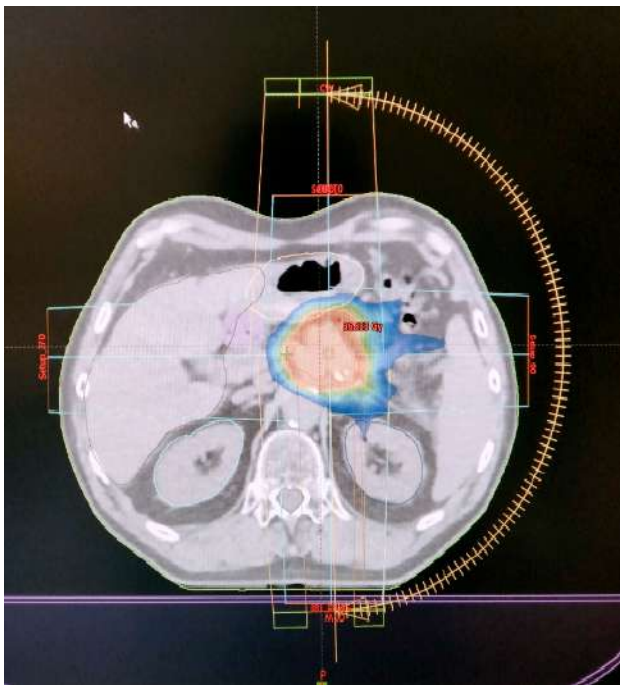

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EVALUATION OF ESTIMATED RISK FOR IPSILATERAL LUNG SECOND TUMORS IN VMAT COMPARED TO 3D-CRT FOR ADJUVANT BREAST RADIOTHERAPY

Code: 68

Aims: The VMAT technique exposes healthy organs close to the target to low diffuse doses, which increase the risk of developing a second cancer.
We investigated the risk of ipsilateral lung (IL) second tumors in VMAT adjuvant breast radiotherapy technique compared to 3D-CRT one.

Methods: We reviewed the radiotherapy plans of the patients treated on right breast from September 2022 to September 2023 at our center. Thirty-five VMAT plans targeting the whole breast with a simultaneous boost to the surgical bed (40.05Gy/15fx and 48Gy/15fx respectively) and 37 3D-CRT plans with sequential surgical bed boost (40.05Gy/15fx to the whole breast and 10Gy/4fx for sequential overdose), were analyzed: we collected the dose-volume histograms (DVHs) of the IL, to study the effect of the different dose distribution.
In order to illustrate the effect of the dosimetric variations in term of second cancer risk we calculated the organ equivalent dose (OED), for both groups, of IL using linear, linear-exponential and plateau models for second cancer risk and then the excess of absolute risk (EAR) using Schneider and Walsh formula.
Finally we linked the EAR (liner-exponential model) with Dmean, related to each treatment plans, using the Spearman correlation coefficient.

Results: In VMAT plans group we report an increased risk of secondary tumors quantified by changes in the EAR parameter (VMAT values is 2 times higher), as reported in Figure 1a. This recorded increase, based on the data available in the literature to date, remains within limits considered justified since no increase in cases of radiation-induced tumors has been observed for patients treated with these doses.
As reported in Figure 1.b, we putted all the EAR (calculated by linear-exponential model) and Dmean for each IL in a graph to find a relationship easily applicable in the study of the treatment plan. For the data collected, this relationship could be non-linear (Spearman correlation coefficient $r=0.80$ p-value<0.001). In the hypothesis of an exponential relationship between EAR and Dmean, we can quantify approximately 23% increase in EAR per Gray. According to the Dmean analyzed, that comply with AIRO Clinical Best Practice 2022 limits, this increase remains within acceptable limits.

Conclusions: According to literature, our study confirmed that VMAT technique in the right breast radiotherapy, concerning the increased risk of secondary tumors IL, could be a valid alternative to 3D-CRT if the AIRO constraints are respected.

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COMPARING TOXICITY IN SOFT TISSUE SARCOMA (STS): PREOPERATIVE RADIO-CHEMOTHERAPY (RTCT) VS RADIOTHERAPY (RT) ALONE

Code: 381

Aims: Pre-operative RT represents a cornerstone in the treatment of STS, despite an increased risk of wound dehiscence when compared to postoperative RT (landmark trials report rates of up to 25%). The addition of preoperative concurrent chemotherapy has been considered to enhance tumor response prior to surgery, although concerns have been raised regarding potential increase in toxicity, surgical complications and treatment interruptions. A matched cohort analysis was conducted in STS patients to assess differences in terms of toxicity, complications and margin status between the RTCT group and the RT alone group.

Methods: Each patient in the RT group was paired with a patient in the RTCT group based on similar age, tumor size, and location in a matching process. Radiotherapy was administered at a dose of 50 Gy in 25 fractions. Chemotherapy consisted of three cycles of Epirubicin-Ifosfamide every 21 days. Clinical and treatment data were collected. The incidence of acute skin toxicity, graded according to the CTCAE v 5.1, along with rates of wound complications and RT interruptions, was compared between the two groups using the Chi-square test.

Results: Eighty-four patients were included, 42 in the RT group and 42 in the RTCT one. Median age was 55 (range 19-83). The use of RTCT was associated with FNCLCC grade 3 disease at diagnosis ($p<0.001$). All patients successfully completed the preoperative treatment regimen

and underwent wide excision, resulting in an R0 resection in 90% of cases (n=77). Acute skin toxicity of grade 2 and 3 was observed in 18 (21%) and 5 (6%) patients, respectively. Wound dehiscence occurred in 13 patients (15%). Treatment interruption was reported in 32 patients, with a median duration of 3 days (range 1-18). There were no statistically significant differences between the RT and RTCT groups regarding wound dehiscence (14% vs 15%, not significant), grade ?2 toxicity (22% vs 33%, not significant) and RT interruption (14% vs 18%, not significant). Furthermore, there was no correlation between the treatment arm and the rate of R0 resection (93% vs 87%, not significant).

Conclusions: Preoperative RTCT in STS patients eligible for surgery did not show increased acute toxicity profile, wound dehiscence or RT interruption. Given the low incidence of marginal resections, larger cohorts are necessary to evaluate the potential benefits of combined treatment in improving R0 resection rate.

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DEEP-INSPIRATION BREATH HOLD VS. FREE BREATHING RADIOTHERAPY IN PATIENTS WITH LEFT- SIDED BREAST CANCER AFTER CONSERVING SURGERY

Code: 429

Aims: The purpose of this study was to compare the distribution to PTV and organs at risk and the delivery time in deep-inspiration breath hold (DIBH) and free-breathing (FB) radiotherapy in patients with left-sided breast cancer undergoing adjuvant radiotherapy after breast-conserving surgery.

Methods: Twenty consecutive patients with left-sided breast cancer were enrolled in this study. Computer tomography scan in FB and BH were acquired for each patient. IMRT treatment planning was performed using Monaco TPS software. The prescription dose on left breast was 42,4 Gy in 16 fractions. OAR's dose constraints were based on "AIRO Breast Cancer Group Best Clinical Practice 2022 Update". Dose-volume histograms were analyzed for heart, left anterior descending coronary artery (LAD), and left lung.

Results: PTV coverage was comparable in both cases. In all cases the dose constraints to OAR were respected. The mean left lung dose (Dmean) for DIBH group was 2.83 Gy (range 1.98-3.92) vs. 2.76 Gy (range 2.09-4.89) in the FB group. The Dmean for heart in DIBH was 0.57 Gy (range 0.32-1.79), as compared to 0.87 Gy

	Free-breathing	DIBH
PTV $V_{44.52}$	1,75 (0,32-4,87)	1,54 (0,09-4,61)
PTV $V_{42,4}$	82,61 (79,08-85,06)	83,51 (76,97-88,79)
PTV $V_{40,28}$	94,28 (91,28-97,13)	94,77 (90,64-97,29)
left lung D_{mean}	2,76 (2,09-4,89)	2,83 (1,98-3,92)
left lung V_{25}	3,24 (0,74-4,82)	3,42 (0,91-4,93)
left lung V_{20}	4,12 (1,38-9,00)	4,2 (1,68-7,4)
left lung V_{16}	5,18 (2,18-10,24)	5,12 (2,56-8,34)
left lung V_8	8,61 (6,07-14,5)	8,72 (6,41-11,54)
left lung V_4	13,83 (11,24-20,75)	14,00 (11,54-16,79)
heart D_{mean}	0,87 (0,40-2,85)	0,57 (0,32-1,79)
heart V_{40}	0 (0-0,1)	0 (0-0)
heart V_{18}	0 (0-4,87)	0 (0-2,08)
heart V_8	0,27 (0-8,5)	0 (0-4,71)
LAD D_{mean}	3,23 (1,15-21,38)	2,11 (1,04-8,87)

(0.40-2.85) with FB. The LAD Dmean in the DIBH group was 2.11 Gy (range 1.04-8.87) and 3.23 Gy (range 1.15-21.38) in the FB group. In table 1 all dose values were shown. Delivery time in DIBH took about 2 minutes longer than for free breathing (9 minutes vs. 7 minutes).

Conclusions: In both cases the plans were clinically acceptable and OAR constraints were widely respected. DIBH treatments required more delivery time than FB treatments. A longer follow up is necessary to demonstrate whether the DIBH treatment is related to greater clinical benefits.

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CEMIPLIMAB – RADIOTHERAPY COMBINATION IN CUTANEOUS SQUAMOUS CELL CARCINOMA (CSCC) INOPERABLE-LOCALLY ADVANCED AND METASTATIC: SAFETY AND EFFICACY PRELIMINARLY PROFILE

Code: 176

Aims: Cemiplimab - the programmed cell death protein- 1 (PD-1) inhibitor - has been approved as first line treatment for patients with metastatic or inoperable-locally advanced cSCC. Radiotherapy (RT) has been shown to modulate the immunogenicity of tumor cells and potentially may improve efficacy of PD-1 inhibitors when delivered concurrently. To our knowledge, there is a lack of literature data among Cemiplimab and RT association and we report our experience.

Paz	sesso	SEDE	INIZIO CEMIPLIMAB	ULTIMO	N CICLI	INTERRUZIONE si= 1 No = 0	MOTIVO	MIGLIOR RISPOSTA
1	M	FRONTE, ASCELLA DX	24/05/2020	30/05/2023	50	1	RC (da maggio 21)	RC
2	F	TEMPORALE SX	03/08/2021	17/01/2023	21	1	RP	RP
3	M	LC dx	24/08/2021	02/01/2024	41	0	RP	RP
4	M	VERTICE	07/09/2021	29/03/2022	9	1	PD	RP
5	M	CUOIO CAPELLUTO	21/09/2021	14/02/2023	21	1	RC	RC
6	F	NASO	16/10/2022	13/06/2023	9	1	TOX	RC
7	F	FRONTALE	09/11/2022	29/11/2022	2	1	PEGGIORAMENTO PS	NA
8	F	CUOIO CAPELLUTO	18/09/2023	02/01/2024	5	0		SD

Paz	Dose totale/frazioni	Tecnica	acute Toxicity RTOG	ULTIMO ACCESSO	DECESSO si= 1, no= 0
1	30 Gy in 10 fr	Roentgen	G1	15/01/2024	0
2	20 Gy in 5 fr	FOTONI	G0	19/10/2023	0
3	60 Gy 24 fr - 50 Gy 20 fr	FOTONI	G2-3	02/01/2024	0
4	55 - 62,5 Gy 25 fr	FOTONI+Roentgen	G1	19/10/2023	0
5	30 Gy in 10 Fr	Roentgen	G1	11/09/2023	0
6	32,5 Gy in 13 fr	ELETTRONI	G2	18/10/2023	0
7	20 Gy in 4 Fr	FOTONI	GO	03/01/2023	1
8	12,5 Gy 5 fr e 20 Gy 5 fr	FOTONI	G0	02/01/2024	0

Methods: Between September 2020 and December 2023, 8 patients with diagnosis of metastatic or inoperable- locally advanced inoperable cSCC where treated with Cemiplimab in association to RT at Radiotherapy Department of Santa Croce e Carle Hospital, Cuneo, and at Radiotherapy Department of Michele e Pietro Ferrero Hospital, Verduno. Radiotherapy was administered to the site of inadequate therapeutic response both in the case of metastatic and locally advanced disease (5 patients) or immediately before or during Cemiplimab infusion (3 patients).

Results: All patients had an ECOG PS 0-2, sex distribution was 4 male and 4 female and others characteristics were summarizes in table 1. RT treatment doses varied from 12.5 Gy in 5 fractions to 62.5 Gy in 25 fractions, but the most used schedules were 20 Gy in 5 fractions and 30 Gy in 10 fractions. RT was delivered with electrons, MV and KV-X ray and during RT treatment Cemiplimab was not administrated. All patients completed RT, 25% of patients developed a cutaneous G2-3 RTOG acute toxicity while for the others no significant cutaneous acute toxicity was reported. 1 patient was lost at follow-up instead 7 patients were alive without toxicity and with controlled disease.

Conclusions: Our preliminarly experience suggested that the association Cemiplimab and RT is safety and efficacy for patients in relation to a good toxicity profile and a significant tumor response. Kurian J at all published in literature another similar clinical experience about 7 patients with the same conclusion about integration of RT and Cemiplimab. Data in-vitro suggested that PD-1 inhibitor may improved response to radiotherapy and probably in the future we could have indication of more tailored RT schedules and doses. Further literature data are needed but Cemiplimab and RT may become a valid therapeutic options for these setting of patients.

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RECTAL CANCER IN YOUGER PATIENTS: RETROSPECTIVE ANALYSIS OF AN UNCOMMON POPULATION

Code: 187

Aims: European (ESMO) and American (NCCN) guidelines for rectal cancer are not age-specific and literature on younger patients is still little and conflicting in results. To fill this gap in our knowledge, we investigated the impact of age and ESMO risk's groups on clinical outcomes of young LARC patients treated in the last 15 years.

Methods: LARC patients undergoing long course NCRT and surgery were divided into young (<50/55 years) and old (>=50/55 years). 2017 ESMO rectal cancer clinical practice guidelines were used to classify patients in different risk groups (very early, early, intermediate, bad, and advanced). A 3D conformal RT technique or IMRT was used. Surgery was performed with TME, PME or Hartmann. In the case of local excision, TAMIS, TEM, TAE, have been used. Uni- and multi-variate analysis were performed to identify predictive factors for OS, DFS, MFS and LC.

Results: 790 LARC patients were analyzed: 582 old and 208 young. Median FUP was 97.7 month. 89% of patients under 50 yo belonged to the bad or advanced risk groups with an equal division. In old patients, 83% belonged to the bad or advanced group with a clear dominance of the advanced risk class. OS at 5 and 10 years was 78.9% (IC 95% 75.9 – 82.1) and 65.2% (IC 95% 61.3 – 69.5), respectively. 3y and 5y OS resulted in 85% and 78% in the Under 50 group and 76% and 59% in the Over 50 group, respectively.
Univariate ESMO risk analysis showed a significant impact on OS ($p < 0.001$). In multivariate analysis OS decreases with increasing age and ESMO risk group ($p<0.001$). DFS at 2 and 5y in the entire population was 80.2% (IC 95% 77.3 – 83.3) and 70% (IC 95% 66.5 – 73.7), respectively. 55 yo was the cutoff age to significantly separate the two curves ($p = 0.02$). 2y and 5y DFS in both Under and Over 55 groups were 85.3% and 77.4% and 75.8% and 66.7%, respectively. In multivariate analysis, DFS decreases with increasing age and ESMO risk group ($p<0.004$). Metastatic patients at diagnosis represented 7.2% of patients under 50 years and 7.5% of those over 50, respectively. As for the DFS, the two curves separated significantly ($p = 0.009$) at 55 years of age with a prevalence of metastasis development in the older group.

Conclusions: Young patients with LARC seem to have a better survival outcome (OS, DFS and OS). ESMO risk group confirmed age as an important factor for survival benefits. A multicenter prospective study including genomic and clinical information, would be useful.

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TOTAL BODY IRRADIATION: TOWARDS 3D VMAT - A SINGLE EXPERIENCE

Code: 186

Aims: TBI is a technique used as part of the conditioning for allogeneic bone marrow or stem cell transplant due to the higher survival and lower relapse risk following TBI plus etoposide compared with chemo alone. To reduce the risk of side effects we created rival VMAT TBI plans to conventional 2D ones. Feasibility and first dosimetric results were evaluated.

Methods: From May 2023, 3D TBI plans using VMAT technique were created in 6 pediatric patients For the 3D plans, patients were simulated with a mask over the head and a full body vacuum bag for immobilization. Two patient's orientation (head-first and foot-first) 5mm slice thickness computed tomography (CT) images for the whole body of each patient were obtained. PTV was defined as the entire body contracted to 5 mm below skin. The aims were to deliver a uniform dose of 12 Gy to the PTV, limiting the mean lung dose (MLD) to < 9 Gy. Lung OAR was intended as the lung with a 1cm expansion into lungs organ to account for intra-fraction motion and ensure the full dose coverage of the ribs. Eclipse 15.6 TPS was used to optimize VMAT beams.PTV was split from the top of the skull to mid-thigh and from mid-thigh to feet. From 5 to 7 total isocenters were used to cover the whole-body. Each isocenter of the upper part of the body had 2 off-set 6 MV VMAT arcs rotating through 360° while in the lower part only one, was used. The width of the field was set to 40 cm and the field length restricted to a maximum of 20 cm with a 2 cm overlap region at the iso. The collimator was rotate to 90° for each of these off-set arcs. MU rate was set at 80 MU/min.

Results: TBI process timing and dosimetric parameters for the target and OAR were analyzed. D95% of the PTV was between 87% and 92% with a Dmax between 118% and 120%. MLD resulted between 7.5 Gy and 9.2 Gy. Each arch resulted in 150-180 MU. TBI process timing resulted higher than a 2-D treatment one for the simulation and planning part that required around 40' and 6 to 7 hours vs 20' and 40' in a 2-D conventional one, respectively. The total beam-on time was calculated around 20' as for a 2D conventional TBI delivery.

Conclusions: 3D VMAT resulted in a safe technique to create TBI plans. Patient's position during the treatment appeared more comfortable. Despite a higher planning time, a 3D VMAT technique let to be more aware of the dose distribution leading to the possibility to compare TBI treatments from different Institutions and to spare OAR, if necessary. Daily IGRT ensure a higher accuracy.

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SARCOPENIC OBESITY IN CERVICAL CARCINOMA: A STRONG AND INDEPENDENT PROGNOSTIC FACTOR BEYOND THE CONVENTIONAL PREDICTORS (ESTHER STUDY - AFRAID PROJECT)

Code: 422

Aims: Locally advanced cervical cancer (LACC) presents a significant treatment challenge, with about one-third of patients experiencing treatment failure post concurrent chemoradiation (CRT). Predictive models incorporating patient demographics, cancer stages, and recurrence risks are increasingly relevant for personalized treatment. Nutrition-related parameters such as body mass index (BMI), sarcopenia (SP), and sarcopenic obesity (SO) have been identified as potential prognostic factors, yet their comprehensive impact remains underexplored.

Methods: This retrospective study assessed the relationship between nutrition-related parameters and the prognosis of LACC in a cohort of 173 patients from the ESTHER study, treated from July 2007 to July 2021. Parameters such as BMI, SP, and SO were evaluated alongside clinical prognostic factors. Survival outcomes, including local control (LC), distant metastasis-free survival (DMFS), disease-free survival (DFS), and overall survival (OS), were analyzed using Kaplan-Meier and Cox regression methods.

Results: Advanced age, lower hemoglobin levels, higher FIGO stages, and lower total radiation doses were significantly associated with poorer outcomes. Univariate analysis revealed significant correlations between BMI and DMFS, DFS, and OS, with normal weight patients displaying higher survival rates. However, these associations were not confirmed in the multivariate analysis. SP was not correlated with any of the outcomes considered while SO was identified as an independent negative predictor of LC (HR: 2.257, 95% CI: 0.933-5.457, p=0.071), DFS (HR: 5.289, 95%CI: 1.298-21.546, p=0.020), and OS (HR: 2.645, 95%CI: 1.275-5.488, p=0.009) (Table 1).

Table 1. multivariable analysis; only statistically significant values are shown.

Parameter	Values	Patients N (%)	LC			DMFS			DFS			OS		
			HR	95%CI	P	HR	95%CI	P	HR	95%CI	p	HR	95%CI	p
Age (years)	<55	77				1	rif.	**0.024**				1	rif.	**0.003**
	55 ≤ age <70	62				1.336	0.642 – 2.781	0.438				2.052	0.936 – 4.502	0.073
	≥70	34				2.919	1.334 – 6.388	**0.007**				4.403	1.878 – 10.322	**<0.001**
Total dose (Gy)	≤ 75	129										1	rif.	**0.016**
	> 75	44										0.368	0.163 – 0.831	
FIGO stage	I-II	77	1	rif.	0.083	1	rif.	**0.019**	1	rif.	**0.031**	1	rif.	**0.008**
	III	73	2.128	0.858 – 5.227	0.103	2.664	1.318 – 5.384	**0.006**	2.148	1.187 – 3.884	**0.011**	3.077	1.515 – 6.250	**0.002**
	IV	23	3.210	1.135 – 9.083	**0.028**	2.676	0.974 – 7.352	**0.056**	2.124	0.959 – 4.707	0.063	2.496	0.873 – 7.139	0.088
Hb	<10	16	1	rif.	**<0.001**				1	rif.	**0.024**	1	rif.	**0.010**
	10 ≤ Hb <12	42	0.395	0.155 – 1.009	0.052				0.394	0.168 – 0.922	0.032	0.400	0.147 – 1.087	0.072
	≥12	115	0.129	0.049 – 0.340	**<0.001**				0.347	0.161 – 0.747	**0.007**	0.227	0.086 – 0.601	**0.003**
BMI	< 18.5	7							1	rif.	**0.060**			
	18.5 ≤ BMI <25	90							1.014	0.227 – 4.534	0.986			
	25 ≤ BMI <30	49							1.982	0.452 – 8.690	0.364			
	≥ 30	27							0.537	0.069 – 4.160	0.552			
SO (SP mean-2DS)	0	148	1	rif.	0.071				1	rif.	**0.020**	1	rif.	**0.009**
	1	23	2.257	0.933 – 5.457					5.289	1.298 – 21.546		2.645	1.275 – 5.488	

Legend: 95%CI: 95% Confidence Interval; BMI: body mass index; DFS: disease free survival; DMFS: distant metastasis free survival; FIGO: International Federation of Gynecology and Obstetrics; Hb: hemoglobin; HR: hazard-ratio; LC: local control; OS: overall survival; SO: sarcopenic obesity; SP; sarcopenia.

Conclusions: The study highlights the prognostic significance of established factors like age, hemoglobin levels, FIGO stage, and radiation dose in LACC. It also underscores the potential of nutrition-related parameters, particularly SO, as independent predictors of clinical outcomes. These findings advocate for the inclusion of body composition metrics in prognostic assessments and treatment planning for LACC patients. Further research is needed to validate these results and elucidate the mechanisms underlying the observed associations, which may lead to more personalized therapeutic strategies.

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CYBERKNIFE UH-SBRT FOR LOCALIZED PCA: A PRELIMINARY REPORT FROM THE PRO-SPEED PROSPECTIVE TRIAL

Code: 433

Aims: To compare dose distributions and dosimetric data between previously in-silico generated and new patient- delivered plans of ultra-hypofractionated (UH) SBRT with CyberKnife® (CK) radiosurgery system (Accuray Inc., Sunnyvale, CA), using image-guided virtual fiducial markers tracking, for localized prostate cancer (PCa) with concomitant focal boost to the dominant intraprostatic lesion (DIL).

Methods: Dose distribution plans coming from the first 15 patient-delivered plans treated from December 2022 to October 2023 were compared with 15 previously generated in-silico CK SBRT plans from our previous dosimetric planning study. A SIB of 40 Gy in 5 fractions (8

Gy/fr) was prescribed to the DIL while a total dose of 36.25 Gy (7.25 Gy/fr) was prescribed to the whole prostate plus proximal part of seminal vesicles every other day, using a 5mm isotropic expansion margin, except 3mm posteriorly, for prostate gland planning target volume (PTV-p) and 3 mm isotropic margin for PTV of the DIL (PTV-d).

Results: A total of 30 plans were compared for this preliminary study. Age, comorbidity, PCa stage, DIL position and PTV volumes (PTV-p and PTV-d) of the two populations compared were similar.
Every in-silico and patient-delivered SBRT plans reached the dose gradient (+10.34%) needed for the SIB prescription and fully achieved the primary planning goal of D95% > 95% for both PTVs. However, the comparison of dose coverage objectives established that small statistically significant difference exists.
Compared to the previous in-silico generated SBRT plans, the SBRT-delivered plans showed a slightly reduction in dose coverage for PTV-d and of PTV-p. Concerning the organs at risk (OARs), both in-silico and delivered plans maintained the dose distribution well below all the prescribed OARs dose constraints, but small differences were noticed. Finally, the median beam-on time in the patient-delivered plans increased by 5 minutes (27 vs 32).
A summary of the main differences regarding the main OARs and PTV dose coverage are reported in Table 1.

Conclusions: The preliminary dosimetric data coming from the first 15 patients treated in the mono-institution phase 2 PRO-Speed Trial, confirm the feasibility hypothesis from the former in-silico planning study. Moreover, the comparison of the median values of PTV dose coverage and OARs dose constraints, proved that only small significant differences exist. These encouraging results need to be confirmed with longer follow-up data and with a larger cohort.

Table 1. Summary of the main differences regarding PTV dose coverage and OARs constraints

PTV Dose coverage	CyberKnife Delivered	CyberKnife Silico
PTV-d (40 Gy)		
D98%	99,52%	100,57%
D95%	100,30%	101,45%
D2%	115,84%	115,77%
V100%	96,50%	98,50%
V110%	21,20%	26,10%
PTV-p (36.25 Gy)		
D98%	94,84%	95,36%
D95%	96,30%	96,99%
D2%	109,03%	103,53%
V100%	76,10%	81,60%
V110%	0,90%	3,40%
Critical organs at risk	**CyberKnife Delivered**	**CyberKnife Silico**
Rectum		
V18 Gy	23,65%	20,30%
V29 Gy	9,00%	6,20%
V33 Gy	4,05%	2,50%
V36.25 Gy	0,70%	0,30%
Rectum posterior wall		
$D1_{cc}$	15,48 Gy	15,56 Gy
Bladder		
V36.25 Gy	3,3 cc	4,5 cc
V18 Gy	19,25%	15,90%
Femoral Heads		
V15 Gy (Right)	0,80%	0,30%
V15 Gy (Left)	0,00%	0,00%
Penile Bulb		
V29 Gy	0,75%	1,80%

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HYPOFRACTIONATED REIRRADIATION WITH PROTON THERAPY: FEASIBILITY AND ACUTE TOXICITY OF THE FIRST 3 PATIENTS TREATED FOR PELVIC TUMOR RECURRENCES

Code: 432

Aims: The present study aims to report the technical feasibility and acute toxicity of reirradiation (re-RT) using hypofractionated proton therapy (PT) for curative treatment of recurrent pelvic malignancies of the first three patients treated in our PT center between November 2023, and January 2024.

Methods: Indication for PT re-RT of each case presented in this preliminary report, underwent a collegial discussion in an internal RT meeting for mutual approval. Prior to every treatment, a CT simulation scan was conducted and a customized mask was also molded (if required), plus a personalized immobilization system was selected depending on RT site. All PT treatments were performed using the "Proteus® One", a single-room PT system by IBA, employing Pencil Beam Scanning - IMPT technique for precise dose delivery. Target volume localization was accomplished through daily computed tomographic imaging (CBCT-KV) before every PT session. Prior RT plans were considered and cumulative doses were converted into equivalent doses in 2 Gy fractions (EQD2) to adhere dose constraints for different reirradiation site.

Results: The first patient underwent re-RT for intravaginal recurrence of urothelial carcinoma, receiving a total dose of 36 Gy (RBE) in 12 fractions (overall treatment time-OTT 20 days) with G2 perineal pain and G2 vaginal bleeding at the end of PT (both present at the beginning of RT).
The second patient underwent re-RT for a postero-lateral pelvic wall recurrence following exploratory laparotomy for HPV+ cervical carcinoma, receiving a total dose of 36 Gy (RBE) in 12 fractions (OTT 18 days) with G1 local asymptomatic edema at the end of PT. The third patient underwent re-RT for pre- sacral recurrence from rectal carcinoma following surgical resection. For the latter, the total dose administered was 35 Gy (RBE) in 5 fractions (OTT 11 days), and no toxicity was reported post-PT. All patients completed their treatment without interruptions or severe toxicity (Grade ≥3) and are currently in good health.
Clinical data and critical OARs dose constraints are summarized in **Table 1.**

Conclusions: Hypofractionated re-RT with PT using the "Proteus One" system proved to be feasible for the first three treated patients. The observed acute toxicities were generally mild, with no treatment interruptions reported. This preliminary investigation indicates the potential efficacy and safety of PT in reirradiation scenarios, warranting further exploration and consideration for broader clinical applications.

Table 1. Summary of clinical data and critical OARs dose constraints

Clinical data	First Patient	Second Patient	Third Patient
Age	77	38	56
Gender	Female	Female	Male
TNM	reT4, cN0, cM0	ypT2, ypN0, cM0	T0, rN1, cM0
Clinical remarks	Vaginal bleeding	Colostomy	Atrial fibrillation
Time of previous RT	08/2022	03/2021	03/2019
Total dose from 1° RT	64 Gy (32 Fr)	53 Gy (25 Fr)	45 Gy (25 Fr)
PT site (re-RT)	Vagina	Postero-lateral pelvic wall	Pre-sacral recurrence
Time interval from re-RT (months)	16	32	57
Dosimetric data			
Maximum dose (0.03_{cc}) EQD_2 to sacral plexus from first RT - α/β 2	NA	42.75 Gy	42.75 Gy
Maximum dose (0.03_{cc}) EQD_2 to sacral plexus (PT re-RT) - α/β 2	NA	45 Gy	78.75 Gy
Maximum dose (0.03_{cc}) EQD_2 to intestinal cavity from first RT - α/β 4	56 Gy	43.5 Gy	43.5 Gy
Maximum dose (0.03_{cc}) EQD_2 to intestinal cavity (PT re-RT) - α/β 4	0 Gy	37.1 Gy	43.5 Gy
Maximum BED (0.03_{cc}) to cauda from first RT - α/β 4	60.4 Gy	NA	61.5 Gy
Maximum BED (0.03_{cc}) BED to cauda (PT re-RT) - α/β 4	0 Gy	NA	65.3 Gy
EQD2 dose to target (PT re-RT) - α/β 10	39 Gy	39 Gy	49.58 Gy

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IS IMRT A SOLUTION FOR HEART SPARING ACCORDING TO THE DEGRO CONSTRAINTS? A MONOISTITUTIONAL EXPERIENCE IN 30 PATIENTS

Code: 125

Aims: Left-sided breast cancer radiotherapy (RT) might lead to relevant cardiac toxicities; modern techniques, such as rotational intensity modulated RT (IMRT) or deep inspiration breath-hold RT, are available to limit the dose to the heart and cardiac subvolumes, whereas free breathing tangential IMRT seems not to be an option to obtain an adequate sparing of the heart. In this setting, the importance of dose parameters related to heart sparing is becoming crucial. This study aims to report our dosimetric data and to retrospectively evaluate adherence to DEGRO breast cancer expert panel recommendations for heart constraints (https://doi.org/10.1007/s00066-018-1378-z), in a cohort of left sided breast cancer patients treated at IEO with Direct TomoTherapy® IMRT.

Methods: After publication of DEGRO recommendations, internal constraints were updated adding left ventricule V5%.Left-sided breast cancer patients treated with breast surgery and receiving RT with TomoTherapy® Hi-Art System in direct modality at the IEO between January and March 2023 were considered for the analysis. Patients received post-mastectomy RT to the chest wall (CW) and infra/supraclavicular nodes or RT to the whole breast +/- boost, both using a 15-fr schedule (2.67 Gy/fr).Institutional applied constraints were collected; others DEGRO constraints not considered as planning objectives were retrospectively evaluated.

Results: A total of 30 patients were included, with a median age of 53.5 years (IQR 4.6-62.6 years). Of them, 27 received RT to the breast +/- boost with a median breast CTV of 528 cm3 (range 403-753 cm3) and 3 patients received RT to the CW and regional nodes with a median CW-CTV of 498 cm3 (range 254-658 cm3). A comparison of the median values among institutional and DEGRO planning objectives is reported in **Table 1**. Median values according DEGRO were respected in all the treatment plans except for Dmean to the left anterior descending artery (LAD) and for LAD V30%; indeed for LAD Dmean there is a difference in the IEO and DEGRO constraints (< 25 Gy vs < 10 Gy, respectively) while for LAD V30% no corresponding constraint is applied in the IEO planning.

Conclusions: Although Direct Tomotherapy IMRT in free breathing is not recommended to achieve a relevant sparing of the heart and cardiac subvolumes, our experience shows that DEGRO constraints are mostly respected. This data supports the improvement of personalized treatments, in terms of techniques and treatment volumes, taking into account patient's cardiac risk factors.

Table 1. Summary of the results

Planning objective	DEGRO constraints	IEO constraints	Cohort median value (range)	N of patients respecting constraint value according to DEGRO (%)
Heart D_{mean}	*< 2.5Gy*	*< 3.2 Gy*	1.9 Gy (0.5-3.0 Gy)	25 (83%)
Left ventricle D_{mean}	*< 3Gy*	*na*	3.1 Gy (0.7-6.0 Gy)	15 (50%)
Left ventricle $V_{5\%}$	*< 17%*	*< 17%*	12.6% (0-27%)	25 (83%)
Left ventricle $V_{23\%}$	*< 5%*	*na*	4.0% (0-11%)	20* (71%)
LAD D_{mean}	*< 10Gy*	*< 25 Gy*	**12.4 Gy (1.3-20.2 Gy)**	10 (33%)
LAD $V_{30\%}$	*< 2%*	*na*	**15.5% (0-49%)**	8 (27%)
LAD $V_{40\%}$	*< 1%*	*na (LAD V45% < 1%)*	0% (0-14%)	27 (90%)

**data not available for 2 patients*

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REAL-WORLD EXPERIENCE ON REGORAFENIB IN GBM RECURRENCE: DOES RADIOTHERAPY VOLUME IMPACT ON TOXICITY OUTCOMES?

Code: 485

Aims: The therapeutic choice for glioblastoma (GBM) recurrence, despite multimodal approach in first-line, remains a challenge. Inphase 2 REGOMA trial, regorafenib improved overall survival (OS) at first progression
after radio-chemotherapy. Some real-life studies showed similar results in terms of OS but a higher rate of adverse effects. The aim of this observational real-world experience was to assess tolerability of regorafenib
in our clinical practice and the potential impact of treatment volume on toxicity outcomes.

Methods: Consecutive patients with GBM treated with regorafenib were included. Data collected were: patient demographics, performance status (PS), number of cycles, number of previous lines of treatment, toxicities, treatment discontinuation, survival data and Clinical Target Volume (CTV) in cc. OS and Progression-Free Survival (PFS) defined as the time from first administration of regorafenib to tumour progression were estimated using the Kaplan-Meier method.

Results: Sixty-one patients were included (40% males and 60% females). Median age was 55 years (range 24-76). All patients had a PS between 0-2. MGMT status was methylated for 29 (47.5%), unmethylated for 23 (37.7%), while in 9 (14.7%) patients data were not available. All the patients previously received radiotherapy and median CTV was 181 cc. Fifty-eight (98.2%) received regorafenib as second-linetreatment; 3 (1.8%) as third-line due to a recurrence occurred before January 2018, with a median number of 3 cycles (range 1-14). Surgery at the time of relapse was performed in 15 (9,1%) patients. The most common adverse events Grade 1-2 were fatigue (70%), rash and desquamation (14.1%), hand-foot skin reaction (9.2%), hypertension (15%), hyperbilirubinemia (3%), hypertransaminasaemia (18%) and seizure (8%). The most common Grade 3-4 were oedema (14%), rash (4.8%), neutropenia (1.6%) and thrombocytopenia (1.6%). Median PFS was 3 months (95% confidence interval: 3-5) and OS 20 months (95% confidence interval: 18-24). In multivariate analysis, no statistically significant correlation was found between treatment volumes and toxicities.

Conclusions: In this real-life experience tolerability profile of regorafenib was manageable, without correlation between radiotherapy volume and toxicities, including oedema and seizures. Fatigue occurred most frequently, with potential impact on quality of life. It may be crucial to identify other parameters, including patient-related, potentially correlated with toxicity profile.

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DOSIMETRIC AND TOXICITY ANALYSIS OF ULTRA-HYPOFRACTIONATED ADJUVANT RADIOTHERAPY IN ELDERLY BREAST CANCER PATIENTS: PRELIMINARY REAL-WORLD SINGLE CENTRE EXPERIENCE

Code: 572

Aims: Moderate hypofractionation is the standard of care for adjuvant radiotherapy (RT) for breast cancer (BC). In 2020 Brunt reported that a dose of 26Gy in 5 daily fractions (frs) is noninferior to the existing standard of 40Gy in 15frs and safe in terms of toxicity. These promising findings appear practice changing especially for elderly patients (pts). Our preliminary retrospective analysis aims to report dosimetric characteristic and preliminary toxicity results of elderly BC pts treated with this schedule.

Methods: Patient selection included women aged older than 70 undergoing RT (26Gy over 1 week) after breast surgery. Target volumes included residual breast or chest wall. Treatment planning used both 3D- Conformal (3D-CRT) and VMAT techniques. Dose constraints were according to FAST-Forward trial[1] and following dosimetric parameters reported: Heart V1.5 and V7Gy, Mean Heart Dose (MHD), Ipsilateral Lung V8 and Mean Lung Dose (IMLD). Normal tissue effects were assessed by clinicians according to CTCAE v5.0.

Results: Between July 2020 and October 2023, data of 23 consecutive pts (median age 82, range 75-88) receiving 26Gy over 1 week were analyzed. BC side was left in 65%. Infiltrating ductal carcinoma recorded in 87%, infiltrating lobular carcinoma in 13%. Pathological node status was pN1 in 35% while pT2 stage in 26%. Ki67 > 25%, positive receptors and negative Her2 recorded in 70%, 91% and 96% respectively. Four plans realized with VMAT modality and 19 with 3D-CRT planning. Mean PTV: 524 cc (range 97-959). Only in 1 patient Heart V1.5Gy not respected (V1.5: 45% - Mean 6.86%, range 0-45%). No other deviations recorded for Heart V7Gy (mean 0.47%, range 0-3.4%) and Ipsilateral Lung V8Gy (mean 7.9%, range 2.5-12.5%) constraints. MHD has been 56.8cGy (range 0-176) while IMLD 223cGy (range 106-323). The 5fr schedule required daily CBCT and 3D surface imaging for monitoring intra- fraction motion. Compliance with RT was 100%. After a median follow up of 9 months (range 3-26), only 1 patient showed a local relapse (4%). Any adverse event in the breast/chest wall occurred in only 22% pts: two pts showed mild breast induration, 2 pts breast or chest wall mild edema, 1 slight telangiectasia (4%). No pts received adjuvant chemotherapy and adjuvant hormonal therapy prescribed to 96%.

Conclusions: Although a short follow up and a small sample size, this preliminary real-world single centre analysis showed dosimetric feasibility and good tolerance of ultra-fractionated adjuvant RT for elderly BC pts

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THE GROWING ROLE OF NEXT-GENERATION IMAGING IN PROSTATE CANCER MANAGEMENT: A CROSS-SECTIONAL SURVEY EXPLORING CLINICAL PRACTICE OF URONCOLOGISTS IN THE NORTH-EASTERN ITALY; ON BEHALF OF GUONE (GRUPPO URO-ONCOLOGICO DEL NORD-EST)

Code: 75

Aims: Next Generation Imaging (NGI) technologies such as mp-MRI and total-body NGI (tbNGI) modalities (WB-MRI, 18F/11C-Choline, 18F-Fluciclovine and 68Ga/18F-PSMA PET/CT or PET/MRI) are becoming increasingly available for the management of patients with prostate cancer (PCa). Due to the lack of univocal recommendations based on clinical data comparing NGI with conventional imaging modalities (CIM), to date their use in the different PCa settings is debated. The present survey was developed by the Gruppo Uro-Oncologico del Nord-Est (GUONE) to describe the current clinical practice in the North-Eastern Italy.

Methods: A cross-sectional survey was conducted by administering an anonymous online questionnaire to uro- oncologists (medical oncologists, radiation oncologists, urologists) practicing in North-Eastern Italy, using Google Forms® platform. Use of NGI was investigated in: primary staging of PCa; management of biochemical (BCR) and local recurrence (LR); restaging in metastatic hormone-sensitive PCa (mHSPC), metastatic castration-resistant PCa (mCRPC), non-metastatic CRPC (nmCRPC) and oligomet-PCa.

Results: 100 uro-oncologists accessed and completed the survey with a 100% response rate for each item (Tab1).
In N/M staging of newly diagnosed PCa, the use of tbNGI increases in accordance with NCCN risk groups (Fisher's exact test: $p<0.01$); in this setting, medical specialty and years of professional practice did not significantly affect this attitude.
Restaging with tbNGI is the prevalent choice in case of BCR after radical prostatectomy. Moreover, as the PSA value rises, there is a parallel increased use of tbNGI ($p<0.01$).
In case of suspected LR, tbNGI plus mp-MRI is the most selected option, particularly among radiation oncologists ($p=0.03$).
Overall, restaging with tbNGI is preferred in mHSPC, mCRPC and nmCRPC patients in case of biochemical progression only as well as for concomitant biochemical and clinical progression. Only in nmCRPC a trend to significance ($p=0.07$) was registered to indicate a greater propensity of participants towards CIM in case of concomitant biochemical and clinical progression.

Conclusions: This survey describes an uro-oncology scenario in North-Eastern Italy characterized by an expanding role of NGI modalities in staging/restaging of PCa, in the management of advanced disease and in the assessment of treatment response. Prospective studies and RCTs are needed to resolve many of the controversial issues emerging in this survey, in order to develop a standardized use of NGI.

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THE EMERGING ROLE OF ARTIFICIAL INTELLIGENCE IN PROTON THERAPY: A REVIEW

Code: 463

Aims: Artificial intelligence (AI) has made a tremendous impact in the space of healthcare, and proton therapy is no exception. This review delves into the emergent role of AI in proton therapy, evaluating its development, advantages, intended clinical contexts, and areas of application.

Methods: Scopus and PubMed databases were searched for manuscripts in the field of "proton therapy" that also included terms related to "artificial intelligence." For each paper, the publication date, abstract, URL, DOI, and BibTeX entries were collected. To assist in the analysis, the large language model ChatGPT was employed to answer questions about the topic of each paper and summarize their conclusions.

Results: A total of 76 papers were included in the review, the majority of which (71 papers, or 93%) was published in 2020-2023. Most papers did not focus on a body region or cancer site, but among those that did, head & neck (19 papers), prostate (9 papers) and brain (9 papers) were the most studied ones (Figure 1).
The manuscripts were categorized into 7 different categories based on their topics:

- AI for dose prediction and calculation (24 papers): AI can help predicting and calculating the optimal radiation dose, as the accuracy of the dose calculation has a direct impact on the treatment outcome.
- AI for synthetic data generation (14 papers): Synthetic data is artificially generated data, not collected from real patients, which can be used to augment existing datasets.
- AI for treatment planning, support, and delivery (10 papers): the applications of AI encompass enhancing the quality and efficiency of treatment planning, improving the resilience and adaptability of treatment plans, facilitating real-time monitoring and dose verification.
- AI for image enhancement and quality (6 papers): AI models can enhance and improve the quality of the medical images, potentially offering clinicians clearer insights and improving the accuracy and robustness.
- AI for outcome prediction (6 papers): AI can be employed to estimate and forecast the consequences of radiotherapy treatment, its side effects, toxicities, or endpoints.
- AI for anatomical delineation and segmentation (3 papers): AI is a potential ally for identifying and segmenting anatomical structures in medical images by DL techniques.
- Other (13 papers)

Conclusions: From optimizing the treatment planning process to enhancing the precision in predicting potential side effects: our review highlights the potential of AI in enhancing PT and mitigating its intrinsic challenges.

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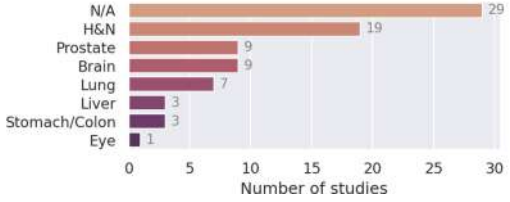
Figure 1. Number of studies focusing on each specific body region. Most papers did not cover a particular region or cancer site (N/A). *List of abbreviations: H&N (Head and neck).*



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ASSESSING THE IMPACT OF COMORBIDITIES ON UHRT TOXICITY PROFILES IN PCA: A REAL WORLD EXPERIENCE

Code: 541

Aims: Despite clinical trials showing UHRT's non-inferiority to conventional RT in treating localized PCa, patients with a high number of comorbidities frequently are overlooked for this treatment, potentially denying them a curative option.
The aim of the present study is to evaluate the toxicity profiles of a real-world cohort of PCa patients who underwent curative UHRT±SIB on DIL±ADT and to assess the influence of pre-treatment Charlson Comorbidity Index (CCI) on acute and late RT-related side-effects.

Methods: Patients with localized PCa treated with radical UHRT at a single institute were retrospectively studied. Risk categorization followed NCCN guidelines and baseline age-adjusted CCI was calculated. Maximum GI/GU acute and late toxicities were assessed via the RTOG scale.
Patients were categorized into 5 CCI subgroups and their impact analyzed via Chi-square test.

Results: From 2012 to 2021, 890 patients met inclusion criteria. Median age at diagnosis was 76 years (IQR 72-79) with a median iPSA of 7.4 ng/ml (IQR 5.2–10.4). The most common risk class was unfavorable intermediate (327, 37.4%), then favorable intermediate (202, 23.1%), low (188, 21.5%), and high/very
high (156, 17.9%). A total of 364 patients (41%) received ADT for a median of 8 months (IQR 6–12).
All patients received UHRT on prostate in 5fx on alternate days, with a dose/fx within 6.5-7.25 Gy±SIB on DIL with a dose within 37.5-40 Gy. Median prostate CTV was 60cc (IQR 46–77.15). Median follow-up was 2.48 years (IQR 1.48–3.45).
Median baseline CCI score was 4 (IQR 3-5). Diabetes mellitus (14.6%), localized second malignancy (12.9%) and heart failure/myocardial infarction (7.0%) were the most frequent comorbidities.

Table 1. Maximum late GU/GI toxicity per CCI group.

Maximum late GU Toxicity				
CCI group	**G0**	**G1**	**G2**	**G3**
1 - 2	45 (12%)	22 (16%)	4 (8%)	0 (0%)
3	116 (31%)	44 (32%)	19 (40%)	3 (60%)
4	119 (32%)	35 (26%)	14 (29%)	1 (20%)
5 - 6 - 7	87 (23%)	34 (25%)	8 (17%)	1 (20%)
8 - 9 - 10 - 11	7 (2%)	1 (1%)	3 (6%)	0 (0%)
Total	**374**	**136**	**48**	**5**
Maximum late GI Toxicity				
CCI group	**G0**	**G1**	**G2**	**G3**
1 - 2	59 (12%)	10 (20%)	2 (13%)	0 (0%)
3	158 (32%)	17 (35%)	4 (25%)	2 (22%)
4	152 (31%)	10 (20%)	6 (38%)	1 (11%)
5 - 6 - 7	112 (23%)	12 (24%)	4 (25%)	1 (11%)
8 - 9 - 10 - 11	10 (2%)	0 (0%)	0 (0%)	5 (56%)
Total	**491**	**49**	**16**	**9**

Acute toxicities included 122 (13.7%) G≥2 GU and 43 (4.8%) G≥2 GI events. Larger prostate CTVs were significantly linked to acute GU toxicities ($p<0.05$).
Data on maximum late toxicities were available for 565 patients (63.5%), with 53 (9%) experiencing late G≥2 GU toxicities and 25 (3.4%) experiencing G≥2 GI toxicities. Significant correlation was found between acute and maximum late toxicities ($p<0.05$).
Toxicity details by CCI-score are shown in Table 1, where a significant relationship was observed between higher CCI and higher late GI toxicity ($p<0.05$), but not for late GU toxicity.

Conclusions: UHRT is a safe and effective treatment, showing excellent GI/GU toxicity profiles. CCI scores have shown low impact on toxicities, thus, UHRT should be proposed as a treatment option independently from patient's comorbidities.

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THE EVOLUTION OF IMAGING MODALITIES IN OMHSPCA: A SHIFTING PARADIGM

Code: 102

Aims: This research aims to extensively evaluate the change in clinical practice regarding the chosen imaging method before metastasis-directed therapy (MDT) in oligometastatic hormone-sensitive prostate cancer (omHSPCa), using a historical cohort of patients.

Methods: The study included patients diagnosed with metachronous omHSPCa who had ≤ 5 metastases, undergoing RT MDT treatment between 2014 and 2022 at the IEO in Milan, Italy. Analytical techniques employed included the Kruskal-Wallis test and ANOVA.

Results: We included 248 patients and a total of 469 MDTs. Specifically, 54% (135 patients) underwent more than one course of MDT.
In terms of the imaging methodologies utilized to determine the indication for MDT at the first clinical recurrence, PET Cho was the predominant technique (111 treatments, 45%), followed by PET PSMA (92 treatments, 37%), RM Whole-Body (39 treatments, 16%), and conventional imaging techniques (6 cases, 2.4%). When comparing the average number of lesions detected by each imaging method, no statistically significant difference was observed ($p = 0.32$) (Fig. 1a).

Upon evaluation of the PSA levels at the time of imaging detection, it was observed that WB RM was performed with an average PSA of 1.62 and a median PSA of 1.06. In contrast, PET PSMA showed an average PSA of 1.72 and a median of 1.02. PET Cho had an average PSA of 3.61 and a median of 2.22, while traditional imaging methods documented an average PSA of 4.80 with a median of 1.31. A subsequent Kruskall-Wallis analysis revealed significant differences in the medians across these groups, evidenced by a p-value of less than 0.05 (Fig. 1b).
A deeper exploration into the data revealed shifts in the preferred imaging method for all MDTs throughout the study period. The analysis segmented treatments into three time intervals: those before 01/01/2015, those between 01/01/2015 and 01/01/2020, and those administered after 01/01/2020 (Fig. 1c).

Conclusions: The evident shift from conventional to new generation imaging with enhanced sensitivity underscores the evolving landscape of MDT, showing the tight connection between the imaging modality and the PSA levels. The enhanced sensitivity of new generation techniques has led to a decrease in PSA levels at the time of imaging, establishing them as the preferred method for directing MDT.

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Fig. 1a

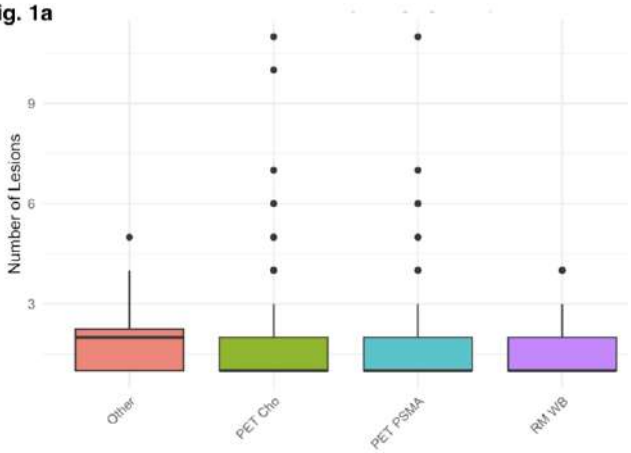


Fig. 1b

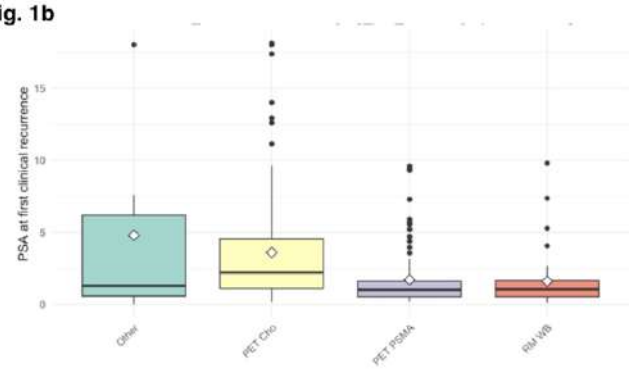
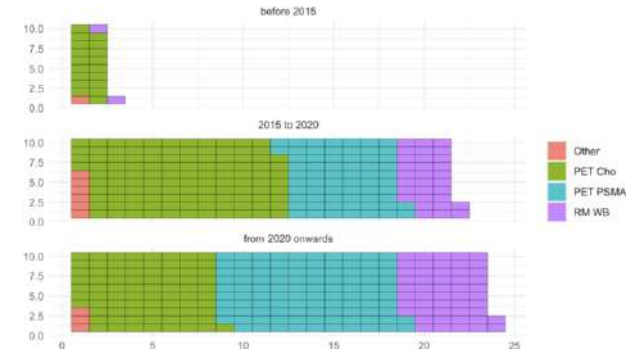


Fig. 1c



ROLE OF RADIOTHERAPY TO THE PRIMARY IN METASTASTIC HORMONE SENSITIVE PROSTATE CANCER: PRELIMINARY RESULTS OF A SINGLE INSTITUTIONAL EXPERIENCE

Code: 247

Aims: To evaluate oncological outcomes of patients affected by newly diagnosed, radiologically confirmed, metastatic prostate cancer treated with radiotherapy on the primary.

Methods: From January 2019 to December 2023, 21 patients affected by ab initio metastatic prostate cancer, with no previous radical treatment, received radical radiotherapy to the primary tumor. Radiation treatment was delivered with helical IMRT or VMAT with moderate or ultra hypofractionated schedules. Besides the prostate gland, 19 patients were irradiated to the seminal vescicles and 4 to the pelvis, with an additional boost to positive nodes in 3 cases. Ten oligometastatic patients (47%) also received radiotherapy to the metastases. All patients underwent hormone therapy before and during RT. Toxicity was assessed according to CTCAE scale v4.0. The primary endpoint was biochemical control. Secondary endpoints were local control and toxicity.

Results: Median FU was 18.7 months (range 3-61). Patients and treatment characteristics are listed in table 1. We measured PSA before radiotherapy and 2-3 months after completion. Median PSA before radiotherapy was 1.72 ng/ml (range 0.02-33). Biochemical response was evaluated in 20 patients: one patient ended the treatment in December 2023 so PSA was not available at the time of this analysis. Median PSA after radiation was 0.195 ng/ml (0.006-1.6). One patient did not reach biochemical response after radiotherapy. Three patients (15%) experienced biochemical and eventually clinical progression after the end of radiotherapy (median 8 months, range 7-10), so two of these patients underwent a switch in systemic treatment and further irradiation on the sites of metastasis. No toxicity >G2 was recorded; 1 case of diarrhea G2 and 3 cases of moderate LUTS appeared during RT; mild nycturia was the most common acute and late toxicity. At last follow-up all patients were alive: 17(85%) without evidence of disease, 1 with local disease, 1 with distant metastases, and 1 with both local and distant failure. Biochemical and local control were achieved in 17 (85%) and 18 (90%) patients, respectively. Biochemical control at 2 yy was 83.7%. Local control was 94.1% at 2 yy and 75.3% at 3yy.

Total patients		***21***
Median age		76
range		63-88
Staging		
T2c		3 (15%)
T3a		5 (23%)
T3b		10 (47%)
T4		3 (15%)
N1		13 (62%)
N0		8 (38%)
M1A		2 (10%)
M1B		14 (66%)
M1A+M1B		5 (24%)
Metastatic Burden according to CHAARTED criteria		
LOW		19
HIGH		2
ISUP Grade Group		
GG2		5
GG3		5
GG4		8
GG5		2
unknown		1
Diagnostic imaging		
MRI		16
CT		8
Bone scan		12
Choline-PET		1
PSMA-PET		15
PSA at diagnosis		
Median		22.34
Range		4,4 - 276
Androgen deprivation therapy		
LHRHa		17
ANTI-ANDROGEN		1
MAB		3
Median Duration (months)		4
Range		1-39
Chemotherapy before RT		2
Radiotherapy on primary tumor		
Data range		22/01/2019 – 18/12/2023
Technique		
IMRT Helical		19 (90%)
VMAT		2 (10%)
RT Volumes		
Prostate		2(10%)
Prostate + SV		15 (71%)
Pelvis + Prostate + SV		4 (19%)
Boost on N		3
Doses		
UltraHypofx		4
32.5 Gy in 5 fx		1
35 Gy in 5 fx		2
36.25 Gy in 5 fx		1
Moderate Hypofx		
64 Gy in 20 fx		15
70.2 Gy in 27 fx		2
Radiotherapy on metastasis		
Number of patients		10 (47%)
Number of treated metastasis		
1 mts		9
2 mts		1
Doses		
30 Gy in 5 fx		2
35 Gy in 5 fx		4
60 Gy in 20 fx		2
64 Gy in 20 fx		2
Acute toxicity during treatment		
GI	G0	17
	G1	3
	G2	1
GU	G0	5
	G1	13
	G2	3
Acute toxicity 0-6 months		
GI	G0	18
	G1	2
	G2	0
GU	G0	9
	G1	9
	G2	2
Late Toxicity		
GI	G0	17
	G1	1
	G2	0
GU	G0	9
	G1	8
	G2	1

Conclusions:
In our experience, radiotherapy to primary tumor results in good biochemical and local control, with an excellent toxicity profile.

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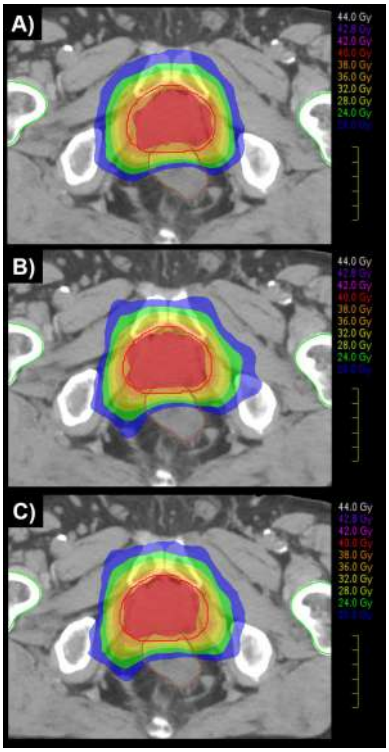
SINGLE-ARC VMAT FOR LOCALIZED PROSTATE CANCER SBRT: IMPROVING TREATMENT DELIVERY EFFICIENCY

Code: 162

Aims: In the last decade, SBRT has gained popularity for the treatment of localized prostate cancer. In ultra- hypofractionated regimens, intra-fraction prostate motion is an important source of treatment uncertainty. As prostate displacement increases with time, a straightforward solution to reduce intra-fractional errors is to minimize delivery time. Prostate SBRT delivered with traditional linacs is commonly planned with multiple arcs, generally two, using flattening filter free (FFF) beams. In this work, double- and single-arc VMAT arrangements were compared in order to minimize beam delivery time and so to reduce treatment uncertainties.

Methods: A retrospective dataset of 10 low- and intermediate-risk patients was used. For treatment simulation, patients were stabilized in supine position (full bladder, empty rectum). CT scans were registered with multiparametric MRI for accurate contouring. The PTV was defined with a 6 mm expansion (3 mm posterior) from the CTV. Three VMAT beam arrangements were compared on VersaHD linac (Elekta): two full arcs 6 MV FFF; one full arc 6 MV FFF; one full arc 10 MV FFF. The prescription dose was 40 Gy/5 fractions. Target and OARs dose constraints were selected for treatment planning comparison. A plan quality index (PQI) was defined to compare achievement of the planning goals. Patient-specific quality assurance (PSQA) plans were delivered to the Octavius 4D phantom to evaluate delivery accuracy. The beam on time (BOT) was compared to evaluate treatment delivery efficiency.



Results: All treatment plans fulfilled all dose constraints. Figure 1 shows examples of SBRT dose distributions obtained with the three arrangements: A) 2 arcs 6 MV FFF; B) 1 arc 6 MV FFF; C) 1 arc 10 MV FFF). No statistical differences were found in the PQI between double- and single-arc arrangements. PSQA plans confirmed the high degree of delivery accuracy for the three arrangements, with mean gamma passing rates >97% (2%/2mm criteria). Contrariwise, statistically significant reductions of the BOT were obtained with single-arc geometries: the average delivery times were 1.6 min (-45%) and 1.3 min (-55%) for 6 and 10 MV FFF respectively.

Conclusions: The high quality, fast and accurate dose delivery of single-arcs indicated the feasibility of this geometry for prostate SBRT. In particular, the significant reduction of the delivery time improve treatment robustness against intra-fraction prostate motion and so patient safety.

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STEREOTACTIC BODY RADIATION THERAPY IN PATIENTS WITH UNRESECTABLE INTRAHEPATIC CHOLANGIOCARCINOMA: CLINICAL OUTCOME, TOXICITY AND PROGNOSTIC FACTORS

Code: 535

Aims: The aim of the study was to assess the efficacy and the tolerance of stereotactic body radiation therapy (SBRT) in patients affected by unresectable intrahepatic cholangiocarcinoma evaluating outcomes, toxicity and prognostic factors.

Methods: All patients with unresectable intrahepatic cholangiocarcinoma were treated with SBRT using volumetric modulated arc therapy (VMAT). Primary endpoint was local control (LC), secondary endpoints were overall survival (OS) and toxicity. We performed an univariate and a multivariable analysis. Acute and late toxicities were recorded according to CTCAE v5.0.

Results: Between 2011 and 2023, 48 patients with unresectable intrahepatic cholangiocarcinoma underwent SBRT. Demographic, clinical and treatment characteristics are shown in Table 1. Fractionation ranged from 30 Gy to 60 Gy in 3-10 fractions. Median BED10 was 78.7 Gy (range 39 – 219.3 Gy). Median follow-up was 15.17 months (1.76 – 145.2 months). Twenty-three patients (48%) underwent chemotherapy. Median LC was 16.6 months, with 1 and 2 years rates of 85% and 62%, respectively. According to RECIST criteria, we observed 14 patients with complete response (29.1%), 4 patients with partial response (8.3%), 19 patients showed stable disease (39.5%) and 11 patients (22.9%) had a local progression. At univariate analysis, cumulative gross tumor volume (GTV) was statistically associated with LC (HR 1.00, p=0.022). Twenty-five patients (52.1%) were alive at the time of analysis and 13 of them (52%) had no evidence of local and metastatic disease. Median OS was 23.8 months, rates of OS at 1 and 2 years were 69.8% (95%CI 53.6 – 81.3) and 47.9% (95%CI 30.9 – 63.1). At univariate analysis, cumulative GTV (HR 1.00, p=0.000), use of chemotherapy (HR 0.34, p=0.020) and surgery (HR 0.37; p=0.020) were predictive for OS. At multivariable analysis, increasing cumulative GTV remained independent negative predictive factor (HR 1.00, p=0.002). Treatment was well tolerated, without acute and/or late toxicity ≥G3.

Conclusions: SBRT offers a noninvasive, effective and safe therapeutic option for patients with unresectable intrahepatic cholangiocarcinoma. Prospective randomized trials are required to determine the efficacy and safety of SBRT compared to and combined with other treatment modalities.

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Table 1. Patients' and treatment's characteristics (n=48)

Median age (range)	76 years (44-86)
Median volume (cc, range) CTV	32.7 (5.4-323)
N° of lesions (n° of patients)	
- 1	40 (83.3%)
- 2	5 (10.4%)
- 3	2 (4.2%)
- 4	1 (2.1)
Chemotherapy	
- Yes	23 (48%)
- No	25 (52%)
Lines of chemotherapy (n)	
- 1	15 (65.2%)
- 2	7 (30.4%)
- 3	1 (4.3%)
Surgery before SBRT	
- Yes	32 (66.6%)
- No	16 (33.4%)

CARDIAC EXPOSURE RELATED TO ADJUVANT RADIOTHERAPY IN PATIENTS AFFECTED BY THYMOMA: A DOSIMETRIC COMPARISON OF PHOTON OR PROTON INTENSITY MODULATED THERAPY

Code: 107

Aims: Radiotherapy for thymoma is delivered post-operatively in case of incomplete surgery or advanced disease.
Given the particular location of thymic lodge and the excellent prognosis of these patients, some of them will be at risk of developing late cardiac toxicities.
Historically considered as a whole organ, more recently the heart is being divided into different substructures in terms of dosimetry, some of which are particularly radio-sensitive. A strategy to reduce dose to heart substructures could be the use of proton beam therapy (PBT), which allows lower distant-to- target dose deposition.

The purpose of this retrospective dosimetric study is to investigate whether PBT compared to photon- therapy could better spare cardiac, given prespecified dose constraints.

Methods: Twenty-nine patients treated with adjuvant radiotherapy with a prescribed dose of 50 Gy in 25 daily fractions for radically resected thymoma were selected; all patients underwent a contrast-enhanced simulation CT. We manually contoured fourteen cardiac substructures (CSs), with the supervision of a team of cardioradiologists. The photon-based plans were optimized in adherence to the Volumetric Modulated Arc Therapy (VMAT) technique, specifically its RapidArc variant. The proton-based plans were optimized in adherence to intensity-modulated proton therapy (IMPT) using the beam spot scanning technique. We used p-Student and p-Fischer to compare the DVH of VMAT versus IMPT plans in terms of Dmax, Dmean and V5Gy. The advantage with IMPT was considered statistically significant if both p- values were less than 0.05.

Results: IMPT demonstrated better sparing of most cardiac substructures in terms of Dmax, Dmean and V5Gy. Left Anterior Descending Coronary Artery was better spared with IMPT in terms of Dmax (18.1±19.5 Gy vs 26.3±17.7 Gy, p=0.000), Dmean (8.2±12.0 Gy vs 12.6±12.3 Gy, p=0.000) and V5Gy (26.5±34.1% vs 55.1±26.6%, p=0.002).
Mean dose (1.6±3.1 Gy vs 4.3±4.6 Gy, p=0.000) and V5Gy (6.3±11.2% vs 22.3±25.9%, p=0.000) to the left ventricle were significantly lower with IMPT.
Similarly, Dmean (6.93±8.76Gy vs 9.57±8.40 Gy, p=0.000) and V5Gy (22.87±25.54% vs 40.13±34.96%, p=0.000) of right atrium were significantly reduced by IMPT.
Finally, IMPT plans more easily achieved the proposed dose constraints.

Conclusions: Cardiac substructures can be successfully spared with IMPT. Clinical studies are needed to estabilish a relationship between dose parameters and the development of cardiac events.

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GYNECOLOGICAL CANCER: FROM IMRT-IGRT TO ADAPTIVE RADIATION THERAPY

Code: 508

Aims: Endometrial cancer is the sixth most common cancer in women worldwide, with over 400,000 new cases per year. Surgery plays a central role in localized disease, while External Beam Radiation Therapy (EBRT) is reserved for cases of inoperable disease and in the adjuvant setting, especially for patients with intermediate-high and high-risk disease, both in combination with systemic treatments and as monotherapy. Cervical cancer ranks as the fourth most commonly diagnosed cancer in women globally. The standard treatment for locally advanced cervical cancer involves concurrent EBRT with cisplatin, followed by brachytherapy. Concerns regarding the treatment of gynecological cancer with Intensity-Modulated Radiation Therapy (IMRT) or Volumetric Modulated Arc Therapy (VMAT), primarily due to the potential for geographical miss resulting from complex and varied movement within the cervix–uterus complex during and between fractions. This movement depends on factors such as bladder and rectal filling and tumor regression during radiotherapy.

Methods: To address this concern, Adaptive Radiotherapy (ART) techniques modify radiotherapy plans based on images acquired during treatment. Strategies such as Internal Target Volume (ITV) definition, scheduled replanning or a Plan of the Day (PotD) approach have been employed, but they have limitations like large planning target volume (PTV) margins or increased workload.
Recent technological progress has given rise to advanced approaches such as Online-Adaptive Radiation Therapy (oART), incorporating daily replanning facilitated by Magnetic Resonance (MR) or Cone Beam Computed Tomography (CBCT) guidance. The Ethos platform allows for daily online adaptation of the target and organs at risk (OARs) contours based on daily CBCT imaging.

Results: Recent studies suggest that using CBCT-guided oART in pelvic EBRT for gynecological tumors can significantly reduce doses to OARs while maintaining tumor control.

Conclusions: Despite encouraging dosimetric data, methodological correlation with adverse event reduction requires further confirmation. Therefore, since Ethos has recently been acquired in our center we are actively working to design a prospective study to validate the real clinical benefit from CBCT-guided oART in gynecological treatments. In particular, we would like to evaluate CTV coverage and PTV margins in adapted plans versus non-adapted plans, dosimetric improvements to CTV and OARs and how these correlate with a reduction of acute and late toxicities.

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IMPLEMENTATION OF SURFACE-GUIDED RADIOTHERAPY (SGRT) FOR BREAST CANCER TREATMENT: PRELIMINARY EXPERIENCES AND CURRENT DEVELOPMENTS IN A SINGLE CENTRE.

Code: 590

Aims: Breast cancer is the most common neoplasia among women, with 30% of cases attributed to malignant breast tumors. Adjuvant radiotherapy plays a crucial role in the postoperative context, both for in situ and invasive carcinoma. The combination of conservative breast surgery and adjuvant radiotherapy is now well-established in common practice, while dose fractionation and target extension are still under investigation. Even in cases of total mastectomy, adjuvant radiotherapy has demonstrated a significant reduction in the local recurrence rate and an increase in overall survival. Considering the substantial caseload, particularly in centers managing over 600 breast carcinoma patients annually, it becomes imperative to mitigate the risk of errors and alleviate the workload for technicians, to guarantee both safer and more efficient treatments. In this context, Surface Guided Radiation Therapy (SGRT) emerges as a promising technique.

Methods: This recent technology enables mapping of the patient's body surface, providing a reference map for accurate positioning and continuous monitoring of body movements within a wide field of view.

Results: The effectiveness of SGRT in identifying positioning errors, without need for repetition of additional imaging such as cone beam CT (CB-CT), significantly reduces total treatment time, shortening the positioning and control phase. In our center, we have successfully implemented SGRT systems developing a specific protocol for breast cancer treatment. The approach involves CB-CT in the first three sessions, followed by SGRT if the mapping of the body surface is congruent. CB-CT is then performed only every five sessions to verify any anatomical changes during treatment.

Conclusions: Although we currently have preliminary data regarding the application of SGRT, we are actively engaged in collecting and analyzing more detailed information. The in-depth analysis of this data could become the focus of future studies aimed at providing a comprehensive analysis of SGRT for breast cancer treatment. In particular, we want to compare set-up errors and reproducibility of target position in IGRT vs SGRT, with a focus also on patient's comfort and RTTs workload. This in perspective of supporting ongoing research and high-quality evaluation of new technologies in the clinical setting.

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REAL-TIME DOSE MINIBEAM DELIVERY METHOD USING SCINTILLATING MATERIALS

Code: 288

Aims: Mini-beam radiotherapy (MBRT) is a novel preclinical approach to radiotherapy (RT), which is based on the use of small parallel beams of radiation (x-ray or protons) to create a highly modulated dose pattern. It has been developed to achieve higher normal tissue sparing compared to conventional RT, while allowing larger doses of radiation. The aim of this study is to perform real-time dose measurements in MBRT using radioluminescence imaging (RLI).

Methods: MBRT was delivered using an image guided small animal irradiator (SmART, PXI, 225 kV x- ray source), where a specific collimator was installed, giving a 20 x 20 mm field size and 1 mm peak-to- peak distance. To evaluate RLI for real-time MBRT dose measurements, different setups were investigated. A scintillator film Gd2O2S:Tb was positioned vertically just below the collimator to visualize the MB shape along the beam axis. The scintillator film was then embedded in four 2.5 mm thick plexiglass slabs to take into account scatter radiation. Two plastic scintillators (Eljen EJ 200) 5 x 5 x 5 cm or 5 x 5 x 1 cm were used too. The RLI signal was detected using a CMOS camera placed at 90 deg from the beam axis and the PVDR was measured. Monte Carlo (MC) simulations were also performed using TOPAS for comparison with the experimental results. To mimic a preclinical MBRT irradiation setting, a mouse phantom was placed on top of the 5 x 5 x 1 cm plastic scintillator slab. Optical images were taken before irradiation (bright field) and during irradiation (RLI). Bright field and RLI images were then superimposed.

Results: We found that RLI can be used to visualize the preclinical MB delivery in real-time. Using the scintillator film alone we measured a PVDR equal to 15 in line with MC simulations. When the film was embedded in the plexiglass slabs, the PVDR dropped down to 4 probably because of reflections and scattering of optical photons in the slabs. The same happened with the scintillator cube. When the mouse phantom

was irradiated, superposition of optical and RLI images allows us to clearly see the minibeams on the slab and, thus, to determine the precise location where the mouse was irradiated.

Conclusions: We proposed an RLI optical method to measure MB dose delivery in real-time using radioluminescence imaging. The PVDR values obtained with RLI matches the PVDR obtained with TOPAS MC simulation. RLI of a preclinical irradiation setting allows us to determine the location of minibeams delivery in real-time.

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DOSIOMIC ANALYSIS OF HYPOFRACTIONATED PROSTATE TREATMENTS: FEATURES ROBUSTNESS AND POSSIBLE APPLICATION IN PREDICTING CLINICAL OUTCOMES

Code: 561

Aims: Artificial intelligence (AI) has become increasingly integrated into radiology, nuclear medicine, pathology, and recently, radiotherapy as a valuable adjunct to clinical practice, aiming to predict clinical outcomes and support decision-making processes. This study focuses on a monocentric, retrospective analysis of patients treated under a Hypofractionated regimen (60Gy in 20fz) for prostate carcinoma, evaluating the robustness of dosiomic features in case of patient positioning errors or anatomical changes during radiotherapy.

Methods: The Dosiomics is the radiomic analysis of dose maps from treatment plans in order to develop predictive models for clinical outcomes. It is crucial to assess the robustness and repeatability of dosiomic features, considering potential patient positioning errors and anatomical changes during radiotherapy. 30 prostate carcinoma (Prostate exclusive target) treatment plans are considered in this study. Dosiomic features robustness is evaluated on dose maps recalculated after random isocenter displacements (simulating patient positioning errors and anatomical changes). First-order dosiomic features are extracted for each patient and their deviation from the reference values (obtained from the original plan) is assessed. Features demonstrating stability are used to train an AI model to predict post-treatment PSA values and other clinical outcomes.

Results: Certain dosiomic features remained independent of isocenter displacements within the considered range, making them suitable for training predictive models. Conversely, some features exhibited less stability, suggesting challenges in their reproducibility. Preliminary results show that training an AI model based on robust dosiomic features to predict clinical outcomes is feasible.

Conclusions: While certain features demonstrated stability against displacements, others showed considerable variability. Training AI models using invariant dosiomic features appear feasible, emphasizing their importance for robust results. Future studies should explore whether stable dosiomic features are decisive for AI models or if their information gain is negligible.
Conducting a robustness study before training predictive dosiomic models is essential to ensure the use of resilient features and enhance the effectiveness of AI in clinical applications.

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STEREOTACTIC RADIOTHERAPY IN OLIGOPROGRESSIVE STAGE IV NON- SMALL CELL LUNG CANCER DURING IMMUNOTHERAPY: A MONO INSTITUTIONAL EXPERIENCE

Code: 522

Aims: The management of oligoprogression during, a scenario of limited disease progression during systemic therapy, presents several challenges. Here, we present the case report of our mono institutional experience involving a 78-year-old patient undergoing concurrent ablative stereotactic radiotherapy (SRT) for a left adrenal lesion and mediastinal lymph nodes oligoprogression, while concurrently receiving Pembrolizumab immunotherapy for stage IV Non-Small Cell Lung Cancer (NSCLC).

Methods: For treatment planning, two 4D simulation CT scans for each target were acquired: one for the mediastinal lesion and one for the left adrenal lesion, establishing two distinct isocenters. For a better target and organ-at-risk identification, a diagnostic Fluorine-18-fluorodeoxyglucose positron emission tomography (18F-FDG PET/CT) and a contrast-enhanced diagnostic CT were co- registered. An Internal Target Volume was defined, accounting for physiological organ motion.
SRT was administered using Volumetric Modulated Arc Therapy (VMAT) - Image-Guided Radiation Therapy (IGRT), and daily cone-beam CT (CBCT) scans were acquired. The prescription dose for both targets was 30 Gy in 5 daily consecutive fractions, with both targets treated on the same day. MONACO planning system has been used for planning.

Results: SRT was well-tolerated, with no significant acute or late toxicities reported. Initial 18F-FDG PET/CT evaluation, 3 months after treatment, revealed a favorable local response, characterized by reduced metabolic uptake in both treated lesions and the absence of disease progression. The patient successfully continued immunotherapy during and after radiotherapy.

Conclusions: Our experience demonstrated the successful integration of stereotactic radiotherapy and immunotherapy for the management of NSCLC oligoprogressive disease, providing a feasible and safe treatment option. Further research is necessary to define optimal patient selection criteria, treatment modalities, and their impact on overall survival.

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18F-FET/PET IN THE RADIOTHERAPY TARGET VOLUME DEFINITION IN HIGH GRADE GLIOMA

Code: 148

Aims: 18F-fluoroethyltyrosine (18F-FET) PET is increasingly used in radiation treatment planning for the primary treatment of high grade glioma (HGG) patients additionally to contrast-enhanced MRI. The aim of this study was to investigate tumor volume delineation by amino acid PET, in addition to the use multiparametric perfusion magnetic resonance imaging (MRI), in patients with untreated HGG o with brain recurrence.

Methods: HGG patients or patients with brain recurrence undergoing 18F-FET PET examination before primary radio(chemotherapy) from 12/2022 to 12/2023 were included. Target volume definition was performed on basis of a gross tumour volumes (GTV) including all contrast enhancing areas on MRI. 18F-FET PET was performed, after total or subtotal resection for RT planning to visualise the metabolically active tumour remnant and after gross total resection to detect metabolically active tumour at the border of the resection cavity. Biological tumour volumes (BTV) were semi-automatically created and fused with MR-based gross tumour volumes (MRGTVs). PET-MRGTV volumes were built through a fusion of the corresponding MRGTV and BTV volumes.

Table 1. Tumour and target volumes

PT	DIAGNOSIS	BTV (cm^3)	$_{MR}$GTV (cm^3)	$_{PET-MR}$GTV (cm^3)	RT Dose
1	Glioblastoma WHO IV	26.80	177.6	286.8	VMAT-SIB: 54/60/66 Gy (1.8/2/2.2 Gy)
2	Glioblastoma WHO IV	24.30	160.1	289.6	VMAT: 56 Gy (2 Gy)
3	Glioblastoma WHO IV	99.6	156.3	228	VMAT: 60 Gy (2 Gy)
4	Glioblastoma WHO IV	73.06	176.7	258.8	VMAT-SIB: 60/66 Gy (2/2.2 Gy)
5	Glioblastoma WHO IV	36.81	22.4	52.1	VMAT-SIB: 54/60 Gy (1.8/2 Gy)
6	Glioblastoma WHO IV	1.44	75.3	152.9	VMAT-SIB: 54/60/66 Gy (1.8/2/2.2 Gy)
7	Glioblastoma WHO IV	1.08	4.7	20.4	VMAT: 60 Gy (2 Gy)
8	Glioblastoma WHO IV	140	211.4	262.4	VMAT: 50 Gy (2 Gy)
9	Glioblastoma WHO IV	1.93	42.9	81.9	VMAT: 60 Gy (2 Gy)
10	Oligodendroglioma	14.45	46.3	89	VMAT: 60 Gy (2 Gy)
11	Oligodendroglioma	1.35	136.8	208.7	VMAT: 60 Gy (2 Gy)
12	Oligodendroglioma	67.30	74.9	108.8	VMAT: 50 Gy (2 Gy)
13	Astrocytoma Recurrence	72.50	73.7	122.4	HSRT: 27 Gy (9 Gy)
14	Astrocytoma Recurrence	0.63	2.5	7.4	HSRT: 27 Gy (9 Gy)
15	Astrocytoma Recurrence	4.10	26.1	62.2	HSRT: 20 Gy (5 Gy)
16	Oligoastrocytoma Recurrence	5.69	1.7	5.1	HSRT: 30 Gy (6 Gy)

BTV: Biological tumour volumes; **$_{MR}$GTV**: MR-based gross tumour volume; **VMAT**: Volumetric Modulated Arc Therapy; **VMAT-SIB**: Volumetric Modulated Arc Therapy-Simultaneous Integrated Boost; **HSRT**: Hypofractionated Stereotactic RT

Results: 16 HGG patients were included: 9 Glioblastoma WHO IV, 3 Oligodendroglioma and 4 recurrence (3 astrocytoma and 1 oligoastrictoma recurrence). Median age was of 53 years (range 32–75, 10 male, 6 female) at the beginning of radiation therapy treatment. Gross total resection was performed in 9 patients, subtotal resection in 7 patients. Tumours were mostly located in the frontal (n = 4) and temporal lobe (n = 7) followed by the parietal (n = 5).
BTVs was 35.72 cm3 (range 0.63-140 cm3). MRGTVs was 86.83 cm3 (range 1.7-211.4 cm3) and by definition smaller than PET-MRGTVs (139.78 cm3, range 5.1-289.6 cm3). A total dose of 60 Gy (50-66 Gy) in 30 fractions was the most frequently used regimen and hypofractionated stereotactic RT (HSRT) for brain recurrence (dose 20-30 Gy in 3-5 fractions) (**Table 1**).

Conclusions: Target volume delineation of HGG patients can be improved through 18F-FET PET imaging prior to primary radiation treatment, since vital tumour can be detected more accurately, suggesting that the metabolically active tumor volume is critically underestimated by contrast enhanced MRI. 18F-FET PET imaging may help to improve target volume delineation accuracy for radiotherapy planning.

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STEREOTACTIC BODY RADIATION THERAPY (SBRT) IN HEPATOCELLULAR CARCINOMA (HCC): FEASIBILITY AND EFFICACY, PATIENT SELECTION AND PREDICTORS OF OUTCOME

Code: 421

Aims: Hepatocellular carcinoma (HCC) is the most common primary liver malignancy. Stereotactic body radiotherapy (SBRT) has emerged as a valuable option in early to advanced-stage disease, as defined by the Barcelona Clinic Liver Cancer (BCLC) system. Our study aims to evaluate the use of SBRT in HCC patients and to identify predictors of outcome and toxicity.

Methods: We retrospectively reviewed HCC patients treated at our institution between November 2011 and December 2022. Patients were treated with SBRT to a maximum of 5 concurrent lesions up to a maximum diameter of 6 cm each. Tumor delineation was performed on a 4D contrast-enhanced simulation CT, including arterial, venous, and parenchymal phases, with MRI co-registration.

Results: SBRT was performed in 171 patients to 289 HCC localizations. Median age was 76 years (range 20-91), with a median follow-up of 12.7 months. Rates of OS at 1 and 2 years were 84.3% (95%CI 76.9–89.5) and 72.4% (95%CI 62.1–80.3). Median OS was 49.3 months. In univariate analysis, the only predictive factor for OS was the presence of varices (HR 2.24, 95% CI 1.14-4.37; p=0.018). Median LC was not reached.
Rates of LC at 1 and 2 years were 91.4% (95%CI 87.3-94.3), and 82.4% (95%CI 75.3–87.6). At univariate analysis, use of alcohol (HR 2.50, 95%CI 1.24 – 5.04; p=0.010), previous systemic therapy (HR 2.50, 95%CI 1.15–5.39; p=0.020), BED10 (HR 0.98, 95%CI 0.97–0.99), and number of lesions (HR 1.49, 95%CI 1.12–1.98), were statistically significant for LC. At multivariable analysis, only BED10 remained an independent predictive factor (HR 0.98, 95%CI 0.97–0.99; p=0.010). Median PFS was 13.2 months, with 1 and 2 year-rates of 55.8% (95%CI 47.3–63.4) and 34.3% (95%CI 25.5–43.3). At univariate analysis, both previous local (HR 1.80, 95%CI 1.06 – 3.05; p=0.028) and systemic treatment (HR 2.71, 95%CI 1.59 – 4.60; p=0.000), together with BCLC classification (HR 1.66, 95%CI 1.21 – 2.29; p=0.002), and number of lesions (HR 1.28, 95%CI 1.03 – 1.60; p=0.021) were predictive for PFS. At multivariable analysis, only systemic therapy (HR 2.19, 95%CI 1.20 – 4.00; p=0.010) and BCLC stage (HR 1.50, 95%CI 1.07–2.09; p=0.016) remained significant for PFS.OS

Conclusions: SBRT is a safe and effective treatment for HCC, with excellent rates of LC and a favorable toxicity profile. Negative prognostic factors for OS and PFS include higher BCLC grade and prior systemic therapy. Therefore, better outcomes may be achieved in fit and therapy-naïve patients with early-stage BCLC class.

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SURVIVAL OUTCOMES AND PREDICTORS OF RESPONSE IN OLIGOMETASTATIC RECTAL CANCER TREATED WITH SBRT

Code: 167

Aims: Colorectal cancer (CRC) is a term used in research and clinical practice to refer to both colon cancer (CC) and rectal cancer (RC), particularly in the metastatic setting. However, these two entities differ in their embryological origin and anatomy, reflecting the different management approaches, with very little evidence on oligometastatic rectal cancer (ORC). This study aims to evaluate outcomes and predictive factors in oRC patients treated with Stereotactic Body Radiation Therapy (SBRT).

Methods: In this retrospective analysis, we included all patients diagnosed with rectal adenocarcinoma and treated at our center with SBRT for a maximum of five oligometastases in three organs. The primary endpoints included overall survival (OS), local control (LC), and progression-free survival (PFS). Univariate and multivariate analysis was performed to evaluate significant predictive factors.

Results: Our study included 88 patients who underwent a total of 142 SBRT treatments on 231 oligometastases. The median follow-up was 21 months. The study showed a median OS of 47.8 months, with OS rates at 1-year and 3-year OS of 97.7% (95%CI 91.2 – 99.4) and 59.7% (95%CI 48.0 – 69.6). respectively. At univariate analysis, lung metastases (HR 0.48, 95%CI 0.28 – 84.1; p=0.010), and incomplete ablation (HR 1.73, 95%CI 1.00 – 2.99; p=0.047) emerged as significant predictors of OS and remained significant at multivariable analysis (HR 0.48, 95%CI 0.27 – 0.83; p=0.009 and HR 1.76, 95%CI 1.02 – 3.05; p=0.041). Median LC was not reached, rates at 1 and 2 years were 77.1% (95%CI 66.7 – 84.5), and 70.5% (95%CI 59.4 – 79.1). None of the analyzed risk factors was correlated with LC. The median treated volume was 9,6 cm3 and had no impact on either OS or LC. Median PFS was 7.6 months, with PFS rates at 1 and 2 years of 38.6% (95%CI 28.4 – 48.6) and 13.3% (5.7 – 22.1) respectively. Male gender (HR 0.59, 95%CI 0.35 – 0.99), and incomplete ablation (HR 3.63, 95%CI 2.16 – 6.08), were significantly correlated with poor PFS in both the univariate and multivariate analysis.

Conclusions: This large retrospective study shows how lung metastases are associated with poor OS, while complete ablation improves both OS and PFS in oRC patients undergoing SBRT. In contrast to recent evidence in oligometastatic colon cancer, the outcomes in oRC are not impacted by the number of metastases or total tumor volume. This demonstrates further differences between these two diseases and highlights the need for separate analyses.

	n	%
Number of patients	88	
Number of treated lesions	231	
Number of treatments courses	142	
Gender		
Male	63	72%
Female	25	28%
PS		
0	61	69%
1	19	22%
2	8	9%
Treated Metastases per treatment course		
1	82	58%
2	39	27%
3	16	11%
4	3	2%
5	2	1%
Treated organs per patient		
1	84	94%
2	4	4%
3	0	0%
Presence of untreated lesions		
None	52	58%
Yes	36	40%
Systemic therapy (ST) before SBRT		
No	21	24%
Yes	67	75%
of which		
1-line only	32	48%
2 lines of ST	23	34%
3 or more lines of ST	12	18%
Number of treatments per patient		
1	52	58%
2	25	28%
3	9	10%
4 or more	2	2%
Location of treated metastases		
Liver	45	19%
Lymphnodes	24	10%
Lung	152	66%
Others	10	4%
Treatment		
Median number of fractions	4	(3-10)
Median delivered dose	48 Gy	(20-75 Gy)
Median BED	105,6	(45-262 Gy)
Median CTV sum	9,6 cm3	(0,7-203,5 cm3)

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IN VIVO DOSIMETRY FOR CLINICAL PRACTICE IN GYNECOLOGICAL CANCER BRACHYTHERAPY WITH IR-192 SOURCE: A QED DIODE SETUP PROPOSAL

Code: 458

Aims: Brachytherapy treatments with a High Dose-Rate (HDR) source require the introduction of an in vivo dosimetry in order to assure the correct delivery of the dose. The proposed workflow aims to investigate the correlation between the dose predicted by the Treatment Planning System (TPS) using three- dimensional (3D) reconstructed Computed Tomography (CT) images and the dose measured by diode detectors, originally intended for conventional radiotherapy, under the clinical condition of HDR brachytherapy of the cervix uteri.

Methods: In order to perform the diode calibration, a CT was taken of a custom 3D-printed water phantom (Figure) with the diode inserted at 15 cm of distance from the applicator. A mock treatment plan was then realized, activating all dwell positions in the first 3 cm of the applicator with an uniform dwell time setup. The absolute dose was obtained from the TPS dose estimation (Elekta Oncentra Brachy 4.5.2).
During each session, a QED diode (1115000-2) was applied on the patient at the level of the iliac crest with a bolus of at least 6 cm in water to mimic TPS calculation conditions. A CT-based HDR was performed with a prescribed dose per fraction of 5-7 Gy to the clinical target volume. Measurements were taken on the patient's skin and were compared with those calculated by the treatment planning system, in terms of absolute and relative dose difference.

$$AD = D_m - D_{TPS}$$

$$RD = \frac{D_m - D_{TPS}}{D_{TPS}} * 100\%$$

With: AD the absolute dose difference, RD the relative dose difference, D_m the dose measured by the diode and D_{TPS} the dose calculated by the TPS

Results: The preliminary measurements showed a good agreement between measures and calculations. The observed trend between treatment sessions was in line with expectations, making these diodes a suitable tool for in vivo dosimetry measurements. In particular, as shown in Figure 2 and 3, it was observed that a reasonable threshold for AD and RD accuracy assessment could be 2.5 cGy and 20%, respectively

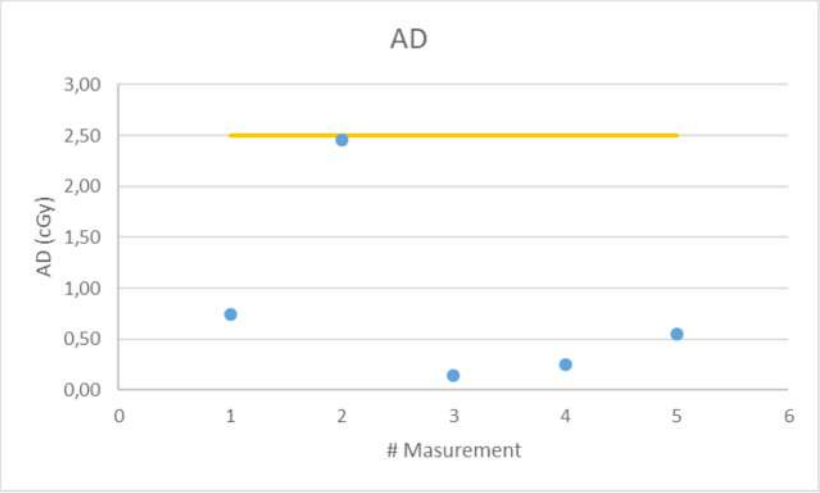

Figure 2: Absolute difference for each measurement performed

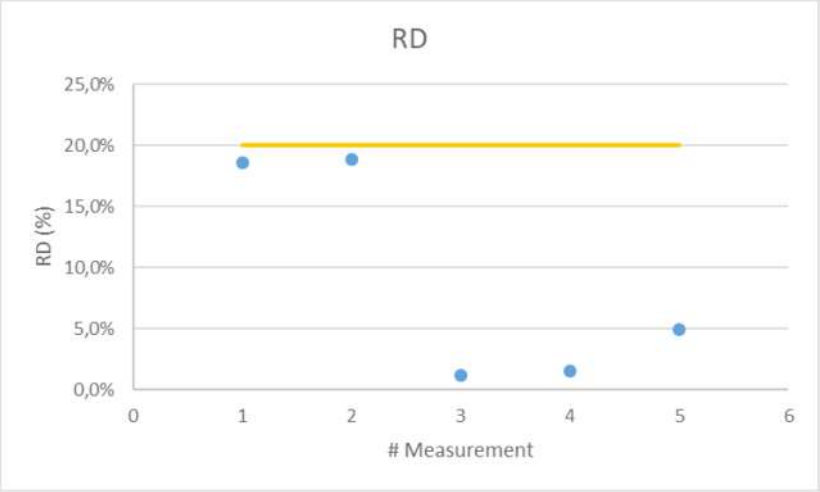

Figure 3: Absolute difference for each measurement performed

Conclusions: Preliminary results show that the accuracy and reproducibility of the measurement system are correlated for routine clinical use and provide a reasonable threshold for estimating the accuracy of dose delivery. Therefore, further measurements are required to make the protocol robust, including the increasing of the number of diodes to 3 to improve the spatial accuracy, and possibly narrowing the proposed tolerance range.

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CARDIAC TOXICITY FOR MAMMARY CHAIN IRRADIATION FOR III STAGE HER2 NEGATIVE BREAST CANCER PATIENTS

Code: 317

Aims: Patients with locally-advanced-stage breast cancer are typically treated including regional lymph nodes irradiation. The role of Internal Mammary Chain (IMC) irradiation remains controversial due to an increased risk of cardiac toxicity. To maximize survival benefits of IMC radiotherapy, dose to heart and left anterior descending coronary artery (LAD) should be minimized. Aim of our work was to analyze the dosimetric effect of IMC irradiation for III stage HER2-negative breast cancer patients and to evaluate acute and late cardiac toxicity.

Methods: Ninety HER2-negative breast cancer patients treated between January 2020 and December 2022 with pathological III stage were retrospectively selected. All patients received chemotherapy before surgery or before radiotherapy and 86.6% of them also received hormonal therapy. They all underwent radical mastectomy and axillary node dissection and received radiotherapy to chest wall, to supraclavicular fossa and to IMC with a total dose of 40.05 Gy. Left-sided breast cancer radiotherapy was realized for 53.3% of patients with the deep inspiration breath-holding technique while the remaining 46.7% of patients received right breast radiotherapy. Volumetric-modulated arc therapy treatment plans were realized with *Raystation (v11B)* Treatment Planning System. Mean LAD-PRV and mean heart doses were calculated. Echocardiography (ECHO) and electrocardiography (ECG) were performed before chemotherapy treatment and then patients were routinely assessed every 3 months by ECHO and ECG.

Results: All cases met the PTV coverage dose constraints and chest wall-, supraclavicular node- and IMC-PTV coverage was adequate. Mean dose of LAD-PRV was 296 cGy for right-side breast and 628 cGy for left- side breast. Heart mean dose was 272 cGy for right-side breast and 298 cGy for left-side breast. The median value of the maximal dose of LAD-PRV was 338 cGy for right breast and 752 cGy for left breast. Heart mean dose was 272 cGy for right breast and 298 cGy for left breast. With a median follow-up of 26 months, no ECHO changes were observed after treatment. T-wave abnormalities at ECG without clinical evidences were observed for 38.8% of patients.

Conclusions: Our analysis shows that internal mammary chain irradiation for locally advanced breast cancer HER2 negative patients appears not to influence cardiac toxicity especially with modern radiotherapy modalities such as volumetric-modulated arc therapy and deep inspiration breath-holding technique.

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STEREOTACTIC RADIOTHERAPY FOR OLIGOMETASTATIC PATIENTS WITH BRAIN METASTASES: RESULTS OF DOSE CALCULATION COMPARISON BETWEEN TOMOTHERAPY AND LINAC- BASED TECHNIQUES

Code: 315

Aims: Stereotactic irradiation is often used in brain oligo-metastases treatment. Recent advanced treatment modalities and different dose calculation alghorithms allowed different output dose characteristics. The aim of this study was to compare dosimetric aspects of stereotactic radiotherapy through the use of two techniques: LINAC-Based (LB) versus Helical Tomotherapy (HT) modalities.

Methods: Eight oligometastatic patients with single brain metastasis who received radical stereotactic radiotherapy, were included in the analysis. Gross Tumor Volume (GTV) was defined by contouring the visible lesions on MRI images and Planning Treatment Volume (PTV) obtained by 2 mm isotropic extension of the GTV. Each contouring dataset of the patients was replanned with both tomotherapy (Raystation v11B TPS) and LINAC-based treatment planning system (BrainLab Elements v 1.5 TPS). The LB modality was realized with FFF beams. The delivered dose was 27 Gy in three fractions (9 Gy per fraction). For each treatment plan, the Paddick Conformity Index (PCI), the inverse Paddick Conformity Index (iPCI), the Gradient Index (GI), the PTV-coverage values, the beam-on time and the volume receiving 18Gy (V18) were calculated and compared for both treatment modalities. Results were analyzed with Wilcoxon signed-rank test.

Results: Each patient had only one brain metastasis treated and the median volume of lesions was 3 cc. PTV coverage, PCI and iPCI were similar for both treatment modalities: mean values were respectively 95.7%, 0.84, 1.2 for LINAC-based and 95.7%, 0.81, 1.2 for tomotherapy. GI and beam-on time were statistically significantly lower with LB with a mean value of GI of 4.0 versus 6.6 for HT and with a beam-on time of 199 seconds for LINAC versus 517 seconds for tomotherapy. Also V18 improved with CBL with a median value of 6.7 cc compared to 8 cc with HT.

Conclusions: In our study among the two treatment modalities and alghoritms analyzed, the LINAC-based had the best dose gradient with similar values of PTV coverage, PCI and iPCI compared to tomotherapy. Also the beam-on time with LB system was lower respect to HT. The LINAC-based approach also provided significantly better V18 values compared with HT improving toxicity profile with the same efficacy. The outcome of our preliminary analysis has encouraged us to preferably treat patients with LINAC-based modality in order to obtain better dose distribution improving toxicity profile and shortening treatment time.

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INTRODUCING THE ROLE OF CONCURRENT RADIO- CHEMOTHERAPY IN HIGH-RISK APPENDICEAL MUCINOUS NEOPLASMS

Code: 502

Aims: Appendiceal cancers, including appendiceal mucinous neoplasms (AMN), pose treatment challenges due to their rarity and diversity. While surgery is the primary approach, uncertainties surround adjuvant therapies. This study retrospectively examines three high-risk AMN cases treated with surgery, followed by systemic and radiation therapy, aiming to provide insights into the efficacy of adjuvant treatments.

Methods: Three high-risk AMN patients treated at our institution from 2018 to 2020 were retrospectively selected for the study. Due to the lack of standardized guidelines, cases were discussed at a tumor board, and adjuvant multimodality treatment involving radiotherapy and chemotherapy was proposed. Radiotherapy involved planning with CT scans for accurate target delineation and dose calculation. During contour delineation, the gross tumor volume (GTV) was outlined, including the tumor bed and surgical clips. Subsequently, the clinical target volume (CTV) and planning target volume (PTV) were delineated, with a 5 mm expansion from GTV to CTV to adjust for daily setup errors and organ motion. The prescribed dose to the PTV was 45 Gy, administered in daily fractions of 1.8 Gy (5 fractions per week). Chemotherapy was administered using a 5FU continuous infusion regimen based on 5FU 225 mg/m2 IV infusion over 24 hours daily (1–5 or 1–7) every week for five weeks, with patients pre-screened for DPD enzyme activity to prevent adverse events. Acute toxicities were monitored weekly, while late toxicities were recorded during follow-up, assessed using the Common Terminology Criteria for Adverse Events (CTCAE version 5.0).

Results: Dosimetric evaluations demonstrated successful targeting of the treatment area with minimal radiation exposure to surrounding tissues. Patients experienced manageable gastrointestinal side effects during treatment, with no significant hematological or genitourinary toxicities. Late toxicity assessment revealed mild gastrointestinal symptoms as the most common adverse events. Following a median follow-up of 29.3±6.1 months, all patients remained disease- free, achieving 100% rates of progression-free and overall survival.

Conclusions: This study suggests re-evaluating the role of adjuvant radiotherapy in high-risk AMN patients, especially those with unresectable disease or high-grade cytologic atypia. Ionizing radiation may contribute significantly to reducing local-regional recurrence and distant metastasis rates in these patients.

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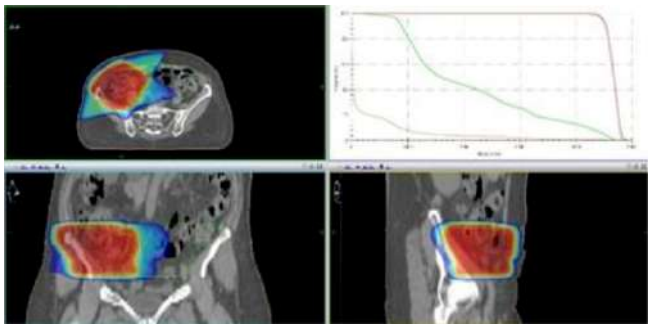

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NUTRITIONAL PREHABILITATION IN HEAD AND NECK CANCER

Code: 26

Aims: La malnutrizione è un problema comune tra i pazienti affetti da cancro alla testa e al collo e può avere effetti negativi sulla salute complessiva e sugli esiti del trattamento. La preabilitazione nutrizionale è una strategia potenziale per ottimizzare lo stato nutrizionale di questi pazienti. Questa revisione sistematica aveva l'obiettivo di identificare e descrivere gli interventi di preabilitazione fisica e nutrizionale che hanno un impatto positivo sullo stato di salute.

Methods: È stata condotta una revisione sistematica della letteratura nelle banche dati PubMed/Medline, Embase, CINAHL, Scopus, Web of Science e Cochrane Library, inclusi anche documenti di letteratura grigia; su
1.215 risultati, sono stati inclusi 8 studi. La valutazione della qualità degli studi e del rischio di bias è stata condotta in accordo con i critical appraisal tools proposti dalla JBI. Il protocollo di questa revisione sistematica è stato registrato nel database del National Institute of Health Research con il numero di registrazione del protocollo PROSPERO: CRD42022377567.

Results: Gli interventi preabilitativi multimodali che combinano consulenze nutrizionali, integratori nutrizionali orali ed esercizi di deglutizione per la prevenzione della disfagia hanno mostrato esiti positivi nel mantenere l'apporto calorico, il peso corporeo, la capacità di deglutizione e nel

ridurre l'incidenza di fibrosi nel tratto gastrointestinale superiore, migliorando contemporaneamente la qualità della vita.

Conclusions: Nonostante il numero limitato di studi clinici disponibili in letteratura, i risultati suggeriscono che gli interventi di preabilitazione nutrizionale hanno un effetto positivo sullo stato nutrizionale e sugli esiti clinici dei pazienti con cancro alla testa e al collo, contribuendo a mitigare il rischio di malnutrizione e migliorare il benessere generale.

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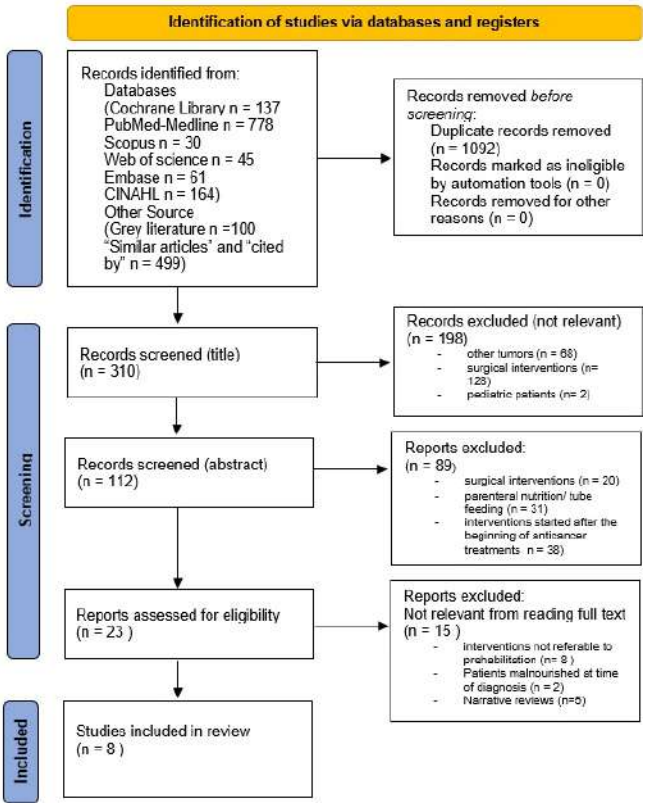
Figure 1: Prisma flow-chart of the process of articles inclusion



HYPOFRACTIONATED PALLIATIVE VOLUMETRIC MODULATED ARC RADIOTHERAPY. "RTOG 8502 QUAD SHOT" FOR ADVANCED HEAD AND NECK CANCER: A SINGLE-INSTITUTIONAL EXPERIENCE

Code: 268

Aims: This study aims to report on our institutional experience of volumetric modulated arc radiotherapy in the locally advanced incurable head and neck by cyclical hypofractionated regimen (RTOG 8502 'QUAD SHOT')

Methods: From jan 2022 to dec 2023 We evaluated 14 incurable patients (ps ecog 2-3, stage 3-4) with Squamous cell head & neck cancer. The patients were treated with at least one cycle of the RTOG 8502 regimen. Median follow-up was 7 months (range 3-30). Two daily fractions of 3.5 Gy were delivered with an interval of at least 6 h for 2 consecutive days, totaling 14 Gy over 4 fractions. This was repeated every 3 weeks for a total of three cycles. No concurrent systemic therapy was performed. Replanning was Done every 3 weeks. Radiation reactions were assessed by RTOG criteria. Tumor response was assessed by recist criteria. From the start of treatment, all the patients were regularly assessed daily during treatment and weekly during planned gaps in treatment. Detailed clinical evaluations were done by thorough local examination of the patients and all the patients were followed up regularly on outpatient basis for a period of at least 6 months at 1-month interval. Survival was measured from the 1st day of treatment.

Results: Partial response was achieved in 3 patients and symptom relief in 10 of 14 patients. Clinical response (partial response or symptom relief) was achieved in 13 patients. Patients who received 2 or more treatment cycles achieved better responses. The number of completed cycles was 3 in 6 patients, 2 in 2 patients, and 1 in 5 patients. Median survival was 5 months. 3 patients completed all three treatment cycles and they are alive with cancer. Only one patient is being treated with cetuximab after the third cycle of protocol with the good clinical local response Grade 2 toxicity was observed in four patients, but no acute Grade ≥ 3 or late toxicity was observed.

Conclusions: In locally advanced head-and-neck cancer patients particularly with poor performance status or elderly patients who need of some form of local therapy for symptom control and palliation, the hypofractionated palliative RT regimen (Quad Shot) offers an effective and quick treatment option which is beneficial both clinically and in logistics issue. RTOG 8502 'QUAD SHOT' regimen provides excellent rates of palliative response with minimal associated toxicity. Patients who are able to complete greater number of RT cycles have higher rates of palliative response and overall survival.

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STEREOTACTIC BODY RADIATION THERAPY FOR THE RE-IRRADIATION OF LOCAL RELAPSE OF PROSTATE CANCER: RESULTS IN TERMS OF OUTCOMES AND TOXICITY

Code: 334

Aims: To retrospectively evaluate toxicity and outcomes of re-irradiation (re-RT) for local relapse in patients with Prostate Cancer treated with previous definitive or post-operative radiotherapy (RT).

Methods: Thirty-six patients affected by local relapse after previous definitive or post-operative RT were treated with Stereotactic Body Radiotherapy (SBRT) in our institute. Treatment dose was 25-30 Gy in 5 fractions. Gastrointestinal (GI) and genitourinary (GU) toxicity was reported according to Common Terminology Criteria for Adverse Events score version 5. Endpoints were biochemical relapse free survival (BRFS) and distant metastases free survival (DMFS), assessed with Kaplan-Meier analysis. Univariate and multivariate Cox regression was carried out to evaluate the association between clinical factors and survival outcomes.

Results: Twenty-six patients received re-RT after definitive RT and 10 after post-operative RT. At time of re-RT median PSA was 2.57 ng/ml (range 0.23-13.10) and local relapse was detected with choline- PSMA-PET or MRI in 18, 17 and 1, respectively. Median CTV was 17.8 cc (range 1-93.1). In 39% of patients the target corresponds to macroscopic relapse, while in 61% target was the whole prostate or prostate bed. Median follow-up was 28.2 months. No late > 2 side effects were collected. Only one patient experienced GI toxicity (G2), while GU side effects were observed in 8 patients (6 G1 and 2 G2). Median BRFS survival was 19.0 months, with 1- and 2-years BRFS rates of 63.5% (95%CI 42.5–78.6) and 37.0% (95%CI 17.5–56.8), respectively. At univariate analysis, PSA value at time of reirradiation was a predictive factor for BRFS (HR 1.43, 95%CI 1.19– 1.73; p=0.000). DMFS rates at 1 and 2 years were 88.0% (95%CI 66.8–96.0) and 72.4% (95%CI 48.1–86.8), respectively. Median DMFS was 19.6 months in with reirradiation of the relapsing nodule, while was not reached in patients treated on the whole prostate gland or surgical bed. At univariate analysis, irradiation of the macroscopic relapse vs the whole gland/bed (HR 5.91, 95%CI 1.35–25.80; p=0.018) and increasing PSA at time of reirradiation (HR 1.20, 95%CI 1.01–1.41; p=0.030) were negative predictive factors. At multivariate analysis, treatment of the macroscopic relapse only remained an independent predictive factor (HR 4.48, 95%CI 1.09–18.37; p=0.037).

Conclusions: Re-RT in patients treated previously with definitive or post-operative RT was safe and showed promising results in terms of toxicity and biochemical outcomes.

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IMPACT OF LATERAL LYMPH NODES ON CLINICAL OUTCOMES IN NEOADJUVANT RADIOCHEMOTHERAPY FOR LOCALLY ADVANCED RECTAL CANCER: MONOINSTITUTIONAL PRELIMINARY RESULTS

Code: 585

Aims: Neoadjuvant Chemoradiotherapy followed by Total Mesorectal Excision in Locally Advanced Rectal Cancer with positive Lateral Lymph nodes (LLNs) is a standard of care. Clinical results published in the literature reported the impact of pre- and post- treatment LLNs on clinical outcomes. The aim of this preliminary study was to evaluate if LLNs could have this predictive value.

Methods: From 2015 to 2021, 98 patients with LARC were retrospectively analyzed. The presence of metastatic lymph nodes and their eventual persistence were studied through MRI. A first evaluation was conducted on patients with *versus*without pretreatment LLNs (LLNs+ vs LLNs-, respectively). After treatment and the restaging MRI, a second analysis was conducted in LLNs+ group. According to Ogura et al. and Sluckin et al., we divided this group in: responders with pre- treatment lymph nodes >7 mm and post-treatment lymph nodes <4 mm and not-responders with pre-treatment lymph nodes >7 mm and post-treatment lymph nodes >4 mm. The measurement of the LLNs were referred to their short axis. The Kaplan-Meier method was used to estimate Overall Survival (OS), Disease-free Survival (DFS) and Local Control (LC), in both evaluations. A P-value less than 0.05 was considered statistically significant.

Results: The median age of patients was 67 years (F: 36 and M: 62). Pre-treatment LLNs were detected in 15 patients (range of 8-18 mm) at baseline MRI. Regarding to LLNs locations, a prevalence was detected for internal iliac lymph nodes (58%). The first analysis between LLNs+ vs LLNs- groups showed the following results: 3-years LC and OS of 88% and 90% in LLNs+ group *versus*94% and 93% in LLNs- group. Disease-free survival was similar in the both groups: 88% in LLNs+ *versus*89% in LLNs-. Regarding the second analysis, in the group of patients with pretreatment LLNs+, 7 patients were defined as responders and 8 not-responders. Figure 1 showed the impact of post-treatment pathological LLNs on OS and DFS: 3-year DFS and OS were 100% in responders *versus* 88% and 90% in not responders, respectively.

Conclusions: Although the preliminary nature of this study and the small sample of analyzed patients, it was observed a worse local control and survivals in those with the presence of LLNs compared to their absence or their regression, confirming the hypothesis of their involvement in the progression of LARC.

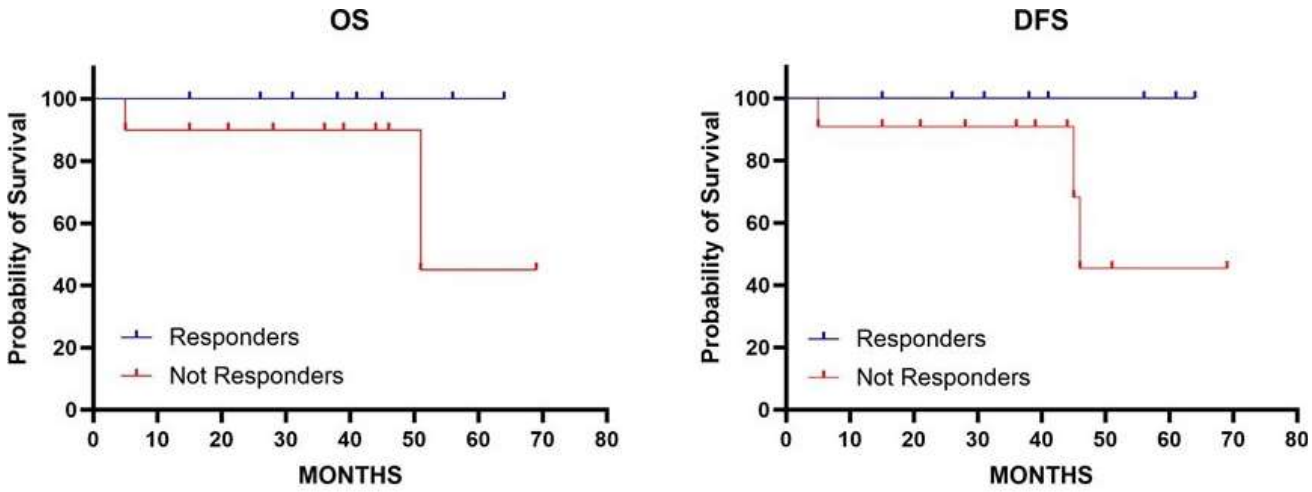

Figure 1. Overall (OS) and Disease-free (DFS) survivals in responders (blue) vs not responders (red) patients for Lateral Lymph nodes.

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GLIOBLASTOMA IN ELDERLY PATIENTS: A MONO- INSTITUTIONAL EXPERIENCE

Code: 436

Aims: Glioblastoma shows a pick of incidence on the fifth/sixth decade of life. Due to ageing of the population, the risk of under-treatment is an open question in elderly population. The aim of the present study was to evaluate the toxicity and clinical outcomes in patients > 65 years old with Glioblastoma treated with concomitant Radiation Therapy (RT) and Temozolomide.

Methods: The study was conducted retrospectively in 50 patients who underwent Chemoradiotherapy between 2015 and 2023. The treatment schedule was delivered in standard fractionated RT (60 Gy, 2 Gy/fraction) or hypofractionated RT (40,05 Gy, 2,67 Gy/fraction) and Temozolomide administered at daily dose of 75 mg/m^2. MRI was performed before treatment and at 3-6 months after the ending of RT. Adverse effects were classified according to RTOG scale. Time-to- progression (TTP) and Overall Survival (OS) were analyzed using Kaplan-Meyer method. A univariate analysis using the Cox proportional regression analysis was performed to evaluate the effect of age, sex, dose on OS. A P-value < 0,05 was considered statistically significant.

Results: The median age was 71 (65-85) years old. 30 patients were male and 20 female. 17 patients underwent hypofractionated radiotherapy schedule. Temozolomide was administered in the whole analyzed population. Treatment tolerability toxicity analyses showed that the severe (?G3) hematological toxicities were: thrombocytopenia in 8 (16%) patients and leucopenia in 2 (4%) patients. Regarding toxicities ?G2, we registered thrombocytopenia in only 2 patients (4%). No other toxicities were documented. The median OS and TTP were 16 months and 12 months, respectively, at the median follow-up time of 12 months (range: 1-56 months) (Figure 1). Cox regression analysis reported no association between OS and age but a light advantage in female and in conventional regimen: Hazard Ratio=0,6 and Hazard Ratio=0,7 respectively.

Conclusions: Considering the relatively good toxicity profile and the efficacy of treatment, our experience supports the use of the standard schedule RT and Temozolomide even in elderly Glioblastoma population.

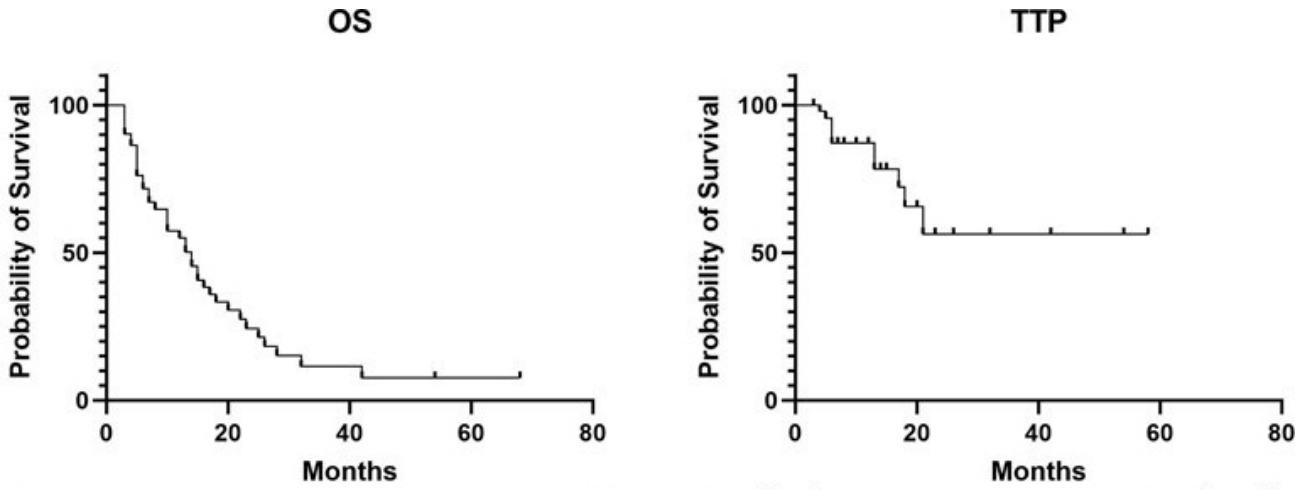

Figure 1: Kaplan-Meyer analyses for Overall Survival (OS) and Time-To-Progression (TTP)

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PATHOLOGICAL COMPLETE RESPONSE AND TOXICITY IN LOCALLY ADVANCED RECTAL CANCER: A 10 YEARS MONOINSTITUTIONAL EXPERIENCE

Code: 592

Aims: In the setting of neoadjuvant Radio-Chemotherapy for Locally Advanced Rectal Cancer (LARC), a single- institution experience was reported in order to evaluate the toxicity and the impact of pathological responses on Overall Survival (OS), Cancer Specific Survival (CSS), Disease Free Survival (DFS) and the Local Control (LC).

Methods: From 2012 to 2022, 178 patients with LARC were retrospectively analyzed. All patients underwent radiotherapy with a simultaneous integrated boost (55 Gy, 2,2 Gy/fraction) to mesorectum and concomitantly administered capecitabine. Toxicities were recorded by the RTOG/EORTC scale. Mandard tumor regression grade (TRG) and pTNM staging system were used to classify pathological responses, particularly the pathological complete response (pCR) i.e the absence of residual cancer. Patients were divided in: pCR (pT0N0) and Not-pCR (pT>0N>0), according to pTNM and in good responders (TRG1-2) and partial/not responders (TRG3-5), according to Mandard TRG. The Kaplan-Meier method was used to estimate OS, CSS, DFS and LC. A P-value less than 0.05 was considered statistically significant.

Results: The median patient age was 68 years and the median follow-up of 42 months. We observed low severe toxicity rate. Acute Grade 3 lower bowel toxicity and Grade 3 cutaneous toxicity were reported in 2 (1.1%) patients, respectively. Late Grade>3 lower bowel toxicity was reported in 6 patients (3%) and late Grade>3 cutaneous toxicity was registered in one patient. There were reported no other severe acute and late toxicities. 168 patients underwent surgery and anterior resection was performed in 106 patients (59%), followed by Transanal Endoscopic Microsurgery in 20 (12%). Pathological Complete Response and good responders (TRG 1-2) rates were of 36% and 62%, respectively. The 10-year OS, CSS, DFS and LC rates 75%, 92%, 81% and 88%, respectively. In pCR patients, the 10-years OS, CSS, DFS and LC were: 89%, 95%, 88% and 92% respectively. In good responders (TRG1-2), the 10-years OS, CSS, DFS and LC were: 87%, 94%, 87%, 91%. In both these setting of patients, statistically significance was found in OS curve: p=0.01 in pCR group and p=0.09 in TRG1-2 group (Figure1).

Conclusions: Neoadjuvant chemoradiotherapy with dose intensification in LARC patients resulted in favorable long- term oncological outcomes specially with a high pCR rate, an optimal impact of Mandard Tumor Regression Grade OS and with an acceptable toxicity.

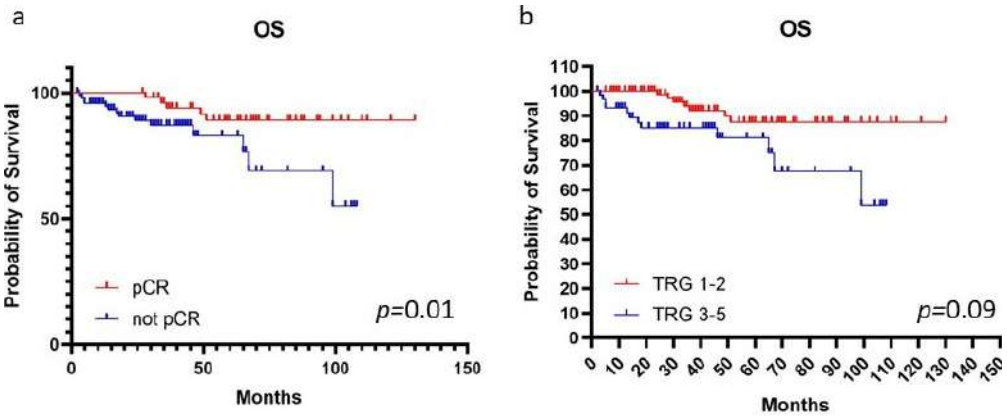

Figure 1. Kaplan Meyer curves for OS a) in pathological complete response (pCR) and b) in good responders according to Mandard tumor regression grade (TRG1-2). Both curves showed statistically significance.

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FAST-FORWARD REGIME: OUR EXPERIENCE

Code: 119

Aims: Moderate hypofractionation is the standard of care for adjuvant whole-breast radiotherapy (RT) after breast-conserving surgery for breast cancer (BC). Recently, 10-year results from the FAST and 5-year results from the FAST-Forward trial evaluating adjuvant whole-breast RT in 5 fractions over 5 weeks or 1 week have been published. We evaluate acute and late RT toxicities in women treated with 26 Gy in 5 daily fractions in our institution.

Methods: From November2020 to October2023, 55 early BC-patients(median age 73 years,64-88)were treated with 26,5 Gy in 5 fraction in a week using VMAT(35/55 pts)and IMRT(20/55)and daily IGRT.Inclusion criteria were: pT1/pT2 invasive BC,no or limited axillary involvement(pN0/pN1),age≥65years.12pts(21%)underwent deep-inspiration breath-hold.Target volumes and organ at risk were defined and plan were evaluated according to the FAST-Forward trial planning objectives.The main exclusion criteria are carcinoma in situ, mastectomy and chemotherapy.Pts underwent follow-up clinical visits documented with photographs at the end of RT and 1, 3,6,12,18,24and36 months after RT-end to evaluate acute and late adverse effects according to CTCAE v. 5.0.

Results: The two techniquesVMATandIMRT are equivalent in terms of adequate dose distribution. All plans have the same dosimetric behaviour in both the mean and max dose.There are no hot spots.Lung and heart dose constraints were never exceeded.Most of pts were T1(82%),while the remaining wereT2(18%).78% of the pts were axillary status negative, only22% were pN1.30(54%) of the cases were right breast,25(46%) were left breast.No patients interrupted radiotherapy.Median follow up was 10months(range3-40). At the end of RT 15 pts(27%)hadG1 breast erythema which was resolved in the next 2-3 weeks.One month later,we found only 2 cases of self-resolved G1 breast fibrosis and 1case of new-onsetG1breast hyperchromia,which persisted for 4months.Three months later we found one benign mastitis.One patient experienced a keloid in the chirurgical area one year later.No G≥2 erythema(acute skin toxicity)was detected.No patients reported cardiac major events,nor pulmonary acute toxicities.Late Skin toxicities were collected 6 months post Rt (5 pts:G1fibrosys),1years later(1ptsG1fibrosys),2years later(NoneG1),3years later(noneG1).No early ipsilateral breast tumour recurrence was observed.

Conclusions: Our analysis confirmed that weekly ultrahypofractionated whole breast RT is effective and safe in terms of acute and late skin toxicities.

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UHRT IN PCa: A CLINICAL IMPACT ANALYSIS FROM REAL WORLD EXPERIENCE

Code: 580

Aims: Randomized clinical trials demonstrated the non-inferiority of UHRT to conventional RT in patients with localized PCa. Despite an increased cost-effectiveness and expanded RT access, UHRT adoption remains variable.
The aim of the present study is to evaluate the oncological outcomes of a real-world cohort of PCa patients who underwent curative UHRT±SIB on DIL±ADT.

Methods: Patients with localized PCa who underwent radical UHRT between 2012 and 2021 were retrospectively included. Continuous variables were presented using the mean, median, and interquartile range (IQR), whereas categorical variables underwent frequency analysis. Toxicities were documented following the RTOG scale, and biochemical PFS was examined using the Kaplan-Meier method.

Results: From 2012 to 2021, a total of 890 patients matched included criteria. General cohort characteristics are reported in **Table 1**. Median age at diagnosis was 76 years (IQR 72 - 79) and median iPSA was 7.4 ng/ml (IQR 5.2 – 10.4).

Patients were stratified according to risk classes as follow: 327 (37.5%) as unfavorable intermediate, 202 (23.1%) as favorable intermediate, 188 (21.5%) as low, 156 (17.9%) as high/very high.
All patients underwent UHRT in 5 fractions with a dose/fx within 6.25 and 7.25 Gy every other day, 361 (40.6%) underwent a boost on DIL(s) with a dose/fx within 7.5 and 8 Gy.
Overall, 364 patients (41%) underwent ADT, according to clinical staging and performance status, with a median duration time of 8 months (IQR 6 – 12).
Median follow-up was 2.48 years (IQR 1.48 – 3.45) with a median last PSA of 0.56 (IQR 0.21 – 1.23) ng/ml.
A total of 85 patients (11.5%) experienced a biochemical progression (BP), with a median time from RT treatment of 30 (IQR 19 - 50) months. One, 2 and 3 years biochemical DFS rates were 98.7%, 93.3% and 88.6%, respectively.
Clinical progression (CP) was observed in 70 patients (7.5%); 46% (32) was unfavorable intermediate, 32% (22) was high/very-high risk, 10% (7) was favorable intermediate and 13% (9) was low risk group.
Local recurrence was registered for 25.8% (18) of patients; the other reported CPs were 42.9% (30) lymphnodal, 25.7% (18) bone and 5.7% (4) visceral.
At last FU, 10 (1.35%) patients died for other causes than PCa, 669 (90.8%) were alive with no evidence of disease and 71 (9.6%) were alive with disease.

Conclusions: As evidenced by this real-world cohort, UHRT is safe and effective for patients with localized PCa and it should be more widely integrated into current clinical practice.

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Table 1. General cohort characteristics and follow-up data.

Pts characteristics	n (%)
Risk class	n=873
Low	188 (21.5)
Favourable intermediate	202 (23.1)
Unfavourable intermediate	327 (37.5)
High	145 (16.7)
Very High	11 (1.2)
cT	n=882
cT1	393 (44.6)
cT2	452 (51.2)
cT3	36 (4.0)
cT4	1 (0.2)
HT	
YES	364 (40.9)
NO	526 (59.1)
Dose prostate	
32.5	57 (6.4)
35	459 (51.6)
36.25	374 (42.0)
Dose DIL	n=361
37.5	332 (91.7)
40	29 (8.3)
Last follow-up status	n=726
NED	633 (87.2)
AWD	79 (10.8)
DIED for other causes	14 (2)
Clinical Progression	n=70
Local recurrence	18 (25.7)
Lymphnodes	30 (42.9)
Bone	18 (25.7)
Visceral	4 (5.7)

STEREOTACTIC BODY RADIATION THERAPY (SBRT) FOR CHALLENGING LIVER METASTASES: A RETROSPECTIVE DATABASE

Code: 32

Aims: Liver is a common site of metastatisation. Surgery has always been the gold standard for hepatic lesions, but most of patients are not operable. Radiofrequency and microwaves ablations are also invasive and have limits related to lesions' size or location. Radiotherapy did not have a role in the treatment of liver metastases, but technological advances have lowered the toxicities and improved the outcomes. However, only few studies report the use of stereotactic body radiotherapy (SBRT) for large or multiple lesions, or metastasis located near dose-limiting organs at risk. We aim to collect the data of patients treated with SBRT for these challenging liver oligometastases.

Methods: We analysed 208 patients (316 liver lesions) treated with SBRT from 2013 to 2022. For every patient, we collected data about primary site, Charlson Comorbidity Index (CCI), liver volume and systemic treatments. For every lesion, we determined the setting (diameter $\geq$ 4 cm, number of metastasis $\geq$ 3, proximity with critical OARs), the oligometastatic state and the previous execution of local and systemic therapies. Primary endpoint was Overall survival (OS), secondary endpoints were local control (LC), progression free survival (PFS), out-field intrahepatic progression (OF-IHPFS) and toxicity.

Results: Median follow up was 17.1 months. OS rates at 1, 2 and 3 years were 78.9% (95%CI 72.0 – 84.2), 52.0% (95%CI 43.5 – 59.9), and 34.1% (95%CI 26.9 – 42.3), negatively related with rectal tumor and high metastatic volume at univariate and multivariable analysis. LC at 1, 2 and 3 years was 96.5% (95%CI 93.2 – 98.2), 96.0% (95%CI 92.4 – 97.9), and 95.0% (95%CI 90.7 – 97.4), associated with previous local ablative therapy (LAT) at univariate and multivariable analysis. Median PFS was 7.03 months, with 1,2- and 3-years rates of 24.5% (95%CI 18.6 – 30.8), 9.7% (95%CI 5.8 – 14.6), and 7.1% (95%CI 3.8 – 11.6), related with histology and lines of systemic therapy.

Conclusions: Our results confirm the feasibility of SBRT for liver metastasis also in difficult scenarios, with excellent local control and low toxicity profile, independent from histology, size and location but related to previous lines of systemic and local therapies and high tumor burden. Further studies are needed to define the real critical hepatic lesion and the optimal timing of SBRT in oligometastatic patients.

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SBRT FOR PROSTATE CANCER USING RADIXACT TOMOTHERAPY WITH SYNCHRONY FIDUCIAL TRACKING: A SINGLE CENTRE EXPERIENCE ON EFFICACY AND TOLERABILITY

Code: 301

Aims: The use of SBRT in the treatment of prostate cancer has increased significantly. SBRT is a highly conformed EBRT technique that allows the delivery of a limited number of high-dose fractions on the target volume and to minimize the dose to adjacent organs. The management of intrafraction prostate motion is necessary for the precise delivery. Aim of this study is to evaluate efficacy and safety in patients with localized prostate cancer undergoing SBRT using Radixact® Tomotherapy with Synchrony® fiducial tracking, a real time motion tracking and correction system.

Methods: This work analyzes 27 prostate cancer patients, underwent SBRT from June 2022 to January 2024. 6 (22%) were at low risk, 8 (30%) at favorable intermediate risk, 10 (37%) at unfavorable intermediate risk and 3 (11%) at high risk. ADT was prescribed based on risk group. Three gold fiducial markers were placed in the prostate under ultrasound guidance before CT scan, to visualize the position and movement of the prostate before and during the treatment and allow to apply corrections in real time. The total dose administered was 36.25 Gy in 5 fractions, every other day, by Radixact® Tomotherapy with Synchrony® fiducial tracking. The required target coverage was at least 95% of the PTV volume with at least 95% of the prescribed dose. CTCAE V 5.0 was used to evaluate acute and late toxicity, GI and GU.
PSA was used as a serum marker to assess response to treatment.

Results: Median age of the patients was 75 (range 56-83) years. Median follow up was 9 months (range 0-19). The treatment was well tolerated by the majority of patients. All patients completed the planned treatment, without requiring interruptions. No acute and late GU and GI toxicities? G3 were observed. For acute GU toxicity, 16 (59%) patients reported symptoms, but only 1 (4%) presented G2 toxicity. For acute GI toxicity 7 (26%) patients presented symptoms, but also in this case only 1 (4%) with G2 toxicity. 21 patient data for late toxicity and efficacy are currently available. 6 (29%) patients experienced late GU toxicity, all G1. 3 (14%) patients reported late GI toxicity, of which 2 (9%) were G2. All patient achieved a significant reduction in PSA.

Conclusions: This work demonstrates that prostate SBRT using Radixact® Tomotherapy with Synchrony® is safe and effective, however it is necessary to expand the sample and longer follow up to evaluate late toxicity and clinical outcome.

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RADIOTHERAPHY ON HEART NOT ONLY AN ADJUVANT TREATMENT

Code: 319

Aims: For long time, Radiotherapy Treatment was very limited for cardiac mal ignancies both for their low incidence a nd for the sensitivity of the heart to radiation injury. However modern radiatio n techniques, such as intensity-modulated radiation therapy (IMRT) and volumetric modulated arc theraphy (VMAT) enable the increase of radia tion dose and minimize side effects.

Methods: In 57-year-old man, dysponea and chest pain were clinical manifestation of cardiac tumor diagnosed with chest CT scan of left atrium (with diameter of 5.5 x 6 cm). After surgical exerisis of atrial mass, histological examination showed cardiac mixoma.
Only three months later, the patient showed cardiac symptoms and a CT scan showed relapse of neoplasia. The relapse was surgically removed and a new histological evaluation concluded for a myxoid sarcoma. Some months later chest CT showed a further inoperable recurrence. The patient was defined not amenable to chemotherapy. Radiant treatment was propose as unique and non invasive therapeutic possibility.
Before proceeding radiant treatment, cardiac magnetic resonance imaging (MRI) was performed and it defined the degree of atrial mass invasiveness to the posterior wall and to the left pulmonary veins (fig.1).
Subsequently the patient was subjected to CT scan centering. An image fusion was carried out with the images of the centering CT and those of MRI for a greater definition of the processing volumes. The Planning Target Volume (PTV) included myxoid sarcoma mass with an expansion of 0.5 mm, and as organs at risk (OAR) the heart not affected by disease, the esophagus and the left and right lung and the spinal cord. With the VMAT, imaging technique (IGRT) total dose (TD) of 45 Gy were delivered in 25 fractions. Before each treatment, CBCT images (Cone

BEAM CT) were acquired and the sessions were performed under electrocardiographic monitoring.
The treatment ended without significant side effects. After 40 days, Cardiac MRI showed a reduction of the cardiac mass whose current diameter is 2.5 x 3.0 cm.
After the improvement in respiratory and cardiac symptoms, the patient began chemotherapy treatment.

Results: Today, after a year from diagnosis, the patient is still alive and presents a moderate-degree heart failure, he is in oxygen therapy and keeps doing chemotherapy with gemcitabine and docetaxl.

Conclusions: Our date suggest postsurgical radiotherapy associated with chemotherapy as a effective adjuvant therapy able to improve survavial.

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SRS TREATMENT FOR PRIMARY SPINAL CORD ASTROCYTOMA IV: A CASE REPORT

Code: 185

Aims: Spinal cord astrocytomas (SCAs) are intramedullary neoplasms that make up 6–8% of spinal cord tumors. Among them, anaplastic Astrocytomas (WHO grade III), and Glioblastoma multiforme (WHO grade IV) are included. Due to their relative rarity, no large patient series are available thus currently there is no consensus to manage SCAs. Although Gross Tumor Resection (GTR) is the best required approach, in spinal Glioblastoma series it is not always achievable. Moreover higher radiation doses are not allowed due to the radiation spinal cord tolerance. Thus Stereotactic RadioSurgery (SRS) could be a helpful option. Herein a case report treated with SRS in our centre.

Methods: A 40 years old woman went to our observation complaing of neurological impairment of extremities and neck, sphynteric incontinence and hyperestesia on trunk. Cervical MRI showed an epidural mass on the anterior side of the spinal cord at C3-C6 vertebrae level, measuring 35 mm in CC, 26 mm in LL and 8 mm in AP sides. Partial resection showed a diagnosis of Atrocytoma IV. Due to her neurological condition critical for the set-up, SRS was chosen as treatment.

Results: PTV consisted of GTV + 1 mm; to GTV 15 Gy and PTV (GTV+ 1 mm) 14 Gy with a dose fall off of 12 Gy Dmax to the surrounding spinal cord were prescribed. The plan consisted of VMAT 3 arcs and 6 MV photon beams; refence point was 100% to GTV with 95,2 % of normalization. The mean dose to GTV was 15. Gy; the mean dose to PTV was 14.52 Gy. The Dmax to the spinal cord was 14 Gy. Treatment was delivered during the same day of simulation. Steroids and mannitol were supplied. Neurological deficits of arms and necks improved within two days. Then she started Temozolomide for 6 cycles. No toxicities on surrounding normal tissue were recorded. Six months later MRI showed at C4-C6 vertebrae level a fibrotic lesion without contrast enhancement.

Conclusions: Due to rarity of intraspinal primary tumors like malignant astrocytomas, no standard treatments are provided. Literature data suggest that SRS is a safe and effective treatment option for primary tumors of the spine and spinal cord as we recorded in this case.

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INITIAL EXPERIENCE WITH TTFields (OPTUNE™) IN AN INOPERABLE GLIOBLASTOMA AFFECTED PATIENT

Code: 138

Aims: A new FDA-approved treatment involving electric fields (TTF) alternating at 200 kHz called Optune™ therapy is now available for recurrent Glioblastoma (GBM) as monotherapy and in combination with temozolomide for new diagnosed GBM on the light of the evidences on its benefit in survival. Here we report our initial experience on the first patient with left frontal GBM not surgically fit, treated with Supp protocol and TTF -Optune™.

Methods: The patient is a 42-year-old woman who first presented with neurological impaiment of all extremities being in a vegetative state. Imaging on MRI documented a large cystic inoperable tumor in the left lobe extending over the midline and the corpus callosum with brain stemA mass effect and severe edema was described. She underwent cystic fluid aspiration and biopsy showing a diagnosis of Glioblastoma (GMB). Then she received radiation therapy 40.05 Gy and concomitant chemotherapy with temozolomide 75 mg/m2/die followed by consolidation temozolomide (TMZ) with TTF.

Results: After the concomitant phase, the MRI showed a stable disease with a new morphology of the necrotic tumor pattern and an unexpected neurological improvements, consisting of a more reactive state. She started the use of TTFields during the first cycle of consolidation TMZ. Neurological symptoms improved. The control brain MRI showed still a stable disease with a tissue loss as a large necrotic area. After 4 months from the diagnosis, she is still alive and reactive, continuing TMZ consolidation with TTFields. No sides effects have been recorded.

Conclusions: Non invasive TTFields (Optune™) device appears to be a safe and efficacious integrated modality for the treatment against GBM in daily clinical practice.

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ADAPTIVE INTERVENTIONAL RADIOTHERAPY (BRACHYTHERAPY) IN THE MANAGEMENT OF CERVIX CANCER: IS IT FEASIBLE PLAN SECOND INTERVENTIONAL RADIOTHERAPY FRACTION ON THE BASIS OF THE FIRST FRACTION PLAN?

Code: 575

Aims: The study's objective was to determine whether it would be feasible to treat subsequent fractions of intracavitary brachytherapy using a computed tomography (CT)-based plan of the first fraction, based on the assessment of the physical dosimetric variations between successive treatments.

Methods: 140 3D CT image datasetbased plans of 35 patients (35 × 4 CT = 140 plan) who have received intracavitary or intracavitary plus interstitial IG-IRT treatment for cervix cancer between July 2023 and November 2023 were analyzed.
To assess variations in applicator position over the 6-hour gap, dosimetric values for OARs (D2cc) and CTV coverage values (V95%) were considered. For validating the overall treatment efficacy, in EQD2 D98% and D90% dosimetric values were also assessed for HR-CTV, in addition to D98% in EQD2 as the dosimetric value for IR-CTV. In plan A, the dose was further optimized to cover HR-CTV and IR-CTV, ensuring no compromise in the target dose. Both dosimetric and coverage parameters were expressed in terms of mean and standard deviation. Variations in dosimetric values and CTV coverage were evaluated using paired t-tests for comparison of means, considering any p-value less than 0.05 as statistically significant.

Results: The analysis of the data presented in this study highlights non-significant findings for dosimetric values of OARs. The analysis of the V95% and D98% for HRCTV and V95% and D98% for IRCTV have been found significant difference between plan A and plan B. Despite the significant findings in CTV coverage, the dosimetric values in EQD2 for D98% and D90% for HR-CTV adhere to the minimum standards of the GYN GEC-ESTRO guidelines concerning the overall treatment, with an average value of 87.7±11.3 Gy and 143±16.5 Gy respectively, and minimum values of 78.6 Gy and 94 Gy. For IR-CTV the average dosimetric value of D98% in EQD2 is (85.4±11.2) Gy with a minimum value of 62.2 Gy, compared to the GYN GEC-ESTRO guidelines reference value is 60 Gy. The analysis of the D90% for HRCTV have been found no significant difference between plan A and plan B.

Conclusions: When treating subsequent fractions using the CT image-based interventional radiotherapy plan of the first fraction, the dosimetric variation for the tumor and organs at risk is within an acceptable level.

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ASSESSING THE PREDICTIVE ROLE OF VOLUMETRIC CHANGES IN SOFT TISSUE SARCOMAS OF THE EXTREMITIES FOLLOWING NEOADJUVANT RADIOTHERAPY

Code: 156

Aims: To evaluate the radiological response of localized, high-grade, primary soft tissue sarcomas (STS) of the extremities treated with neoadjuvant radio(chemo)therapy, using RECIST, Choi criteria, and volumetric changes.

Methods: Fifty-nine patients (median age 52 years, range: 16-84) with STS underwent pre-operative external beam radiotherapy (RT), receiving a median dose of 50 Gy. MRI scans of the affected region and chest TC +/- PET were performed before RT, after RT (before surgery), and during follow-up (FU). All MRIs were reviewed by a single radiologist specializing in musculoskeletal oncology, using semi-automatic software (Carestream Vue PACS c 12.2.6.2000019) for volume measurements.

Results: MRI scans were conducted at a median of 5.71 weeks before and 4.43 weeks after RT. The median percentage change in maximal tumor diameter was -12.50% (range -74.63% to +92.78%). According to RECIST and Choi criteria, partial response was seen in 20.34% and 55.93% of cases, stable disease in 71.90% and 27.12%, and progressive disease in 8.47% and 16.95%, respectively. Tumor volume decreased in 43 out of 59 patients, with a median change of -37.00% (range from +415% to -99.00%). The log-rank test revealed that radiological responses evaluated by RECIST, Choi criteria, and volume changes did not significantly impact 5-year local control, distant metastasis-free survival, disease-free survival, or overall survival (Table 1).

Conclusions: Our analysis indicates that neither RECIST and Choi criteria nor volumetric changes effectively predict oncological outcomes. This suggests the necessity for exploring additional parameters or predictive models that could more accurately forecast treatment response and patient prognosis in soft tissue sarcomas of the extremities following neoadjuvant radio(chemo)therapy.

Table 1: actuarial results and univariate analysis.

Variable	Value	Nr Pz	5-year LC	p	5-year-DMFS	p	5-year DFS	p	5-year OS	p
Choi	CR+PR	33	100.0%	.	71.4%	0.531	71.4%	0.531	100.0%	0.217
	SD+PD	26	100.0%		59.4%		59.4%		94.7%	
RECIST	CR+PR	12	100.0%	.	58.3%	0.794	58.3%	0.794	100.0%	0.631
	SD+PD	47	100.0%		67.6%		67.6%		97.4%	
Volume	≥ -37%	31	100.0%	.	65.9%	0.409	65.9%	0.409	95.8%	0.317
	< -37%	28	100.0%		66.5%		66.5%		100.0%	

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BASAL CELL CARCINOMA: A RARE CASE OF BONE METASTASIS

Code: 305

Aims: Bone metastases of basal cell carcinoma (BCC) are very unusual.In this setting of disease available therapeutic options are limited. To our knowledge, in literature there are no cases of bone metastases from BCC treated with external beam radiation therapy (EBRT) without any systemic treatment.

Methods: We reported a rare case of bone BCC metastasis in a 79-year-old man who previously underwent surgery on right nasal wing and subsequent radiotherapy, on residual disease for a total dose of 40 Gy (2 Gy/fraction) in April 2016, in another institute. His first relapse was in July 2019 and, because of the patient's refusal to undergo any surgical or medical treatments, he was referred to our institute for a radiation oncology consult; then, he was re-irradiated on the right nasal wing for a total dose of 50 Gy (2 Gy/fraction). After 20 months of follow up, bone lesion was documented by means of 18 F-FDG computed tomography (CT) / Positron Emission Tomography (PET) and confirmed by the biopsy. Due to the osteolytic characteristics of the bone lesion in L4, the patient underwent vertebroplasty surgery and was candidated to EBRT with palliative and consolidative intent. EBRT consisted of Volumetric Modulated Arc Therapy (VMAT) in a daily schedule for a total dose of 20 Gy (4 Gy/fraction). After three months by the end of EBRT, 18-F FDG CT/PET revaluation showed a metabolic partial response. The patient died of other causes in May 2023.

Results: In our case we recorded an improvement on painful symptoms and partial response with a good disease local control in absence of any side effects.

Conclusions: To our knowledge, our experience is the first case in literature that reported VMAT for bone BCC metastasis. In the present case report, VMAT was a safe and effective option in this unusual clinical scenario.

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DEVELOPMENT AND VALIDATION OF A RISK MODEL FOR LOCAL FAILURE IN PANCREATIC CANCER AFTER SBRT.

Code: 456

Aims: To develop and validate a predicting model of local failure (LF) based on geometric GTV uncovered by high-dose radiotherapy (50Gy) in patients (pts) with locally advanced pancreatic cancer (PC).

Methods: Two cohorts of PC pts received chemotherapy and SBRT: the discovery cohort (50 pts) and the validation cohort (91 pts). Univariate and multivariable survival analyses (UVA/MVA) were performed to evaluate LF association with GTV size and the extent of GTV not covered by high-dose RT.
We defined a set of incomplete GTV-covering levels: GTV75 (=yes if less than 75% of the GTV was included in the 50 Gy isodose), GTV70, GTV50, and GTV30. Variables with $p \leq 0.2$ at UVA were included in MVA.

Results: In the discovery cohort, 12 pts experienced LF. The GTV size ($p=0.007$) and GTV70=yes ($p=0.2$) were selected as risk factors. GTV size was dichotomized as below/above 25 cc. Dichotomized GTV size and GTV70 were used to build a 3-level Geometric Score (GS) for the prediction of the risk of LF:
- Low Risk (LR) if "GTV<25cc AND GTV70=no";
- Intermediate Risk (IR) if "GTV>25cc OR GTV70=yes";
- High Risk (HiR) if "GTV>25cc AND GTV70=yes".

The model classified 10 pts in LR, 21 pts in IR, and 19 in HiR classes. Pts categorized at HiR had a significantly higher probability of LF: HR=6.9 (95%CI 1.5-32.9) compared to LR, and HR=13.2 (95%CI 3.6-48.4) when compared to IR. 10/12 LFs are in the HiR group. The actuarial probability of LF was 62% in the HiR group vs 7% in the others. The mean time (MT) to LF is 38, 35, and 23 months (mo) for the LR, IR, and HiR classes, respectively.
In the validation cohort, pts were subdivided into: 8 in LR, 60 in IR, and 14 in HiR. The likelihood of LF doesn't significantly differ across the 3 classes ($p=0.082$). Only the HiR and IR were found significant ($p=0.037$). This may be due to the small number of events relative to the total number of pts in each class (LR: 3 events out of 8 patients). LR and IR were merged to create a 2-class GS. Low-Intermidiete risk class (L-IR) owns GTV<25 ccs or GVT70=no, and HiR has no favourable variables.
The 2-GS can predict LF with HR=0.5 (95%CI 0.15-1.85) for L-IR and HR=1.48 (95%CI 0.36-5.98) for HiR ($p= 0.042$). The LF probability at 15 mo is 34% for L-IR and 44% for HiR. The MT to LF is 32 and 20 mo for the LIR and HiR classes, respectively.

Conclusions: Although the 3-GS is not validated, a large GTV size coupled with an incomplete (<70%) covering of GTV from the high dose highly increases the risk of LF in PC pts, as confirmed in the 2-GS.

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COMPARISON BETWEEN CONTOURING PRE AND POST ESTRO ACROP GUIDELINES IN PATIENTS TREATED WITH NEOADJUVANT CHEMOTHERAPY AND PROSTHETIC RECONSTRUCTION POST MASTECTOMY: OUR EXPERIENCE

Code: 481

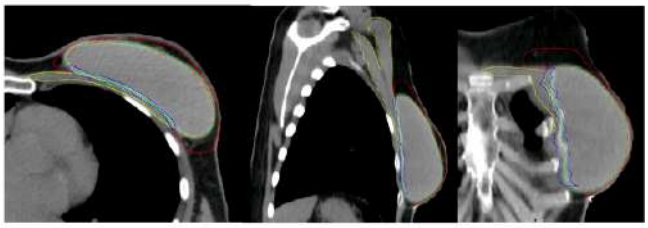
Aims: Post-mastectomy prosthetic reconstruction is increasingly common in breast cancer patients undergoing neoadjuvant chemotherapy. In our study we compared volumes of pre and post ESTRO ACROP giudelines contouring in our clinical practice and observed the aesthetic outcomes and the incidence local and distant recurrences.

Methods: From January 2019 to June 2023 we selected the data of 18 patients who fit the following criteria: patients with T2-4 N0-2 M0 at the diagnosis, neoadjuvant chemotherapy, subjected to mastectomy (Nipple- sparing and Skin-sparing) and prosthetic reconstruction (with prostetic implant or expansor), Radiation therapy (using schedule of 25 or 15 fractions), follow-up of no less than 6 months. We compared the volumes of treatment using the ESTRO ACROP Guidelines (as shown in Figure 1) and we evaluated the pattern of recurrence, toxicity (cutaneous, cardiac, pulmonary) and time to progression.

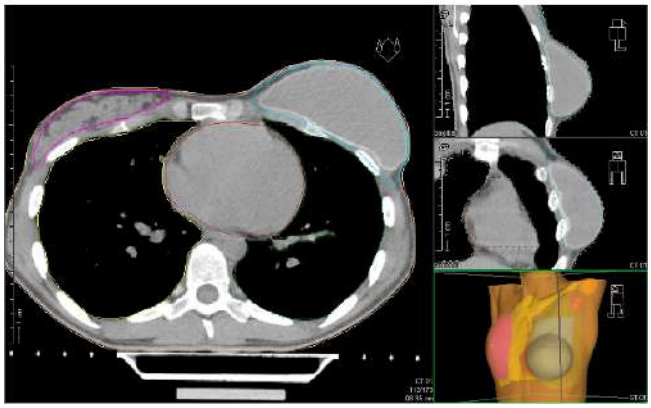
Results: Of the eighteen patients analyzed, 10 patients fitted all the inclusion criteria. Among these, only one patient showed regional recurrence located outside the ESTRO-target volume, in the medial margin of the implant with infiltration of the chest wall. One patient had distant recurrence after 2 years. 3 patients showed mild skin and cardiac toxicity, no prostetic shrinkage or damage were assessed.

Conclusions: The ESTRO ACROP guidelines are a fundamental tool in standardizing the definition of contouring volumes ensuring optimal aesthetic and survival outcomes.

Figure 1. Comparison between ESTRO ACROP guidelines.



Our Contouring.



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IMPACT OF GASTRIC VOLUME ON SBRT FOR LOCALLY-ADVANCED PANCREATIC CANCER: SINGLE CENTER STUDY

Code: 424

Aims: To evaluate if daily variability in gastric filling may impact the efficacy and safety of SBRT in pancreatic cancer.

Methods: We retrospectively evaluated the treatment plans and Cone Beam Computed Tomography (CBCT) of patients with locally advanced pancreatic cancer treated with 50 Gy in 5 fractions according to Verona protocol. For each patient on each CBCT the stomach was contoured, by a TSRM, named Stomac1 in the first CBCT up to the fifth Stomac5 in the last one. The contouring was then reviewed and validated by a radiation oncologist. Of each patient, the difference in gastric filling was assessed in terms of percentage difference of cc (% cc) from the contoured stomach on the simulation CT and the percentage standard deviation (% SD). The effective dose received by the new stomach structures both daily and in total was then re-calculated. At last, it was evaluated if the new stomach structures overlapped with the planning target volume receiving 50 Gy (PTV50) and for how many cc. These dosimetry data were correlated with acute and chronic toxicity assessed according to the CTCAE v5 scale.

Results: Twenty-three pts treated from 2016 to 2019 were evaluated. Mean age 64 (range 46-79). 14 male and 9 female pts.115 stomach structures were contoured, 5 for each patient. The tumor was located at the head of the pancreas in 8 pts, at the isthmus in 11 pts and at the tail in 4 pts.

Table 1 shows as first the volume in cc of the stomach structures in CT sim and CBCT and the difference in filling in mean value and % SD. The second value in each column after the / represents the maximum dose received by the new stomach structure in the recalculated treatment plans

Table 1.

TC PLAN (*cc* / Gy)	CBCT1 (*cc* / Gy)	CBCT2 (*cc* / Gy)	CBCT3 (*cc* / Gy)	CBCT4 (*cc* / Gy)	CBCT5 (*cc* / Gy)	MEDIA cc CBCT	dev std %	diff % volume stomaco tra CBCT e TC	DOSE TOTALE EFFETTIVA Gy
169,2 / **35,0**	*244,1* / **50,1**	*209,8* / **50,4**	*155,4* / **35,6**	*196,4* / **42,5**	*188,6* / **48,4**	198,86	*16,23%*	17,53%	**45,4**
332,7 / **7,70**	*322,7* / **4,50**	*284,2* / **3,20**	*275,4* / **4,50**	*285,3* / **5,00**	*297,3* / **6,20**	292,98	*6,26%*	-11,94%	**4,7**
158,3 / **26,6**	*132,5* / **28,0**	*177,7* / **46,5**	*125,4* / **29,5**	*116,8* / **33,1**	*170,1* / **31,6**	144,5	*19,06%*	-8,72%	**33,7**
165,4 / **34,1**	*241,3* / **33,9**	*447,7* / **28,0**	*249,1* / **28,4**	*246,6* / **29,5**	*159,5* / **30,8**	268,84	*39,71%*	62,54%	**30,1**
226,6 / **21,7**	*290,3* / **16,0**	*349,6* / **19,1**	*365,1* / **28,1**	*330,0* / **23,9**	*228,2* / **31,1**	312,64	*17,55%*	37,97%	**23,6**
186,5 / **25,8**	*234,9* / **30,3**	*219,3* / **11,1**	*202,9* / **34,0**	*205,0* / **15,2**	*339,2* / **17,8**	240,26	*23,63%*	28,83%	**21,7**
258,7 / **28,7**	*226,9* / **51,5**	*229,7* / **48,8**	*176,9* / **50,7**	*233,7* / **30,4**	*189,1* / **35,2**	211,26	*12,43%*	-18,34%	**43,3**
329,7 / **28,3**	*254,7* / **39,7**	*263,7* / **46,1**	*192,7* / **47,5**	*295,2* / **48,5**	*247,4* / **45,0**	250,74	*14,84%*	-23,95%	**45,3**
169,1 / **20,7**	*178,2* / **20,2**	*156,8* / **25,1**	*152,9* / **24,5**	*307,6* / **32,7**	*184,5* / **35,2**	196	*32,57%*	15,91%	**27,5**
168,2 / **29,1**	*168,2* / **22,5**	*134,0* / **25,6**	*103,0* / **25,7**	*126,2* / **20,5**	*83,1* / **24,2**	122,9	*26,26%*	-26,93%	**23,7**
314,9 / **12,8**	*289,2* / **15,7**	*222,5* / **10,9**	*253,1* / **14,1**	*256,6* / **17,7**	*162,7* / **12,6**	236,82	*20,14%*	-24,80%	**14,2**
205,3 / **27,4**	*181,8* / **28,2**	*190,0* / **29,2**	*174,2* / **34,1**	*159,1* / **30,5**	*206,6* / **30,1**	182,34	*9,71%*	-11,18%	**30,4**
173,7 / **23,7**	*288,5* / **1,70**	*206,2* / **25,5**	*161,2* / **21,9**	*162,5* / **24,9**	*154,3* / **24,9**	194,54	*28,99%*	12,00%	**19,8**
118,5 / **27,0**	*217,7* / **31,1**	*299,4* / **45,7**	*351,3* / **44,2**	*275,1* / **30,6**	*287,9* / **37,4**	286,28	*16,78%*	141,59%	**37,8**
116,6 / **28,1**	*150,2* / **25,9**	*131,9* / **27,1**	*117,3* / **36,9**	*167,3* / **26,6**	*310,5* / **35,8**	175,44	*44,35%*	50,46%	**30,5**
130,4 / **14,2**	*207,6* / **10,0**	*123,5* / **8,80**	*113,4* / **14,8**	*140,1* / **13,2**	*119* / **15,0**	140,72	*27,50%*	7,91%	**12,4**
156,3 / **29,4**	*145,2* / **30,4**	*169,5* / **30,4**	*174,9* / **30,7**	*150,3* / **34,7**	*154,2* / **32,9**	158,82	*8,04%*	1,61%	**31,8**
196,6 / **19,5**	*313,5* / **21,8**	*242,6* / **20,8**	*210,1* / **19,7**	*311,6* / **29,3**	*265,8* / **19,8**	268,72	*16,61%*	36,68%	**22,3**
299,6 / **25,4**	*267,0* / **27,2**	*280,0* / **27,0**	*234,4* / **27,6**	*252,6* / **30,5**	*302,6* / **29,6**	267,32	*9,73%*	-10,77%	**28,4**
207,6 / **30,2**	*333,4* / **25,7**	*273,9* / **30,9**	*222,0* / **30,0**	*226,1* / **22,9**	*134,5* / **27,4**	237,98	*30,81%*	14,63%	**27,4**
109,1 / **25,8**	*151,9* / **31,0**	*170,2* / **30,1**	*190,8* / **30,1**	*199,1* / **30,3**	*287,1* / **30,7**	199,82	*26,09%*	83,15%	**30,5**
148,7 / **27,1**	*165,3* / **28,3**	*141,5* / **31,1**	*151,1* / **30,7**	*154,7* / **28,7**	*131,3* / **30,6**	148,78	*8,71%*	0,05%	**30,2**
195,0 / **30,8**	*399,8* / **40,1**	*295,3* / **35,4**	*253,9* / **34,2**	*207,8* / **35,3**	*195,8* / **36,0**	270,52	*30,44%*	38,73%	**36,2**

for each CBCT. The last column contains the effective dose received by the stomach. The dose constraint of Dmax<35 Gy has been exceeded in 5 patients. Overlap between the of the new PRV stomach of each new stomach structure with the PTV50 occurred in only one patient for 1.1 cc. No acute or chronic toxicities above G2 occurred in any patient evaluated.

Conclusions: The stomach has considerable interfraction variability that however in our series did not impact the quality of treatment in terms of safety and efficacy. The maximum dose indicated in the literature as constraints (Dmax<35 Gy) was exceeded but did not cause increased toxicity. Future evaluations on larger case series should be done to assess if dose escalation is feasible in SBRT for pancreatic cancer patients.

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HYPOFRACTIONATED RADIOTHERAPY FOR CUTANEOS CARCINOMA: ROUTINE CLINICAL PRACTICE IN TIMES OF COVID-19

Code: 455

Aims: The COVID-19 pandemic has had a significant impact on Radiotherapy (RT) facilities; there has been a reduction in the delivery of treatments due to the logistical and organizational challenges created by the pandemic. Conventionally fractionated radiotherapy posed challenges during the COVID-19 crisis in terms of accessibility and compliance; for these reasons hypofractionated radiotherapy has been used with success, providing higher doses per fraction with fewer sessions. Based on these experiences, we used hypofractionated RT for pts with Non-Melanoma Squamous Cellular Carcinoma (NMSC) and continued this strategy even after the pandemic, as this approach not only mitigated the risk of exposure to infectious agents, but also proved to be very useful regarding the care of elderly patients with poor compliance.

Methods: Between November 2021 and November 2023, 70 patients (pts) diagnosed with NMSC were treated with radical radiotherapy at our center, of which 27 were selected to receive a treatment plan aimed at minimizing the number of admissions to our department. 9 pts (33.3%) had a diagnosis of Basocellular Carcinoma (BCC), 18 pts (66.6%) had a diagnosis of Squamous Cellular Carcinoma (SCC), all patients had a head-neck region pathology. 5 (18,5%) pts were female, 22 (91,5%) pts were men, with a median age of 85 (range 66-99). RT prescription dose was 50-60 Gy in 10 fraction (5-6 Gy/fx bi-weekly) The treatment was performed by electrons beam in 22 pts (81.5%) and by photons in 5 pts (18.5%).

Results: Grade 2 erythema was observed in 20 pts (74%), Grade 1 erythema in 5 pts (18,5%), and Grade 3 erythema with moist desquamation occurred in only 2 pts (7,4%). At the time of the analysis, in December 2023, with a median follow up of 12 months (range 1 - 24), 21 pts (77.7%) present local control (LC), 2 pts (7,4 %) present stable disease (SD), 3 pts (11,1%) had a progression disease (PD), 1 pts (3.7%) died.

Conclusions: The biweekly RT schedule is a safe and well-tolerated treatment option. This program can benefit elderly patients with complex medical conditions and fitter patients by reducing their hospital presence, inspired by the logistics of the COVID pandemic. The flexibility of this solution helps to solve the challenges of patient management, ensuring better compliance and reducing logistical challenges for radiotherapy facilities, as well as freeing up treatment slots for new patients to reduce waiting lists.

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FEASIBILITY AND TOLERABILITY OF WHOLE LUNG VMAT IRRADIATION IN PAEDIATRIC AND TEENAGE PATIENTS USING ACTIVE BREATHING CONTROL SYSTEM

Code: 392

Aims: to demonstrate the feasibility of VMAT whole lung irradiation (WLI) using Elekta Active Breathing Coordinator™ (ABC) system to safely treat paediatric and teenage patients (pts) with sarcoma lung metastases.

Methods: We retrospectively identified pts ≤18 years referred for WLI using ABC at our centre from 2022 to 2023. Volumetric intensity modulated arc therapy (VMAT) plans adequacy was analysed reviewing DVHs records and calculating conformity index (CI) and homogeneity index (HI) using ICRU formulas. ABC tolerability and acute toxicities were assessed from machine and clinical records reporting procedures duration (from the site set up to the end of each irradiation) and acute toxicities (CTCAE v5.0).

Results: 4 pts with sarcoma lung metastases (2 Ewing and 2 Ewing like) received VMAT WLI using ABC system. The ages of pts were: 15, 15, 13 and 8 years. All pts received a training on how to hold their breath prior to simulation using ABC with the aim of tolerate a breath-hold time of 20-25 seconds and an inhalation threshold of 1.2-1.5 litres. A breast board device was used to raise pts arms during planning CT and treatment. All plans were performed using Raystation treatment planning system v.10B using two coplanar 357° arcs with the goals to have an adequate coverage of the PTV (≥ 95% of the prescribed dose) and to limit the maximum dose to spinal cord, heart and liver (<105% of the prescribed dose). A total dose of 18Gy in 12fr or 15 Gy in 10 fr (5fr/w) was prescribed depending on age. One patient received a further SBRT boost to a pulmonary nodule. PTV goals and OARs limits were always respected. The mean CI and HI were 0.9 and 0.1. All pts were able to comply treatment without interruptions. Mean machine time for each daily fraction was 24.22 minutes. No acute toxicities >G2 were recorded. One pts contracted an asymptomatic SARS-CoV2 infection 11 days after WLI without sequels. Another pts, previously treated with high dose chemotherapy, presented a G3 thrombocytopenia during the SBRT boost. Pts underwent a chest X-ray at 10 days and a Chest CT at 3 months and no pulmonary injury was recorded.

Conclusions: VMAT WLI in paediatric and adolescent patients using active breathing control system was found to be feasible and well tolerated. The average machine time necessary to carry out each radiation fraction using ABC system does not exceed that normally reserved for adult patients. No acute toxicities were reported during WLI and at the radiologic revaluations.

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THE ADOPTION OF 1.5 TESLA MRI-LINAC FOR THE TREATMENT OF NON-HODGKIN LYMPHOMA INVOLVING HEAD AND NECK SITES: A CASE SERIES

Code: 457

Aims: MRI-Linac provides superior soft tissue image quality and allows daily re-contouring of gross tumor and clinical target volume, enabling adaptive treatment. This could be crucial for the treatment of lymphomas, considered their tendency to rapidly shrink in response to irradiation.

Methods: clinical and dosimetric data of the first 7 patients affected by non-Hodgkin lymphoma (NHL) involving head and neck (H&N) sited treated with Elekta Unity® 1.5 T MRI-Linac were prospectively collected, integrated with relevant data from medical records and analyzed.

Results: main characteristics of the patients are summarized in Table 1, 6 patients had B-cell lymphoma (two DLBCL, two MALT, one follicular and one mantle-cell) and one T-cell/NK lymphoma. Intent of RT was radical for 4 patients (in the T-cell/NK case followed by chemotherapy), salvage treatment for 2 and CAR- T bridging for one.
Two patients presented orbital localizations and 5 cervical lymphnode sites (in two cases with concomitant nasopharyngeal and in one with oropharyngeal disease).
Median GTV was 16.47 cc (range 1.14 - 194.07 cc), median CTV 147.27 cc (25.63 – 496.64 cc) and median PTV 246.75 cc (51.19 – 709.45 cc).
Prescribed dose was 2 Gy per fraction up to 30 Gy for 2 patients, 36 Gy with a sequential boost of 4 Gy for another two, 24 Gy for one patient and 50 Gy for the T-cell/NK case. The patient that received bridging therapy before CAR-T was treated with a dose of 3 Gy/fr and was the only one that did not complete RT, as after 8 of the 10 scheduled fractions treatment was suspended for G4 febrile neutropenia (not due to RT).
All the patients experienced acute toxicity, maximum grade was G1 for 5 patients and G2 for two at the end of RT. Most common side effects included mucositis (71%, 42% G2), dermatitis (57%, all G1), esophagitis (57%, 43% G2), xeroftalmia (43%, all G1, 100% of patients with orbital disease), dysgeusia (43%, G2 29%), epiphora (G1 29%) and pharyngodynia (G1 29% G1). One month after radiotherapy six patients still experienced G1 toxicity, but no toxicity grade ≥ 2 was reported.
After a median follow up of 166 days, no patient experienced local or systemic disease progression; first radiological assessment was performed in 5 patients after a median of 69 days, reporting complete response for all the cases.

Conclusions: radiotherapy for NHL with H&N localization using a 1.5 T MRI-linac was feasible, with no > G2 toxicity and optimal response rate and disease control.

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Table 1.

Patients' characteristics	
Age	median 59.7 years (range 48.5-70.5 years)
Histology	Diffuse large B-cell lymphoma 2 patients Mucosa-associated lymphoid tissue lymphoma 2 patients Follicular lymphoma 1 patient Mantle cell lymphoma 1 patient T-cell/Natural killer cell lymphoma 1 patient
Stage	Stage I 5 patients Stage II 1 patient Stage IV 1 patient
Setting	First diagnosis 5 patients Relapse 2 patients
Treatment modality	Exclusive radiotherapy 4 patients Sequential treatment with chemotherapy 3 patients
Time from diagnosis to RT	median 6 months after diagnosis (range 1.5-30.7 months)
ECOG performance status	PS 0 4 patients PS 1 3 patients

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ACUTE TOXICITY: IMPACT OF BREAST VOLUME IN EARLY BREAST CANCER PATIENTS TREATED WITH THREE-DIMENSIONAL CONFORMAL RADIOTHERAPY (3D- CRT): A SINGLE – INSTITUTION RETROSPECTIVE ANALYSIS – UPDATE 2023

Code: 283

Aims: The aim of this study is an update the previous study, inserting the number of patients treated in 2023 to evaluate acute skin toxicity and the impact of breast volume in early breast cancer patients treated with hypofractionated (HF RT) after breast conserving surgery (BCS).

Methods: This is an update of the data previously included in the study to which the patients treated in the last year (2023) at our center have been added. As well as the patients observed in the previous retrospective study (from June 2017 to December 2022), patients with early breast cancer received BCS (pT1-2, pN0 R0 M0) and were treated with 3D hypofractionated RT (40 Gy in 15 fractions). Acute skin toxicity was monitored according to the CTCAE scale. In the previous analysis, as shown in many literature studies, a link is observed between acute skin toxicity and large breast volume. Large breast volume seems to be a risk factor for acute adverse events independently of dose inhomogeneity and regardless of the conformal radiotherapy technique or fractionation schedule.

Results: 398 patients were included in the study: 281 were treated from June 2017 to December 2022 and 117 were treated from January to November 2023 with hypofractionated RT (HF). Patients that received the hypofractionation showed slightly better results, with G 1 toxicity was predominant for all sub- groups analyzed while the percentage of patients with > G2 toxicity was the highest in the subgroup of large breasted patients. In patients treated in the last year, compared to those examined in the previous study, this was highlighted: 24% vs 36% no toxicity ; 68% vs. 57% skin toxicity G1; 8% vs.6 % skin toxicity G2 and 0% vs. 1% skin toxicity G3. A significant statistical difference wasn't observed ($P > 0.05$).

Conclusions: The volume of treatment has an important effect on skin reactions with the number of events increasing considerably at larger volumes. Overall, there is a benefit in favor of hypofractionation in terms of acute skin toxicity. From the data analyzed there appears to be a slight increase in acute toxicity of grade G1 and G2 in the group of patients with brest volume >1000cc, as obtained in the previous analysis. It seems likely that the large volume of treatment could increase toxicity but it is necessary to increase the number of cases in order to obtain statistically significant data.

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MANAGEMENT OF ORAL MUCOSITIS (OM) IN HEAD AND NECK CANCER (HNC) IN RADIOTHERAPY WITH LOW LEVEL LASER THERAPY (LLLT): PRELIMINARY EXPERIENCE

Code: 218

Aims: Severe radiaton induced oral mucositis (OM) is a frequent acute toxicity in HNC treatment associate to nonadherence of therapies for bad quality of life without standardized preventing strategy. Aim of this study was evaluate efficacy and safety of low level laser therapy (LLLT) in management and control of OM in patients (pts) with HNC during radiotherapy (RT) or radiochemotherapy (RTCT). Primary Endpoint was rates adherence to the therapy.

Methods: We enrolled 6 pts with radical or post-operative pourpose with HNC Squamous cell carcinoma, locally advanced, G2-G3, for RT exclusive or concomitant RTCT at Total Dose of 60-69,96 Gy. First day of RT, was suggest oral hygiene, no smoke, no spicy or hot meal, sodium bicarbonate mouthwashes, oral barrier agents to prevent G1 RTOG oral mucositis. However between III-IV week of RT at a median dose of
30-42,4 Gy, when OM worsened (G2-G3 RTOG scale) with important pain, edema and solid or liquid dysphagia, xerostomia, anorexia and loss of weight were prescribed steroids, benzydamine, analgesics with low benefit, so pts underwent to Diode Laser (Wavelength 980-Lasotronix-Poland) in Continuous Emission at 1Watt. Each lesion was treated in defocalized mode for 1 minute with a handpiece dedicated to photo-biomodulation; rinse with antimycotic and antinfiammatory has been always suggested too. Each session was repeated weekly at least 3 times (considering in some instances general clinical condition did not allow further treaments).

Results: Patients referred immediatly post treatment pain remission and possibility to go back to eating variably persisting in the following days with an overall high compliance to LLLT, as not invasive and not painful. Pts continued RT encouraged by LLLT results as an important help for pain. Our data suggested an important improvement for Quality of Life specially for pain, no interruption of RT due to OM was recorded and it is particularly important in HNC.

Conclusions: The LLLT, seem to be safety reducing incidence of symtoms of severe oral mucositis specially pain and improve compliance-adherence to Radiotherapy and Quality of Life in pts with HNC. The encouraging results suggest implementing LLLT in HNC pts in RT or RTCT.

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PRECISION IN BREAST CANCER RADIOTHERAPY: THE IMPORTANCE OF ARTIFICIAL INTELLIGENCE (AI) AUTOCONTOURING FOR PERSONALIZED TREATMENT

Code: 446

Aims: Radiation therapy is crucial in treating breast cancer, requiring precise delineation of anatomical structures for efficacy and safety. This study aims to compare human and AI delineations of the organs at risk (OARs), conducting a thorough qualitative and quantitative analysis. The research explores the benefits and limitations of using AI-driven technologies in this context.

Methods: In this study, 15 patients diagnosed with right breast cancer underwent simulation CT scans, with contouring structures generated using Siemens' "DirectORGAN 2.0" AI software on the go.Sim CT system. We compared AI generated contours with manual delineations by radiation oncologists. Identical radiation therapy plans were executed for each patient using both sets of contours. To gauge correspondence or disparities, dimensional similarity indices such as DICE (DSC), overlap, maximum, and average Hausdorff distance (HD) were calculated for each organ at risk. Additionally, differences in dose were assessed by analyzing Dose-Volume Histograms (DVHs) specific to each set of structures. The analysis was made using custom code developed in Matlab 2023b and Varian Treatment Planning System.

Results: Manual contour adjustments led to a reduction in OAR volumes of 4.58%±2.90% compared to those generated by AI contouring. The average DSC and HD were 0.96±0.02 and 1.82±1.04 mm, respectively, indicating a high degree of similarity. Dosimetric constraints, particularly for heart and lungs, were evaluated for each patient. Both adaptive workflows demonstrated comparable results, with minimal differences observed in mean dose for homolateral lung (0.16±0.58) and V20% relative to lung (0.34±0.93). All constraints were within acceptable limits, emphasizing the reliability of both manual and AI-driven contouring in meeting dosimetric criteria.

Conclusions: The autocontouring devices employing deep AI algorithms, as investigated in this study, demonstrate accuracy and adaptability under the supervision of competent medical personnel. While proving to be valuable support for doctors, they are not positioned as alternatives to human expertise. Ongoing efforts involve extending the study to encompass additional anatomical regions and a larger sample size, aiming to further validate the practical implications and scope of these AI-driven tools in clinical applications.

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OAR	Dice index	Overlap index	Average Hausdorff index
Left Breast	0.95 ± 0.03	0.94 ± 0.06	1.88 ± 1.70
Heart	0.97 ± 0.03	0.97 ± 0.03	1.05 ± 0.77
Left Lung	0.97 ± 0.02	0.97 ± 0.03	0.25 ± 0.21
Right Lung	0.98 ± 0.02	0.98 ± 0.03	0.36 ± 0.45
Spinal Cord	0.97 ± 0.02	0.96 ± 0.03	0.58 ± 1.33

Tab. 1 - Mean values and standard deviations of dimensional simalarity indices on a study population of 15 patients.

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SBRT AND SYSTEMIC THERAPY FOR PATIENTS WITH OLIGOMETASTATIC RENAL CELL CARCINOMA

Code: 151

Aims: Renal cell carcinoma (RCC) is an aggressive malignancy, and often carries a poor prognosis, especially in metastatic patients. RCC has traditionally been considered radio-resistant with a limited role for conventional fractionation as a local approach. However, since the advent of stereotactic body radiation therapy (SBRT), radiotherapy has been increasingly used in the management of metastatic RCC (mRCC). The aim of our analysis is to evaluate the role of SBRT as Metastasis-Directed Therapy for synchronous and metachronous oligo- metastatic (OMD) RCC pts in terms of local control and delay of prescription of Next-line Systemic Therapy (NEST).

Methods: A monocentric retrospective data collection was performed. Between 02/2019-07/2023, 97 treatments in 61 pts were delivered with CyberKnife™ (Accuray, Sunnyvale, CA, USA). All metastatic sites were considered. Tumor response was evaluated using the response evaluation criteria in solid tumors (RECIST). Time to NEST was calculated from the end of SBRT to the start of any new systemic therapy. Progression-free survival (PFS), Local Control (LC) and overall survival (OS) were calculated via the Kaplan-Meier method.

Results: Median follow-up was 13.9 (0-61.9) months. Median time between primary tumor diagnosis and SBRT for OMD was 62.2 (0-356.7) months. Median prescribed dose was 30 Gy (16-60) in a median of 3 (1-8) fractions, at a median isodose of 80% (63%-85%). For 47 treatments (48.4%) concomitant systemic therapy was prescribed. Median Biological Equivalent Dose (BED), calculated with tumor specific a/b coefficient of 3, was 146.7 (66.7-378) Gy. OS of all pts at 12- and 24-months was 87.1% and 63.6%, respectively. Twelve- and 24-month LRFS was 81.8% and 78.7%, respectively. At the last follow-up NEST was necessary for 11 pts (25 lesions). Median time to NEST was 8 (1.6-30.8) months. NEST-free survival at 12- and 24-months was 70.7% and 63.2%, respectively. Median NEST-free survival for pts with SBRT only was not reached, and was 30.8 months for pts with SBRT and systemic therapy. Six-, 12- and 24-months NEST-free survival was 85.1%, 82%, and 69% for pts with SBRT only vs 76.5%, 56.6% and 56% for pts with SBRT and systemic therapy (p=0.15), probably due to the selection of pts with more advanced disease for systemic therapy.

Conclusions: SBRT is a feasible and effective treatment in patients with mRCC with good LC. These results of combined local and systemic treatments should be verified in prospective trials.

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CORRELATION BETWEEN HISTOPATHOLOGICAL RISK FACTORS AND CLINICAL OUTCOMES IN PATIENTS WITH CERVICAL CANCER UNDERGOING SURGERY AND ADJUVANT RADIO(CHEMO)THERAPY

Code: 82

Aims: There is yet a gap in knowledge regarding the ideal management of patients with intermediate/high-stage cervical cancer. We examine the correlation between histopathological risk factors and clinical outcomes in our patients undergoing surgery followed by adjuvant treatment.

Methods: We retrospectively examined 82 patients who underwent radical hysterectomy and adjuvant radio(chemo)therapy for intermediate-high cervical cancer (IB-IIB) from 2019 to 2021. Histopathological risk factors, including tumor extension, lymph node involvement, LVSI (lymphovascular space invasion), tumor size, margin and node status and tumoral residual were assessed. The effects of clinical and pathological factors on local control (LC), disease-free survival (DFS) and overall survival (OS) were evaluated in univariate and multivariate analyses.

Results: After a median follow-up of 48 months, the locoregional failure rate was 6.1% for entire popoluation. The 2- and 5-year overall survival (OS) and disease-free survival rates were 98.7% and 96.1%, and 85.9% and 81.4%, respectively. Separate sub-group analyses in patients with intermediate risk or high risk also did not reveal any significant survival benefit of combined treatment in either of the sub-groups. No severe acute toxicity was observed, late grade ≥ 3 toxicity developed in 1 patient.

Conclusions: The role of adjuvant treatment in cervical cancer is debated. Further studies are needed to update the risk categories that may benefit from adjuvant treatment.

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PROTON BEAM RADIATION THERAPY FOR HEAD AND NECK ADENOID CYSTIC CARCINOMA: TRENTO PROTON- THERAPY CENTER EXPERIENCE

Code: 602

Aims: Locoregional control (LC) in adenoid cystic carcinoma (ACC) is dose-dependent, initial results with particle therapy are promising. We report our experience with pencil beam scanning-proton theapy (PBS- PT) in 81 patients with pathologically confirmed adenoid cystic carcinoma (ACC) of the head and neck.

Methods: Treatment records of patients treated with PBS-PT between March 2016 and March 2023 were collected. Median age of patient was 55 years (range, 18-80 years). 41 patients were male and 40 female. All tumours were hystologically confirmed. In 45 patients tumors were located in major salivary glands (60,8%), in 36 patients in minor salivary glands. Most patient were treated in post-operative setting, R0, R1, and R2 were respectively 22 (29%), 34 (42%), and 19 (23,4%), 6 patients underwent Protontherapy as definitive treatment. 8 patients had previously been irradiated with photons with a median dose of 63 Gy (range 45-70), less time between the two irradiation was 12 months. Median total PT dose was 64 GyRBE (range, 45-74 GyRBE). Neck was irradiated only in case of node positivity, all patients had cranial nerves irradiation. No one patient performed chemotherapy.

Results: Median follow-up period was 40,3 months (5-70 months). Treatment was well tolerated, most represented acute toxicity was radiation induced dermatitis grade 1 or 2 in 53 patients, grade 3 in 16 cases, the second most rapresented was mucositis in 42 patients, 6 of them developed grade 3. No acute toxicities more than G3 were observed. Most represented late toxicities were cutaneous in 17 patients and trisma in 16 patients, 1 patient reported carotid stenosis, 1 wound dejuice, 1 oronasal fistula, 2 cases of radionecrosis (1 of temporal lobe, 1 of brainstem) at 8 and 28 months respectively, 1 case of flap detachment was reported.
At the time of the analysis 65 patients were alive, 40 of them were free from disease, 3 alive with controlled diesease, 7 patients had in field local relapse, 15 patients relapse at distance mostly in the bone or lung. 13 patients had died for local or at distance progression. No patient developed neck recurrence.

Conclusions: High-dose conformal proton beam radiation therapy resulted in very encouraging local control rates with a low toxicity profile in patients with adenoid cystic carcinoma of the head and neck. More follow up is necessary to confirm these results.

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ELECTIVE HYPOFRACTIONATED HEMIPELVIC IRRADIATION WITH SYMULTANEOUS INTEGRATED BOOST IN THE NODAL OLIGORECURRENT PROSTATE CANCER: AN INSTITUTIONAL EXPERIENCE.

Code: 258

Aims: Patients with biochemical recurrence following primary prostate cancer (PCa) treatment often experience a relapse in the pelvic lymph nodes (LNs)**.** There is an open question about the best radiotherapy in this setting (SBRT vs ENRT), taking into account not only the oncological outcomes and relapse patterns but also the different toxicity and overall treatment time.

Methods: We retrospectively collected data regarding patients with PCa treated with elective hypofractionated hemipelvic nodal irradiation (EHhpNRT) and simultaneous integrated boost (SIB) for a LN oligorecurrence (1 node) after prostatectomy, prostate radiotherapy or their combination. All patients were staged with a PSMA-PET following a biochemical relapse. No concomitant androgen deprivation therapy (ADT) was administered. Toxicity (CTCAE 4.0), biochemical progression free survival (BPFS, as an increasing of PSA after a biochemical response) and time to castration resistant prostate cancer (CRPC free survival) were the endpoints analyzed.

Results: From 03/2021 to 10/2023, nine (9) patients were treated with 25 Gy in 5 daily fraction on the ipsilateral hemipelvis (internal and,external iliac,obturator and common iliac LNs) with a SIB up to 35 Gy on the nodal oligorecurrence PSMA-PETdetected . Median PTVs were 276.9 cc (range 207.2 - 415.1) for the elective hemipelvic volume and 8.7 cc (range 6.1-16.9) for the nodal PSMA+ve target volume. Mean doses to the bowel ranged from 3.02 Gy to 10.41 Gy with a median of 5.66 Gy. After a median follow up of 25.5 months (range 3.7-34.6), no acute or late toxicities were detected. At the time of the analysis, all the patients were alive : 4/9 pts were biochemical or disease free; 5/9 pts had a relapse PSMA-PET diagnosed (3 pts in controlateral hemipelvic nodes, 1 pt M1a and 1 pt M1b), of these 3 pts are on ADT, one patient was treated with EHhpNRT on the contralateral pelvis and the other one was treated with SBRT only. Median pre-RT PSA was 1.14 ng/ml (range 0.34-8.46). Median post-RT PSA was 0.39 ng/ml (range 0.07-3.72). 1-yr, 2-yr and median BPFS for the whole population were 75%, 56.3% and 25 months, respectively. So far no patient has developed a CRPC disease

Conclusions: According to our experience, EHhpNRT with a SIB in selected pts with nodal prostate cancer oligorecurrence is safe and feasible, providing a good biochemical control with a short overall treatment time.

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SHORT-COURSE STRATEGY FOR RECTAL CANCER: FOR WHOM AND WHY? A REAL-WORLD EXPLORATORY ANALYSIS

Code: 225

Aims: Short-course radiotherapy (SCRT) is an effective strategy for locally advanced rectal cancers (LARCs) in a neoadjuvant setting: it means only one-week RT, with a low impact on patients (pts)' routine, and a benefit in terms of healthcare costs and waiting list, comparing to long-course RT. Its use also finds a clinical rationale in metastatic pts, to achieve local disease control. Moreover, the choice of scheduling immediate or deferred surgery after SCRT fosters new therapeutic approaches. The present work aims to report the ten-year experience of a single large-volume RT Department, to take a picture of clinical practice in this scenario.

Methods: Pts who completed a neoadjuvant SCRT course followed by surgery between 2012 and 2021 were retrospectively collected. RT was performed using IMRT or 3D-CRT scheduled in 25 Gy/5 fraction. Post- operative complications were graded according to the Clavien-Dindo Classification. Association of pts, tumor, and treatment characteristics with overall survival (OS), postoperative complications, and downstaging were also investigated.

Results: Sixty-four pts met the inclusion criteria. The choice of SCRT was mainly driven by comorbidities, advanced age, and/or the presence of metastasis at diagnosis. Forty-three (67%) pts had LARCs, while 21 (33%) were at IV stage. Twenty-two pts (34%) underwent chemotherapy before SCRT, while post- operative chemotherapy was prescribed in 20 cases (34%). Thirty-six out of 64 pts (56%) underwent immediate surgery (within 4 weeks), while 28 (44%) deferred surgery (after 4 weeks). A median follow- up of 3.0 years (IQR 1.6-4.6) was observed, and 33 pts (52%) were alive at the end of the observation period. At 1 year, local relapse incidence was 6% (95% CI: 2-14%), and OS was 92% (95% CI: 82-97%). Interestingly, OS was not found to be different stratifying pts according to the presence of metastases at diagnosis, while a trend was found between reduced OS and advanced age, male gender, increased neutrophil-lymphocyte ratio (NLR) and deferred surgery. Dividing pts according to the time of surgery (immediate vs deferred), downstaging was significantly higher in the case of deferred surgery (68% vs. 31%, p=0.003), as expected (**Table 1**).

Table 1. Association of patient, tumor, and treatment characteristics with overall survival, postoperative complications, and downstaging.

Variable	Overall survival					Post-op Clavien-Dindo grade				Downstaging		
	N	Death	No (N=34)	No (N=34)	P-value	0 (N=33)	1-2 (N=19)	3 (N=12)	P-value	No (N=34)	Yes (N=30)	P-value
Age at diagnosis												
<70	25	9	Ref.	-	-	11 (44)	9 (36)	5 (20)	0.59	14 (56)	11 (44)	0.71
70+	39	22	2.18	0.99-4.77	0.051	22 (56)	10 (26)	7 (18)		20 (51)	19 (49)	
Sex												
Female	20	13	Ref.	-	-	11 (55)	6 (30)	3 (15)	0.87	12 (60)	8 (40)	0.46
Male	44	18	0.53	0.26-1.11	0.091	22 (50)	13 (30)	9 (20)		22 (50)	22 (50)	
CCI												
≤3	43	19	Ref.	-	-	23 (53)	11 (26)	9 (21)	0.57	24 (56)	19 (44)	0.54
>3	21	12	0.82	0.40-1.71	0.60	10 (48)	8 (38)	3 (14)		10 (48)	11 (52)	
Hb												
Hb<12.2	28	16	Ref.	-	-	14 (50)	10 (36)	4 (14)	0.55	18 (64)	10 (36)	0.11
Hb>12.2	26	9	0.65	0.29-1.47	0.30	17 (65)	6 (23)	3 (11)		11 (42)	15 (58)	
Missing	10	6				2	3	5		5	5	
NLR												
NLR<4.22	25	10	Ref.	-	-	12 (48)	8 (32)	5 (20)	0.33	15 (60)	10 (40)	0.66
NLR>4.22	26	15	1.87	0.84-4.18	0.13	17 (65)	7 (27)	2 (8)		14 (54)	12 (46)	
Missing	13	6				4	4	5		5	8	
Mets at diagnosis												
No	43	20	Ref.	-	-	24 (56)	12 (28)	7 (16)	0.60	22 (51)	21 (49)	0.65
Yes	21	11	1.05	0.50-2.21	0.89	9 (43)	7 (33)	5 (24)		12 (57)	9 (43)	
Weeks between RT and surgery												
Less than 4 weeks	36	15	Ref.	-	-	18 (50)	11 (31)	7 (19)	0.96	25 (69)	11 (31)	**0.003**
Four or more weeks	28	16	1.87	0.91-3.86	0.090	15 (54)	8 (29)	5 (18)		9 (32)	19 (68)	

Conclusions: The present work confirms that the SCRT strategy is a valuable option for the treatment of rectal cancer both in case of LARC and metastatic disease. Further investigation is warranted to find pts who could most benefit from this approach and the best timing between RT and surgery.

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LEFT BREAST CANCER RADIOTHERAPY: FREE BREATHING VERSUS DIBH TECHINQUE USING BRAINLAB EXACTRAC DYNAMIC

Code: 184

Aims: Nelle pazienti radiotrattate per cancro al seno sx il rischio a lungo termine dell'insorgere di malattie cardiache è tra i più importanti data la vicinanza del cuore al target. Si è indagata l'utilità in termini di riduzione di dose a cuore e LAD dell'impiego della tecnica DIBH nell'irradiazione di queste pazienti mediante l'utilizzo di BrainLAB Exactrac Dynamic. Inoltre sono stati valutati i tempi di trattamento in DIBH e la compliance delle pazienti sottoposte a terapia in inspirazione profonda.

Methods: Sono state esaminate 7 pazienti trattate per cancro al seno sx in DIBH impiegando Exactrac Dynamic v.1.1.3 e TrueBeamSTx Varian. Sono state acquisite una TC di simulazione a respiro libero ed una in inspirazione forzata. L'inspirazione è stata controllata con sistema Real-time Position Management di Varian. Le immagini acquisite sono state inviate ad ARIA oncology information system di Varian per il contouring e la pianificazione del trattamento è stata effettuata utilizzando il sistema Eclipse di Varian impiegando tecnica IMRT ed energia 6x. Contornazione e pianificazione sono state effettuate sulle immagini a respiro libero e in inspirazione forzata per comparare i valori MHD MeanHeartDose, HeartV25Gy, LAD MeanDose, LAD MaximumDose. I tempi medi di trattamento in DIBH sono stati confrontati con quelli di 7 pazienti trattate per cancro al seno sx a respiro libero. Dalla somministrazione di un questionario dedicato l'ultimo giorno di terapia sono stati estrapolati i dati relativi alla compliance delle pazienti trattate in DIBH.

Results: In DIBH si sono ottenute le seguenti medie di valori: MHD 1.47Gy, LAD MeanDose 5.70Gy, LAD MaximumDose a 15.27Gy, HeartV25Gy 0.13%; mentre in free breathing le medie sono MHD 2.52Gy, LAD MeanDose 13.63Gy, LAD MaximumDose a 32.54Gy, HeartV25Gy 1.98%. I tempi medi di terapia in DIBH sono in generale sovrapponibili a quelli a respiro libero. Dai questionari somministrati è emerso che le indicazioni dei tecnici durante la terapia sono state semplici da seguire e il sistema di guida visivo fornito da BrainLAB è intuitivo.

Conclusions: La DIBH è risultata utile per il risparmio di dose a cuore e LAD nelle pazienti radiotrattate per cancro al seno sx. Inoltre è emerso che tale tecnica non comporta un significativo aumento dei tempi di terapia e le pazienti sono in grado di mantenere una buona compliance per la durata della terapia.

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BILATERAL BREAST IRRADIATION USING VOLUMETRIC MODULATED ARC THERAPY (VMAT) TECHNIQUE: A CASE REPORT

Code: 476

Aims: Synchronous bilateral irradiation of both mammary glands was a challenging task due to technical difficulties and limited evidence supporting an optimal technique to improve treatment outcomes. The purpose of this case report is to share our experience in treating bilateral early breast cancer (EBC) with VMAT technique.

Methods: Patient was CT scanned and then treated in the supine position, with both arms above the head, in free breathing technique. The photon therapy plans were created using VMAT technique, with a single isocenter posterior to the sternum and with 2 or 3 partial arcs ranging between 220° and 140°. CTVs were contoured according to ESTRO consensuns guidelines. The delivered fractionation scheme was 40 Gy in 15 fractions (2,67 Gy per fraction). Planning objectives, for CTV, wereV95% ?98% and V107%?2%. Dose contraints for normal tissue were: Heart V17?5% and V35?1%; Lung V17? 25% and mean dose? 16Gy (each lung) (Stick et al). Patient tolerance was periodically assessed according to CTCAE scale.

Results: The pazient was a 60 yrs old female, PS1. At screening, she had radiological and following hystological diagnosis of bilateral EBC (cT1 in both breast), without nodal involvment. On october 2023 she underwent to bilateral breast conservation surgery, with diagnosis of EBC pT1pN0 Luminal B on the left and pT1bpN0 Luminal A on the right breast. After multidisciplinar discussion, she was prescribed adjuvant ormoal therapy and adjuvant bilateral radiotherapy (RT). The treatment plan was elaborated at our Radiotherapy Unit. All the constraints were satisfied and all the objectives were met. Patient will begin RT in the next few days. We will follow her with clinical assessment to evaluate both acute both chronic toxicity.

Conclusions: In our experience, bilateral breast irradiation using VMAT technique was feasible. It is our goal to follow the patient over time to analyze the safty of this treatment and to expand study sample.

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VMAT HYIPPOCAMPAL AVOIDANCE IN PROPHYLACTIC CRANIAL IRRADIATION FOR SCLC PATIENTS: MONOINSTITUTIONAL EXPERIENCE

Code: 509

Aims: To evaluate feasibility, oncological outcome and pattern of failure of prophylactic cranial irradiation (PCI) in patients with complete response for limited stage or good response for extensive stage small cell lung cancer (SCLC) following primary treatment, perfomed with hippocampal avoidance (HA-PCI) using volumetric modulated arc therapy (VMAT) technique.

Author	Title	Journal	Year	Results
Hsu et al	Whole brain radiotherapy with hippocampal avoidance and simultaneous integrated boost for 1-3 brain metastases: a feasibility study using volumetric modulated arc therapy.	RedJ	2010	The VMAT was able to achieve adequate whole brain coverage with a mean mean hippocampal dose of 5.23 +/- 0.39 Gy.
Prokic et al	Whole brain irradiation with hippocampal sparing and dose escalation on multiple brain metastases: a planning study on treatment concepts.	RedJ	2013	The SIB technique achieved better sparing of the hippocampus, with a mean dose of 7.55±0.62 Gy and 6.29±0.62 Gy when 5-mm and 10-mm avoidance regions were used, normalized to 2-Gy fractions.
Gondi et al	Preservation of memory with conformal avoidance of the hippocampal neural stem-cell compartment during whole-brain radiotherapy for brain metastases (RTOG 0933): a phase II multi-institutional trial	JCO	2014	113 patients received HA-WBRT, with this protocol: dose to 100% of the hippocampus could not exceed 9 Gy, and Dmax was 16 Gy. Mean relative decline in Hopkins Verbal Learning Test from baseline to 4 months was 7.0%, significantly lower in comparison with the historical control.
Redmond et al	Prospective study of hippocampal-sparing prophylactic cranial irradiation in limited-stage small cell lung cancer	RedJ	2017	Patients received PCI 25 Gy/10 fractions, with a mean hippocampal dose <8 Gy and ≥90% of the brain receiving 90% of the prescription. A diverse battery of neuropsychological testing was performed at baseline and 6 and 12 months after PCI. There was no significant decline in performance between baseline and 6 or 12 months for any of the tests.
Brown et al	Hippocampal avoidance during whole-brain radiotherapy plus memantine for patients with brain metastases: Phase III Trial NRG Oncology CC001	JCO	2020	518 patients were randomly assigned to HA-WBRT plus memantine or WBRT plus memantine. Risk of cognitive failure was significantly lower after HA-WBRT vs WBRT (0.74; 95% CI, 0.58 to 0.95; P = .02). There was less deterioration in executive function at 4 months (23.3% v 40.4%; P = .01) and learning and memory at 6 months (11.5% v 24.7% [P = .049] and 16.4% v 33.3% [P = .02], respectively).
Yang et al	Hippocampal avoidance whole-brain radiotherapy without memantine in preserving neurocognitive function for brain metastases: a phase II blinded randomized trial.	Neuro Oncol	2021	This trial enrolled 70 patients with brain metastases and randomly assigned them to receive HA-WBRT or C-WBRT. At 4 months HVLT-R was -8.8% in the HA-WBRT arm and +3.8% in the C-WBRT arm (P = 0.31). At 6 months, HA-WBRT showed favorable perpetuation of HVLT-R (mean difference = 2.60, P = 0.079) and significantly better preservation of the HVLT-R recognition-discrimination index (mean difference = 1.78, P = 0.019) and memory score.
Belderbos et al	Phase 3 randomized trial of prophylactic cranial irradiation with or without hippocampus avoidance in SCLC (NCT01780675).	JThorac Oncol	2021	168 patients were randomized to standard PCI or HA-PCI of 25 Gy in 10 fractions. 29% of pts on PCI and 28% of pts had HA-PCI Decline on the Hopkins Verbal Learning Test (p = 1.000). Performance on other cognitive tests were similare over time between the groups.
Dios et al	Randomized phase III trial of prophylactic cranial irradiation with or without hippocampal avoidance for small-cell lung cancer (PREMER): a GICOR-GOECP-SEOR study.	JCO	2021	150 patients with SCLC were enrolled to receive standard PCI with HA and tested for neurocognitive function. Decline on memory (delayed free recall) at 3 months was lower in the HA-PCI arm (5.8%) vs with the PCI arm (P = .003). There was no differeneces on oncologolical outcomes.

Methods: We offered HA-PCI to patients without progression after initial therapy for SCLC, with good performance status (PS). Patients had to have a negative baseline MRI brain scan with gadolinium prior HA-PCI. According to European guidelines, we prescribed 25 Gy in 10 fractions once daily over 2 weeks to the whole brain. The hippocampus volume was identified using pre-treatment MRI and a 5 mm isotropic expansion was used to create the hippocampal avoidance zone (HAZ) (RTOG 0933). Planning aims were (according to Redmond et al): mean hyppocampal dose <8Gy and at least 90% of prescribed dose delivered to 90% brain target. Additional constraints were hippocampal maximus dose <12Gy and PTV D2%<120%. All patients had daily cone-beam CT. After PCI, all patients had three monthly MRI brain scans as well as three monthly total body CT scans. Neurocognitive assessment (it means cognitive disturbance and concentration impairment) and toxicities were evaluated according to CTCAE scale. In table 1 we have summerized main studies involving HA-WBRT.

Results: Currently, we analyzed one patient (female) with stage III, PS 1. The patient received primary chemotherapy in association with radiotehrapy, with mild toxicities. She experienced a good response at the radiological evaluation after primary treatments and so she underwnt to HA-PCI in our Radiotherapy Unit on january 2024. For planning, all the constraints were satisfied. She had no acute toxicities during PCI. There was no difference in neurocognitive function before and after completion of HA-PCI. She has currently moved into our follow up protocol.

Conclusions: In our experience, HA-PCI with VMAT technique is a safe and feasible alternative to standard PCI for patients with SCLC to prevent neurocognitive dysfunction.

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PRECISION IN BREATH-HOLD: NAVIGATING LUNG LESION STEREOTACTIC RADIOTHERAPY WITH MINIMAL MARGIN AND MAXIMUM ACCURACY

Code: 544

Aims: Our study focuses on assessing the consistency of target positioning during breath-hold (BH) in lung lesions treated with stereotactic body radiotherapy (SBRT). Since a different position of Clinical Target Volume (CTV) was noted despite the correct reproducibility of the BH window and the set-up correction on the bone, we aim to investigate the potential reduction of margins and sparing of healthy tissue, possible thanks to image-guided online correction (IGRT).

Methods: We analyzed 9 BH CT scans and 57 BH cone-beam CT scans (CBCT) of 9 lung cancer patients who underwent SBRT with BH technique. Four patients (pts) received treatment in 8 fractions (fx), while five received treatment in 5 fx. All pts underwent BH-CT and tracking using the RPM system (VARIAN). The position of the lesion was checked and corrected online daily before treatment. First, we corrected set-up on bone structures, then we fine- tuned the position of the CTV to ensure that it was exactly within the PTV.
To quantify the residual CTV position error after correction on bone structures, we used the Eclipse Treatment Planning System (TPS) offline.
Our procedure included:
Aligning the CT and CBCT scans based on the bone structures.
Verifying the real CTV position on CBCT.
Measuring the CTV position differences between BH CT and BH CBCT, tabulating the displacements in the spatial directions (x, y, z) and calculating the mean and standard deviation for each patient and for overall population.
Determining the required additional CTV-PTV margins in cases of non-correction of residual CTV error after bone match using Van Herk formula $M=2.5\Sigma+0.7\sigma$.

Results: Despite BH, our analysis showed uncertainties in lesion position after daily setup corrections based on bone landmarks, requiring further adjustments on soft tissue. The recorded random errors (σ) were 0.03, 0.04, and 0.19 for the x, y, and z directions, respectively, with systematic errors (Σ) of 0.07, 0.26, and 0.40. When calculated using the Van Herk formula, the additional margins for not correcting CTV errors with BH CBCT on soft tissue were as follows: x(LL):0.22 cm, y(AP):0.7cm, z(CC):1.15 cm (Table 1).

Table 1: Compensatory Margin (cm) needed by residual position errors of the GTV after correction based on bone structure.

	x	y	z
M	-0,02919	0,053083	-0,15128
σ	0,034558	0,045185	0,193518
Σ	0,078831	0,268097	0,406329
Suggested Margin	0,221269	0,701873	1,151285

Conclusions: Our results emphasize the importance of online imaging in these treatments. The use of IGRT with a second-order adjustment of the residual error of the GTV position after correction to bone structures can avoid a compensatory CC margin of 1.15 cm and thus prevent unnecessary irradiation of healthy lung tissue.

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EFFICACY OF SINGLE-VERSUS MULTI-FRACTION RADIOTHERAPY FOR BONE METASTASES PAIN MANAGEMENT IN DEVELOPING COUNTRIES: A META-ANALYSIS

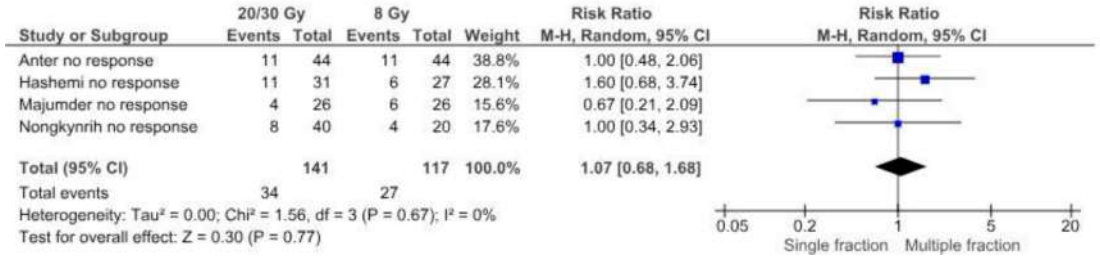
Code: 87

Aims: This study aims to assess the efficacy of palliative radiotherapy (RT) for managing pain in patients with bone metastases (BM), with a particular focus on single-fractionation versus multi-fractionation RT. Despite existing evidence from high-income countries suggesting comparable effectiveness between these two approaches, there is a notable scarcity of data pertaining to low/middle-income countries (LMICs).
This gap is significant, given the resource constraints in LMICs that potentially prolong diagnostic and treatment processes and amplify patient load. Consequently, this research undertakes a meta-analysis to evaluate the relative effectiveness of single versus multiple fractionation of palliative RT for BM in LMICs.

Methods: An extensive literature review was conducted independently by two researchers across PubMed, Cochrane, and Scopus databases. From the initial 333 records screened, 4 randomized trials involving 282 patients from Iran, India, and Egypt were included in this meta-analysis.

Results: All trials compared single-fraction RT (8 Gy) with multiple fractions (20 Gy in 5 fractions or 30 Gy in 10 fractions). Pain relief efficacy was measured using the Visual Analog Scales (VAS) in two trials, the Numeric Rating Scales (NRS) in one trial, and a 4-level pain scale in another trial. The parameter of non- response rate was assessed at 1 month in three trials and at 3 months in one trial. The comparative analysis of the non-response rates between single and multiple fractions revealed no significant difference (Relative Risk [RR] = 1.07; 95% CI: 0.68-1.68).

Figure 1. Forest plot of no response rate between multiple fractions versus single fraction palliative radiotherapy.



Conclusions: The findings show that single-fraction RT is as effective as multi-fraction RT in pain management for BM patients also in LMICs. Given the resource constraints in LMICs, the adoption of single-fraction RT could mitigate resource utilization and expedite patient treatment timelines.

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EFFICACY AND SAFETY OUTCOMES OF CHEMO- IMMUNOTHERAPY IN PATIENTS WITH RECURRENT/METASTATIC HNSCC: A RETROSPECTIVE ANALYSIS

Code: 346

Aims: KEYNOTE 048 added PDL1 CPS score to the other factors usually considered by oncologists in the choice of a personalized therapeutic approach for patients with squamous cell carcinoma of the head and neck (HNSCC) not eligible for curative treatment. This report aims to analyze data on efficacy and safety outcomes in a cohort of patients treated in our center with first line systemic therapy (FLST) from 2021.

Methods: Data about stadiation, prognostic factors and treatment were retrospective collected from patients with recurrent/metastatic HNSCC treated in our center with FLST according to CPS. The primary endpoints were overall survival (OS) (time from the start of FLST to death or last date of follow-up) and progression- free survival (PFS) (time from the start of FLST until death or progressive disease). Toxicity data were reported according to CTCAE v4.0.

Results: 39 patients who underwent FLST in our center between Jan 2021 and May 2023 were included in this retrospective study, with a median follow-up of 9 months [95%CI 1.2-16.8]. Patient and treatment characteristics are reported in Table1. Median age was 62.8 years and PS ECOG mostly 0-1 (90%); CPS resulted negative in 8 (21%), >1 in 9 (23%) and >20 in 22 (56%) patients. 16 patients (41%) had distant metastases, the others locoregional disease not eligible for radical treatment.
EXTREME schedule (3 without 5FU) was chosen in the 8 CPS-negative patients; 20 of the CPS-positive cohort received Platinum+5FU+Pembrolizumab (PFP) (3 without 5FU) and 11 Pembrolizumab alone.
Considering all patients, median OS was 9 months [95%CI 3.1-14.8], 1-year OS was 46%, 2-year OS 20%; median PFS was 5 months [95%CI 3.4-6.5]; 1-year PFS 21%. In the CPS positive cohort, pembrolizumab group had a median OS of 9 months [95%CI 3.5-14.5] and 1-year OS of 38%; PFP group had median OS of 10 months [95%CI 0-23.9], 1-year OS 45% and 2-year OS 30%. At univariate analysis, younger age was associated with longer survival with a median OS of 17 months [95%CI 4.2-29.7] and 5 months [95%CI 1.7-8.3] for patients aged <70y and >70y respectively (p=0.01). Regarding toxicity, we reported 15 events > G3; the most frequent were mucositis (4) and neutropenia (4) in chemotherapy groups; only 3 occurred with Pembrolizumab alone.

Conclusions: In our cohort, patients with recurrent/metastatic HNSCC had efficacy and safety outcomes in line with published chemo-immunotherapy data (KN048). Younger age was significantly associated with longer survival.

SEX			
Male		21 (53.8%)	
Female		18 (46.2%)	
AGE (years)		Median age: 62,8y (22-85)	
<70		24 (61.6%)	
≥70		15 (38.4%)	
PS ECOG			
0		24 (61.6%)	
1		11 (28.2%)	
2		4 (10.2%)	
SMOKING			
Never smoker		11 (28.2%)	
1-20 p/y		7 (18%)	
≥20 p/y		21 (53.8%)	
PRIMITIVE SITE			
Oral Cavity		22 (56.4%)	
Oropharynx		11 (28.2%)	
Larynx		4 (10.2%)	
Nasal cavity and paranasal sinuses		1 (2.6%)	
Hypopharynx		1 (2.6%)	
HPV STATUS (OPC n=11)			
HPV+		7 (63.6%)	
HPV-		4 (36.4%)	
CPS STATUS (PDL1)			
CPS negative		8 (20.5%)	
CPS 1-20		9 (39.1%)	
CPS > 20		22 (56.4%)	
SITE OF DISEASE AT FIRST LINE ST			
Local (T)		30 (76.9%)	
Regional (N)		29 (74.4%)	
Distant (M)		16 (41%)	
CPS SCORE	TREATMENT CHOICE		
0 (n=8)	Platinum+5FU+Cetuximab	5 (62.5%)	
	Platinum+Cetuximab	3 (37.5%)	
>1 (n=31)	Platinum+5FU+Pembrolizumab	17 (54.8%)	
	Platinum+Pembrolizumab	3 (9.7%)	
	Pembrolizumab	11 (35.5%)	
TOXICITIES (≥G3+)		EXTREME	PF-PEMBRO	PEMBROLIZUMAB
Skin toxicity		3 (0)	0	1 (1)
Nausea and Vomiting		1 (1)	2 (1)	0
Neutropenia		1 (1)	4 (3)	0
Hypothyroidism		0	2 (0)	2 (1)
Mucositis		1 (0)	4 (4)	0
Anaemia		2 (0)	4 (2)	0
Thrombocytopenia		1 (0)	2 (0)	0
Liver toxicity		0	0	1 (1)

Table 1. Patients, disease and treatment characteristics

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COMPARATIVE DOSIMETRIC ANALYSIS BETWEEN FREE BREATHING AND DEEP INSPIRATION BREATH-HOLD TECHNIQUES IN THE ADJUVANT RADIOTHERAPY FOR LEFT-SIDED BREAST CANCER AND EVALUATION POTENZIAL BENEFITS OF A RESPIRATORY TRAINING

Code: 253

Aims: The purpose of this study is to evaluate the benefit of the Deep Inspiratory Breath-Hold (DIBH) technique performed with the Respiratory Gating for Scanners (RGSC; Varian Medical Systems,
USA) system, as regards the left lung, heart and left anterior descending artery coronary (LADAC) sparing and to evaluate the correlation between dosimetric improvement and threshold amplitude of DIBH, including potential benefits of a respiratory training before the simulation.

Methods: Fourty-four patients (pts) with left-sided breast cancer (LSBC) after breast conservative surgery treated in our institution were enrolled. All pts underwent two sequential CT simulations in supine position: the first in free breathing (FB) and the second in DIBH, using the RGSC system. Six pts underwent a respiratory training session in treatment position before a CT simulation and the threshold of DIBH was registered. A combined tangential and volumetric field has been used for treatment plans for both CT scans. The DVH were generated for both plans. 40.5 Gy and 48 Gy with SIB were prescribed respectively in 29 pts and 15 pts. The deep inspiration amplitude in DIBH and the average respiratory excursion in FB were recorded. Paired t-test was performed to compare dosimetric values between DIBH and FB plans and correlation analysis was sought between threshold amplitude of DIBH and dosimetric parameters and between pts underwent or not to training session.

Results: A significant dose reduction ($p<0.05$) with DIBH compared to FB was recorded in all analysed parameters regarding heart (Dmean, Dmax, V5, V10, V20, V30), left lung (Dmean, V5, V10, V20) and LADCA (Dmean, Dmax, V5). In particular, reductions of 45%, 44% and 15% respectively for the mean heart dose (MHD) (1.4 Gy vs 2.6 Gy, $p<0.001$), maximum LADAC dose (13.1 Gy vs 23.6 Gy, $p<0.001$) and mean ipsilateral lung dose (5.4 Gy vs 6.3 Gy, $p<0.001$) were obtained with DIBH. Greater reductions of MHD and LADAC Dmax, although not statistically significant, between patients with or without respiratory training were observed (respectively 53% vs 41% and 45% vs 42%). No specific threshold that can give improved dosimetry value was identified.

Conclusions: DIBH in adjuvant radiotherapy for LSBC leads to significant dose reduction to heart, LADCA and left lung, proving to be an important and effective therapeutic option. Performing respiratory training could become a valuable option for achieving better DIBH. Further studies are needed to verify the validity of this approach.

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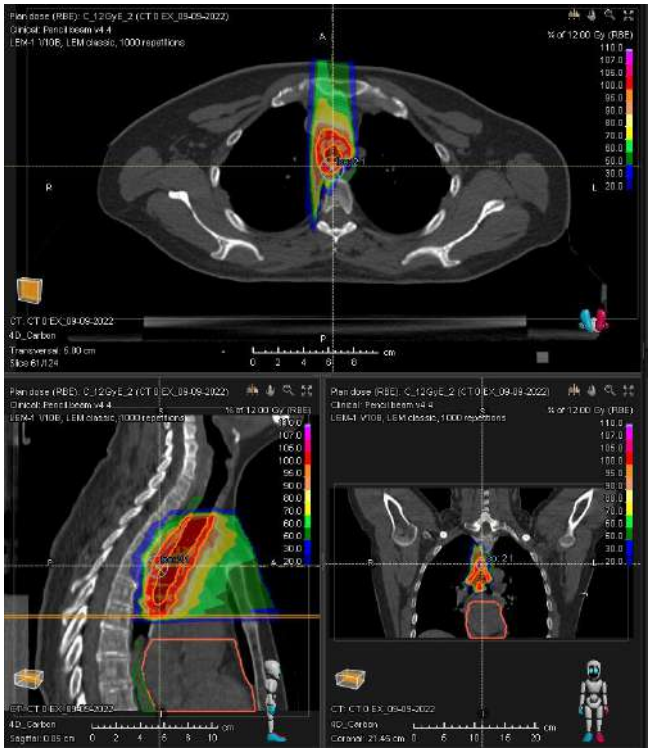
PARTICLE BEAM RADIOTHERAPY (PBRT) IN ADENOID CYSTIC CARCINOMA OF THE LOWER AIRWAYS: A MONOCENTRIC EXPERIENCE

Code: 263

Aims: Adenoid Cystic Carcinoma (ACC) is a rare salivary gland tumor that can arise in both major and minor salivary glands, including those located in larynx, trachea and bronchus. When feasible, radical surgery is the gold standard but require a demolitive approach. Particle beam radiotherapy (PBRT), due to its high precision and effectiveness in targeting tumors while sparing healthy tissue, is emerging as a promising option for such cases.

Methods: This is a retrospective preliminary study on consecutive patients who underwent PBRT alone or a mixed beam radiotherapy (RT) approach (PBRT+photons) for a lower airways ACC. Local control (LC), overall survival (OS), distant progression-free survival (DPFS) were evaluated from the end of treatment. Acute and late toxicity were scored according to CTCAE 5.0.

Results: Nine patients (median age 46, range 14-83) with stage III-IV ACCs, treated between September 2017 and June 2023, were enrolled. One patient was lost during the follow-up and excluded, and the analysis was carried out on 8 patients (3 males and 5 females). Seven (87.5%) patients received a radical mixed beam RT for unresectable disease, consisting of an early carbon ion RT (CIRT) boost (range: 9-15 GyRBE, for a total of 3-5 fractions) followed by photon RT (range: 50-54 GyRBE, for a total of 25-27 fractions). One patient (12.5%) underwent a postoperative proton therapy up to a total dose of 66 GyRBE, 2 GyRBE/fraction. After a median follow-up of 12.5 months (range: 4-32), the median LC was 12.5 months (range 4-32). Overall, the median DPFS was 12.5 months (range 4-32), and we recorded 3 cases (37.5%) of multiple distant metastases (bone,organs) in patients with a stage IV at diagnosis. The median OS was 10 months (range 4-32). Concerning toxicity, the treatment was tolerated without interruption. No acute/late toxicities≥3 were experienced, but 3 patients (37.5%) showed acute toxicities (one G1 actinic pneumonitis, one G2 dysphagia, and one G2 erythema) and 1 patient a late G1 pulmonary fibrosis.



Conclusions: Despite preliminary, our results suggest that PBRT is a potential effective treatment for this difficult-to-cure patients, both in a radical and in adjuvant setting with a favourable toxicity profile. Further analyses with an extended follow-up period and a larger sample size are necessary to validate this hypothesis. A strong national collaboration is warranted considering the rarity of the histology and the challenging anatomical scenario.

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PATTERN OF FAILURE AFTER POSTOPERATIVE RADIOTHERAPY PLUS CONCOMITANT AND ADJUVANT TEMOZOLOMIDE IN MALIGNANT GLIOMAS

Code: 359

Aims: To evaluate the recurrence patterns in patients with newly diagnosed malignant gliomas treated with Volumetric Modulated Arc Therapy (VMAT) plus concomitant and adjuvant temozolomide (TMZ), according to the ESTRO-EANO Target Delineation Guideline 2023.

Methods: Between June 2019 and June 2022, 80 patients with newly diagnosed malignant gliomas underwent neurosurgical resection. They were classified based upon the relative tumor volume reduction in 3 groups: complete resection, partial resection and biopsy. After 4-6 weeks 67 patients underwent postoperative radiotherapy conventionally fractionated (60 Gy/30 fractions) plus concomitant and adjuvant temozolomide. All patients underwent magnetic resonance simulation (MR-SIM) and CT simulation (CTSIM) followed by imaging registration. The better Volumetric Modulated Arc Therapy (VMAT) technique was performed. DVH and Conformity Index plan comparison were employed to check the adequacy of the plan. A total dose of 60 Gy (2Gy/die) was delivered to the volume of the enhancing tumor plus surgical cavity, without FLAIR alteration, plus a margin of 1.5 cm. The failure pattern was analyzed using MR scans and compared with the planning computed tomography. According to the new WHO classificatio 2021, patients affected by anaplastic astrocytoma IDH wild type have been reclassified as affected by glioblastoma Grade 4. The diagnosis of glioblastoma was restricted to tumors IDH wild type.

Results: All patients completed the treatment. After a median follow-up of 10.5 months (range 3-48) The median 2-y overall survival and time to progression were 14 months and 8 months, respectively. Overall survival and time to progression data show the benefit of both complete surgical resection and combined radio- chemotherapy. Complete surgery and adjuvant chemotherapy were both independent predictors of better clinical outcome. The main pattern of failure was "central desease" in almost 85% of patients, marginal in 8% and distant in 7% of patients. Our data revealed a significant difference in failure pattern based on IDH status.

Conclusions: Our results compare favourably with those found in the literature. Most disease recurrences are central according to the ESTRO-EANO Target Delineation Guideline. Reclassify patients according to the new WHO Classification underlines the importance of knowledge of immunohistochemical and molecular data for their prognostic and predictive value.

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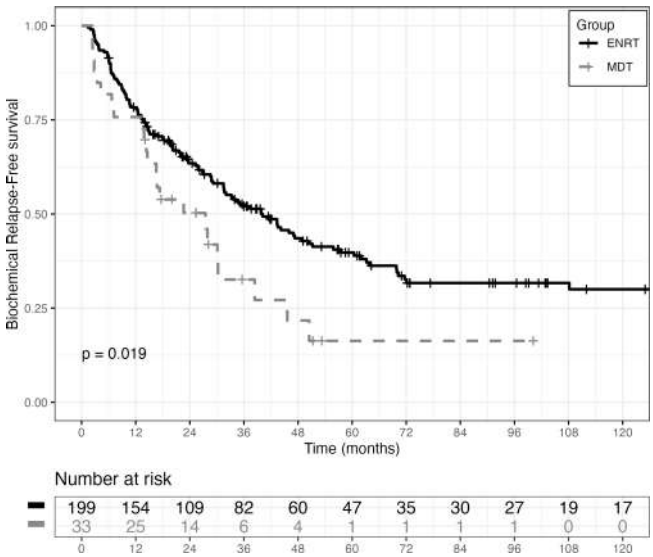
BETTER BIOCHEMICAL CONTROL AFTER ENRT VS MDT FOR PROSTATE CANCER LYMPH NODE RELAPSE: RESULTS OF A PRELIMINARY MONOINSTITUTIONAL ANALYSIS

Code: 142

Aims: Better biochemical control (BC) for patients with prostate cancer (PC) was registered with Extended nodal radiotherapy (ENRT), both for radical and salvage treatments, in prospective randomized phase III trials. A multi-institutional retrospective analysis observed better outcomes for selected patients treated with ENRT vs Metastasis Directed Therapy (MDT). We report our institution results in two cohorts of patients treated with salvage ENRT and positron emission tomography (PET)-guided simultaneous integrated boost (SIB) on PET positive LN vs PET guided MDT.

Methods: From 02/2005 to 11/2021, 305 patients were treated for 781 LNM with ENRT or MDT for PC LN relapses. In some cases, the ENRT/MDT were repeated for subsequent relapses; only the first treatment was considered for this analysis. MDT treatments for synchronous metastases were considered together, as a single treatment, even when they were delivered with different treatment plans. Thus, 232 patients were analyzed: 199 patients treated with ENRT at a median total dose (TD)= 51.8 Gy/28 fr, and PET-guided SIB to a median TD= 65.5 (50-74.2) Gy in 28 (25-30) fractions, and 33 patients treated with MDT at a median TD=35 Gy (25-65) in 5 (3-30) fractions. Median number of metastases per patient was 2 (1-32) for ENRT and 1 (1-4) for MDT. [11C]-choline PET/CT was used for 188 patients and [18F]-PSMA PET/CT for 42 patients.



Results: Median follow up was 103.3 months [interquartile range, IQR 57.5;142.4] for the ENRT group and 35.6 months [IQR 25.4;77.1] for the MDT group. Five-year biochemical relapse-free survival (bRFS) was 39.8% for ENRT vs 16.3% for

MDT (p=0.019) (See Fig.1). Five-year clinical recurrence-free survival was 60% for ENRT group and 36.9% for the MDT group (p=0.09)

Conclusions: The two groups of patients are unbalanced for the total number of patients and median follow-up. However, despite an unfavorable disease burden (up to 32 positive LN, determined mainly with choline PET/CT for ENRT vs up to 4 LN, determined with PSMA PET/CT, for MDT), as for radical and salvage treatments (POP-RT and NRG Oncology/RTOG 0534 SPPORT trial), we observed better bRFS in the ENRT group. Prospective studies should verify the effectiveness of the two treatments in patients with lymph node recurrence.

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EVALUATION OF THE PSYCHOLOGICAL AND SOCIAL IMPACT OF PERMANENT MARKS ON PATIENTS IN FOLLOW-UP AFTER RADIOTHERAPY

Code: 49

Aims: The aim of this study was to evaluate in the population of cancer patients in follow-up the psychological and social impact of body image changes caused by oncological treatments, such as surgical scars and permanent tattoos performed for radiotherapy.

Methods: During follow-up check-ups, we administered a questionnaire about body image (BI) consisting from a 10-items scale constructed in collaboration with the Quality of Life Study Group of EORTC, with 4 new questions relating to the specific impact of tattoos on self-image.

Results: From September 2022 to February 2023 the body image scale modified (BISM) questionnaire was submitted to a population of 500 cancer patients. The interviewed sample comprised 259 male (51.8%) and 241 female (48.2%) with a median age of 68 years (range 34-89). Among the population the most common primary tumors were: prostate cancer (n=190; 38%); breast cancer (n=177; 35.4%), lung cancer (n=62; 12.4%) and colorectal cancer (n=31; 6.2%).
More than 32% of patients believe that their body has undergone changes due to cancer treatments, and in 21.4% to 25.4% of cases, a reduction in physical and sexual attraction is reported. This discomfort is related to surgical scars in 22.4% of patients. Our study shows that 9% of patients feel physically less attractive due to RT tattoos, and 6.8% of patients reported being influenced in the way they dress or experiencing general discomfort when looking at themselves naked in the mirror.
Globally, the preference for RT without permanent tattoos was reported in 17% of patients. A global dissatisfaction over Body Image was reported by 37.1% of women and 7.4% of men, with a physical and psychological discomfort caused by permanent tattoos reported in 14.2% of women and 1.3% of men.
In a subgroup of 132 women aged 35-65 with thoracic tumors, the percentage arises to 58.3% and the preference for radiotherapy without permanent tattoos was reported in 29.5%.

Conclusions: Body image is an important endpoint in assessing quality of life since cancer treatment can result in major changes in patients' appearance. This study revealed that permanent marks, such as surgical scars and tattoos for radiotherapy, have a psychological and social impact on oncological patients, underscoring the importance of addressing patients' body image concerns and exploring alternative approaches to enhance their well-being during follow-up.

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REAL-WORLD ANALYSIS OF TREATMENT RELATED TOXICITY FOLLOWING PROSTATE SBRT

Code: 293

Aims: The aim of this retrospective analysis is to assess treatment-related toxicity of radical Stereotactic body radiation therapy (SBRT) for prostate cancer (PCa), considering different parameters.

Methods: Patients with confirmed localized PCa, regardless of risk class or prostate volume, received linac-based SBRT every other day using Volumetric Modulated Arc Therapy to the prostate and seminal vesicles. All patients were positioned supine with an empty rectum and a filled bladder for reproducibility and motion control. Androgen deprivation therapy (ADT) was prescribed as guidelines indicates. Alpha- blockers were prescribed at the beginning of the radiation treatment to prevent side effects to all patients. Maximum acute and late toxicity were assessed with CTCAE v.5, while patient-reported outcomes and biochemical control were evaluated through IPSS questionnaires and PSA serum levels, respectively. A logistic regression analysis was performed to evaluate potential associations between patient, tumor, or treatment factors and adverse clinical outcomes.

Results: From April 2020 to November 2023, 136 patients underwent SBRT with a 12-month (0-40) median follow-up. Table 1 displays their baseline demographic and clinical charactetistics, along with treatment details. Median CTV and PTV were 52 (20-134) cc and 99 (48-221) cc, respectively. Fifty percent of patients received ADT. Acute G3 Gu toxicity occurred in two patients, with 18.3% experiencing G2 events. No acute G > 2 GI toxicity was observed, and 9.5% had G2 GI events. Late GU toxicity included 1.5% G3, 1.5% G2, and 23% G1. No late G>2 GI toxicity occurred; G2 and G1 GI toxicity were 0.7% and 3.7%. Univariate analysis did not identify any factor significantly associated with GI late toxicity. At multivariate analysis Prostate volume correlated with acute G>1 GU toxicity (P=0.0366), age at radiotherapy with acute G>1 GI toxicity (P=0.0309), and previous abdominal surgery with late G>0 GU toxicity (P=0.0476). Median IPSS was 9 (0-27) at baseline and 6 (1-21) at the last follow-up, with 17.6% experiencing a >1-point worsening. Lower baseline IPSS with a cutoff of 9 was identified as protective against IPSS decline in multivariate analysis (P=0.0058).

Conclusions: This study shows that SBRT is a safe and well-tolerated treatment for localized prostate cancer, and strict patient selection criteria may not be essential if a thorough protocol for preparation and monitoring is followed, although long-term follow-up is required for confirmation.

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LOCALLY ADVANCED RECTAL CANCER (LARC) IN THE "TNT Era": A RETROSPECTIVE EVALUATION OF A MONO-INSTITUTIONAL CASE SERIES

Code: 474

Aims: To evaluate the feasibility, toxicity, and efficacy of total neoadjuvant therapy (TNT) - encompassing Radiotherapy (RT) and Neoadjuvant Chemotherapy (nCT) - followed by surgery in patients (pts) with high-risk locally advanced rectal cancer (LARC) treated in our center.

Methods: We retrospectively analyzed LARC pts underwent TNT program decided by a multidisciplinary team (MDT) based on MRI findings.
TNT programs included induction chemotherapy (iCT), consolidation chemotherapy (cCT), or both (sandwichCT), long-course chemoradiation (LCCRT), or short-course radiotherapy (SCRT).
We analyzed demographics, compliance, and toxicity (CTCAE v5.0), sphincter-sparing surgery (SSS) and pathological response rate.
In addition, we evaluate Distant Metastases, and Overall Survival rates, using descriptive statistics.

Results: Between May 2021-February 2024, a consecutive cohort of 52 LARC patients underwent TNT in our institution. 40 male, 12 women, with median age of 65 yrs (range 34-84 yrs).
MRI stage at baseline was: cT4 in 14 pts (27%), cT3N2 in 28 pts (54%) and positive mesorectal fascia (MRF+) in 30 pts (58%).
At the time of data analysis, 17 pts (33%) received iCT, 28 pts (54%) received sandwichCT and, finally, 7 pts (13%) received cCT.
RT was delivered with Volumetric Modulated Arc Therapy (VMAT) technique, with 4 pts receiving SCRT (8%) and 45 pts (92%) receiving LCCRT with a boost up to 50-55Gy on macroscopic T with corresponding mesorectum and positive nodes.
All but 6 pts (10%) completed the planned treatment schedule due to 2 allergic reactions to Oxaliplatin, 2 pts with G3 gastrointestinal (GI) toxicities, and 2 pts with G3 cardiac toxicities.
To date 38 pts underwent surgery, SSS with anterior resection of the rectum was performed in 36 pts (95%), with the remaining requiring Miles Surgery. Surgery was performed after a median of 13 weeks. Pathological partial and complete responses were achieved in 20 (53%) and 13 pts (34%), respectively. With a median follow-up of 15 months: 1 pt (2%) died from other causes, and 3 pts (6%) developed oligometastatic disease 13 months after R0 surgery

Conclusions: TNT has proven to be feasible, safe, and effective, as demonstrated by low toxicity rate and high adherence to planned treatment. Moreover, TNT revealed a high rates of pCR (35%) and disease-free survival (94%).
A longer follow-up is desirable to determine if these short-term benefits translate into improved overall survival and disease control.

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TOTAL NEOADJUVANT THERAPY (TNT) IN ELDERLY RECTAL CANCER PATIENTS: A POSSIBLE RESOLUTION TO A QUESTION OF GROWING RELEVANCE, FROM A MONOINSTITUTIONAL RETROSPECTIVE STUDY

Code: 478

Aims: The incidence of rectal cancer in the geriatric population is expected to increase: despite that , guidelines for the treatment are very limited, due to their lack of inclusion or insufficient representation in clinical trials. Therefore, establishing the best therapeutic strategy remains an unresolved issue: real word data can contribute to generate evidence in terms of efficacy and safety of TNT, in this group of pts.

Methods: We retrospectively examined elderly patients (>70yrs) with LARC (cT4-T3N+/MRF+), who underwent TNT program, assessed via comprehensive geriatric assessment (CGA) and multidisciplinary discussion.
All pts received induction chemotherapy (iCT), consolidation chemotherapy (cCT) or both (sandwichCT) and long-course chemoradiation (LCCRT) or Short Course RT.
After TNT, patients were either shifted to Non-Operative Management (NOM) following a clinical complete response (cCR) on MRI or proceeded to surgery 8 wks after TNT.
We evaluated acute and late toxicities (CTCAE v5.0), adherence to planned TNT, and clinical and pathological response

Results: From November 2021 to November 2023, 17 elderly patients (>70yrs) underwent TNT at our center (13 male and 4 female). 11 pts (65%) were MRF+, 4 pts (23,5%) cT4 ,13 pts (76,5%) cT3N+. Median age was 74yrs (70-84yrs).
12 pts (70,5%) received sandwichCT, 5 pts (29.5%) underwent iCT with oxaliplatin-based CT in combination with Capecitabine in 14 pts (82%) and 5FU in 3 pts (18%).
All but one pt completed the planned schedule: one pt (6%) discontinued oxaliplatin due to an allergic reaction and continued with capecitabine monotherapy.
All pts were treated with capecitabine based LCCRT (median total dose 55Gy), only one pt received IC 5-FU.
The most common adverse events were G1-2 diarrhea (n=12, 70,5%), G1-2 anemia and/or plts count decreased (n=11, 64%) and peripheral neuropathy (n=2, 12%).
At the time of analysis, 2 pts (12%) achieved cCR on MRI and were shifted to NOM. 13 pts (76%) underwent surgery and 2 pts (12%) are in presurgical evaluation.
In the surgery group, all pts received sphincter saving surgery with RAR.
At the pathological analysis, TRG distribution, according to Mandard score, was: TRG 1 (pCR) in 5 pts (38%) , TRG 2 in 7 pts (54%) and TRG 3 in 1 pt (8%) .
After a median FUP of 16,7 months (range 11-29 months), all pts are alive without local and distant relapse.

Conclusions: Our small experience has demonstrated that TNT is a safe and effective treatment modality even in this subgroup of patients.

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MODERATE HYPOFRACTIONATION IN INOPERABLE LOCALLY ADVANCER BREAST CANCER

Code: 526

Aims: Breast cancer surgery is the primary treatment for most types of breast cancer. The effectiveness of neoadjuvant treatment has led to an expansion of its indications from locally advanced to highly chemo- sensitive early-stage breast cancers, aiming to increase conservative treatments, in place of more invasive surgery, and to improve long term outcomes. This paper describes our recent experience in the treatment of locally advanced inoperable breast cancer with moderate hypofractionated radiotherapy with systemic therapy.

Methods: In 2023 more than 800 women with breast cancer were evaluated by multidisciplinary team in preoperative setting.
10 patients were considered inelegible for surgery for comorbidities or anesthesia risks and were evaluated for definitive radiotherapy treatment. 4 patients refused radiotherapy (accepting only endocrine therapy) and 6 patients were trated with moderate hypofractionated radiotherapy. After TC scan, a plan of treament was elaborate in 3D conformal tecnique with two tangential fields or with multiple fields or with volumetric modluated arc therapy. Radiation was delivered in 15 fractions, 2.67 Gy for a total breast and nodal volume (IàIV livel) dose of 40.05Gy and contestually was delivered 3.5 Gy to the tumor site for a total dose of 52.5 Gy. One patient was treated with palliative intent: 30 Gy in 10 fractions at tumor site. The median follow-up was 6 months.

Results: In 2023, 6 women were treated with hypofractionated radiotherapy. 1 patient had luminal A subtype, 3 luminal B and 2 patients have Her2 overexpression. 3 patients presented with N3 nodal involvement, 2 have cT4 stage for cutaneous involvement, one had cT2N2 disease. All women receveid systemic therapy (4 endocrine therapy and 2 chemotherapy and biological treatments). After 6 months the 5 patients treated with curative intention gained reduction in the tumour volume, whilst the one treated with palliative intention had a nodal progression. 2 had acute cutaneous toxicity grade 2 consistinf of erithema. Other toxicity were not reported.

Conclusions: Definitive hypofractionated radiotherapy allows a good local control, with acceptable toxicity but a longer follow up and a greater sample is needed to assess more robuste results.

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DOSIMETRIC EVALUATION OF ROBUST INTENSITY MODULATED PROTON THERAPY VERSUS PTV-BASED VOLUMETRIC ARC RADIATION THERAPY IN PERIPHERAL LUNG SBRT: TARGET COVERAGE AND NORMAL TISSUE SPARING COMPARISON

Code: 194

Aims: To investigate the dosimetric differences between Intensity Modulated Proton Therapy (IMPT) and photon Volumetric Modulated Arc Therapy (VMAT) in peripheral lung SBRT treatment planning.

Methods: Twenty patients with >3cm peripherally located lung lesions were retrospectively evaluated. Gated IMPT and VMAT plans were independently created on the end-exhale and end-inhale phases, respectively, using three contiguous phases to create an ITV. An SBRT fractionation regimen of 48-60Gy[RBE] in 4-8 fractions was adopted. IMPT plans were optimized on the CTV using robust planning with a 4mm ITV-to- collimator edge margin. VMAT treatments were planned on a PTV obtained by a 3mm isotropic ITV expansion. The comparative analysis encompassed target coverage, conformity index (CI), gradient index (GI), and chest wall, ribs, and lungs–ITV dose parameters. Wilcoxon-Mann-Whitney test (alpha=0.05) assessed the statistical significance. A Lyman-Kutcher-Burman (LKB) model was created to assess radiation-induced late toxicity probability.

Results: Both techniques successfully achieved all dosimetric objectives, except for the ribs constraint, which was exceeded in 2 IMPT plans and 13 VMAT plans. All the IMPT doses to the chest wall, ribs, and lungs were significantly lower than those by VMAT plans. On average, the organs at risk (OARs) biological effective dose (BED3) was reduced by 36.2Gy for chest wall D2cc ($P=0.020$) and 43.5Gy for ribs D2cc ($P<0.001$). Nevertheless, the probability of rib fractures ≥G2 decreased only by 2.3% on average. The mean lungs–ITV volume receiving 53.5Gy (BED3 equivalent of V20Gy) passed from 3.0% to 1.3% ($P<0.001$), with no clinical differences in the incidence of radiation pneumonitis. The target coverage was kept above 95% in both IMPT and VMAT plans, but ITV D99% and CTV D99% were higher in VMAT plans (ITV: 95.2% vs 98.3%; CTV: 95.4% vs 98.8%). A 3mm/3.5% robust evaluation revealed that in the worst scenario, CTV coverage did not drop below 93.6% for IMPT and 98.4% for VMAT. No statistically significant differences were observed in terms of CI and GI.

Conclusions: The VMAT optimization resulted in greater plan robustness compared to IMPT. Anyway, IMPT plans maintained a clinically acceptable CTV coverage, while providing a significant reduction in the dose to the OARs compared to VMAT plans. The LKB model did not identify a significant translation of these dose reductions into a decrease in late toxicities in lung patients undergoing SBRT.

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QUANTIFYING INTRAFRACTION MOTION IN PROSTATE SBRT: ANALYSIS FROM INITIAL CLINICAL EXPERIENCE WITH A 4D TRANSPERINEAL ULTRASOUND REAL-TIME MONITORING SYSTEM

Code: 192

Aims: This study aimed to quantify intrafraction motion using a 4D transperineal ultrasound (TPUS) real-time monitoring system in linac-based prostate SBRT.

Methods: Forty fractions from ten patients with localized prostate cancer treated with 36.25Gy/5fx or 30Gy/3fx since July 2023 were investigated. PTV was obtained by a 3mm isotropic expansion from CTV. Patient setup was achieved through CBCT soft-tissue matching. A TPUS automatic probe fixed to the treatment couch was used for intrafractional monitoring of the prostate. The system interrupted the beam delivery when the threshold of 2.5 mm was exceeded for >5 seconds in any of the three spatial directions. Unless the offset was transient, the patient was repositioned by repeating CBCT or using the coordinates recorded in the system. Couch-relative shifts of the prostate, from the beginning of the setup to the end of treatment delivery, were analyzed for all fractions to capture the real intrafraction motion as a function of time.

Results: Intrafractional TPUS tracking was successfully performed in all fractions. The treatment session's median [range] duration was 6.6 minutes [5.1 – 29.3], while the delivery time was less than 2 minutes on average. At least an intervention in the couch position was required in 6 (15%) fractions, while a transient prostate movement outside the 2.5mm threshold was observed in 2 (5%) fractions during the delivery phase. The couch-relative shifts analysis revealed that the mean (SD) shifts of the prostate were -0.21 (0.55), 0.53 (0.42), and -1.35 (0.97) in lateral, longitudinal, and vertical directions, respectively. The prostate motion mainly occurred in the posterior direction, while in the longitudinal direction it was likely restricted by the probe pressure towards the perineum. The minimum timeframe for a >3mm prostate shift in any direction over all analyzed fractions was 4.3 minutes. The same time was 9.7 minutes for >5mm shifts. The probability of >3mm movements increased from 5% (2/40) within 5 minutes to 30% (6/20) within 6.6 minutes. There were no fractions with prostate deviations >5mm within 8 minutes, while 40% (4/10) trespassed this margin thereafter.

Conclusions: Intrafraction monitoring with TPUS was feasible and effective. Keeping treatment time below 8 minutes with standard 5 mm/3 mm posterior margins minimizes the impact of intrafraction motion in prostate SBRT. Tighter margins may require a real-time monitoring device.

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PERSONALIZED CONTRAST-ENHANCED 4D-CT IMAGING FOR TARGET VOLUME DEFINITION IN ABDOMEN SBRT

Code: 191

Aims: To report our institutional implementation of 4D-CT simulation combined with individually synchronized intravenous contrast injection for better target volume delineation and breathing motion management in abdominal SBRT.

Methods: Since March 2022, thirteen patients with pancreatic (n=6) and liver (n=7) tumors were treated with 33-35 Gy and 50-60 Gy in 5 fractions, respectively. Each patient underwent two sequential 4D-CT scans: one at baseline and one contrast-enhanced (e4D-CT) with personalized delay times to achieve the expected contrast phase in the tumor region. Previous diagnostic triple-phase CT scan determined the optimal contrast phase. Uniform protocol parameters included a flow rate of 2.5 ml/s, a contrast volume adjusted to the patient's weight, and 2mm slice thickness. HU values of the aorta on the e4D-CT provided peak and washout contrast times. Different patient characteristics were analyzed to identify correlations with the quality of the enhancement.

Results: All e4D-CT scans yielded clear delineation of anatomical structures and vessels. The contrast medium significantly improved tumor visibility over all phases of the breathing cycle in 10 out of 13 cases. The delay time scheduled within the e4D-CT acquisition protocol varied from 0 to 37 seconds. Most liver lesions were imaged in the arterial phase, while pancreatic tumors were most visible in the venous phase. Four cases included a customized early-intermediate phase. The mean differences in HU relative to the adjacent vessels and liver parenchyma obtained for pancreatic and liver tumors were -90 HU and +43 HU, respectively. The aortic HU analysis revealed that the median (range) peak contrast and washout plateau times were 53.5 s (45.2-56.7) and 69.3 s (65.4-72.5), respectively. Age, performance status, aortic diameter, and other comorbidities showed no correlations with the three instances of scarce enhancement.

Conclusions: Individually synchronized e4D-CT simulation was feasible and resulted in optimal tumor enhancement and vessels definition over the whole breathing cycle. The main limitation was the reliance on calculating the patient-specific delay times from contrast injection to the CT scan. Nonetheless, our approach mitigates uncertainties in radiotherapy planning, by addressing the poor target visibility and respiratory motion challenges. This enables the delivery of higher doses of SBRT with minimal resource investment.

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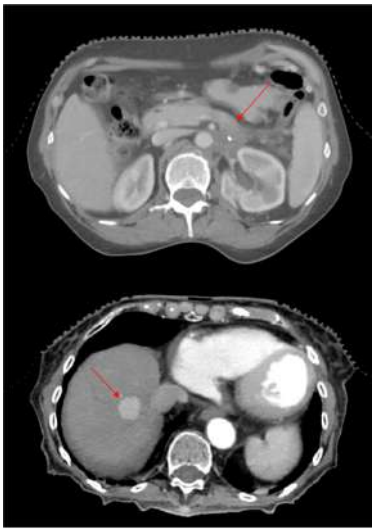

Figure 1. Contrast-enhanced 4D-CT of a venous phase for a pancreatic lesion (top) and of an arterial phase for a liver lesion (bottom).

PREDICTIVE FACTORS FOR CLINICAL OUTCOMES AFTER SINGLE-ISOCENTER LINAC-BASED RADIOSURGERY FOR SINGLE AND MULTIPLE BRAIN METASTASES

Code: 377

Aims: To report on clinical outcomes and identify predictive factors associated with improved treatment results in Linac- based Stereotactic Radiosurgery (SRS) and fractionated Stereotactic Radiosurgery (fSRS) for single and multiple brain metastases (BM).

Methods: One-hundred patients (108 treatments) received either 14-21 Gy in a single fraction (n=88) or 27 Gy in three fractions (n=20) using Linac-based single-isocenter coplanar FFF-VMAT technique between March 2020 and December 2023. Clinical and radiological follow-ups were retrospectively analyzed to assess treatment outcomes. Kaplan-Meier analysis was performed to evaluate local control (LC), intracranial disease-free survival (iDFS), and overall survival (OS). Log-rank test and Cox regression analysis were carried out to assess differences between cohorts and to identify predictive factors.

Results: The population consisted of 50 females and 50 males, with a median age of 69 years (29-86). Lung (53%) and adenocarcinoma (66%) were the most frequent tumor histology. The median follow-up was 11 months (2-64). At the time of analysis, 39 patients were still alive. A total of 214 BM (1-10) with a median volume of 0.24 cc (0.01-8.77) were irradiated, with a median minimum dose of 21.2 Gy (11.1-28.9). Nineteen (8.9%) local failure events and 1-year LC rate of 90.1% were observed. On treatment-basis, 17 (15.7%) local recurrences in at least one treated BM and 52 (48.1%) intracranial progression occurred. The median LC, iDFS, and OS were 6 months (1-47), 5 months (1-46), and 7 months (1-47), respectively. Patients with lung adenocarcinoma and mutated tumors had better treatment responses, while ≥2 lines of systemic therapy led to worse outcomes. Chemotherapy was identified as a risk factor for iDFS and OS. Female patients showed significantly better LC and OS. Polymetastatic patients exhibited inferior OS, whereas synchronous BM were not related to outcomes. No statistically significant differences were found for number of treated lesions, target volume, dose, patient age, and performance status. At multivariate analysis, lung tumor, ≥2 lines of systemic therapy, and chemotherapy remained independent factors associated with OS.

Conclusions: Linac-based SRS/fSRS treatments with single-isocenter coplanar FFF-VMAT technique were feasible and resulted in encouraging LC outcomes. Patient prognosis remains poor, mostly determined by tumor histology and systemic progression, irrespective of the radiation treatment.

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ADAPTIVE RADIOTHERAPY FOR PROSTATE CANCER WITH DAILY CBCT- GUIDED VMAT: EXPERIMENTAL ANALYSIS OF DOSIMETRIC AND RADIOPROTECTION BENEFITS CONSIDERING DLG.S 101\20

Code: 542

Aims: To evaluate the efficacy in terms of radiation protection and improvement of therapeutic workflow for patients with prostate cancer(PC) treated with volumetric modulated arc therapy (VMAT) guided by daily cone-beam computed tomography(CBCT).

Methods: 20 patients with PC treated in our Institution were included.They underwent RT using VMAT technique(total dose 60Gy to the seminal vesicles and 72 or 75.43Gy to prostate in 30-36 sessions).Our standard IGRT protocol include volumetric CBCT for the first 3 sessions and then twice a week,with two-dimensional OBI verification for the other sessions.Planning target volume (PTV)margins with the standard protocol were 6mm in all directions and 4mm posteriorly.Scan parameters of CBCT were analyzed to determine dosimetry and effective dose absorbed by the patient during the acquisitions.The CTDIw dose index was calculated using a PMMA phantom to obtain the effective dose of each CBCT acquisition.The experimental protocol included daily CBCT before each RT session,with a reduction of PTV margins by 2mm in all directions and 1mm posteriorly.Collected data were analyzed using appropriate statistical methods to evaluate the optimized dose-volume histograms(DVH),comparing them with those of the standard treatment.

Results: Application of the intensive IGRT protocol with reduced PTV margins led to a significant percentage reduction of irradiated volume for the main pelvic at risk organs (OAR's), maintaining comparable dose coverage to the PTVs. This gain justifies and compensates the increase of effective dose to the patient from 60-68 mSv to 140 mSv, for the standard and the intensive protocol respectively. Furthermore, our analysis included a technical-practical comparison focused on the daily workflow of RT and the associated machine time.From an analysis conducted on 7 patients,it was found that the use of pre-treatment CBCT required a slightly longer total average execution time of the RT session compared to the use of OBI(2.5 minutes longer, range: 1.5-3.5 minutes),but this slight treatment increase does not affect the overall scheduled time session.

Conclusions: The use of daily CBCT with reduced PTV margins produces only a slight and acceptable increase in treatment time and effective dose delivered to the patient and it's justified from a dosimetric and radioprotection point of view.

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LOCAL CONTROL OF A MALIGNANT ECCRINE SPIRADENOMA INVADING SKULL ACHIEVED BY EXTERNAL BEAM RADIOTHERAPY (EBRT). A CASE REPORT

Code: 496

Aims: Malignant Eccrine Spiradenoma is a rare malignant tumor which originates from the eccrine glands. It was first described in 1972. MES has a locally invasive and metastatic potential and to date no therapeutic standard is available for this disease. Particularly, there is only one case report in literature of MES treated with EBRT. Our goal is to describe the therapeutic efficacy of External Beam Radiotherapy in achieving local disease control in a patient affected by metastatic MES with skull invasion.

Methods: The radiotherapy treatment was administered on Linac Synergy with 3DCRT external beam technique, using a once-weekly hypofractionated schedule with a total dose of 40 Gy in 8 sessions.

Results: In July 2023, a 62 years old male patient, affected by MES of the skull base with stable lung metastasis treated in 2022 with chemotherapy, presented to the oncology clinic with an exophitic, ulcerated and bleeding lesion of the occipital region. The lesion measured 6*8 cm and cranial MRI showed occipital bone erosion. The case of the patient was discussed at the local Multidisciplinary Team dedicated to Skin cancers. Given the high risk of neurological sequelae due to a surgical approach, external beam radiotherapy was performed. Hence the patient have been treated with EBRT from to, (total dose received: 40 Gy), achieving a reduction of the lesion of an half and a complete reduction of bleeding, which is persisting at the time this report is written.

Conclusions: In this report proved efficacy in achieving local control in a patient with a heavily treated MES. The patient experienced a significant shrinkage in tumor volume and a complete resolution of bleeding. Thus, EBRT might prove effective in the treatment of this rare tumor. Given the rarity of the disease, prospective randomized trial regarding the efficacy of radiation therapy in MES are not easily feasible. Hence, a retrospective cohort study might provide evidence to support the use of EBRT in MES.

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THE POTENTIAL PROGNOSTIC ROLE OF METABOLIC RESPONSE OF 18F-FDG PET/CT IN LOCALLY ADVANCED CERVICAL CANCER AFTER RADICAL CHEMORADIOTHERAPY: A SYSTEMATIC REVIEW

Code: 373

Aims: In locally advanced cervical cancer (LACC), chemoradiotherapy (CRT) represents the standard of care. Despite 18 fluorodeoxyglucose positron emission tomography-computed tomography (^{18}F-FDG PET-CT) is recommended to assess the extension of disease at diagnosis and in the post treatment response, its role as prognostic tool is still unknown. The aim of this systematic review is to investigate the prognostic role of metabolic response of ^{18}F-FDG PET-CT after CRT in LACC patients.In locally advanced cervical cancer (LACC), chemoradiotherapy (CRT) represents the standard of care. Despite 18 fluorodeoxyglucose positron emission tomography-computed tomography (^{18F}-FDG PET-CT) is recommended to assess theextension of disease at diagnosis and in the post treatment response, its role as prognostic tool is still largely unknown. The aim of this systematic review is to investigate the prognostic role of metabolic response of ^{18}F-FDG PET-CT after CRT in LACC patients.

Methods: We systematically reviewed the literature according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines to identify studies up to December 2023. The literature search was performed on PubMed and Scopus, using the following combination of medical subject headings (MeSH) and keywords "Uterine Cervical Neoplasms", "^{18}F-FDG PET-CT", "locally advanced cervical cancer", "chemoradiotherapy". The search was restricted to the English language. The timeframe 2010–2023 as year of publication was considered. Studies assessing metabolic response after CRT in LACC were included. All abstracts and full-text articles were screened independently by four authors. Discrepancies were resolved through discussion with a third part.

Results: After the literature research, 9 studies fulfilled the inclusion criteria and were included in this review. Metabolic response after radical CRT treatment was significantly related to better clinical outcomes (including relapse free survival, overall survival, cancer specific survival, progression free survival) and to lower local relapse. Incomplete metabolic response was a predictive factor for distant metastasis and cancer related deaths.

Conclusions: Current data highlight the potential role of metabolic response of ^{18}F-FDG PET-CT after CRT to predict survival outcomes. LACC patients are likely to benefit from this imaging technique in the follow up management. Patients with incomplete metabolic response could be addressed to further additional therapeutic strategies.

AUTHOR, yrs	STUDY TIPE	PTS (n)	TREATMENT	PET-CT PROCEDURE	BEST PROGNOSTIC BASED PARAMETERS	PET RESPONSE	DFS	OS
Beriwall et al (2012)	retrospective	155	CRT+BT	POST TREATMENT (10-16 week)	CMR	CMR 112 (72%) RMU 29 (18.7%) IMU 14 (9%)	78 % at 3yy 31% at 3yy 0% at 3yy	NR
OH et al. (2013)	retrospective	60	CRT+BT	PRE, DURING and POST TREATMENT (1 month)	CMR	CMR= 43 (72,8) RMU=12 (20,33) + IMU= 4 (6,78)	NR	95% at 2 yrs 25% at 2 yrs
Onal et al 2014)	retrospective	152	CRT+BT	PRE and POST TREATMENT (3-9,8 months)		CMR 122 (80%) RMU+IMU 30 (18%)	64,3% at 4 yrs 0% at 4 yrs	66,9% at 4 yrs 12,4% at 4 yrs
Siva et al (2015)	prospective	105	CRT+BT	POST TREATMENT (3-6 months)	CMR	CMR 73 (70%) IMU 22 (21%)	86 % at 5 yrs 0% at 5 yrs	93% at 5 yrs 22% at 5 yrs
Scarsbook et al (2017)	retrospective	96	CRT+BT	PRE and POST TREATMENT (3 months)	CMR	CMR 40 (41,7%) RMU 17 (17,7%) IMU 15 (15,6 %)	NR	90% at 3 yrs 37% at 3 yrs 8% at 3 yrs
Lima et al (2018)	retrospective	82	CRT+BT	POST TREATMENT (3-12 months)	CMR	CMR 57 (69%) RMU+ IMU 25 (31%)	NR	90% at 5 yrs 30% at 5 yrs
Liu et al (2018)	prospective (randomized)	55	CRT CDDP vs GEM	POST TREATMENT (2-3 months)	CMR	RMU 9 (16%) Equivocal 13 (24%) CMR 33 (60%)	NR	0% at 5 yrs 73% at 5 yrs 88% at 5 yrs
Knight et al (2020)	retrospective	131	CRT CRT+BT CRT/S CRT/BT/S	POST TREATMENT	RMU	RMU 44 (33.6%) CMR 87 (66,4%)	29,7% at 5 yrs 67,4% at 5 yrs	52,5% at 5 yrs 85,1% at 5 yrs
Onai et al (2021)	retrospective	173	CRT+BT	PRE and POST TREATMENT (3.9 months)	CMR	CMR 122 (80%) RMU 23 (13%) + IMU 7 (5%)	NR	61% at 5 yrs 21% at 5 yrs

CRT= chemoradiotherapy; BT= Brachytherapy; S = Surgery; CMR= Complete Metabolic Response; RMU= Residual Metabolic Uptake; IMU= Increased Metabolic Uptake; NR= Not Reported

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UNEXPECTED RESULTS FROM THE MULTICENTER ARISE STUDY: CANCER TYPE IS THE PREDOMINANT FACTOR IN NON-CANCER PAIN MANAGEMENT

Code: 100

Aims: This investigation sought to elucidate the suboptimal management of non-cancer-related pain in oncology patients, with a focus on those receiving radiotherapy. The study aimed to identify determinant factors that predict the effectiveness of pain management in this demographic.

Methods: A detailed examination of a subset of participants from the ARISE study was undertaken, targeting those reporting non-malignant pain. We collected comprehensive demographic and clinical data, alongside pain intensity ratings. The Pain Management Index (PMI) was utilized to evaluate the adequacy of pain management. Advanced computational analyses, including Least Absolute Shrinkage and Selection Operator (LASSO) algorithm and the Classification and Regression Tree (CART) analysis, were employed to establish a predictive model for pain management outcomes.

Results: The cohort included 446 individuals reporting non-cancer pain. The PMI revealed that a substantial 73.1% of patients received inadequate pain management. Notably, 83.8% of breast cancer patients were found to have suboptimal pain management, in contrast to 63.6% of patients with other cancer types.
Geographically, breast cancer patients in northern Italy had a lower incidence of inadequate pain management (67.7%) compared to their counterparts in southern and central regions (86.6%).
Furthermore, in the latter, younger patients under the age of 50 reported a higher prevalence of poorly managed pain (92.9%) compared to older patients (85.4%). Among non-breast cancer types, gastrointestinal cancer patients reported better management outcomes (PMI<0: 62.5%) relative to those with other cancer diagnoses (PMI<0: 66.5%). Within this group, individuals with head and neck tumors experienced a more favorable pain management outcome (PMI<0: 59.6%) as opposed to a higher rate of inadequacy in others (PMI<0: 68.5%) (Table 1).

ALL PATIENTS 73.1 (446)					
NON-BREAST CANCER 63.6 (236)			BREAST CANCER 83.8 (210)		
NON-GI CANCER 66.5 (422)		GI CANCER 62.5 (24)	SOUTHERN ITALY 86.6 (368)		NORTHEN ITALY 67.7 (78)
NON-H&N CANCER	H&N CANCER		AGE < 50 YEARS	AGE ≥ 50 YEARS	
68.5 (47)	59.6 (399)		92.9 (49)	85.4 (397)	

Table 1: Predictive model for inadequate pain management: Red numbers represent the proportion of patients with inadequate pain management (PMI < 0), while the figures in brackets represent the total number of patients within each respective group. (H&N: head and neck; GI: gastro-intestinal).

Conclusions: The findings definitively confirm the inadequacy of non-cancer pain management in the oncological patient population. The disparities in pain management are influenced by cancer type, patient age, and geographic location within Italy. The study underscores the urgent need for tailored pain management protocols and highlights the need for further research to define the contributing factors to these disparities, with the ultimate goal of enhancing pain management strategies for oncological patients.

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CLINICAL IMPLICATIONS OF TRANSITIONING FROM TYPE-B TO TYPE-C ALGORITHMS IN LUNG STEREOTACTIC BODY RADIATION THERAPY (SBRT) TREATMENT PLANNING

Code: 491

Aims: This study aims to investigate the dosimetric variations resulting from the transition from a type-b to a type- c algorithm in lung SBRT planning and to evaluate their potential effects on patient outcomes, specifically local response and toxicities.

Methods: A cohort of 145 patients treated between 2014 and 2021 underwent VMAT treatment using a 10 MV FFF beam. Dose prescriptions varied, with 38 patients receiving 50 Gy in 5 fractions and 108 receiving 48 Gy in 4 fractions. The AAA algorithm (type-b) was used for 105 patients, while Acuros (type-c) was used for the remaining 40. Plans were recalculated using the alternate algorithm, and dose differences were assessed for coverage (PTV mean dose) and sparing of OARs (Lungs-CTV V20Gy). Mean PTV density was also examined. Clinical responses and toxicities were categorized according to the CTCAE V.5.0.
Univariate analysis, employing Fisher's exact test, and multivariate logistic regression were conducted to explore the impact of the algorithm and density parameters on response and toxicity.

Results: The median follow-up was 19.2 months (range 2-78 months), with 25.8 and 9.3 months for type-b and type- c sets, respectively. Mean PTV density was -578±139 HU, and the mean PTV dose difference was 5±4%.
The correlation coefficient between PTV dose difference and mean density (HU) was -0.744 ($p<0.01$). No significant differences were observed in OARs (<0.1%). Univariate analysis of the algorithm showed no significant differences, with p-values of 0.86, 1.00, and 0.17 for response, late, and early toxicity, respectively. In multivariate analysis, none of the considered variables were significant, except for target density showing a p-value of 0.07 with acute toxicity as the dependent variable. Further investigation using a Mann-Whitney test for patients with toxicity revealed a lower mean HU value (p-value=0.08), although not statistically significant.

Conclusions: Despite notable dose differences during algorithm transitions, no statistically significant impact on response or toxicity was observed. These findings support the implementation of a type-c algorithm without altering dose prescriptions. While PTV density did not show statistical significance, it may be a crucial factor, prompting further exploration with larger datasets. In scenarios with very low densities, strategies should be developed to prevent excessive fluence and potential dose escalation beyond established clinical practices.

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ROBUST OPTIMIZATION VS PTV OPTIMIZATION PLANNING PILOT PROTOCOL FOR LOCALLY ADVANCED LUNG CANCERS: TIME FOR GOING BEYOND PTV?

Code: 182

Aims: The planning target volume (PTV) represents the conventional, mainstream planning solution to account for uncertainties occurring during the radiation treatment (RT) such as setup-errors with the aim to ensure the CTV receives the prescribed treatment dose. Generated from an isotropical expansion of CTV-ITV, the PTV exposes a not negligible amount of healthy tissues to potentially uncessary and preventable high doses. In the case of lung cancers, this could impact both on treatment toxicity and on response to therapies including immunotherapy with a potential reduction of RT cure rates. Therefore, we elaborated a clinical protocol to evaluate the advantages of a novel planning technique based on Robust Optimization (RO) in comparison with standard PTV.

Methods: Patients affected by unresectable STAGE III non-small cell lung cancer (NSCLC) and by limited small cell lung cancer (SCLC) will be enrolled. 4D simulation CT (10 phases) will be performed to generate the ITV. Two planning approaches will be compared: 1) ITV-based RO technique: ITV (obtained from CTVs delineated on the 4DCT) will be used to perform RO with 0.5 cm setup uncertainties in cardinal directions and 2) standard PTV optimization technique, with the PTV= ITV + 0.5 cm isotropic expansion. All plans will be normalized to have at least 95 % of the prescribed dose, i.e. 57 Gy, at the 95% of the target volume. Robust optimized plans should satisfy V95 $\geq$ 95% in all perturbed scenarios. Plans will be compared in terms of nominal and robust target coverage, doses to the organs at risk including coronary arteries and the estimated dose to the immune system (EDIC). The NTCP values for pulmonary and cardiac toxicity according to the model developed by Appelt et al and Defreane et al, respectively, will be evaluated.

Results: At least 25 patients will be enrolled in a two-year period. Patients will be treated with the robust optimized plan instead of the PTV plan in case of comparable target coverage and in presence of any reduction of healthy tissue doses, especially lung and cardiovascular structures doses. One-year local control data will be also collected and compared with historical data.

Conclusions: The potential of RO to ensure adequate target coverage and spare healthy tissues in lung cancer RT will be tested in this trial: in case of positive results the RO technique will constitute a solid and novel alternative to standard PTV optimization technique which could augment the rate of cure of integrated treatments in this setting.

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SAFETY OUTCOMES OF COMBINATION OF LUNG SBRT AND TKI IN OLIGOPROGRESSIVE EGFR METASTATIC NSCLC: A MONOCENTRIC EXPERIENCE

Code: 177

Aims: First-Line EGFR TKI represent the SoC for mNSCLC harboring EGFR mutation. Nevertheless, some pts develop acquired resistance in less than 1year.In case of OligopPD, the addition of local treatment with SBRT, by eliminating drug-resistant tumor cells in the progressing lesions, allows pts to continue their first line therapy. Safety represents the major issue in combining TKI+Lung RT; in literature,2 retrospective studies reported severe pneumonitis by combining RT and Osimertinib. Based on these data, in our daily clinical practice, our MDT decided to withhold TKIs from 2 days before until 2 days after RT. We report here the outcomes of our experience.

Methods: We retrospectively reviewed clinical and radiological data to identify Oligoprogressive pts in the lung while on TKI treatment based on routine TBCT scan with iodine contrast. Before SBRT, all patients underwent 4DCT scan with respiratory gating for managing respiratory motion of the lesions. All SBRT was delivered with VMAT 6XFFF and daily CBCT was performed. Pts were told to withhold TKI from 2 days before until 2 days after RT.SBRT dose was decided based on the location of the lesions ,previous treatment plan and/or dose at OARs(especially trachea and main bronchus).

Table 1. Main acute adverse effects (CTCAE 5.0)

	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Radiation Pneumonitis	5	0	0	0	0
Radiation Esophagitis	0	0	0	0	0
Asthenia	6	0	0	0	0

Results: From March 2020 to June 2023,14 pts on TKI treatment received Lung SBRT for Lung OligoPD. Median age at diagnosis was 69.4(55-82).All were diagnosed with metastatic adenocarcinoma,10 pts(71%) received Osimertinib as first line treatment,2 pts(14%)received Erlotinib, and 2 pts(14%)received Afatinib.4 pts were switched at Osimertinib for PD, before receiving RT and still on ongoing.Overall,18 Lung lesions were defined as safely treatable with SBRT by a Radiation Oncologist during MDT evaluation. The most common SBRT fractionation schedule was 50 Gy/5 fx(8 pts),followed by 40 Gy/5 fx(3 pts).Other pts received,respectively,55 Gy/5 fx (1pt),48 Gy/4 fx(1 pt),35 Gy/5 fx(1 pt) and 30 Gy/5 fx(1 pt).No G2-4 acute respiratory toxicity was recorded;5 patients(35%)developed acute G1radiation pneumonitis(according to CTCAE 5.0.)Asthenia G1 was observed in 6 pts. In terms of late respiratory toxicities, only 5 G1(35%)were recorded. No delay in resuming TKI therapy was observed. Median PFS was 10 months(36-6);sample size and follow-up time were too small for any OS calculation.

Conclusions: In our series, Lung SBRT for OligoPD during TKI was safe and feasible, with a positive trend in PFS. Data from large series or randomized trials are needed to confirm safety and efficacy benefit with this approach.

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PLEOMORPHIC DERMAL SARCOMA OF THE SCALP: TREATMENT MANAGEMENT IN A CASE REPORT

Code: 397

Aims: Pleomorphic dermal sarcoma (PDS) of the scalp is a rare tumor which has usually a slow developement, but occasionally shows a rapid growth and it has low rate of local recurrence (LR). Surgical resection is the mainstay of treatment, with or without adjuvant radiotherapy (RT). Case series of PDS have reported LR rates from 7-35% and distant metastases (DM) in 2–20% of cases [1]. We present a case report treated in our Institution.

Methods: In November 2019 a 76 years old patient with a 2 cm reddish bullous lesion of the scalp was evaluated by a plastic surgeon. First excision found an histology of undifferentiated PDS (CD10 and S100 positive, p40 negative, ki67 25%) with positive deep margin. A surgical enlargement was done in August 2020, showing a 4 mm focus of PDS distant 5 mm from the deep margin of resection. Staging with total body computed tomography (CT) did not show LR or DM. From December 2020 to January 2021 a postoperative RT was performed on the tumoral bed of the scalp, at the total dose of 60 Gy with conventional fractionation (6MeV electrons with bolus). A field's margin of at least 1 cm from the tumoral bed was applied. RT was well tolerated, with skin erythema grade 2 according to CTCAE scale v4. Negative follow-up (FU) until Avril 2021 when a nodule in the inferior left lung lobe appeared on TC and showed an high captation on positron emission tomography (PET).

Results: In May 2021 an atypical resection of this left lung nodule was performed, with histology of PDS metastasis. No adjuvant chemotherapy was realised because of an impaired renal function. Nowadays, after a FU of 37 months from the end of scalp RT, patient is alive and in good clinical conditions, without local or distant relapse.

Conclusions: Radical surgery and, when indicated, adjuvant RT at recommended doses for soft tissues sarcomas, can be safe and effective for the treatment of a rare tumor like PDS of the scalp, permitting a good control of disease and a reduction of LR.

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RISK FACTORS OF ACUTE ASPIRATION PENUMONIA (AAP) DURING RADIATION TREATMENT IN OROPHARYNGEAL CANCER PATIENTS: A RETROSPECTIVE ANALYSIS

Code: 558

Aims: Pre-treatment dysphagia with silent aspiration is present in 15% of H&N pts and risk of clinical acute aspiration pneumonia is concerning. This study aimed to identify risk factors related to patients and to radiation treatment, that could help to prevent clinical AAP during radiation treatment.

Methods: Patients with locally advanced oropharyngeal squamous carcinoma treated from August 2021 to December 2023 with full IMRT+ CDDP based Chemotherapy were retrospectively evaluated. AAP was scored with CTCAE v.5 criteria. We analysed patient and tumour and radiation related risk factors for AAP, as tumor involvement of larynx, presence of nasogastric feeding tube and/or tracheostoma, mean radiation dose on larynx. The correlation between AAP and presence of tracheostoma and involvement of the larynx (sovraglottic +/- glottic) was performed using Chi-square test while correlation between AAP and Dmean Larynx was calculated with the point-biserial correlation.

Results: We found 23 patients with oropharyngeal cancer, 3 female and 20 male, median age was 66 years (54-83). Grade 3-4 AAP was observed in 7/23 pts (30%), 1 case of grade 5, and 1 case with grade 1 found in CT scan. Larynx was involved in 19/23 pts thus the median of the mean dose of larynx was 50 Gy (30-67 Gy). We found a statistically significant association between the presence of a nasogastric feeding tube and aspiration (**p = 0.04**). However, we did not found a statistically significant relationship between AAP and the presence of tracheostoma (p =0.5), involvement of the larynx (sovraglottic +/- glottic) (p=0.2), and the Dmean Larynx (p = 0.6).

Conclusions: We observed a 35% of symptomatic AAP (G > 2). Our findings showed a significant association between the nasogastric feeding tube and the incidence of AAP in patients treated for oropharyngeal cancer, underscoring the clinical relevance of nutritional support methods in managing dysphagia. However, the lack of a significant correlation between the Dmean Larynx and aspiration challenges the hypothesis that radiation dose to the larynx directly influences aspiration risk. In our Institution a multiprofessional preliminary evaluation of patients including pre-treatment aspiration risk determination and rigorous assessment of pre-treatment dysphagia is now implemented in all H&N cancer patients, to assure a correct selection of patients to undergone PEG.

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SURFACE GUIDED-DEEP INSPIRATION BREATH HOLD IN ULTRA-HYPOFRACTIONATED WHOLE BREAST IRRADIATION FOR EARLY STAGE LEFT- SIDED BREAST CANCER PATIENTS: A MONO-ISTITUTIONAL ANALYSIS

Code: 492

Aims: In twenty consecutive left-sided breast cancer (BC) patients treated with breast conserving surgery (BCS), the present study aims at evaluating dosimetric parameters and treatment delivery of a post-operative ultra-hypofractionated whole breast irradiation (WBI) administered using a Surface Guided - Deep Inspiration Breath Hold (SG-DIBH) delivered with AlignRT® System. DIBH and free breath (FB) plans were compared.

Methods: All patients received 26 Gy in 5 fractions to the whole breast. Two planning CT scans were acquired: the first with patient in FB for surface reference and tattoos alignment, the second with patient in DIBH. For each patient treatment plans were performed both on FB-CT scan and on DIBH-CT scan, using a three- dimensional conformal radiotherapy (3DCRT) technique. Dose-volume specifications for plan evaluation were as follows: D95%?95%, V105%<5%, V107%<2% and Dmax<110% for breast-PTV, V8Gy<15% for the left lung, V1.5Gy<30% and V7Gy<5% for the heart and LADA Dmean<6Gy.

Results: Doses to the left lung, heart and LADA emerged as significantly lower in DIBH plans, reaching a reduction of 13% for the left lung V8Gy, 60% for the LADA Dmean and 84% for the heart V7Gy (Table 1). Regarding treatment delivery, the average of the maximum shift value in all directions, calculated after co-registration of digitally reconstructed radiographs (DRRs) with 2D kV-portal images, was < 0.5 mm for all patients. All patients easily completed treatment and patient compliance was high.

Conclusions: SF-DIBH WBI with AlignRT® System resulted feasible and reproducible. At the present, in our Institution, SG-DIBH is the standard treatment for all left-sided BC patients.

ROI	Objective	DIBH	FB	p
Left lung	V8 <15%	12.0% ± 1.5%	13.8% ± 1.9%	= 0.001
Heart	V1.5 < 30%	6.4% ± 4.3%	13.6% ± 6.4%	= 0.000
	V7 < 5%	0.5% ± 0.5%	3.0% ± 2.0%	= 0.000
LADA	Dmean < 6 Gy	2.7% ± 1.4%	6.8% ± 3.6%	= 0.000

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HYPOFRACTIONATED VERSUS CONVENTIONALLY FRACTIONATED RADIATION THERAPY WITH TEMOZOLOMIDE FOR PATIENTS WITH GLIOBLASTOMA: AN INSTITUTIONAL EXPERIENCE

Code: 141

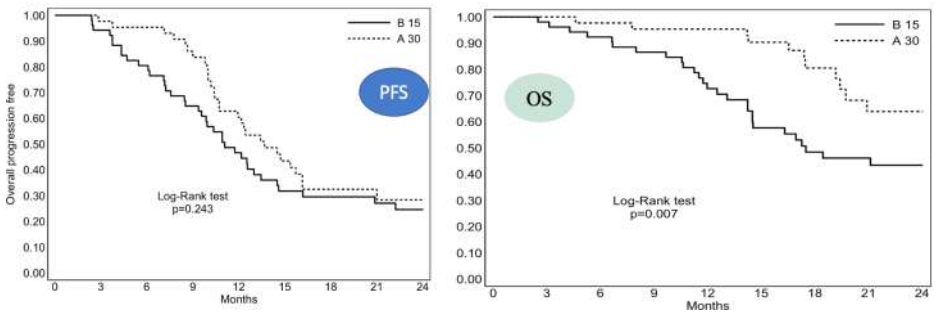
Aims: Hypofractionation Radiotherapy (HF-RT) may have a radiobiological rational, a patient convenience and a healthcare resource advantages over conventionally fractionated radiation therapy (CF-RT) in glioblastoma (GBM). Furthermore, simulated integrated boost (SIB) HF-RT is an effective and safe treatment. We report monoistitutional experience in terms of progression free survival (PFS), Overall survival (OS) and RT related toxicities of GBM patients treated with HF-RT and CF-RT.

Methods: From November 2019 to April 2023, patients with IDH-wildtype GBM treated with HF-RT (52.5Gy/15 fractions) or CF-RT (60Gy-70 Gy/30 fractions) were selected. Volumetric modulated arc therapy was performed for all patients. Concomitant temozolomide (75mg/mq/die) and adjuvant chemotherapy (TMZ 150-200 mg/mq/5 days q 28) were administered. OS and PFS were estimated using the Kaplan-Meier method.

Results: Ninety-five patients were treated (HF-RT:53, CF-RT:42). With a median follow-up of 24 months (range 9-63) median age was 64 and 54 years for both HF-RT and CF-RT groups. With regards to the entire population, the median OS at 1 year was not yet reached. In CF-RT and HF-RT group, estimated time to progression was 13,7 and 11,1 months, respectively (p=0.243). In terms of OS, CF-RT group presented a median OS of 28,8 vs 17,5 months of HF-RT group (p=0.007).In figure 1 main clinical outcomes of two groups are reported. No acute or late neurological side effects of grade ≥ 2 were reported during RT. Grade 3-4 hematologic toxicity occurred in five cases.

Conclusions: CF-RT represents the standard of care in GBM patients while HF-RT is a treatment modality well established in elderly and poor-prognosis patients. Even though further investigations are ongoing, a statistically significative difference exists in terms of OS between Hypo-RT and CF-RT. This study presents different limits, especially the retrospective nature and inhomogeneity of the sample (in terms of performance status, age, type of surgery, prognosis, RT dose and so on). In this context, further investigation, with a greater amount of data, are mandatory, in order to assess the best standard approach.

Figure 1 Progression Free survival (PFS) and Overall survival (OS) of two groups: hypofractionated radiotherapy-A, conventional fractionated Radiotherapy -B



A GENERAL OVERVIEW OF THE RESULTS AFTER ONE YEAR OF USE OF THE LATTICE RADIATION THERAPY

Code: 197

Aims: The Lattice Radiotherapy (LRT) allows to treat unresectable bulky cancers with an heterogeneous high- gradient dose distribution and a safe dose escalation. With this technique, multiple localized high-dose islands (vertices, Vs) were created within the tumor volume, alternated with a certain degree of separation from lower dose regions (valleys). LRT enhances its action inducing bystander and abscopal effects. We describe one year's experience with LRT.

Methods: In 2023 we treated 15 patients (pts) with bulky tumors. From 3 to 32 cylindrical or spherical Vs were created in the tumor volume, with a diameter of 1 cm and a separation of 1.5/2 cm between each vertex and the next in the axial plane, using a geometric arrangement created by a grid tool of the Treatment Planning System. We used Montecarlo algorithm and VMAT radiotherapy. Tumor volume ranges from 48,530 cm3 to 1417,608 cm3. Vs volume ranges from 1,172 cm3 to 42,544 cm3. In 3 cases a moving-strip technique was used, because the tumors were really bulky (in Fig.1 a right leg's sarcoma of about 30 cm). Mean Vs/tumor volume ratio was 3,01%. The doses ranges from 6 Gy/1 fr to 60 Gy/30 fr to the CTV and from 12 Gy/1 fr to 60 Gy/4 fr to the Vs. 9 cases were treated with a concurrent approach, 6 cases with a sequential one. We planned to achieve a goal of ≥ 95% prescription dose coverage to at least 95% of the targets. The constraints for Organs At Risk normally employed were used.

Results: 13 pts completed the treatment without toxicities and interruptions, 2 pts ended the treatment a few sessions earlier. LRT allowed to deliver ablative doses without excessive toxicity to the surrounding normal tissues, compared with standard treatment. We observed remarkable relief of initial symptoms (dyspnea, pain, functional impotence) after the treatment and, where follow ups were available, reduction of the tumor volume and SUV values. Tumor reduction ranges varies from to 8 to 45 mm (mean 25 mm), SUV reduction ranges from 3.7 to 15.6 (mean 9.5). In Figure 2, before vs after CT of a patient with a bulky mediastinal mass.

Conclusions: After one year, LRT confirmed its safety and efficacy and it can be used for the treatment of bulky cancers, thanks to the delivery of a very high dose inside the tumor and an higher local control without adding any extra toxicity in the peripheral normal tissue. We hope to add more pts to our experience and increase our knowledge of this technique to optimize its use in the clinical practice.

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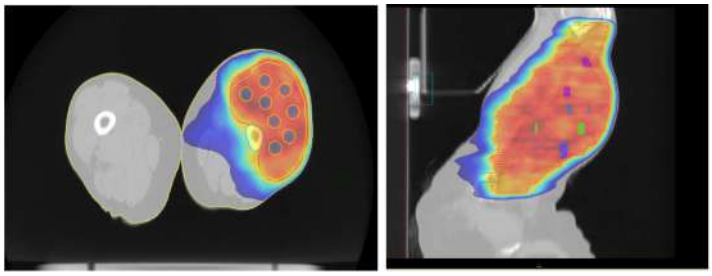

Fig. 1 A case of a sarcoma of the right leg (Patient in position "Feet first").

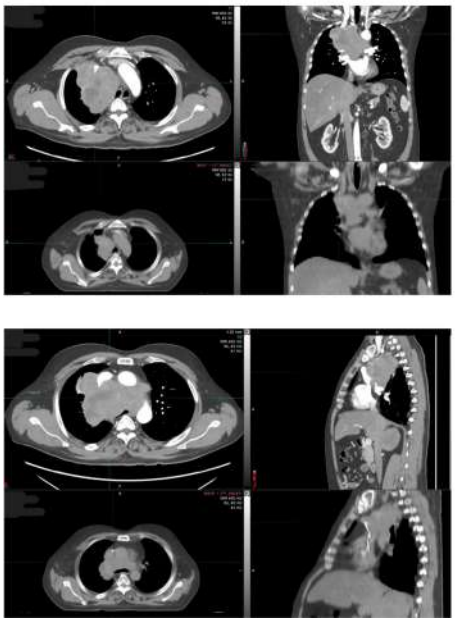

Fig. 2a Before the treatment CT (above) vs after 2 months CT (below) of a patient with a bulky medistinal mass. Axial and coronal view.

Fig.2b Axial and sagittal view.

ROLE OF METASTASES DIRECTED RADIOTHERAPY IN DELAYING SYSTEMIC THERAPY IN OLIGOMETASTATIC PROSTATE CANCER PATIENTS

Code: 356

Aims: Metastasis-directed therapy (MDT) using SBRT is a safe treatment for patients(pts) with oligometastases. This approach can prolong disease-free survival and delay the initiation/change of systemic therapies. We retrospectively analyzed, biochemical progression-free survival (b-PFS), toxicity, and delayded systemic treatment in oligometastatic prostate cancer (PC)pts.

Methods: Between 2018 and 2023 28 oligometastatic PC pts(36 lesions) with 1/5 bone or nodal lesions were treated with the Cyberknife System (CK). Lesions were diagnosed with PSMA-PET and treated with 21/36 Gy in 3/5 fractions. We calculated: median follow-up (FU), median nadir value after primary therapy, time between primary therapy, onset of bone or lymph node lesions, median nadir value after MDT, time free from change of systemic therapy at 1-2 year.

Results: Bone lesions were located in: spine(12),ilium(1),sternum(4),clavicle(1),rib(1). Nodal lesions were in the lumboaortic region(15),thoracic region(3). Median FU was 17 months (mo)(4-60) for pts treated on bone lesions,11 mo (3-26) for 10/14 pts treated on lymph node lesions (4were lost to FU).8 pts were treated with primary radiotherapy,8 with adjuvant radiotherapy,4 with salvage radiotherapy. Median nadir value after primary therapy was 0.05ng/ml(0-1.32) and time to onset of metastatic sites after primary therapy was 3years(1-25). Before MDT,6 pts did not receive any systemic therapy, 18 only ADT, 4 ADT+ARSI.
Median pre-MDT PSA was 0.855ng/ml(0.0-4.64) and median post-MDT PSA was 0.25 ng/ml (0.0-1.02). There was no toxicity above G1(RTOG scale).
Among 14pts with mtx bone, 4 pts had a median ADT-free bPFS of 17mo; 4 pts, treated before MDT with ADT, had a median bPFS of 15mo, 2pts treated before MDT ADT+ARSI, had a median bPFS of 13 mo; 4pts had biochemical relapse at a median time of 11mo and changed systemic therapy. Among pts with lymph node lesions, 10 did not change therapy, of these 3 had a median ADT-free bPFS of 16mo; 6 pts, treated before MDT with ADT, had median bPFS of 13 mo; 1 patient, treated before MDT with ADT+ARSI, had a bPFS of 3 mo; four pts were lost to FU. Overall, the time free from change of systemic therapy at 1 year was 84.2%; at 2 years it was 57.7%

Conclusions: MDT with the CK for relapsed PC is a safe treatment with promising results in terms of b-PFS and delay in initiation/change of systemic therapies. This minimally invasive approach finds great compliance in pts, but requires further evaluation in future clinical trials.

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ASSESSMENT OF MIGRATION OF INTRAPROSTATIC FIDUCIAL MARKERS DURING RADIOTHERAPY

Code: 566

Aims: Prostate motion throughout the course of radiotherapy (RT) is a significant concern. Employing intraprostatic fiducial markers (FM) as surrogate for prostate gland position relies on the assumption that these FM remain rigidly fixed within the prostate. This study aimed to assess marker stability by monitoring the distances between implanted markers (FMD) over the entire duration of RT.

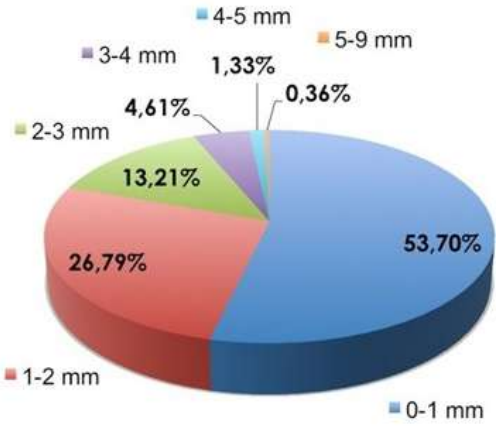
Methods: From January 2007 to December 2023, a total of 280 patients diagnosed with early-stage, T1-T2 N0M0 prostate neoplasia, with a Gleason score of ≤7 and PSA < 10, underwent transrectal implantation of three radio-opaque FM. Patients meeting additional criteria such as the absence of intraprostatic calcifications, favorable anatomy, no prior TURP, and providing informed consent were further selected for the study.
The analysis focused on 70 out of the total 280 patients who underwent image-guided RT (IGRT). Three markers were implanted per patient at the base (A), middle (B), and apex (C) of the prostate. Following marker implantation, all patients underwent computed tomography (CT sim) with a slice thickness of 1 mm, conducted at least one week post-implantation. Additionally, daily cone-beam CT (CBCT) scans were utilized to verify FM positions before each treatment session.
Retrospectively, CT sim images and daily CBCT scans were used to record the coordinates (x, y, z) of the FM. The distances between markers (FMD), such as AB, BC, and CA, were measured as: $X_1X_2=\sqrt{(x_1 - x_2)^2 + (y_1 - y_2)^2 + (z_1 - z_2)^2}$

FMD variations throughout the entire course of RT were calculated as D1,10…n – D0 = ΔD1, 10…n; where D0 represented the initial FMD observed on the CT sim.

Results: The mean absolute variation of all FMDs was 1.28 ± 0.65 mm. The largest observed variation in FMD was 9.1 mm. 94% of recorded variations were 3 mm or less, with 80% being 2 mm or less (Fig 1). No correlation was identified between FMD variations and initial prostate volume. A simultaneous progressive reduction of FMDs was observed in 70% of patients, which correlated with prostate shrinkage.

Conclusions: FM are now considered as a standard practice in modern prostate radiotherapy, particularly when dose escalation is being considered. The results obtained indicate minimal variations in the relative position of the markers (1.28 ± 0.65 mm) without significant marker migration, confirming that FM serve as a reliable surrogate for prostate location in IGRT treatment. Severe complications from fiducial implantation are rare.

Figure 1 :Absolute variations distribution



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ULTRA-HYPOFRACTIONATED RADIOTHERAPY WITH FIDUCIAL MARKERS FOR PROSTATE CANCER: INTRAFRACTION ORGAN MOTION EVALUATION AND CORRECTION

Code: 581

Aims: Ultra-hypofractionated radiotherapy, employing higher doses per fraction of radiation for low or intermediate-risk prostate cancer, is now recognized as a viable alternative to conventional normofractionated or moderately hypofractionated EBRT schedules. Understanding and addressing both inter- and intrafraction setup and organ motion of the prostate are crucial for minimizing irradiation to surrounding healthy tissues. In this study, we assessed intrafraction motion by monitoring the position of fiducial markers throughout the session.

Methods: Patients with a prostatic volume less than 100 cc and good urinary function, as indicated by an IPSS score of less than 20 and uroflowmetry, were selected for ultra-hypofractionated radiotherapy. Three intraprostatic fiducial markers were implanted to delineate the target volume and assess inter- and intrafraction organ motion.
Planning CT 1 mm slices with optimized bladder filling and an empty rectum, was conducted; a bladder catheter was utilized for urethra delineation. Fusion of planning CT with multiparametric MRI aided in defining the clinical target volume (CTV) and organs at risk. A CTV-to-PTV margin of 3 mm and a 3 mm margin for the urethra PRV were applied.
The treatment regimen consisted of 5 fractions of 7 Gy administered every other day. Cone-beam CT (CBCT) was performed prior to each session to correct interfraction prostate position using fiducial markers. Additionally, KV images were captured at every 30-degree gantry rotation during treatment to monitor intrafraction organ motion. Each KV image was reviewed online, and if a marker's position exceeded the predefined tolerance (2.5 mm), delivery was halted, and shifts/rots were made to correct the error.

Results: The treatment was well tolerated, with no Grade 3 acute or chronic toxicity observed. Utilizing a bladder catheter allowed for optimization of the treatment plan by sparing the urethra, adhering to a Dmean constraint of 32.5 Gy based on literature data. The tolerance for marker position was consistently maintained, resulting in only a few treatment sessions being interrupted. Our study demonstrated that marker position changes were minimal, less than 3 mm, supporting us in confirming the limited expansion from CTV to PTV.

Conclusions: In conclusion, the positioning of fiducial markers proved to be an excellent indicator of prostate position, facilitating precise treatment delivery while minimizing radiation exposure to surrounding organs.

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INTEROBSERVER CONTOURING VARIABILITY IN POSTOPERATIVE STEREOTACTIC RADIOTHERAPY OF BRAIN METASTASES

Code: 71

Aims: To investigate interobserver variability (IOV) of target volume delineation in post-surgery stereotactic radiotherapy (SRT) of brain metastases.

Methods: Eighteen radiation oncologists participated in a virtual contouring laboratory as part of a nationwide multistep prospective study, regarding the management of postoperative SRT of brain metastases. The referral expert for each participant center received five cases, with relative imaging (pre and post-surgery T1 post gadolinium MRI), and CT simulation without contrast. Clinical cases were selected in order to evaluate various scenarios in relation to size, location and local extent of brain metastases pre-surgery.
Specifically, case 1 concerned a supratentorial lesion < 4 cm with dural/venous sinus contact from triple negative breast cancer. Case 2 involved an infratentorial lesion > 4 cm with dural/venous sinus contact from NSCLC. Case 3 was a supratentorial lesion < 4 cm with no contact from HER2+ breast cancer. Case 4 was an infratentorial lesion < 4 cm with no contact from NSCLC; finally, the case 5 consisted in a supratentorial lesion > 4 cm with dural contact from triple negative breast cancer. For each case, all radiation oncologists were required to delineate the clinical tumor volume (CTV), independently.

Results: A total of 79 CTV was received. Results of IOV are showed in Table 1. For case 3, one CTV had a volume of 3.4 cc and a mean Dice of 0.3 (0.23-0.39, SD 0.05), strongly deviating from the others. Therefore, it was excluded from the calculation of the global mean Dice. Similarly, for case 5 one volume had a major deviation with a volume of 67.9 cc and a mean Dice of 0.57 (0.45-0.69, SD 0.07). In general, CTV of case 3 showed the higher agreement as demonstrated by a mean Dice of 0.78, with minimum value of 0.72.

Conclusions: In this analysis a contouring variability was observed, increasing in case of brain metastases with dural/venous sinus contact and infratentorial location; moreover, a disagreement was observed in the inclusion and the definition of surgical tract. After this evaluation, we performed a nationwide webinar with the aim to promote the sharing of best standard care and to potentially improve equability and uniformity of the clinical practice. A further analysis is ongoing on the assessment of IOV post-webinar and the impact of educational event.

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Table 1

	Volume (cc)	Dice similarity coefficient
	Mean (smallest-larger)	Mean (95% CI)
CTV Case 1	20.9 cc (15.2-35.5)	0.70 (95% CI, 0.62-0.77)
CTV Case 2	45.3 cc (28.7-61.3)	0.72 (95% CI, 0.61-0.76)
CTV Case 3	18.4 cc (3.4-25.4)	0.78 (95% CI, 0.72-0.82)
CTV Case 4	8.1 cc (3.4-14.7)	0.70 (95% CI, 0.58-0.76)
CTV Case 5	30.6 cc (19.5-67.9)	0.74 (95% CI, 0.7-0.78)

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TOTAL MARROW IRRADIATION: IMPACT OF REDUCED CT-TO-DELIVERY TIMEFRAME ON DOSE AND POSITIONING ACCURACY

Code: 33

Aims: Total Marrow and Lymph-node Irradiation (TMLI) is a challenging technique employed in the pre- transplantation conditioning regimen for hematopoietic malignancies. TMLI aims to irradiate bone marrow, lymph nodes, and spleen sparing nearby organs at risk, reducing toxicities associated with standard total body irradiation. Due to the complexity of contouring and planning optimization, TMLI typically takes several days, leading to perform simCT 15 days before treatment (CT-15). We evaluated the possible benefit of performing a simCT with reduced CT-to-delivery timeframes and its impact on clinical workflow.

Methods: Since 2010, our center has treated 130 patients with TMLI using volumetric modulated arc therapy (VMAT) based on the simulation CT-15 using a personalized immobilization system developed by our team. Image-guided radiotherapy (IGRT) using cone beam CT (CBCT) was employed on each isocenter. Shifts and matching quality were evaluated by an expert radiation oncologist on a scale of 1-5. For the latest 18 patients, a second simCT was performed 4 days before treatment (CT-4) to assess anatomical changes compared to CT-15 and evaluate its impact on treatment plan. Deformable registration was used to map PTV from CT-15 to CT-4. Dosimetric analysis and CBCT matching was evaluated for CT-4 and compared to CT-15. The statistical analysis was performed using the Mann-Whitney test ($p<0.05$).

Results: A total of 857 CBCT scans were analyzed, of which the last 164 performed also the CT-4. No significant difference in the CBCT/CT-15 matching were observed between the first 693 and the last 168 scans, with an average and standard deviation of 5.3±7.4 mm vs. 5.5±4.2 mm. Image quality agreement was sub- optimal (<4) in 13% of cases. Quality agreement of CBCT/CT-4 was higher with no cases ranked <4 (figure 1). A significant PTV_D98% reduction was observed using CT-4 (92.7 ± 4.1 % for CT-4 vs. 98.0
± 1.5 % for CT-15) (table 1). In 11% of cases important differences were observed between the two CT scans, leading to plan re-optimization using CT-4. This rapid optimization was feasible by artificial intelligence (AI) tools developed by our team.

Conclusions: Our study highlights the benefits of reduced CT-to-delivery timeframes for the TMLI. CT-4 improved agreement with CBCT compared to CT-15. These findings support the use of AI-based tools to streamline plan optimization and enhance accuracy and efficiency in TMLI delivery. This study was part of AuToMI project to automate TMLI planning.

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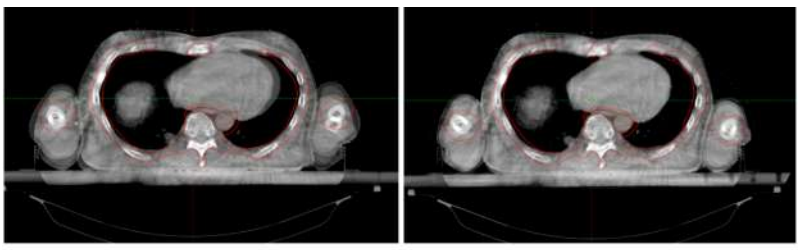

Figure 1: representative axial view of the matching between the simulation CT at -15days and CBCT, and the simulation CT at -4days and the CBCT.

STEREOTACTIC RE-IRRADIATION FOR LOCAL RECURRENCE AFTER RADICAL PROSTATECTOMY AND RADIATION THERAPY

Code: 78

Aims: Prostate cancer recurrence in patients previously treated with radical prostatectomy and radiation therapy is challenging, especially due to the risk of bladder and rectal toxicity. Re-irradiation could be an option, and here we present the results of the retrospective evaluation of the results in the cases treated in our institution.

Methods: From July 2019 to March 2022 12 pts underwent salvage reirradiation with stereotactic body radiotherapy for local prostate cancer recurrence in the prostatic bed. The median total dose of SBRT was 30 Gy (range 25-35) in 5 fractions. Thirteen robotic stereotactic treatments were performed and fiducial markers tracking was used in 77% of cases. In the first RT course, the prostatic bed received a median 2Gy equivalent dose of 72 Gy (range 70-74). Median time from previous radiotherapy to ReRT was 92 months (range 35-208). The median cumulative 2 Gy equivalent dose (considering both RT course) was 148 Gy, while median BED was 345 Gy (α/β 1.5). Androgen deprivation therapy (ADT) was used concomitantly with SBRT in 7/12 (58%) patients (only first-generation ADT in 5 patients and Androgen Receptor Targeted Agents in 2 cases). Biochemical and clinical relapse-free survival were analyzed, and post- treatment toxicities were assessed according to the Common Terminology of Adverse Events v.5 criteria.

Results: One patient (previously treated with cryotherapy) presented grade 3 cystitis and urethral pain and another one (treated in two different local relapses in the prostatic bed) presented only grade 3 hematuria. At the last follow up all toxicities recovered. A patient died in a car accident two months after the end of the RT before the first follow-up visit. All other patients had a biochemical response. With a median follow-up of 34 months (range 12-54), 5/12 patients (42%) had a biochemical relapse, 2/12 (17%) had an out-of-field clinical relapse, but none presented local recurrence. Two- and 3-year biochemical relapse-free survival (bRFS) were 63% and 50%, while clinical relapse-free survival (cRFS, out of field) were 92% and 80% respectively

Conclusions: Salvage stereotactic reirradiation for local recurrence in the prostatic bed may offer a local encouraging control with acceptable toxicity. Prospective studies are needed to confirm these oncological outcomes and to better define the population that could most benefit from this treatment.

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IS THERE AN IMPACT OF AUTOIMMUNE RHEUMATOLOGICAL DISEASES ON ADJUVANT RADIOTHERAPY IN BREAST CANCER? A MONO-INSTITUTIONAL EXPERIENCE

Code: 567

Aims: Autoimmune rheumatologic diseases (ARDs) have historically constituted an absolute or relative contraindication for Radiotherapy, due to increased RT-related toxicity and the possible exacerbation of the rheumatologic disease. ARDs are more frequent in females than in males (F:M 4:1); in women, breast cancer is the most common malignancy, accounting alone for 31% of female cancers. This study analyzed the acute and late cutaneous toxicity in ARDs patients occurred during post-surgery breast Radiotherapy, in order to verify any differences in toxicity levels compared to the non-ARDSs population.

Methods: Patients with breast cancer and ARDs treated between 2013 and 2023 were retrospectively reviewed for RT-related toxicity. The ARDs group (experimental group) was compared with a control group in a 1:2 ratio (control group), homogeneous by age, type of treatment, dose and treatment site. Acute and late toxicities were based on RTOG scales. A P-value less than 0.05 was considered statistically significant.

Results: We considered 44 women with ARDs (mean age 61 yrs). In this group, the most used RT schedule was a conventional fractionation (50-54 Gy) for 32 patients (72.7%); hypofractionation (40-44 Gy) was administered in 12 cases (27.3%). In the control group, 88 patients (1:2 ratio) received radiotherapy (median age 62 yrs) with a conventional treatment (50-54 Gy) in 64 patients (72.7%) and with hypofractionation schedule (40-44 Gy) in 24 patients (27.3%). All patients in both groups experienced acute toxicities. The overall acute skin toxicity rate was 80.4% in control group vs 86.4% in experimental group (p=0.681). Specifically, G2 toxicities were 22% in control group vs 31% in experimental group, while G3 acute toxicities were 2,3% in both groups. A statistically significant difference was observed in late G2 toxicity, which was 0% in control group vs 6.82% in experimental group (p=0.035), respectively.

Conclusions: In our experience, patients with ARDs did not show significant differences in terms of toxicity, with results comparable with the control group. Therefore, ARDs do not represent an absolute or relative contraindication to post-surgical Radiotherapy treatment of breast cancer.

BRIDGING RADIOTHERAPY TO CAR-T CELL THERAPY IN RELAPSING/REFRACTORY NON- HODGKIN B LYMPHOMA: A SINGLE CENTER EXPERIENCE

Code: 409

Aims: Chimeric antigen receptor (CAR) T-cells are autologous genetically engineered T cells recognizing tumor surface antigens. CAR-T cell based therapies have revolutionized the treatment of refractory or ralapsing Lymphoma.In this setting, radiotherapy (RT)can be used as a bridge therapy for patients with chemorefractory disease or as salvage treatment. We evaluated patients affected by Diffuse Large B cell Lymphoma (DLBCL) relapsing/refractory to chemotherapy (CRR), receiving radiation as a bridge therapy to anti-CD19 CAR T-cells.

Methods: Between March 2023 and January 2024 three patients received bridging radiation before antiCD19 CAR T-cells. All patients were affected by DLBCL CCR and received RT according to different schedules. RT was administrered after leukapheresis in all patients. The patients underwent clinical re-evaluation one month later and instrumental follow-up according to haematological timing.

Results: To date, 3 patients received bridge RT. Median age was 69 years. Median time from the end of RT to CAR-T cell infusion was 30 days. One patient underwent RT on left calf for a total dose of 40 Gy in 20 fractions (fr) and one patient received 20Gy/5fr on sternum, treated with conformal 3 dimensional radiotherapy (3DRT).
The third patient received a total dose of 30Gy/10fr on retroperitoneal localization of bulky disease using volumetric modulated arc therapy (VMAT).
Complete regression of pain was achieved at the first clinical follow up in two patients (one patient has not yet had follow up). No acute adverse events were recorded.
One patient underwent follow-up FDG PET/CT at 2 and 4 months after the end of RT with a complete remission, the other two patients have not yet undergone re-evaluation imaging.

Conclusions: RT appears to be safe and well tolerated. Despite our preliminary experience, the bridge RT Bridge RT appears to be an effective therapeutic option in DLBCL CRR.

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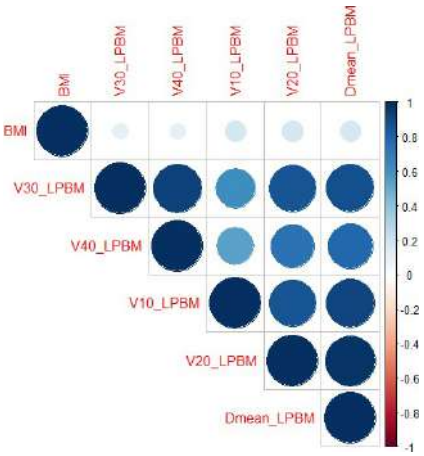
PELVIC INSUFFICIENCY FRACTURES RISK IN CERVICAL CANCER AFTER DEFINITIVE RADIOTHERAPY

Code: 295

Aims: To investigate the correlation between clinical and dosimetric factors with the incidence of pelvic insufficiency fractures (PIF) in patients affected by cervical cancer undergoing radical radiotherapy in association or not with chemotherapy and to find possible dose constraints useful for reducing the risk.

Methods: We reviewed data from cervical cancer patients treated with pelvic external-beam RT in our Institution between 2020 and 2022. For each patient, pelvic bone marrow (BM) was contoured and divided into three subsites: lumbosacral spine (LSBM), ilium (IBM) and lower pelvis (LPBM). Data on the volume of each region receiving 10, 20, 30 and 40 Gy (V10, V20, V30, V40, respectively), Dmean and Dmax were collected. Clinical data such as age, BMI, comorbidities, steroid and hormonal therapy before radiotherapy, menopausal state, smoking status, vitamin D and calcium dosage before and after treatment and diagnosis of osteopenia/osteoporosis on Bone Densitometry were analyzed.

Results: A total of 90 patients were retrospectively analyzed. Twenty-one patients (23%) developed PIF in the treatment field. Our analysis shows that LPBM Dmean is the most relevant dosimetric parameter in the correlation with PIF: in fact, if this is kept below 18.5 cc, the probability of the patient having fractures is reduced to 20%. Keeping this constraint below 13 cc has a PIF probability of less than 10%.



Conclusions: Our preliminary study allowed us to identify the following constraints to reduce the risk of PIF in this population: LPBM Dmean <13 cc (optimal) and <18.5 cc (mandatory). Further investigations are needed to confirm these findings through the inclusion of these parameters in the planning process.

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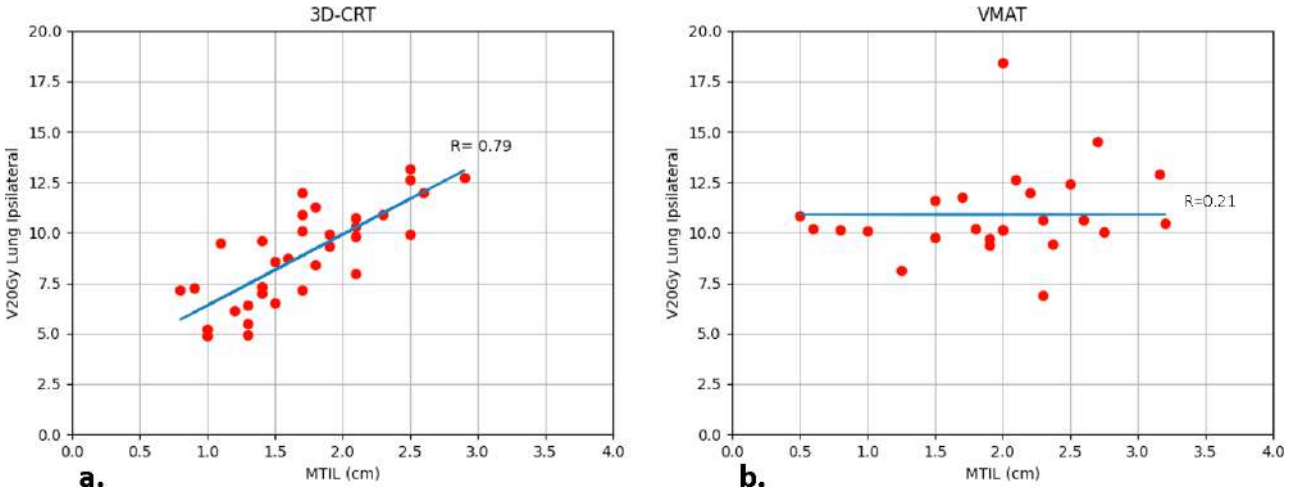
LOOKING FOR A CRITERION TO SELECT THE PATIENTS BENEFITING OF A VOLUMETRIC MODULATED ARC THERAPY (VMAT) TECHNIQUE FOR BREAST ADJUVANT RADIOTHERAPY BASED ON IPSILATERAL LUNG DOSE ANALYSIS

Code: 77

Aims: Exploring benefits in reducing high doses to the ipsilateral lung (IL) in VMAT compared to 3D-CRT technique for adjuvant breast radiotherapy, we sought to identify criteria for determining patients who would benefit most from VMAT technique.

Methods: We reviewed the radiotherapy plans of the patients treated on right breast from September 2022 to June 2023 at our center. Seventy-two radiation plans were evaluated: 35 VMAT technique plans targeting the whole breast with a simultaneous boost to the surgical bed with 40.05Gy/15fx and 48 Gy/15fx, 37 3D- CRT plans with sequential surgical bed boost: 40.05Gy/15fx to the whole breast and 10Gy/4fx for sequential overdose.
The comparison was carried out on the two groups of treatment plans to highlight the dosimetric and isodose conformation differences concerning the reference structures. Therefore, Conformal Index (COIN) values were calculated to compare the isodose conformation to the target and nearby OAR (IL).
We collected the dose-volume histograms (DVHs) of the IL for the patients for both groups; we calculated their mean and standard deviation to detect the dosimetric differences due to the two techniques in term of dose.
For every plan we collected the maximum thickness of IL (MTIL) included within the lateral and medial borders of the target to the central slice in the cranio-caudal direction, and we related it with V20Gy using the Pearson correlation coefficient (R).

Results: Despite the target isodose coverage was similar (CTV V98% > 96%), the VMAT technique appears to be more conformal (55% higher COIN index $p<0.001$), in term of isodose conformation on target and IL dose sparing, compared to the 3D-CRT technique. For both groups, considering the mean IL DVH, the AIRO constrains are respected.



Finally, considering the two previous statements, a link between V20Gy of IL and the MTIL is observed for the 3D-CRT technique (Figure 1.a); this correlation can be considered linear (R=0.79). In the case of VMAT there is no relation between this two value (R=0.21), all data are flatten around V20Gy mean value of 10.8% (Figure 1.b). Therefore, VMAT technique could be more advantageous for patients with an unfavorable anatomical conformations.

Conclusions: According to literature, our study confirmed that VMAT technique in the right breast radiotherapy, concerning the dose conformity respect IL, could be a valid alternative to 3D-CRT; it becomes more advantageous as the MTIL increases.

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STEREOTACTIC RADIOTHERAPY FOR PENILE METASTASIS: CASE REPORT AND SYSTEMATIC LITERATURE REVIEW

Code: 47

Aims: Penile metastases (PM) are a rare clinical presentation mainly related to advanced stages of disease. Considering the low incidence, an optimal treatment approach has not yet been defined; surgery, chemotherapy, and radiotherapy are different options used in the vast majority with palliative intent.
The advances in modern RT can represent an innovative tool in PM management and a curative option.
This paper aims to report the case of a PM patient treated with Stereotactic Body Radiotherapy (SBRT) and perform a systematic literature review of current evidence on the RT approach to PM.

Methods: We reported the case of an 80-year-old patient with PM from primary bladder cancer. Following the surgical approach for the primary tumor, evidence of PM was shown, and the patient was admitted to SBRT treatment on PM after an adjuvant RT course on the pelvis. A 25 Gy in 5 fractions SBRT treatment was performed, and a complete clinical response was shown at the first follow-up.
A Pubmed/MEDLINE and Embase systematic review was carried out. The search strategy terms were [('penile metastasis'/exp OR 'penile metastasis' OR (penile AND ('metastasis'/exp OR metastasis))) AND ('radiotherapy'/exp OR radiotherapy)] and only original articles up to the 24.10.2023 were considered.

Results: A total of 174 studies were obtained using the previously mentioned search strategy, and the analysis was performed on 15 papers obtained following the complete selection process. All reported evidence was focused on the palliative approach of PM showing good results in terms of symptom control.

Conclusions: The potential role of modern RT in the management of PM has yet to be defined. The reported case showed the feasibility and the clinical impact of SBRT in PM treatment.

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APPLICATIONS OF ARTIFICIAL INTELLIGENCE IN RADIATION TREATMENT OF PROSTATE CANCER: A SYSTEMATIC REVIEW

Code: 48

Aims: Radiotherapy (RT) represents a crucial treatment for the management of Prostate Cancer (PC). Artificial intelligence (AI) is changing the paradigms of cancer care providing innovative tools for diagnosis, treatment optimization and outcome prediction. The application of AI in PC RT management is the focus of this review.

Methods: A Pubmed/MEDLINE and Embase systematic review was conducted to investigate the impact of AI to PC RT management. Only original up to date to 06/09/2023 were considered and the resulted 27 articles were referred to specific clusters: adaptive, autocontouring, autoplanning, prediction, synthetic Computed Tomography (CT), quality assurance (QA) and tracking.

Results: In the selected group, the cluster with highest concentration of articles was autocotouring followed by prediction, autoplanning and adaptive RT; to a lesser extent on tracking and QA and lastly Synthetic CT.

Conclusions: AI seem to significantly impact different phases of PC RT workflow even though some experiences have to be validated in clinical studies. Further studies are needed to confirm these the potential role of AI in the personalization of treatments in the era of omics guided treatment.

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CORRELATION BETWEEN HANDGRIP STRENGTH AND SKELETAL MUSCLE INDEX IN HEAD AND NECK CANCER PATIENTS UNDERGOING RADIOCHEMOTHERAPY: INSIGHTS FROM A SINGLE INSTITUTION STUDY

Code: 497

Aims: Sarcopenia, characterized by the gradual decline in skeletal muscle mass, strength, and function associated with aging, poses significant concerns in oncology due to its implications for physical performance, frailty, and mortality. In head and neck cancer, skeletal muscle mass (SMM) has emerged as a crucial predictor for both treatment toxicities, including those related to platinum-based therapies and radiotherapy, as well as overall survival. Computed tomography (CT) imaging at the level of the third lumbar vertebra (L3) is commonly used to assess muscle mass accurately.
This study aimed to explore the relationship between SMM measurements at the third cervical vertebra (C3) and those at L3, utilizing the methodology proposed by Swartz et al. to evaluate sarcopenia risk in our patient cohort.

Methods: Fifteen patients underwent nutritional assessment and Handgrip testing (HGT). Using simulation CT scans, we delineated paravertebral and sternocleidomastoid muscles at the C3 level. Muscle areas were manually contoured on the first slice showing transverse processes and the vertebral arc. The cross-sectional area (CSA) at C3 was converted to CSA at L3 using Swartz et al.'s algorithm. Subsequently, CSA at L3 was adjusted for patient height to derive the skeletal muscle index (SMI). Sarcopenia was assessed using sex- and BMI-specific cutoff values. Univariate ANOVA tested correlations between HGT, SMI, and treatment- related outcomes (toxicity, treatment interruptions), while multivariate logistic regression analysis generated a ROC curve.

Results: HGT exhibited a significant correlation with CSA at L3 (p:0.002, Pearson correlation: 0.55), but not with SMI at L3 (p:0.17, Pearson correlation: 0.25). Neither variable correlated with treatment toxicity but both were associated with treatment interruptions (p:0.027 for HGT and 0.046 for CSA at L3). Logistic regression identified HGT as the sole predictor of treatment interruptions (p:0.047, R2:0.27, AUC: 0.79).

Conclusions: Our initial findings underscore the potential utility of sarcopenia indices in managing head and neck squamous cell carcinoma (HNSCC) patients, warranting further investigation.

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TREATMENT EFFECTIVENESS AND MANAGEMENT OF RECURRENCES IN A SINGLE - ISTITUTION SERIES OF PATIENTS (PTS) WITH GLIOBLASTOMA (GBM)

Code: 121

Aims: To assess patterns of recurrence and overall survival (OS) in a series of patients treated for GBM at our Institution.

Methods: From June 2016 to July 2023, 231 consecutive patients with GBM were treated.
The majority of patients (217/231, 93.9%) underwent surgical resection. Subsequent treatment included concurrent Temozolomide (TMZ) and localized radiotherapy (RT) delivered as VMAT or Tomotherapy. The Gross Tumor Volume (GTV) included the tumor bed and any residual tumor visible on contrast- enhanced (CE) T1 MRI. The Clinical Target Volume (CTV) was determined by a 2-cm expansion on GTV, encompassing FLAIR abnormalities. The Planning Target Volume (PTV) was defined with a 0.3-cm expansion from CTV. Standard RT course consisted in 60 Gy in 30 fractions. Hypofractionated RT course (40.05 Gy in 15 fractions) was administered to elderly patients (70 or older) and those with a poor prognosis. Disease progression was evaluated using the RANO-HGG criteria. An In-field recurrence was defined as if more than 80% of the recurrent tumor was located within the 95% isodose surface; a marginal one if 20-80% of the recurrent lesion was within the 95% isodose surface; a distant one if less than 20% of the recurrent lesion was within the 95% isodose surface.

Results: 231 consecutive patients were evaluated; of these 142 were male and 79 female. Median age at the time of first surgery was 60 (range 30-88). ECOG performance status in each pt was 0-2. 14 pts underwent biopsy, 24 pts a partial resection, 193 pts a gross total resection. Glioblastoma histology was confirmed in all pts. 175 pts underwent RT 60 Gy in 30 Fx plus concomitant TMZ; 56 pts received a hypofractionated RT schedule (40.05 Gy in 15 Fx) plus concomitant TMZ. 83 of the 231 pts relapsed: 83% in field, 7% marginal and 10% out-field. 19 out of the 83 pts underwent a second surgery followed by re-irradiation (reRT) and then a second line chemotherapy, 15 pts a reRT and then chemotherapy, 49 pts a second line chemotherapy only. ReRT doses ranged from 36 to 54 Gy in 18-27 Fx; GTV encompassed tumor or tumor bed (in case of resection) on CE T1 MRI; PTV was driven by a 1-cm expansion from GTV. No G2-G4 toxicities were observed in reRT pts. In the whole series, mean follow-up was 32 months (range 3-88). Median OS from the end of first RT was 20 months (range 3-88).

Conclusions: Our data in terms of OS are comparable to the ones of the literature. Our findings suggest that the use of reRT is a safe and valid option in case of relapse.

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SAFETY AND EFFICACY OF SINGLE - ISOCENTER NON - COPLANAR STEREOTACTIC RADIOTHERAPY (HYPERARC) FOR SINGLE OR MULTIPLE BRAIN METASTASES TREATMENT

Code: 155

Aims: To analyze the clinical impact of HyperArc (HA) technique in our series of patients (pts) treated for single or multiple brain metastases (BMs).

Methods: Pts with BMs and ECOG performance status 0 – 2 treated with HA technique were enrolled in the study; they were retrospectively evaluated as to overall survival (OS) from the end of radiotherapy to the last follow-up or death, and toxicity.

Results: 105 pts (54 males, 51 females) accounting for 274 BMs, treated at our institution from March 2019 to July 2023, were reviewed. Primary tumor histology was NSCLC in 32 pts, SCLC in 4, breast in 20, melanoma in 19, kidney in 9, colon in 5, pancreas in 4, prostate in 2, cardias in 1, thoracic esophagus in 1, base of tongue in 1, adult medulloblastoma in 1, endometrium in 1, bladder in 1, germinoma testis in 1, parotid in 1, rectum in 1, thymic carcinoma in 1. Median age at the time of BM diagnosis was 64 (range 24-83). The average number of metastases in each treatment (Tx) was 2.4 (range 1-12). A single BM was present in 45 among the 105 pts, multiple BMs in 60 pts. The average diameter of the greatest lesion in each Tx was 2.1 cm (range 0.2-5.5). In 5 Tx, the surgical bed was one of the targets. The GTV encompassed the macroscopic contrast enhancing lesion on T1-MRI and was assumed to be equal to the CTV. The PTV was obtained from the GTV plus an isotropic margin of 2 mm. Dose prescription was 27 Gy in 3 fractions (Fx) or 21 Gy in single Fx, related to lesions size and brain localization. All 5 surgical cavities were treated with 27 Gy in 3 Fx. 21 Tx were a 21-Gy single-Fx treatment; among them, the average diameter of the greatest lesion was 0.9 cm (range 0.2-2). 84 Tx consisted in 27 Gy in 3 Fx; the average diameter of the greatest lesion was 2.1 cm (range 0.3-5.5). MRI follow – up was available for all patients; among them, 53 pts had a stable disease, 8 pts an increasing size of the treated lesion, 38 pts an onset of new lesions, 6 pts both. In the whole series, after an average follow-up of 24 months (range 1-47), median OS was 13 months (range 1-47). Patients did not develop G2-G3 toxicities.

Conclusions: HA technique is not only effective in achieving positive outcomes but is also well-suited for patients with significant metastatic burden. Our results underscore the potential clinical utility of the HA technique in the context of brain metastases treatment.

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CARDIAC STRUCTURE-SPARING TECHNIQUES IN LEFT BREAST CANCER PATIENTS

Code: 553

Aims: The aim of our study is to improve target coverage and reduce dose to heart, left anterior descending artery (LAD) and left ventricle (LV) in left breast cancer pts with comorbidities and unfavorable anatomy using volumetric modulated arc therapy (VMAT) or hybrid volumetric modulated arc therapy (H-VMAT) with deep inspiration breath hold (DIBH).

Methods: We analysed 120 breast cancer pts treated from July 2019 to August 2023 with VMAT or H-VMAT in DIBH on breast alone or breast/chest wall and drainage lymph nodes (LN). The dose regimen was 40.5 Gy in 15 fractions (frs) (dose/fr 2.67), with a concomitant simultaneous integrated boost, if indicated, of 48 Gy in 15 frs (dose/fr 3.2 Gy). VMAT plans were generated using 3 arcs in order to reduce the interplay effect due to briefing motion; a virtual 10 mm bolus helped extending the dose fluency outside the body to compensate for small changes in breast shape and volume. In H-VMAT plans 70-80% of the prescription dose was delivered by 3D-CRT fields and the remainder 20-30% by VMAT fields. The median age of pts was 58 years (range 36-80), 36 pts (30%) had a history of heart disease; most pts received chemotherapy before RT. In all pts, echocardiography was performed before starting RT and 1- and 6-months after the end of treatment. Dose constraints were: to the heart Dmean ? 2.5 Gy for breast alone, ? 3 Gy for breast/chest wall plus LN; V8Gy < 15%, D5% < 10 Gy; to the LAD Dmean ? 10 Gy, V30 < 2%, V40 < 1% and to the LV Dmean ? 3 Gy, for breast alone, ? 4 Gy for breast/chest wall plus LN, V5Gy < 17%, V23Gy < 5%.

Results: The treatment was well tolerated in all pts. Median V95% to breast/chest wall CTV and to LN CTV was 98%. We reported a heart Dmean 2.3 Gy and 2.8 Gy, a LAD Dmean 6 Gy and 8 Gy and a LV Dmean 2.8 Gy and 3.5 Gy for breast alone and for breast/chest wall plus LN respectively; heart V8Gy= 6.2%, D5% = 8.6 Gy; LV V5Gy = 7.6 Gy, V23 Gy = 1.8%. The 1- and 6-months echocardiographic control after RT completion showed unchanged cardiac functioning parameters, in particular, no variation in the ejection fraction was detected.

Conclusions: The VMAT and H-VMAT techniques in DIBH are useful in the treatment of left breast cancer pts (especially with cardiac comorbidities and unfavorable anatomy) by ensuring an excellent target coverage and sparing heart, LAD and LV. Long-term follow-up data are needed to assess late toxicity and clinical outcomes for this subset of pts.

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HOMOGENEOUS DOSE DISTRIBUTION TO THE VERTEBRAE IN PAEDIATRIC PATIENTS: A CASE REPORT

Code: 543

Aims: Non-homogeneous radiotherapy dose distribution to the vertebrae in paediatric patients can lead to serious growth problems, such as scoliosis, lordosis, kyphosis and hypoplasia. For this reason, it is essential that the dose delivered to the adjacent vertebrae is homogeneous. We report our experience with a case of neuroblastoma.

Methods: The case concerns an 8-year-old boy with a metastatic M-MycN non-amplified neuroblastoma. The instrumental examinations show in the left thoracic paravertebral region a solid expansion extending from D4 to D7, with involvement of the left neural foramina, and in the sub-carenal region. The patient received induction chemotherapy and subsequent surgery. Histological examination revealed no residual neoplastic lesions. It is agreed for high-dose therapy and re-infusion of autologous stem cells and irradiation of the primitive according to the SIOPEN protocol: 21.6 Gy in 12 fractions. CTV, PTV and OARs were contoured. In particular, adjacent (VBs Adj) and non-adjacent superior and inferior vertebrae (VBs NAdj S/I) were defined, encompassing the primary ossification centres. The VBs Adj are in proximity of the target. For those vertebrae a sufficient dose sparing is challenging and a uniform irradiation is recommended: anterior-posterior and left-right gradients should be kept within 5 Gy. The VBs NAdj S/I are defined as one single vertebra above and below VBs Adj and are to be spared (D5%<15 Gy). PTV dose coverage objective (D95?95% and D107%<2%) and dose constraints for OARs (lungs, heart, PRV spinal cord, vertebrae etc) reported in High Risk Neuroblastoma Study 2 SIOPEN were adopted. The treatment plan has been carried out with a VMAT technique using four 6 MV full arcs. The PTV dose coverage and doses to OARs were evaluated. Dose gradients in VBs Adj were calculated as the difference between D2% and D98%. D5% in VBs NAdj was estimated.

Results: PTV dose coverage and all dose constraints for OARs were respected. A homogeneous dose coverage in VBs Adj was achieved and inspected by a slice-by-slice visual assessment of isodose lines. Dose gradient in VBs Adj results 3.74 Gy. Requirement for D5% in VBs NAdj S/I was satisfied (14.7 and 14.5 Gy respectively). Steep supero-inferior gradients in both VBs NAdj were obtained.

Conclusions: The dosimetric gradient allows homogeneous dose distribution in VBs Adj and dose sparing of VBs NAdj. This avoids abnormalities in the child's growth phase.

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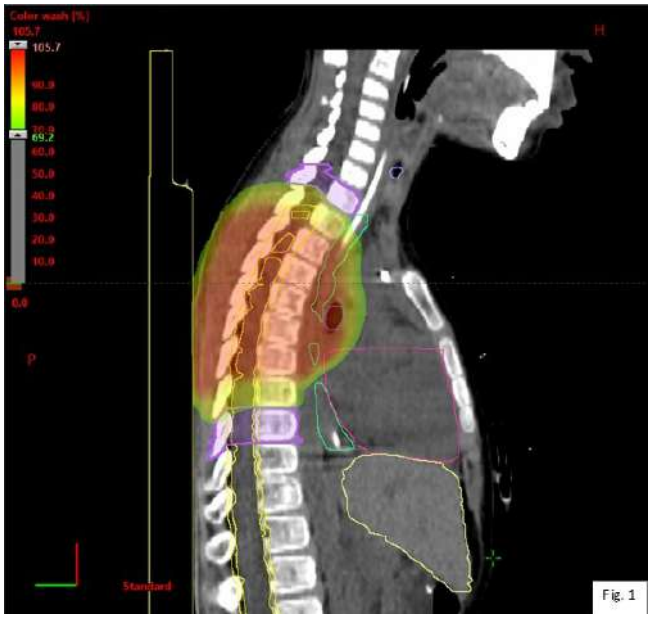

Fig. 1

QUALITY OF LIFE IN RECTAL CANCER PATIENTS AFTER MULTIMODAL TREATMENT AT THE END OF FOLLOW-UP

Code: 171

Aims: Rectal cancer (RC) is a prevalent global malignancy, where multimodal treatment has improved cancer-related outcomes, yet its impact on quality of life (QoL) remains a significant consideration. This study aims to investigate this impact on QoL, intestinal function and sexual health in RC patients (pts) at the end of follow-up (FUP).

Methods: questionnaires were administered to RC pts who underwent neoadjuvant RT (nRT)/ radiochemotherapy (nCRT), followed by surgery and, in selected cases, adjuvant CT. Surgical procedures included anterior (AR) or abdominoperineal resection (APR), with local excision (LE) performed in pts exhibiting a major or complete response after nRT/nCRT. All pts had a FUP exceding 5 years and were disease-free at the time of analysis. Validates questionnaires, EORTC QLQ-CR 29 and C30 (v 3.0), International Index of Erectile Function (IIEF), Female Sexual Function Index (FSFI) and Low Anterior Resection Syndrome (LARS) score were employed. EORTC QLQ scores have range from 0 to 100, with higher scores indicating healthier functioning or a better QoL, except for the symptoms, where higher scores represent a high level of problem. A cut-off value of 60/100 was utilized. IIEF classifies erectile dysfunction severity as serious (1-10), moderate (11-16), mild (17-25), or none (26-30). FSFI has range from 2 to 36, with higher scores reflecting greater sexual satisfaction. LARS scores categorize symptoms as none (0-20), minor (21-29), or major (30-42).

Results: data were collected from April to November 2023 for 42 pts (69% men and 31% women), average age 61 years (range 44-73) at diagnosis. 73,8% underwent AR, 19% APR and 7,2% LE. Grade 3 toxicity was observed as acute and late gastrointestinal (GI) in 14.3% and 4.8%, respectively; none Grade 4.
Global Health status/QoL was>60 in 71,8%. Treatments mainly impacted intestinal and sexual function, with symptoms such as diarrhea (16.7%), insomnia (14.3%), urinary frequency (11.9%), impotence/dyspareunia (21.4%). LARS was major in 4.8%. Social functioning score was ≥60% in 78.6%. Sexual interest reduction (≥60) was reported in 42.8%. FSFI average was 13.8 (range 2-36) and IIEF indicated serious dysfunction in 62%.

Conclusions: at the end of FUP period, approximately 30% of RC pts experienced reduced QoL, primarily linked to GI and genitourinary dysfunctions, impacting social function. These findings emphasize the importance of addressing these aspects in the management of RC patients.

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Functional and symptoms scales in rectal cancer

EORTC functional scale	Score ≥ 60	Missing
Physical functioning	95,2%	0
Role functioning	95,2%	2,4 %
Emotional functioning	88%	2,4 %
Cognitive functioning	88%	2,4 %
Social functioning	78,6%	2,4 %
Anxiety	88%	0
Weight	97,6 %	0
Body Image	90,5%	0
Sexual Interest	42,8%	26,2%

EORTC symptoms scale	Score ≥ 60	Missing
Dyspnoea	0	2,4%
Pain	2,4%	0
Fatigue	2,4%	0
Insomnia	14,3%	2,4%
Appetite loss	0	0
Nausea and Vomiting	0	2,4%
Constipation	9,5%	2,4%
Diarrhoea	16,7%	4,8%
Financial difficulties	11,9%	4,8%
Urinary Frequency	11,9%	0
Urinary Incontinence	0	0
Dysuria	2,4%	0
Abdominal pain	4,8%	2,4%
Ano-rectal pain	7,1%	0
Bloating	9,5%	0
Blood and mucus in stool	0	0
Dry mouth	2,4%	0
Hair Loss	0	0
Taste	2,4%	2,4%
Flatulence	9,5%	42,8%
Faecal Incontinence	4,8%	45,2%
Sore skin	4,8%	45,2%
Stool frequency	2,4%	45,2%
Embarrassment	9,5%	45,2%
Stoma care problems	0	4,8%
Impotence/Dyspareunia	21,4%	26,2%

Erectile dysfunction	Serious (0-10)	Moderate (11-16)	Mild (17-25)	None (26-30)	Missing
	62%	6,9%	13,8%	3,5%	13,8%

LARS	None (0-20)	Minor (21-29)	Major (30-42)	Missing
	69%	26,2%	4,8%	0

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TOTAL NEOADJUVANT THERAPY IN LOCAL ADVANCED RECTAL CANCER: A MONO-INSTITUTIONAL EXPERIENCE

Code: 490

Aims: Because of two large recents randomised ph III clinical trials (RAPIDO-PRODIGE 23), total neoadjuvant therapy (TNT) is a new paradigm for locally advanced rectal cancer (LARC). These two trials have focused on intensification of systemic therapy for localized disease with an aim of reducing the distant relapse rate. On a systematic review were also evident superior rates of pathological complete response (pCR) compared with standard therapy. On the basis of these recents data we proposed TNT approach in patients medically fit with LARC.

Methods: In the last two years 36 patients (pts) were treated in the neoadjuvant setting for LARC: 19pts with standard preoperative radio-chemotherapy, 15pts with TNT. Pts were selected for the TNT approach by age, risk factors and general conditions. They had a median age of 57.6years (range 20-72), and were treated with four to six cycles of chemotherapy (Capox regimen) and standard long course radio-chemotherapy. Pts in the standard group had a median age of 71years (range 50-78). All of the patients in TNT group completed the treatment, while 2 patients of the standard group had to stop radiotherapy at 21 fractions (75%). All patients underwent surgery at about 8-10weeks from the end of the radiotherapy phase. The hystological findings were stratified according to the tumor regression grade (TRG)–CAP guidelines/Ryan modified.

Results: At the hystopathological analyses in the TNT group was found a pCR in 40% of the patients (6pts–TRG 0); the other 60% were partial (6pts–TRG1-2) or minimal response (3pts–TRG3). In the standard group the pCR at the hystological findings were instead 26.4 % (5pts–TRG0), while partial and minimal responses were 36.8% (7pts–TRG1-2) and 36.8% (7pts–TRG3). In the "standard" group of patients were registered more cases of surgical morbidity, probably also because younger and fitter patients were selected for the total neooadjuvant approach. With a median Follow-up of 11 months, no differences were evident between the two groups of patients in terms of local and distant recurrence.

Conclusions: From the analysis of the pathological findings it's evident a trend in increase in pCR with the TNT approach versus the standard one. Our data are not statistically significant, but they reflects the findings from the most recent literature on the subject, with a difference of about 13 percentage points between the two groups. As today many questions remain unanswered, including which patients could benefit the most from this intensive treatment.

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KV-TRIGGERED FIDUCIALS TRACKING AND MAGNITUDE OF INTRA-FRACTION PROSTATE MOTION DURING PROSTATE STEREOTACTIC BODY RADIATION THERAPY (SBRT)

Code: 563

Aims: To evaluate the performance of a LINAC-integrated kV-triggered fiducials tracking system and the magnitude of intra-fraction prostate motion (I-fPM) during Stereotactic Body Radiation Therapy (SBRT) for localized prostate cancer.

Methods: Sixty consecutive patients treated with prostate SBRT at our institution between November 2021 and July 2023 were retrospectively evaluated. Implantation of 3 intra-prostatic fiducial markers was performed for all patients. SBRT was delivered every other day with VMAT, administering 36.25 Gy/5 fractions (85%) or 42.7 Gy/7 fractions (15%) to the PTV. All patients underwent pre-SBRT CBCT, with fiducial markers alignment. I-fPM was monitored during treatment delivery using fiducials tracking with TrueBeam Auto Beam Hold feature, with the acquisition of kV triggered images every 10 degrees of gantry rotation.
Fiducials were auto detected from kV images and compared with a "tolerance structure" (5 mm expansion from each marker center). If any marker center shifted outside the "tolerance structure" contour, treatment automatically was paused and a new CBCT was required for shift correction. Data including number of session interruptions, magnitude of shifts, and SBRT treatment time were analyzed.

Results: Overall, 318 SBRT treatment sessions were analyzed. In 50 (83.3%) patients, at least one beam interruption due to a shift >5 mm occurred. In 37.4% of therapy sessions the treatment was paused, for a total of 225 interruptions; in 16.4%, the treatment was interrupted more than once (range 2-9). The mean (SD) total interruptions per patient and per session were 3.7 (3.7) and 0.7 (1.3), respectively. Considering the shift absolute values, the mean and max value translations were 4.4 (4.4) and 40.5 mm lng, 3.9 (3.2) and 25.3 mm vrt, and 4.0 (3.5) and 26.0-mm lat. Overall, 30.6% of lng and 23.6% of lat shifts were >5 mm PTV margin and 54.9% of vertical shifts >3 mm posterior margin. Shift in lat direction was smaller than in lng ($p = 0.01$) and vrt ($p = 0.04$) directions. Mean fraction total treatment time (TT) was 21.6 (23.8) minutes. In 59% of sessions, TT was 15 minutes, while in 7% was >60 minutes (range 6.3-202 minutes).

Conclusions: KV-triggered fiducials tracking significantly increased daily treatment precision for prostate SBRT. Significant beam interruptions occurred, with not negligible shifts detected, confirming the importance of I-fPM management.

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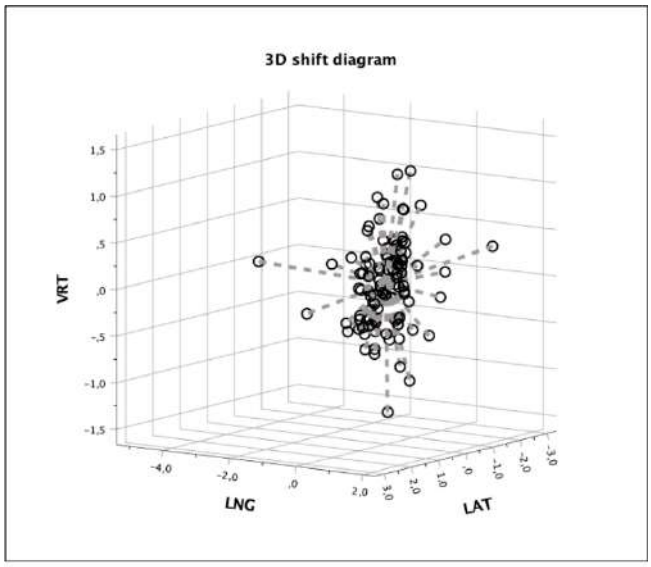

Figure 1. 3D scatterplot of intrafraction translation geometrical shift measured at first SBRT session interruption (n = 199). Black circles represent the combined translation shift (longitudinal + vertical + lateral) as compared to pre-SBRT session CBCT fiducials alignment (barycenter at intersection of dotted gray lines).

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STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR LOCALIZED PROSTATE CANCER: 1-YEAR TOXICITY AND QUALITY OF LIFE RESULTS FROM AN OBSERVATIONAL PROSPECTIVE STUDY

Code: 559

Aims: To report acute toxicity findings and quality of life (QoL) from an observational prospective study of stereotactic body radiotherapy (SBRT) for patients with localized prostate cancer.

Methods: Sixty-one patients (21.3% low-, 59% intermediate- and 19.7% high-risk according to D'Amico classification) treated with prostate SBRT at our Institution from January 2022 to August 2023 were included in the study. SBRT was delivered with volumetric modulated arc radiotherapy (VMAT), administering 36.25 Gy in 5 fractions every other day to the Planning Target Volume (PTV). A simultaneous integrated boost (SIB) delivering 40 Gy to the prostate or 40-45 Gy to the dominant intraprostatic lesion (DIL) was planned for 18 (29.5%) and 19 (31.2%) patients, respectively. In 4 (6.6%) patients a 25 Gy SIB to the pelvis was administered. Fiducial markers tracking was used for all patients, while rectal spacer was used in 44 (72.1%) patients. Genitourinary (GU) and gastrointestinal (GI) toxicity was reported using the CTCAE scoring criteria. A prospective collection of data regarding toxicity and QoL was performed.

Results: Median patient age was 74 years (IQR 70-76). Most patients (50.8%) had cT2 disease and median iPSA was 13 ng/ml (IQR 8-20.5). In 32 (51.5%) patients androgen deprivation therapy (ADT) was administered in accordance with risk group. At a median estimated follow up of 12.1 months (95% CI 10.5-16.7), no serious adverse events (defined as G3) were reported. At SBRT end, 3, 6, and 12 months, G1-2 GU toxicity was observed in 52.5%, 21.3%, 8.2%, and 7.6% of patients, respectively, while G1-2 GI toxicity occurred in 19.7%, 6.6%, 1.6%, and 1.9%, respectively, at the same time-point. Toxicity rate did not correlate with prostate/DIL SIB ($p = 0.26$) or pelvis SIB ($p = 0.47$) administration. QoL evaluation showed a substantial return to baseline for IPSS, ICIQ-SF, EPIC-26, EORTC-QLQ-C30 and EORTC-QLQ-PR25 scores within 3 months following SBRT. In contrast, the sexual domain (IIEF-5) worsened compared to baseline in 34.4% of patients, mostly related with ADT use. All patients experienced biochemical response, with PSA falling to a median of 0.18 ng/ml (IQR 0.03-1.0) at last evaluation. No cancer-specific death occurred.

Conclusions: Data prospectively collected showed very promising results in terms of toxicity and QoL for prostate SBRT. Longer follow-up is needed to evaluate tumor control and late toxicity. In this respect, further enrollment of patients is ongoing.

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CTCAE GENITOURINARY TOXICITY	G1-2 n (%)	
	Acute	Late*
Urinary tract pain	15 (24.6%)	4 (7.6%)
Urinary frequency	31 (50.8%)	2 (3.8%)
Prostate obstruction	4 (6.6%)	1 (1.9%)
Cystitis	5 (8.2%)	0 (0%)
Urinary urgency/incontinence	4 (6.6%)	1 (1.9%)

* Data on 53 patients with 12 months follow up

CTCAE GASTROINTESTINAL TOXICITY	G1-2 n (%)	
	Acute	Late*
Rectal proctitis	4 (6.6%)	1 (1.9%)
Rectal urgency	1 (1.6%)	1 (1.9%)
Rectal tenesmus	6 (9.8%)	0 (0%)
Diarrhoea	6 (9.8%)	0 (0%)
Haemorrhoids	3 (4.9%)	0 (0%)

* Data on 53 patients with 12 months follow up

Figure 1. Common Terminology Criteria for Adverse Events (CTCAE) toxicity for genitourinary and gastrointestinal systems

PRELIMINARY DATA ON THE SAFETY OF RADIOTHERAPY WITH CONCOMITANT PEMBROLIZUMAB IN BREAST CANCER PATIENTS

Code: 154

Aims: As immunotherapy enters the clinical scenario of Breast Cancer (BC) treatment, the feasibility and potential synergy of its concomitant administration with radiation therapy (RT) become paramount considerations. The aim of our prospective study was to assess safety of adjuvant Pembrolizumab with concomitant RT in BC patients.

Methods: Data from patients with triple-negative BC treated with neoadjuvant chemo-immunotherapy with Pembrolizumab (as per Keynote-522 criteria), followed by surgery and at least 1 cycle of adjuvant Pembrolizumab with concomitant RT were prospectively collected.
40.05 Gy in 15 fractions were prescribed to the breast or chest wall, with regional nodes and tumor bed boost being administered when clinically indicated. Left-sided BC patients were treated with deep inspiration breath hold. The study endpoint was to assess the feasibility of the treatment in terms of acute toxicity, evaluated according to the RTOG scale, and rate of discontinuation of RT and/or Pembrolizumab.

Results: We treated a total of 10 patients. Median age was 58 (range: 27 – 68). A median of 8 (range: 4 – 9) cycles of neoadjuvant Pembrolizumab were prescribed. Eight patients received breast-conserving surgery, while 2 patients underwent mastectomy. All patients had an objective response to neoadjuvant chemo- immunotherapy, with 8 pathologic complete response. Before RT, patients received a median of 3 (range: 2 – 4) cycles of adjuvant Pembrolizumab. Volumes of RT included the residual breast and tumor bed boost after breast conservative surgery (8 patients) and chest wall after mastectomy (2 patients). Four patients required regional nodal irradiation.
Grade (G) ≥3 acute toxicity was registered in 2 patients: the first had G4 hepatotoxicity one month after RT which led to permanent discontinuation of adjuvant Pembrolizumab, despite no side effects during the entire course of neoadjuvant chemo-immunotherapy. The other one had G3 electrolyte imbalance due to dysphagia, causing definitive RT interruption and temporary discontinuation of adjuvant Pembrolizumab. Among the remaining 8 patients, only 2 patients experienced G2 skin erythema, with no treatment discontinuation.

Conclusions: Despite our limited cohort, the combination of adjuvant Pembrolizumab with concomitant RT proved to be feasible. Toxicity was limited and consistent with literature. A larger sample and longer follow-up are needed to confirm our hypothesis.

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FAT NECROSIS AFTER ONE-WEEK PARTIAL BREAST IRRADIATION OR STANDARD OF CARE: A CASE-CONTROL STUDY

Code: 150

Aims: One-week external beam partial breast irradiation (PBI) is endorsed as a viable option for early-stage, low risk, breast cancer (BC) patients. Previous analysis evidenced a high fat necrosis rate in those patients who underwent PBI. This study aimed to compare the incidence of fat necrosis after PBI vs hypofractionated whole breast irradiation (WBI) in patients with early-stage breast cancer.

Methods: We pulled out early-stage BC patients who underwent breast conservative surgery and adjuvant radiotherapy between 2009 and 2022. Radiation therapy consisted of PBI of 30 Gy in 5 daily fractions (Fx) (delivered in one week, consecutively) to the tumor bed or WBI (42.4 Gy in 16 Fx). Tumor bed boost and chemotherapy were exclusion criteria.
We matched, with a case-control approach, patients by age, pathological tumor stage and diabetes diagnosis. We retrospectively retrieved data on fat necrosis from yearly mammograms and breast ultrasound reports. The primary endpoint was the incidence of radiologically detected fat necrosis.

Results: From the case-control match, PBI and WBI groups comprised 268 and 267 patients, respectively. No statistically significant differences were observed in age, diabetes and T-stage characteristics (p-values: 0.31, 0.35, and 1, respectively). Crude rates of radiologically detected fat necrosis were 29.1%, and 27.3% in the PBI and WBI groups, respectively. Notably, none of these cases required surgical intervention. The 3-year Kaplan-Meier actuarial rate of fat necrosis was 32.8% (95% CI: 30.0% – 35.6%) for PBI and 22.3% (95% CI: 19.7% – 24.9%) for WBI patients.
Univariate Kaplan-Meier survival analysis revealed a HR of 1.6 [95% CI: 1.1 – 2.2; p = 0.0055] for the fat necrosis rate within the PBI group compared to WBI. Multivariate Cox proportional hazard regression identified significant associations between fat necrosis and diabetes (HR = 1.9, 95% CI: 1.1 – 3.3; p = 0.02) and breast volume (HR = 1.0005 for increase of 1 cc, 95% CI: 1.0001 – 1.0010; p = 0.03). Specifically, for PBI, the analysis revealed an HR of 2.2 (95% CI: 1.2 – 4.0; p = 0.01).

Conclusions: The occurrence of radiologically diagnosed fat necrosis was higher in the PBI group compared to the WBI. Further investigations aiming to identify a lower-dose schedule with comparable efficacy to 30 Gy in 5 Fx but fewer toxicities, particularly for at-risk patients, are warranted.

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STEREOTACTIC BODY RADIATION THERAPY AS A BRIDGE TO NEW LINE OF SYSTEMIC THERAPIES IN OLIGOPROGRESSIVE NON-SMALL-CELL LUNG CANCER

Code: 157

Aims: Stereotactic body radiation therapy (SBRT) has been demonstrated to be effective in improving survival outcomes in an oligometastatic setting, especially for non-small-cell lung cancer (NSCLC). However, less is known regarding the oligoprogressive scenario. In this study, we aimed to evaluate whether SBRT can delay the need to change systemic therapy in a subset of patients with oligoprogressive NSCLC.

Methods: A retrospective analysis was conducted on NSCLC patients undergoing SBRT for extra-cranial oligoprogressive disease, defined as progression in ≤5 lesions during or after the first-line systemic therapy, following an initial complete or partial response. The primary endpoint was Time to Next Treatment (TNT), with secondary endpoints including local control (LC), progression-free survival (PFS), and overall survival (OS). Univariate and multivariate Cox proportional-hazard regressions were performed to identify factors influencing the benefits of SBRT.

Results: Forty-three patients (60 lesions) underwent SBRT at a single Institution. The median age was 68 years (range 43 – 87), and 86.7% had a history of smoking. Systemic treatment included chemotherapy, immunotherapy, and target therapy for 22 (36.7%), 26 (43.3%), and 12 (20%) patients, respectively. First, second and ≥3 lines were administered in 33 (55%), 17 (28.3%), and 10 (16.7%) patients, respectively. The median total dose was 30 Gy (8 – 60) in a median of 5 fractions (1 – 18), with a median biological effective dose, considering an $\alpha/\beta = 10$ (BED10) of 48 Gy (14.4 – 151.2). After a median follow-up of 10 months (1 – 50), SBRT delayed further systemic therapy in 48 (80%) of the cases. Median TNT, LC, PFS and OS were 5 (0 – 47), 7 (0 – 41), 5 (0 – 21) and 8 (0 – 47) months, respectively. One-year Kaplan-Meier estimates for next treatment-free survival, LC, PFS, and OS were 73.4% (95% Confidence Interval [CI]: 66.0% – 80.8%), 83.1% (95% CI: 77.6% – 88.6%), 50.8% (95% CI: 43.1% – 58.5%), and 87.9% (95% CI: 83.2% – 92.6%), respectively. No relevant adverse events were observed. At multivariate analysis, patients with ≥ 3 lines of systemic therapy did not benefit from SBRT (Hazard Ratio 9.7, 95% CI: 1.8 – 52.4; $p = 0.008$).

Conclusions: Our findings show that SBRT represents an effective and viable option for oligoprogressive NSCLC, particularly in patients irradiated early during their systemic treatment's course. Long-term randomized data that test this strategy are awaited.

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TAILORING STEREOTACTIC BODY RADIATION THERAPY FOR OLIGOPROGRESSIVE NON-SMALL-CELL LUNG CANCER USING QUANTITATIVE PET PARAMETERS: PRELIMINARY DATA

Code: 159

Aims: There is limited knowledge on the efficacy of stereotactic body radiation therapy (SBRT) in oligoprogressive non-small-cell lung cancer (NSCLC). This study aims to assess if quantitative parameters of pre-treatment 18F-FDG PET (PET) can predict outcomes for ablative treatments targeting sites of oligoprogression in NSCLC patients.

Methods: NSCLC patients submitted to PET before receiving SBRT for extracranial oligoprogressive disease were retrospectively enrolled in the study. Oligoprogressive disease was defined as metabolic progression in ≤5 lesions during or after the first-line systemic therapy, following an initial complete or partial response. All lesions detected on PET scans were automatically contoured with Fiji software (https://www.petctviewer.org/) with a relative threshold of 41% to calculate total metabolic tumour volume (MTV), total lesion glycolysis (TLG), standardized uptake value (SUV) max, SUVmean, SUVpeak, and the number of contoured lesions. The primary endpoint was the efficacy of SBRT in delaying the initiation of a subsequent line of systemic therapy, expressed as the Time to Next Treatment (TNT). Secondary endpoints included local control (LC), progression-free survival (PFS), and overall survival (OS).

Results: Overall, 28 patients (34 SBRT-treated lesions) were analyzed. The median age was 68 years (range 47 – 84), with 82.2% having a history of smoking. After a median follow-up of 11 months (range 2 – 44), SBRT delayed further systemic therapy in 29 cases (85.3%). The median TNT was 5 months (range 0 – 41), and the one-year Kaplan-Meier estimate for next treatment-free survival was 73.4% (95% Confidence Interval [CI]: 66.0% – 80.8%). In univariate Cox proportional-hazard regression analysis, only MTV and TLG significantly

correlated with a shorter TNT: Hazard Ratios = 1.008 [95% CI: 1,001 to 1,017; p = 0.03] and 1.002 (95% CI: 1,0001 to 1,003; p = 0.03), respectively. However, in the multivariate analysis, PET quantitative parameters did not show predictive value, and no additional correlations were identified for LC, PFS, and OS.

Conclusions: Despite the limited cohort, our preliminary data suggest that MTV, TLG, could be predictive of the effectiveness of SBRT in delaying further systemic treatments for patients with oligoprogressive NSCLC. Larger and prospective studies are needed to confirm these results.

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INTERFRACTION MOTION AND DOSIMETRIC ANALYSIS OF VOLUMETRIC MODULATED ARC THERAPY FOR CRANIOSPINAL IRRADIATION IN ADULT MEDULLOBLASTOMA

Code: 320

Aims: It is currently recommended that adult medulloblastoma patients undergo postoperative craniospinal irradiation (CSI) as a standard form of treatment. Volumetric intensity-modulated arc therapy (VMAT) has been recently introduced as a potential method for CSI. In this report, we present the outcomes of 6 AMB patients concerning their repositioning and dosimetric data.

Methods: Complete CSI and posterior cranial fossa irradiation, or tumor bed boost irradiation with Linac-based VMAT, was performed and evaluated. Patients were immobilized supine with two thermoplastic masks (head, neck, and abdomen) to guarantee the correct position during treatment. CSI treatment plans were performed with three isocenters. To ensure inter-fraction reproducibility during radiation therapy (RT), a single cone-beam CT (CBCT) for each isocenter and real-time surface-guided RT using AlignRT® were
performed daily before and during the RT session. Before treatment, the radiation therapists (RTTs) utilized surface-guided radiation therapy (SGRT) to adjust the patient's position. Subsequently, in all instances, the first cone-beam computed tomography (CBCT) scan was employed to ensure the accurate placement of the patient. Match values of all three translational axes (x = lateral, y = longitudinal, z = vertical) were recorded.

Results: From August 2022 to September 2023, 6 AMBs were treated with CSI: 3 were women and 3 men, with a median age of 32 years (22-42). All cases were classical MB, 4 were low risk, and 2 were defined as high risk due to the metastatic disease. All patients underwent surgery; two received GTR (Gross Tumor Resesction). Low-risk patients received 36Gy for CSI and a 54Gy boost, while high-risk patients received 39Gy for CSI. No significant toxicities greater than G2 were observed during radiotherapy, and only 2 patients reported a decrease in platelet counts (112) without disrupting treatment. The dose to the organs at risk was low and acceptable. The mean doses to heart, lungs, eyes, stomach, and thyroid were 4.4Gy, 8.5Gy, 12Gy, 8.7Gy, and 11Gy, respectively. In terms of repositioning data, 124 CBCT were analyzed for CSI. Inter-fraction CBCT mean values for the study population in all translational directions were inferior to 2mm in more than 90% of cases.

Conclusions: VMAT is a convenient, effective treatment for adult medulloblastoma. SGRT-guided positioning and immobilization with masks reduce inter-fraction motion.

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HYPOFRACTIONED TREATMENT WITH SIB IN PATIENTS WITH BREAST CARCINOMA DIAGNOSIS AFTER CONSERVATIVE SURGERY: ASSESSMENT OF ACUTE TOXICITY, RESULTS OF OUR EXPERIENCE

Code: 206

Aims: Studies on the evaluation of adjuvant treatment in breast cancer after early-stage conservative surgery have demonstrated the validity of hypofractionated treatment compared to conventional treatment, on local control without worsening of long-term cosmetic results and reduction risk of acute toxicity. For tumor bed recurrence it is useful to administer an overdose (boost) sequentially or concomitantly (SIB, simultaneous integrated boost) with irradiation of whole breast. The aim of our analysis is to evaluate the feasibility, safety and acute toxicity of hypofractionated adjuvant treatment with SIB in patients with early stage breast cancer.

Methods: In 2023, 27 patients were treated, aged between 45 and 80 years (average age 62 years), undergoing conservative surgical treatment for breast cancer, histology: 16 invasive ductal carcinoma, 3 invasive lobular, 8 intraductal; stage I, in the absence of lymph node localizations, negative margins, 16 G1, 10 G2, 1 G3 (intraductal carcinoma). All patients were treated with hypofractionated radiotherapy with intensity-modulated SIB (IMRT or VMAT), using LINAC with 6 MV photon beams, for a DT of 40.05 Gy (DF 2.67 Gy) on the whole breast and with SIB on the tumor bed DT 48 (DF 3.2 Gy), assuming those of QUANTEC as dose constraints to the organs at risk. The planning in IMRT took into account possible movements of the patients for an adequate dose on the skin, using the TPS skin flash tool (Varian Eclipse) for IMRT plans, or an artifice on the planning CT for VMAT plans, evaluating the skin flash opportunity based on the comparison of DVHs for VMAT plans with and without skin flash. Adjuvant hormone therapy was prescribed for 93% of the patients taking it during treatment. Acute toxicity was assessed by C.T.C.A.E. Version 5.0.

Results: The evaluation of acute toxicity regarding the appearance of erythema was grade G1 in 94%, grade G2 in 3% and grade G0 in 3%. None of the patients required advanced medications or treatment interruptions.

Conclusions: In our experience, hypofractionated treatment with SIB confirmed the tolerability of the treatment with excellent cosmetic results. The follow up will permit to evaluate the toxicity of the treatment and the cosmetic results.

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ABRUPT TRIAL: TOXICITY PROFILE AND PATIENT-REPORTED OUTCOMES FOLLOWING RADIOSURGERY FOR UNFAVORABLE PROSTATE TUMORS

Code: 290

Aims: To assess late gastrointestinal (GI) and genitourinary (GU) side effects in patients with organ- confined unfavorable prostate cancer (PCa) following RS.

Methods: Thirty pts included in the prospective clinical trial ABRUPT were treated with a single fraction of 24 Gy to the whole prostate with urethra sparing in association with androgen deprivation therapy, as per standard of care. The RS was delivered on Linac platform with Volumetric Modulated Arc Therapy and a real-time prostate tracking system. QoL outcomes (EORTC QLQ-PR25/C30, IPSS and IIEF 5 questionnaires) and the maximum treatment-related genitourinary (GU) and gastrointestinal (GI) toxicities evaluated with CTCAE_v5 scale from 3 months after treatment to the last follow-up were assessed and compared with the baseline. Paired t-test was used to compare pre-RS and post-RS questionnaire scores with Minimal Important Difference (MID) established as a change of >0.5 pooled SD from the baseline. Logistic regression was used to evaluate potential associations between patients', tumor, or treatment-related factors and a worsening of clinical outcomes.

Results: Patients, tumor and treatment characteristics are summarized in Table 1. With a median follow- up of 18 months (6-31), no >G2 late side effects were observed. G2 late GI and G2 late GU toxicities were recorded in 1 and 2 patients, respectively. Any grade GI toxicity was significantly associated to maximum dose to the rectum (P=0.021), while lower baseline QoL score (P=0.025), higher baseline IPSS score (P=0.049), acute GU toxicity (P=0.029), and acute MID in the urinary domain (P=0.045) were significant predictors of any grade GU toxicity. At MVA, only baseline QoL score (OR 0.95, 95% CI 0.89-0.99, P=0.031) and acute GU toxicity (OR 8.4, 95% CI 1.09-64.45, P=0.041) retained their significance. The only statistically significant MID was observed in the urinary domain (P=0.005), with the median value raising from 8 (0–25) to 17 (0–71). Urinary MID significantly correlated with acute urinary MID (P=0.003), acute QoL MID (P=0.029), acute GU toxicity (p=0.030), and lower baseline urinary score (P=0.033). At MVA, only acute urinary MID was identified as predictive factor for late urinary MID (OR 9.7, 95% CI 1.2–80.2, P=0.035).

Conclusions: RS irradiation of the whole prostate with urethra sparing and organ motion control was feasible and well tolerated in patients with organ confined unfavorable PCa. Long-term results are needed to confirm these findings.

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DIFFERENT SAFETY PROFILE EVALUATION OF STEREOTAXIC TREATMENT IN M1B CRPC (CASTRATION-RESISTANT) PROSTATE CANCER WITH SINGLE PELVIC LYMPH NODE LOCALIZATION UNDERGOING CHEMOTHERAPY OR HORMONE THERAPY

Code: 386

Aims: Evaluation of different toxicity profiles of stereotactic treatment in patients with M1b CRPC prostate cancer, after total hormonal blockade, under chemotherapy or ARSI and oligoprogression/oligoresidue on single pelvic lymph node.

Methods: We retrospectively evaluated 19 stage M1b patients in oliprogression/oligoresidue on a single pelvic lymph node lesion during chemotherapy with Docetaxel or ARSI. The stereotactic fractionation was 7 Gy x 5 frz, carried out with the aid of PSMA PET image fusion, imaging daily control by CBCT and positioning correction of the table in all 6 freedom degrees. They were subsequently divided into two groups: group A comprising 10 patients receiving ARSI and group B comprising 9 patients receiving Docetaxel.

Results: The median follow-up was 90-120 days. More than 50%(n°5) of patients subjected to chemotherapy developed type G1-G2 gastrointestinal toxicities such as nausea and diarrhea, resolved by appropriate therapy. All 10 patients receiving ARSI did not report any toxicity.

Conclusions: Our retrospective study results, although small in size, show that patients undergoing sbrt and chemotherapy frequently develope gastrointestinal toxicity, condition that require greater measures to prevent it such as better gastrointestinal preparation and/or adopting different fractions. Further studies with greater statistical power are necessary to better define the most suitable dose/fraction and explain uncertainties regarding the role of weekly or three-weekly chemotherapy treatment schedules.

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EVALUATION OF THE SAFETY AND TOXICITY PROFILE IN RE-TREATMENT, WITH STEREOTACTIC TECHNIQUE, IN PATIENTS WITH GLIOBLASTOMA RECURRENCE AFTER STANDARD THERAPY

Code: 233

Aims: Most glioblastomas recur within 12-18 months, despite a comprehensive approach. Currently there is no standard of care on re-treatment. Our intent is to evaluate the safety and feasibility of reirradiation in patients affected by glioblastoma operated and treated with the Stupp protocol, Radiotherapy (60 Gy in 30 frz) and Temozolamide

Methods: Starting from 2018 to 2024 we retrospectively evaluated 8 patients, who relapsed 10-12 months after surgery mantaining a good KPS: 1-2. The methylation status of the MGMT promoter was unknown. The re- treatment was carried out with two distinct fractionations: 5 Gy x 5 frz or 6 Gy x 5 frz, according to respect constraints dose, without any concomitant chemotherapy. RT planes were contoured by using MR image fusion and previous treatment plans comparison.

Results: Of the 8 re-treated patients only one underwent surgery again with partial radicalization of the recurrence. More than 50 % (n°5) of patients developed RT-related toxicities during RT course, with mild G1 headache and occasional nausea, immediately resolved with an increase in corticosteroid drugs. In the median follow-up (4-6 months) non subacute toxicities was registered

Conclusions: The short follow up does not allow us to comment on the effectiveness of the treatment, but although small in extent, our experience confirms that the re-treatment of recurrent GBM is feasible and without noteworthy acute toxicities. Further evidence is needed to explore efficacy during longer follow-up

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SAFETY AND TOXICITY OF DIFFERENT BRAIN STEREOTACTIC FRACTIONATION IN EGFR MUTATED PATIENTS

Code: 232

Aims: The EGFR mutation is present in approximately 20% of lung cancer patients, characterized by a 15-18 % recurrence risk of brain progression during treatment with TKI. The aims of this study is to evaluate the safety and radio-related toxicity of different brain stereotaxic fractionations in patients with metastatic oncogene-addicted lung cancer.

Methods: We retrospectively selected 20 patients with single brain metastatic lung cancer with EGFR mutated treated with fractionated stereotactic radiotherapy from January 2018 to January 2024. The fractionations used were: 7 Gy x 5 fr, 8 Gy x 3 fr and 9 Gy x 3 fr. All selected patients were taking first generation TKIs and had a PS 0-1 at the CT-sim. All plans were drawn up after image fusion with brain MRI and corticosteroid was prescribed in order to reduce any perilesional edema.

Results: Of the 20 patients selected 5 patients (20%) developed grade 1 (headache and nausea) and grade 2 toxicity (only nausea), within 6 months from the start of treatment with greater incidence in the first 30 days therapy. The 10% of patients developed radionecrosis during follow-up (>6 months.)

Conclusions: The fractionations used and the experience gained highlight how the stereotactic treatment in 5 or 3 sessions is safe and with few neurological toxicity, promptly resolved by pharmacological therapy. Further larger studies are necessary to highlight long-term toxicity and clinical-iconographic efficacy.

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ROLE OF RADIOCHEMIOTHERAPY IN HIGH RISK pT1 RECTAL CANCER PATIENTS THAT REFUSE SURGICAL APPROACH: A RETROSPECTIVE MONOCENTRIC EXPERIENCE

Code: 272

Aims: Patients diagnosed with pT1 rectal cancer (RC) following local resection and exhibiting risk factors should be considered for total mesorectal excision (TME) surgery. Nevertheless, it is worth considering a conservative approach, even though it is not the prevailing standard of care. The aim of this monocentric retrospective trial is to evaluate the role of adjuvant radiotherapy (RT) +/- concomitant chemotherapy (aRT/aCRT) in pT1 high risk RC patients in terms of local recurrence (LC), systemic disease free survival (DFS) and overall survival (OS).

Methods: We retrospectively collected data on pT1 histology RC patients who underwent local resection with at least 1 of these specific histological features: poorly differentiated adenocarcinoma, mucinous adenocarcinoma or Signet ring cell carcinoma, submucosal invasion>1000 microns, positive lymphatic or venous invasion confirmed by immunostaining, grade of budding 2-3. After local resection, patients declining TME surgery received aRT or aCRT. Clinical target volume 1 (CTV1) included the scar and the associated mesorectum, while CTV2 encompassed elective lymph node stations. Planning target volume (PTV1) received 50/55Gy Gy in 25 fractions. Concomitant chemotherapy included 5-FU (225 mg/sqm/day in continuous infusion) or oral capecitabine (1650 mg/sqm/day in chronomodulation). Careful follow-up included rectoscopy and clinical examination every 3 months for the first 2 years, then every 6 months for the next 3 years. Pelvic MRI was performed twice a year. Salvage TME surgery was required for recurrence of disease. LC, DFS and OS were evaluated.

Results: The study included 31 pT1 RC. Median age at diagnosis was 69 (35-86) years. The majority of lesions were located in the lower rectum (64.5%). High budding grade was observed in 54.8% of cases, vascular invasion in 41.9%, and neural invasion in 3.22%. Patients characteristics are reported in Table 1. At 51 (1-148) months median follow-up, we observed 3-year LC of 87% and 3-year DFS of 73%. The 3-year and 5-year OS were 91.1% and 87%, respectively.

Conclusions: This study highlights the potential of a conservative management approach, entailing close surveillance of patients diagnosed with pT1 RC and exhibiting specific risk factors, potentially reducing the need for more aggressive interventions. Further research is needed to validate these results and potentially redefine the standard of care for this patient population.

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	N (%)
Patients	**41 (100)**
Patients with progression	7 (22.6)
Death	5 (12.2)
Age at diagnosis, median	68 (35-86)
Gender	
Female	16 (51.6)
Male	15 (48.4)
Site of lesion	
High rectum	3 (9.7)
Low rectum	20 (64.5)
Medium rectum	6 (19.3)
NA	2 (6.5)
Lesion dimension (mm) median (range)	37.5 (10-150)
Major Axis (mm) median (range)	30 (10-155)
Tmoral budding	
absent	1 (3.2)
present	2 (6.5)
high	8 (25.8)
low	7 (22.6)
NA	13 (41.9)
Vascular invasion	
absent	17 (54.8)
present	13 (42)
NA	1 (3.2)
Grading	
G1	3 (9.7)
G2	20 (64.5)
G3	7 (22.6)
GX	1 (3.2)
Circumferential-intramucosal margin (dichotomous)	
Positive	4 (12.9)
Negative	24 (77.4)
NA	3 (9.7)
Deep margin (dichotomous)	
Positive	20 (64.5)
Negative	11 (35.5)
Neural invasion	
Positive	1 (3.2)
Negative	29 (93.6)
NA	1 (3.2)
Surgey	
Yes	4 (12.9)
No	27 (87.1)

Table 1: Descriptive sample analysis

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REAL-LIFE EXPERIENCE OF SMALL CELL LUNG CANCER LIMITED DISEASE: RESULTS OF THE RETROSPECTIVE BeST COHORT

Code: 255

Aims: Small Cell Lung Cancer (SCLC) accounts for 15% of all lung cancers. Recently, the advent of immunotherapy has increased the overall survival (OS) for the extended disease, while data for the limited disease are to be awaited. To this date, the gold standard for the radical treatment of LD SCLC is concurrent chemoradiotherapy (CRT). However, nowaydays, the prognosis remains poor. This study aims to describe the population and clinical outcomes of a single-center retrospective series on that matter

Methods: Clinical and therapeutic data of patients affected by LD SCLC and treated with CRT from 2017-2023 were collected within the BeST (Brescia Enterprise SCLC treatment) cohort. Descriptive, inferential e regressive statistical analysis was performed using SPSS

Results: Data from 57 patients were retrieved for this study: fifty-one percent were male, the mean age was 70; all of them but three patients, were former or current smokers with a mean of 45 pack/year. Mean Charlson Comorbidity Index was 5,5. Performance status according to ECOG was 0-1 in 79% of the patients and weight loss was present at the onset in 25% of the patients. TNM staging resulted I-IIA in 14%. Forty-one patients received CRT (7 sequential and 34 concurrent), 9 radiotherapy alone and 7 chemotherapy alone. Prophylactic Cranial Irradiation (PCI) was applied in 46% of cases. After a median follow up of 14.3 months 37 patients died; median Progression Free Survival (PFS) and Overall Survival (OS) resulted in 12 and 19 months, respectively. The most common toxicities were haematological.

Conclusions: In real-world practice, patients with LD-SCLC are commonly frail, elderly and comorbid. In the entire population eligible for curative treatment, only 72% of patients ultimately received CRT. In this
analysis PFS was similar to recent randomized trials but OS resulted lower, with acceptable toxicities. It could mean that radical treatment could be effective and safe for unselected patients. Distant and local failure are common and for these cases further treatment options are limited, negatively affecting on OS.

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STEREOTACTIC BODY RADIOTHERAPY ON PRIMARY LESION AND METASTASIS DIRECTED RT FOR OLIGOMETASTATIC BREAST CANCER PATIENTS: AN INTERIM ANALYSIS OF A MONOINSTITUTIONAL STUDY

Code: 245

Aims: The treatment of primary tumor with an ablative intent has already demonstrated to confer a survival benefit for oligometastatic prostate cancer patients. The purpose of this study is to evaluate effects of stereotactic body radiation treatment (SBRT) of primary lesion in oligometastatic breast cancer (OBC) patients, in term of acute toxicity and local control.

Methods: Patients (pts) with histological proof of invasive breast cancer, oligometastatic staged on FDG PET-CT (≤ 5 metastasis), underwent SBRT on primary breast lesion. The prescribed total dose was 40Gy in 5 fractions (8 Gy/fr) to the PTV, obtained from GTV contour plus 3mm-margin. All the metastatic lesions were also treated using stereotactic technique with an ablative intent. Primary endpoint was evaluation of adverse effect of radiotherapy, graded according to CTCAE v5.0. Secondary endpoint was evaluation of response on re-assessment FDG PET-CT.

Results: SBRT on primary and secondary breast cancer lesions were performed for five pts. Median age was 71 years. All patients were taking CDK4/6 inhibitors, which were suspended during RT. Grade 2 acute erythroderma was observed in 1 patient. At a median follow-up of 6 months, a local response was observed, with a mean reduction in maximum diameter of 30% and/or in SUV max of 20% .

Conclusions: The stereotactic treatment of primary breast lesion, associated to a metastasis directed RT, in OBC pts appears safe and effective and may allow to preserve quality of life, avoiding skin ulceration due to the tumor. Further longer follow up and larger studies are needed to confirm these findings and to evaluate the potential survival benefit of this treatment.

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A DOSIMETRIC PREDICTIVE MODEL OF ACUTE TOXICITY AFTER FAST FORWARD IRRADIATION FOR EARLY BREAST CANCER

Code: 338

Aims: Backed by robust clinical evidence demonstrating comparable efficacy and safety to hypofractionated regimens, accelerated radiotherapy regimens, namely the Fast Forward scheme, represent a pioneering strategy for patients (pts) with early breast cancer (EBC) to optimize therapeutic outcomes, while minimizing treatment duration. Recently, 5-year results from the FAST-Forward trial evaluating adjuvant whole-breast radiotherapy in 5 fractions have been published, confirming previous data. This study aimed to develop a dosimetric predictive model for acute toxicity for pts with EBC treated with the Fast Forward scheme.

Methods: Inclusion criteria were defined as per the FAST-Forward protocol. Toxicity was assessed according to Common Terminology Criteria for Adverse Events (CTCAE) toxicity scale
$_{v.5}$ Logistic regression was used to test the predictive model for acute toxicity between the most prevalent acute adverse events and the Planning Target Volume of the Breast (PTVBreast), the Planning Target Volume of the Boost (PTVBoost), Volumes of the PTV receiving the 105% (V105) and the 107% of the prescribed dose (V107). A receive
operating characteristic (ROC) curve was used to identify the cut-off point for significant variables in predicting acute events.

Results: Data from 112 pts treated at our institution from 2020 to 2023 were collected. All patients underwent breast-conserving surgery. Eighty-five (75%) pts were treated with 3DCRT and 28 (25%) pts were treated with VMAT; 30 (26%) pts received a tumor bed boost. After a median follow up of 6 months (IQR 0-12), acute toxicity occurred in 85 (78%) patients. Erythema and fibrosis were the most prevalent, with 77 (69%) pts and 48 (43%) pts experiencing overall mild G1/2 toxicity, respectively. No significant impact of PTVBoost, V105, V107 was detected. Only PTVBreast showed significant association with erythema (p=0.01). ROC analysis showed that PTVBreast > 592,1 cc best predicted erythema, with a positive likelihood ratio of 1.9 (95% CI 1.2-3.1, AUC 0.6, p=0.001) (Fig.1).

Conclusions: These data suggest that higher PTVBreast may increase risk of acute erythema, while fibrosis might have not proven significant due to post-surgical tissue hardening. Larger series are needed to consolidate a predictive model for acute skin toxicity, with potential cosmesis correlation.

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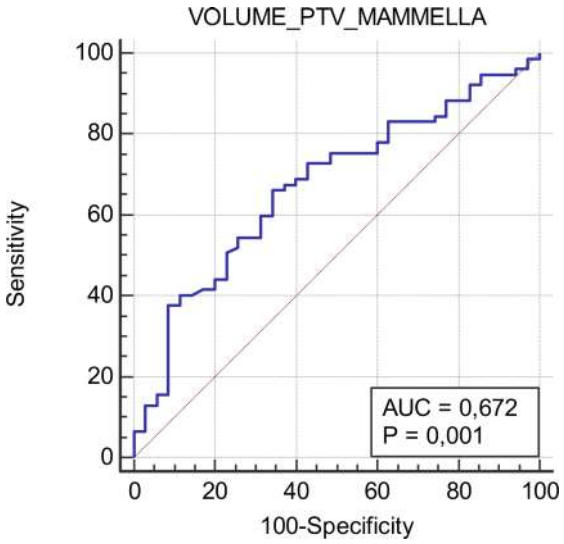

END TO END TESTING OF AN EXTENDED DISTANCE IMRT TECHNIQUE FOR TOTAL BODY IRRADIATION

Code: 599

Aims: Total Body Irradiation (TBI) in San Gerardo Hospital in Monza is delivered with large fields at an extended source- to-skin distance. Recently an extended-distance IMRT-based technique was developed to achieve better uniformity on dose delivery and faster and easier patient positioning. To validate this technique, an end-to-end (E2E) test including simulation, planning and delivery phases was conducted. The main objectives of the E2E test were evaluating time reduction in the different phases, dose uniformity and accuracy.

Methods: An Alderson RANDO Phantom was used with polypropylene pipes filled with water and fixed at the extremities to simulate the limbs. The patient is positioned with bent legs in a whole-body vacuum 200x100 cm (Vac-Lok Cushion, CQ Medical, United States). During treatment, the vacuum cushion is positioned in an adjustable bed at an extended source to the phantom midline distance of 360 cm. Whole-body CT images with a slice thickness of 5mm were acquired with a Philips CT (Brilliance 16 Bigbore). Treatment planning was done using Monaco Treatment Planning System (v. 6.1.3) validated for extended distances. The prescription considered was 12Gy in 6 fractions at the umbilical level. Lungs were the only considered organs at risk, with the prescribed dose between ±5% of the total dose. CNERGY portal imager (Cablon Medical BV, The Netherlands) is used to live check and correct the phantom positioning during treatment. Measurements were performed using previously calibrated semiconductor diodes and thermoluminescence dosimeters (TLDs) at different locations. Treatment was delivered using a VersaHD LINAC (Elekta AB, Sweden).

Results: Each step of the end-to end test was completed smoothly. The treatment plan was optimised in about 2 hours. Time required for treatment delivery phase was about 60 min. In phantom dosimetry confirmed the calculated dose distribution with maximum dose differences within 5%.

Conclusions: The newly developed IMRT TBI technique was capable of delivering a uniform dose to the phantom body. Positioning of the phantom was done smoothly, substantially reducing treatment time. E2E test proved feasibility and reliability of this technique achieving accurate dose delivery.

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CLINICAL TRAJECTORY AND MOLECULAR CHARACTERISTICS OF GLIOBLASTOMA LONG-TERM SURVIVORS

Code: 487

Aims: Median survival in patients (pts) with glioblastoma (GBM) usually is around 12 months. Only few pts survive longer, the 5-year survival rate is still 5–10%. Patient and disease features associated with long-term survival remain poorly defined. The aim of this study was to assess the clinical trajectory as well as the clinical and molecular characteristics in a cohort of long-term GBM survivors treated at the University of Florence (UNIFI).

Methods: Patients with glioblastoma surviving at least 5 years from diagnosis were identified at Unifi. In pts with isocitrate dehydrogenase (IDH) wildtype tumours, prognostic factors were analysed using the Kaplan-Meier method.

Results: 39 GBM long-term survivors were identified. 24 Males (61.5%) and 15 females (38.5%). Mean age at the time of diagnosis was 52 years. KPS was <80 in 9 pts (23%) and >80 in 30 pts (77%). Gross total resection was achieved in 36 pts (93.3%). All pts were diagnosed according to the CNS WHO 2021 5th edition: 31 (79.5%) were IDH-wildtype and 8 (20.5%) IDH-mut.
MGMT status was methylated in 28 pts (71.8%). Adjuvant radio-chemotherapy with temozolomide (TMZ) according to Stupp protocol was performed in all 39 pts with a median of 12 cycles of sequential TMZ. 30 (77%) pts recurred the first time and those were treated as follows: surgery in 2 pts; chemotherapy (CT) in 12 pts, re-irradiation (re-RT) in 2 pts, CT+re-RT in 8 pts, Bevacizumab in 3 pts, CT+Beva in 1 patient, re-RT+Beva in 1 patient. 22 pts had a second relapse and were treated as follows: RT in 10 pts, CT+re-RT in 1 patient, Bevacizumab in 2 pts, CT+Beva in 2 pts, 9 pts didn't receive any further treatment. 6 pts experienced a third recurrence and were treated with: CT in 2 pts, Bevacizumab in 2 pts, CT+Beva in 1 patient, re- RT+Beva in 1 patient while 1 patient did not receive treatment. Median PFS was 32,1 months (95% CI: 25,59-46). No clinical or molecular factors have a statistically significant impact on PFS. Median OS was 72,94 months (95% CI: 49,54-127) and only KPS had a significant influence on OS (P = 0,0215). No correlation on OS was found between patients with one or more recurrences compared to those without any recurrence.

Conclusions: KPS remains a strong prognosticator even in long-term GBM survivors. Freedom from recurrence did not have significant impact on patients' outcome. Larger studies are warranted to identify biomarkers that could lead to an early identification of these small but significant cohort of patients.

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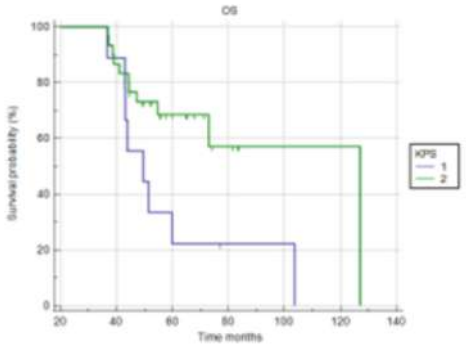

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IMPACT OF USING SGRT IN THE POSITIONING OF PATIENTS WITH BONE METASTASES: TIME AND SET-UPACCURACY

Code: 198

Aims: L'impiego dei sistemi di SGRT per il posizionamento del paziente è ormai parte consolidata nei workflow di molteplici trattamenti radioterapici, di cui è stata ampiamente discussa la validità in termini di accuratezza del set up e riduzione del tempo di trattamento. Il lavoro intende indagare i vantaggi nell'impiego di Brainlab Exactrac Dynamic (versione 1.1.3) per il prepositioning dei pazienti sottoposti a trattamenti palliativi su metastasi ossee. L'obiettivo è preservare l'accuratezza del set-up riducendo al minimo il tempo di trattamento, rendendolo più tollerabile per i pazienti che provano dolore. Inoltre, si valuta la possibilità di eliminazione dei tattoo permanenti, con vantaggi sia per pazienti che per operatori.

Methods: Lo studio ha coinvolto 50 pazienti sottoposti a radioterapia palliativa in 5 frazioni su metastasi ossee singole o multiple. Metà dei pazienti sono stata posizionati utilizzando allineamento sui tatuaggi e il Varian Delta Couch Shift; l'altra metà è stata posizionata utilizzando la guida di superficie di Exactrac Dynamic. La valutazione del dolore è stata eseguita con la scala NRS. La posizione del trattamento è stata verificata quotidianamente con la CBCT e sono stati raccolti i valori degli errori di set-up traslazionali e rotazionali da 250 CBCT. Il tempo di set-up è stato ricavato dai log file del Linac.

Results: L'uso di SGRT ha comportato una riduzione del tempo di posizionamento di circa il 30% rispetto al metodo con i tatuaggi, con un risparmio medio di 2,5 minuti. Gli errori medi di set-up per entrambi i metodi di posizionamento sono sovrapponibili, con una differenza di ±0,04 cm (vrt), ±0,13 cm (long), ±0,10 cm (lat) e una differenza di ±0,1° (pitch), ±0,17° (roll) e ±0,02° (rtn).

Conclusions: La riduzione del tempo di trattamento grazie a SGRT limita possibili interruzioni e riposizionamenti causati da movimenti intra-frazione, particolarmente vantaggiosa per i pazienti con dolore e trattati con dosi più elevate. Inoltre, la maggiore compliance può consentire di trattare più siti in una sola seduta, riducendo il numero complessivo di giorni di radioterapia. L'uso di SGRT può migliorare la qualità di vita dei pazienti e semplificare il flusso di lavoro dei tecnici. L'eliminazione dei tatuaggi può prevenire danni per rischio biologico causati da punture accidentali dell'operatore. Lo studio suggerisce che l'uso di SGRT è un metodo efficace per il preposizionamento dei pazienti sottoposti a trattamenti palliativi sulle metastasi ossee.

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INTENSITY-MODULATED RADIATION THERAPY WITH SIMULTANEOUS INTEGRATED BOOST (SIB-IMRT) FOR PELVIC POSITIVE-LYMPH NODES IN PROSTATE CANCER

Code: 516

Aims: The aim of our study was to evaluate the efficacy and tolerability of intensity-modulated radiation therapy with simultaneous integrated boost (SIB-IMRT), combined with androgen-deprivation therapy, for pelvic positive-lymph nodes (cN1) in prostate cancer.

Methods: We retrospectively analyzed 24 patients with cN1 prostate cancer who received SIB-IMRT between January 2020 and December 2023. All patients enrolled received a total dose of 70 Gy (2.5 Gy/fraction) to the prostatic *plus* seminal vesicles volume, 58.8 Gy (2.1 Gy/fraction) to the pelvic positive lymph-nodes and 50.4 Gy (1.8 Gy/fraction) to the remaining pelvic lymph-nodes chains, in 28 fractions with SIB-IMRT, combined with androgen-deprivation therapy (ADT).

Results: Themedian age was 68.7 years. The median follow-up was 32 months. The 4-year biochemical relapse- free survival (bRFS) was 83.3%; the 4-year prostate cancer-specific survival (pCCS) was 91.6%; the 4-year overall survival (OS) was 83.3%. Only two patients presented local relapse. The 4-year distant metastasis-free survival (DMFS) was 83.3%. *Acute and late Grade 2 urinary toxicity were observed in 16.6% and 8.3%, respectively. Acute and late Grade 2 gastrointestinal toxicity were observed in 12.5% and 8.3%, respectively. No Grade 3 or more acute or late urinary and gastrointestinal toxicities were detected.*

Conclusions: SIB-IMRT for cN1 prostate cancer combined with ADT demonstrates favourable outcomes with acceptable toxicity.

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DEFINITIVE SIMULTANEOUS INTEGRATED BOOST - INTENSITY MODULATED RADIATION THERAPY (SIB-IMRT) PLUS CONCURRENT CHEMOTHERAPY FOR SQUAMOUS CELL ANAL CANCER: A 2-YEAR MONO-INSTITUTIONAL EXPERIENCE

Code: 529

Aims: Anal squamous cell cancer (ASCC) is a rare disease with an increasing incidence, associated with up to 93% of cases to HPV infections. Our study showed the 2-year clinical outcomes of ASCC patients treated in the c*omplex operational units*of *Radiotherapy and Oncology of Ragusa.* The aim of our study was to retrospectively evaluate feasibility, safety and outcomes of our institutional "SIB-IMRT *plus*concurrent chemotherapy schedule" in patients with squamous cell anal cancer.

Methods: Between January 2021 and December 2023, a total of 14 patients with squamous cell anal cancer, stage cT1-4, cN0-3, were treated in our institution with definitive chemoradiation. Radiotherapy was delivered using a SIB-IMRT schedule with a dose of 59.4 Gy to the primary tumor and macroscopically involved lymph nodes and 49.5 Gy to elective lymph node areas, in 33 fractions. All patients received concurrent chemotherapy following the Nigro regimen (5-fluorouracil and Mitomycin C).

Results: Mean age was 66.7 years (range 55–79); mean follow-up was 18 (range 3–24) months. 85.7% of patients had stage II-III. Thirteen patients completed chemoradiation without any treatment break. One patient required three days of treatment interruption due to acute toxicity. The 2-year local control (LC) rate was 85.7%; the 2-year colostomy-free survival (CFS) rate was 92.8 %; the 2-year distant metastases-free survival (DMFS) rate was 85.7 %; the 2-year overall survival (OS) rate was 92.8 %, respectively. Acute grade(G) ≥2 skin toxicity was observed in 14.2% of the patients. No G≥2 gastrointestinal or urinary acute toxicity occurred. Haematological toxicity G≥2 was observed in 7.1% of patients. No G≥2 late toxicity was observed.

Conclusions: Our analysis demonstrates excellent outcomes with minimal toxicityfor the use of definitive SIB-IMRT *plus* concurrent chemotherapy in treatment of squamous cell anal cancer patients.

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RADIOSURGERY FOR HEMANGIOBLASTOMAS: MONOISTITUTIONAL ANALYSIS

Code: 286

Aims: Hemangioblastomas are rare benign vascular tumors of the central nervous system (CNS). Hemangioblastomas can occur either as sporadic lesions or in 20%–25% patients affected by von Hippel- Lindau disease (VHL). Cerebellum and spinal cord are the most common sites. Although surgical resection remains the primary therapy for HB, either radiotherapy (RT) or Radiosurgery (SRS) is considered as a therapeutic option for patients who have undergone previous surgery with subtotally excised lesions as well as for recurrent disease. The aim of this study is to evaluate the efficacy and safety of SRS for patients with diagnosis of intracranial and spinal HB in terms of local control and toxicity.

Methods: We conducted a retrospective analysis of patients treated with SRS for HB at our Institute. A regular radiological follow-up with MR imaging was scheduled at 4–6 month intervals after SRS procedure. The radiosurgical procedures were performed using a CyberKnife® system. Statistical analysis was carried out using SPSS 21.

Results: Data of 33 patients having in total 71 HB lesions treated at our Institute from January 2012 until June 2023 were included. The diagnosis of HB was based on histological findings after surgery, except in 8 patients who did not receive upfront surgery. Fifty-one lesions were intracranial and 20 lesions were spinal. Median age at the time of the first SRS was 44 years (IQR 30-61 years), 15 patients were female and 18 male. Thirteen patients (39%) had a confirmed diagnosis of VHL disease. The median (IQR) follow-up of the entire cohort was 42 months (IQR 23–112 months). Twenty-two patients (67%) were treated for a single lesion, while 11 patients for multiple lesions. The median tumour volume pre-SRS was 250 mm3 (IQR 77-645 mm3). The median prescription dose for single fraction SRS was 15 Gy (IQR 12-18 Gy) while for multi-fractionated SRS was 24 Gy (IQR 21-25 Gy) in 3-5 fractions. Six patients (18%) experienced local failure, 17 (52%) showed stable disease and 9 (30%) partial response. There was no significant toxicity after treatments.

Conclusions: SRS, both in single and multi-fractions settings, is potentially attractive for patients with single or multiple HBs, even though patients with VHL disease may develop more lesions and may be difficult to treat or retreat with repeated surgery and/or conventional radiation techniques without the risk of toxicity. Our results show that SRS can be considered a safe and effective treatment for intracranial and spinal HB.

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SINGLE AND FRACTIONATED RADIOSURGERY FOR SKULL-BASE PARAGANGLIOMAS

Code: 451

Aims: Paragangliomas of the skull base are rare hypervascular low-grade malignancies arising within the autonomic nervous system and surgery is the gold standard treatment. However, non- invasive techniques as stereotactic radiosurgery (SRS) or fractionated stereotactic radiosurgery (fSRS) can be considered for both non-resectable and residual lesions.

Methods: We conducted a retrospective analysis of patients (pts) with histologically or radiologically diagnoses of paragangliomas treated with SRS or fSRS using CyberKnife at our Institute. Each case was examined with MRI, and if MRI was not feasible, 68Ga-DOTATATE PET/CT was employed.

Results: Between 2005 and June 2023 were treated 25 pts (6 male and 19 female) with a median age of 55 years (IQR 44-66 years), harboring 26 lesions. Eleven pts (44%) received surgery while 14 pts (56%) had a radiological diagnosis. Seven pts (28%) underwent SRS, while 18 pts (72%) fSRS (3-5 fractions). The median dose for fSRS group was 25 Gy (IQR 24-25 Gy) with a median prescription isodose line (IDL) of 80% (IQR 79-82%), while for SRS was 12 Gy (IQR 12-12.75 Gy), with a median prescription IDL of 78% (77-82%). Median PTV was 25 cc (IQR 14-34 cc) for fSRS and 4 cc (IQR 2-5) for SRS. After a median follow-up of 72 months (IQR 43-128 months), local control was stable for 15 pts (60%), 9 pts (36%) had a partial response and 1 patient (4%) had local failure after 88 months from fSRS. At the last follow-up, neurological symptoms improved in 7 cases, worsened in 3, and were unchanged in the remaining pts. Among the patients who experienced worsening, one developed vertigo, and two others presented with trigeminal symptoms – one with hypo- paresthesia and another with neuralgia attributed to radionecrosis.

Conclusions: Radiosurgery, in both single and fractionated approach, appears to be a viable and safe therapeutic option for patients with skull-base paragangliomas. Further studies are needed to confirm these data and better analyze doses and fractionation.

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REDUCED INTENSITY CONDITIONING FOLLOWED BY ALLO-HSCT IN PATIENTS WITH REFRACTORY/RELAPSING LYMPHOMAS

Code: 554

Aims: Since standard high-dose chemotherapy followed by autologous haematopoietic stem cell transplantation (HSCT) often fails in patients with lymphomas, allogeneic HSCT (allo-HSCT) with reduced intensity conditioning (RIC) has emerged as an alternative and feasible salvage strategy. RIC wich administer fludarabine +cyclophosphamideor thiothepa and low-dose total body irradiation (TBI) exerts its action through an immunosuppressive effects. It was reported to lower transplant-related mortality in most and improve survival. With the aim of evaluating outcomes after RIC and allo-HSCT, we designed a multi- centre retrospective study enrolling patients with refractory or relapsed lymphomas.

Methods: The study recruited 59 patients, 49 of whom had failed high-dose autologous HSCT (31 males, 28 females; median age 47 years;(range 14-79); mean KPS 90% (range: 70-100)). Patients were affected by Hodgkin's lymphoma (26), T cell lymphoma (11), diffuse B large cell lymphoma (18), mantle cell lymphoma (2) and follicular lymphoma (2). Patients received fludarabine from days −6 to −2, cyclophosphamide/thiothepa on days -5 and -6 and 2-4 Gy total body irradiation on day -1. Allo-HSCT were HLA-matched related (20) or unrelated (39). A post-transplant immunosuppressive strategy was adopted in all patients.

Results: Stable engraftment was achieved in 55/59 patients; non-fatal rejection was observed in 4 patients Acute toxicity rate was 22/59 (37.3)% (6 gastrointestinal, 1 renal, 2 veno-occlusive disease (VOD)). Post-transplant infections occurred in 13/59 patients (22%). Acute graft-versus-host disease (GvHD) was found in 17/59 patients (28.8%). It was grade I in 5 (29.4%), grade II in 9 (52.9.%), grade III in 3 (17.6%) . Chronic GVHD was observed in 11(18,6%) patients (grade I in 7 patients (63.6%) grade II in 4 (36.4%). The median follow-up was 33.5 (1-128) months. Nine patients were lost at follow-up. Disease progression was observed in 14 patients ;11 patients (22%) died, 3 (27.3%) of relapse and 6 (54.5%) of non-relapse. The 5-year Kaplan-Meier probabilities of disease-free survivals were 66.6%.

Conclusions: Allo-HSCT after RIC is a feasible and safe salvage strategy for patients with relapsed and refractory lymphoma. The high response and low relapse rates suggest that lymphoma cells are susceptible to graft-vs-tumor responses.

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OUTCOMES OF PROTON THERAPY IN THE TREATMENT OF SINONASAL CANCERS: A MONOCENTRIC EXPERIENCE

Code: 370

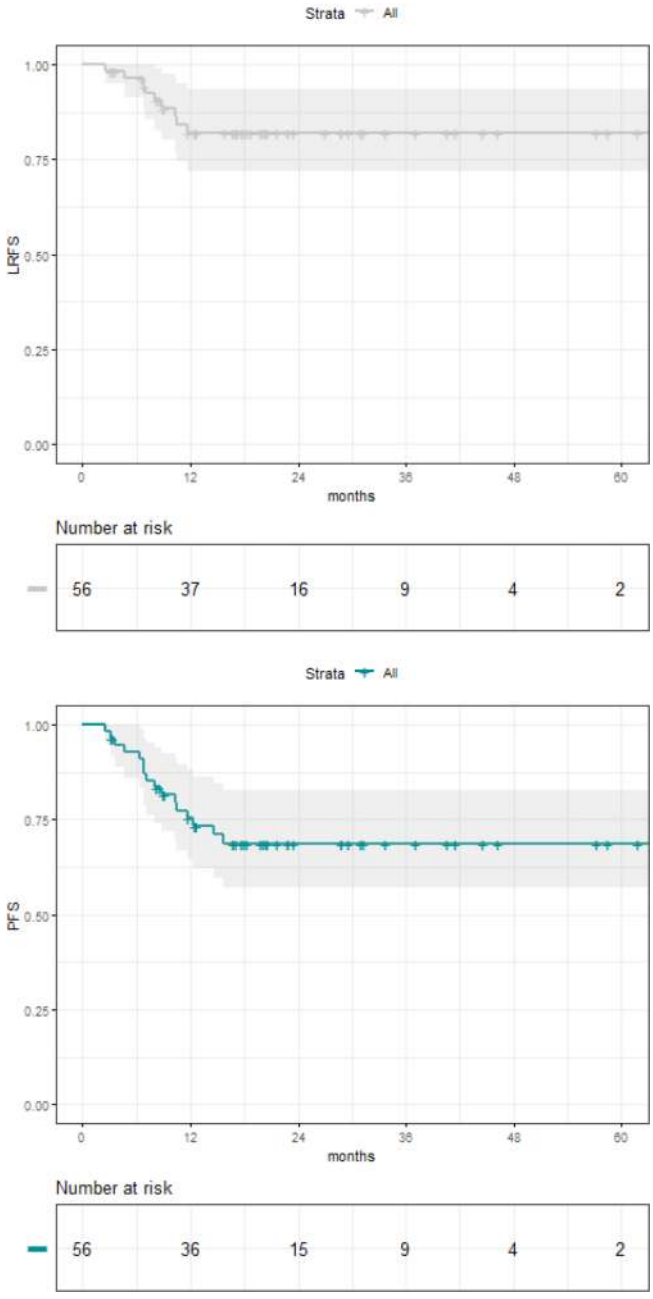
Aims: Sinonasal cancers (SNCs) represents a challenging scenario for radiation oncologists due to their proximity to critical organs at risk (OARs, as optic nerves and brain) and their locally advanced stage at the time of the diagnosis. Proton therapy (PT), thanks to its dosimetric properties, could be exploited in the multidisciplinary management of this disease. Our aim is to evaluate the outcomes of a cohort of patients (pts) with SNCs treated with PT.

Methods: A cohort of 56 pts with SNCs treated from July 2017 to November 2022 with PT were included in this retrospective analysis. Mixed beam treatments and adenoid-cystic histology were excluded. Local Relapse Free Survival (LRFS) and Progression Free Survival (PFS) at 2-years (2-y) were evaluated with the Kaplan Meier. Univariable analysis was performed with Log-Rank test to evaluate the association of clinical and treatment variables with the survival outcomes. Toxicity grading was assessed according to the Common Terminology Criteria for Adverse Events (CTCAE) v5. Univariable analysis (chi-squared and Mann-Whitney U tests) was used in order to identify clinical and treatment factors impacting acute and late G2+ toxicities.

Results: Squamous cell carcinoma was the most frequent histology (34%), followed by Intestinal type adenocarcinoma (27%). Thirty-eight pts (68%) underwent surgery followed by PT. Thirty-one pts (55.3%) were treated with induction and/or concomitant chemotherapy. PT was delivered to all pts with a median total dose of 66 Gy RBE (range 60-70 Gy RBE). With a median follow-up time of 20.16 months (95% CI: 17.13-26.9) 2-y LRFS achieved 81.9% (95% CI: 71.9– 93.4%) and 2-y PFS was 68.7% (95% CI:57-82.9%) (Fig. 1). At univariate analysis, 2-y LRFS and 2-y PFS were significantly better for T2-T3 stage vs T4 ($p = 0.029$ and $p = 0.02$). Dose < 66 Gy RBE was associated with better 2-y PFS ($p = 0.026$). Acute and late max G2+ toxicity were respectively 73.2% and 55.8%. No G4 acute toxicity was reported. One late G4 toxicity was expected due to the involvement of the optic nerve by the disease. The majority of acute and late toxicity G2+ were resolved in the last follow up with the rate of 7.4 % and 3.1% respectively.

Conclusions: PT provided an excellent LRFS and PFS with a safety toxicity profile. In the field of high precision therapy, PT represents a safe strategy in managing locally advanced SNCs. International PT register and randomized clinical trials are needed to optimize pts selection.

Figure 1. Local Relapse Free Survival and Progression Free Survival



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TREATMENT OF LIVER LESIONS BY SBRT: A MONO INSTITUTIONAL STUDY

Code: 143

Aims: The liver is a common organ for primary or metastatic disease. Oligometastatic cancer is defined by a limited number of metastases and number of affected organ systems. In that scenario the patients may potentially be cured, or, at least, progression-free interval and overall survival can be prolonged by an effective local treatment in addition to systemic therapy. Surgical resection provides the greatest potential for cure but accompanying cirrhosis or diminished hepatic function or comorbidities often disallows surgical attempts. Other local ablative modalities are commonly applied, as SBRT. Aims of this study is to evaluate the local control (LC), metastasis free survival out field (MFS o-f), progression free survival (PFS), the rate of conversion in polimetastatic disease (PMD) > 5 metastasis and overall survival of patients treated by SBRT on liver disease and toxicities.

Methods: This is a retrospective study that analyzes a group of patients treated by SBRT on liver lesions in our center. From to 2007 to 2023 we have evaluated 60 patients with 79 liver lesions. The median age was 65 years. The single fraction was administered in the 42% of cases and multiple fractions in the 58 % of cases. Eight (10%) lesion was from a primary liver disease, 90% of lesion were metastasis. Of that 35% were classified as oligometastasis syncronus, 55% oligorecurrents, 7% oligoprogressives, 3% oligopersistents. The primary most represented was colon rectal cancer (44%).

Results: The LC was obtained in 74 % of liver lesions treated by SBRT with rates at 1-, 3- and 5- years of 65%, 56% and 56% respectively. The rates of MFS o-f were 43%, 26% and 19% at 1-, 3 - and 5- years respectively. The rates of PFS were 39%, 23% and 18% at 1-, 3 - and 5- years respectively. The rates of conversion in PMD at 1-, 3- and 5- years were 73%, 63% and 63% respectively. The rates of OS were at 1-, 3- and 5- years 78%, 50% and 35% respectively. We have not registered acute and late toxicities ≥ grade 2.

Conclusions: SBRT is a safe option for the treatment of liver lesions as primitive or metastasis, whit good rates of local control, improving the data of progression of disease and overall survival. Prospective studies are required to further confirm the benefit of this treatment, the right timing and the integrations with systemic therapies.

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MACHINE LEARNING MODEL FOR PATIENT-SPECIFIC QA PREDICTION IN STEREOTACTIC RADIOSURGERY

Code: 80

Aims: Stereotactic radiosurgery (SRS) for multiple brain metastases can be delivered with a single isocenter and multiple non-coplanar arcs. The highly conformal dose distribution can be achieved at the cost of extreme modulation of a linac's mechanical components. Therefore, patient-specific quality assurance (PSQA) is performed by comparing the calculated and measured dose via the gamma passing rate (GPR) to ensure that SRS plans are delivered as intended. However, measurement-based PSQA represents a time consuming workload which, in case of failure, could potentially lead to delays in treatment plan delivery. In this study, a machine learning (ML) model was developed to predict the GPR based on SRS plan parameters.

Methods: Four hundred-fifty-eight patients (1604 arcs) from our internal database were selected. All patients were optimized using HyperArc (Varian) and underwent PSQA. The GPR analyses were performed using 3%/1 mm and 95% action limit criteria. Nineteen plan parameters were used as input features for the ML models to predict the corresponding GPR of the field. A range of tree-based ensemble ML regression models and classifiers, including extra trees, random forest, AdaBoost, and XGBoost, was considered. The performance of the extra trees was assessed on the test set, using mean absolute error (MAE) and absolute error statistics for the regression model, and specificity and sensitivity for the classifier.

Results: Among all models, extra trees was the most promising, with MAE=2.4% on the test set. A small median value of 0.7% was observed in the distribution of the residuals, i.e., the difference between measurements and predictions. At the same time, a tendency to overestimate

REGRESSION	Extra Trees
Mean Absolute Error (%)	2.6
Absolute Error <=3% (% points)	71.2
Absolute Error <=5% (% points)	90.0
Absolute Error <=10% (% points)	97.2
Absolute Error (%) 90th percentile	5.0
Absolute Error (%) 95th percentile	8.2
Absolute Error (%) 98th percentile	10.2
CLASSIFIER	**Extra Trees**
Sensitivity - 95% action limit	0.93
Specificity - 95% action limit	0.60

Table 1: Summary of the prediction performance for the regression and classification extra trees

lower values of the experimental GPR was noticed. The extra trees classification model yielded a sensitivity - fraction of fields with GPR<95% correctly identified - of 0.60 and a specificity - fraction of fields with GPR>=95% correctly identified – of 0.93. Table 1 summarizes the evaluation metrics for the regression and classification models.

Conclusions: ML models can be integrated into clinical practice to provide PSQA outcome estimates for SRS treatments. Our results suggest that such models should undergo comprehensive verification to ensure their reliability and safety before clinical use. Although a regression model can provide an expected value for PSQA, the use of a classifier could offer a simpler and more intuitive indication of the risk of PSQA failure.

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MR-ADAPTIVE RT WITH MR-LINAC 1-5T FOR THE TREATMENT OF PRIMARY HEAD&NECK (N&N) TUMOURS. PRELIMINARY DATA ANALYSIS AND COMPARISON

Code: 425

Aims: MRI is the standard for identification and follow-up of primary h&n tumours. MRI increases accuracy in diagnosis of tumour (T)and disease-related inflammation. Identification of T- volume and organ at risk (OAR) is the central part of radiotherapy process. Conformation of dose to T and OAR, before and during the treatment, is a challenge considering the changes during the treatment. The daily adaptive treatment with MR-Linac can increase T/OAR definition and dose distribution, possiblyobtaining better outcome.

Methods: The data of patients (pts) treated between 9-2022 and 12-2023,after MR-simulation, with MR-Linac IMRT and Helical IMRT are going to be collected in terms of response, dosimetry data and acute toxicities. The preliminary results about patients treated with MR-Linac are reported.

Results: In the accrual period 110 pts had CT simulation for h&n cancer, in all the settings and for all different histology. 77/110 pts had RM simulation. 37/78 were treated on MR-Linac. The pts were treated with both RM-guided RT (MR-Linac) and Helical IMRT. The case mix was different between them. Differences between the two approaches are evident in terms of margin CTV-GTV, waiting time between simulation and RT, numbers of replanning and delivery time (Tab.1).

All pts on MR-Linac were treated using the "adapt to shape"workflow with daily identification of the volumes and replanning. The stage (st) of the pts was st I 10/37; st II 4/37; st III 6/37; st IV 14/37. 26 pts had radio-chemotherapy (17: weekly CDDP; 9: 3w-CDDP). Mucosal toxicity was classified as reported G1: 3, G2: 16, G3: 14; median time between higher grade mucositis and the start of RT was 27 days(d); median duration was 85 d. Cutaneous toxicity was classified as reported G1: 11; G2: 13; G3: 9; median time between the higher cutaneous toxicity and the start of RT was 33 d; median duration was 69 d.; 25 pts had access in the hospital for supportive care. After a median follow up of 188 d 24 pts had first re-staging PET reporting CR in 15 pts; PR in 5 pts (all of these were in RC at the subsequent MRI); 3 pts with unclear response were in RC after MRI; one pt had metastatic disease.

Conclusions: The reported preliminary data show that MR-guides RT with MR-Linac is feasible and safe. The data about toxicity seems in line with those from other technologies. The direct comparison with helical IMRT and the results about late toxicity will be included in the final analysis of these data.

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	IMRT with MR-Linac	Helical IMRT
Number of patients	37	40
Sex M	30	25
Site of disease		
Oropharynx	31	13
Nasopharynx	1	8
Larynx	2	6 (2 post-op)
Hypopharynx	2	2
Paranasal sinus	0	7
Oral cavity	0	2
other	1	2
n° of replanning during RT	1:9 paz; 2: 1paz; resto 0 (median 0,3)	1.3 (median number)
CTV-PTV margin	3 mm	6 mm cranio-caudal; 5 mm axial
days simulation-beginning of the treatment	12	18
Delivery Time	70 minutes	20 minutes

MR-LINAC 1.5T FOR THE TREATMENT OF PRIMARY BRAIN TUMOURS. PRELIMINARY ANALYSIS AND COMPARISON WITH OTHER TECHNIQUES

Code: 404

Aims: MR imaging is the standard of care for identification and follow-up of primary brain tumours. The use of MRI increases accuracy of differential diagnosis between tumour, oedema and high- and low-grade disease. Identification of tumour (T) volumes and organ at risk (OAR) is the central part of the radiotherapy process. Accuracy in identification of Gross tumour volume (GTV) is very high using MRI allowing to decrease CTV volume.

Methods: The data of patients (pts) treated between 9-2022 and 12-2023, after MR-simulation, with MR-Linac IMRT and Helical IMRT are being collected in terms of response, dosimetry data and acute toxicities.The preliminary data about pts treated with MR-Linac are reported. All the pts were included in the prospective Ryma-trial.

Results: All pts with primary brain tumour but those with contra-indication to the use of MR (metallic prothesis, claustrophobia, pacemaker etc) were simulated with MR.
MRI simulation with e.v. contrast consented the identification of early recurrence in 3 patients. Differences in pts and treatment planning features between those treated with IMRT with MR-Linac and with Helical IMRT are showed in Tab.
All the pts treated with MR-Linac, having both hypo and normo-fractionated RT, received chemotherapy with Temozolomide concomitant to RT. Treatment volumes were identified on simulation MRI-T2 and T1 sequences; T2 flair and T1 with contrast were also acquired and used. Organs at risk (optic nerves, optic chiasma and hippocampus) were more easily identified using T1 sequences; differential identification of oedema and low-grade disease was performed using T2 flair sequences. All pts were treated with "Adapt to Shape" workflow using T2 sequences, with daily identification of target and OAR and online replanning. In-room time was slightly longer than that observed in patients treated with Helical IMRT.
Changes in CTV related to target position were daily adapted. T2-MR daily sequences consented to anticipate symptoms related to the oedema in 50% of the cases, prescribing low steroid dose.

Conclusions: The treatment of pts with primary CNS tumours is feasible and safe on MR-Linac. The different MRI sequences, both during the simulation and the treatment, consent the differential identification of tumour and other different conditions. Data regarding toxicity and differences between pts treated with Helical- IMRT are being collected. The personalization of the treatment based on differences in MR features is the next challenge of the therapeutic approach.

	IMRT with MR-Linac	Helical IMRT
Number of patients	41	16
Sex M	21	7
Histology		
glioblastoma	35	10
Astrocytoma	1	3
oligodendroglioma	5	2
other	0	1
Hypo-fractionation	22/44	7/16
CTV-PTV margin	3mm	5 mm axial; 6 mm cranio-caudal
Recurrence/progression identification during RM simulation	3/41	0
In room time	30-40 minutes	20 minutes
days between simulation - RT beginning	9	15,2

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DOSIMETRIC PREDICTORS OF LATE LYMPHOPENIA IN PROSTATE CANCER PATIENTS UNDERGOING WHOLE-PELVIS RADIOTHERAPY: A MULTI- INSTITUTIONAL PROSPECTIVE COHORT STUDY

Code: 562

Aims: This study aims to identify clinical and dosimetric factors predictive of late hematological toxicity (HT) in prostate cancer (PCa) patients undergoing whole-pelvis radiotherapy (WPRT) through a prospective multi- institutional cohort investigation.

Methods: A multi-center institutional review board-approved study (IHU) commenced in September 2012 to assess predictors of toxicity in WPRT, including HT. PCa patients receiving radical or post-surgery radiation were followed for 5 years. Preliminary findings on dose-volume histogram (DVH) predictors of HT were previously reported. Four pelvic bone volumes were delineated: iliac bones, lumbosacral spine, lower pelvis, and whole pelvis. DVHs were generated, and integral doses were computed. Blood tests monitored lymphocytes, neutrophils, hemoglobin, platelets, red blood cells, and white blood cells. Late grade≥2 (G2+) lymphopenia, defined as absolute lymphocyte count (ALC) <800/μL at 2 years post-RT, was the primary outcome. Mann–Whitney tests and logistic regression analyzed DVH parameters and clinical covariates for association with G2+ lymphopenia.

Results: Data from 499 patients were analyzed. Late G2+ lymphopenia incidence was 9.2%. Univariate analysis identified ALC at baseline, smoking status, and lumbosacral DVH (specifically V24Gy, Figure 1) as significant predictors. Performance statistics (average precision: 0.45, F1 score: 0.4, ROC curve AUC: 0.87, McFadden's pseudo-R-squared: 0.27) were calculated. Including acute G3+ lymphopenia improved the model (average precision: 0.52, F1 score: 0.42, ROC curve AUC: 0.88, McFadden's pseudo-R-squared: 0.32).

Conclusions: Lymphopenia post-WPRT for PCa is notable, with a 9.2% 2-year incidence of G2+ lymphopenia. Lumbosacral DVH emerged as a key dosimetric predictor, along with baseline ALC and smoking status. Additionally, acute G3+ lymphopenia correlated with long-term persistence, underscoring its significance in predicting late HT.

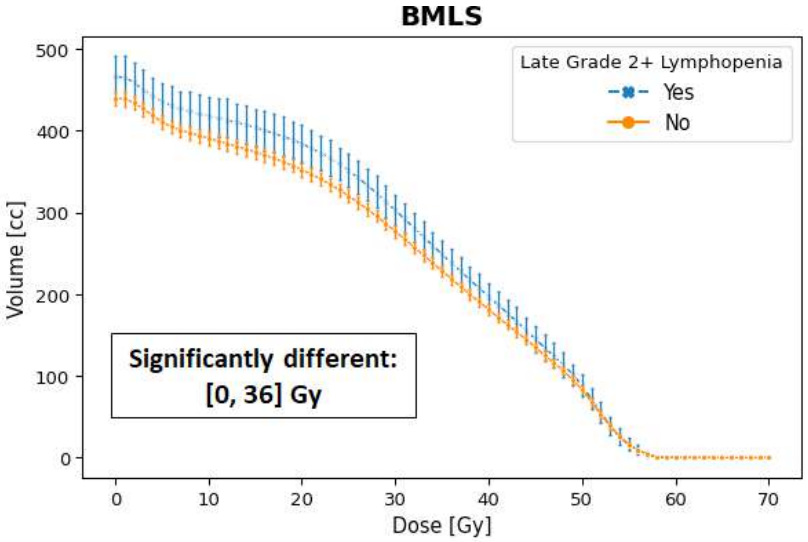

Figure1. Dose-volume histogram (DVH) of lumbosacral spine (BMLS) stratified by the presence of Late Grade 2+ Lymphopenia. DVH parameters from V0Gy to V36Gy resulted significantly different in the two groups with respect to the Mann–Whitney U tests. V24Gy was found to have the lowest p-value.

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CLINICAL PREDICTORS OF LATE GRADE 2+ LYMPHOPENIA FOLLOWING WHOLE-PELVIS RADIOTHERAPY FOR PROSTATE CANCER: A COMPREHENSIVE COHORT STUDY

Code: 551

Aims: To identify predictors of G2+ lymphopenia 2 years post-whole pelvis radiotherapy (WPRT) for prostate cancer (PCa), encompassing various intensity-modulated radiotherapy (IMRT) techniques and intentions.

Methods: Started in 2011, an initial study (IHU) assessed toxicity from WPRT for PCa. The IHU WPRT-TOX prospective cohort study (NCT02803086) extended the research from 2012 across multiple institutes. Data comprised health, comorbidities, and smoking habits, with blood tests collected over a 5-year period to monitor hematological parameters and RT details. Planning Treatment Volume for lymph nodes (PTVLN) data were extracted to explore potential effects on pelvic bone marrow (BM).
Acute G3+ (ALC<500/µL at mid/end of RT) and late G2+ lymphopenia (ALC<800 µL at 24/30 months post-RT) were defined as endpoints. 499 patients with blood tests at specific time points (baseline, mid/end RT, 3-6, 12-18, and 24-30 months) were included. Analysis considered 18 variables, underwent preprocessing with univariate logistic regression and pairwise Spearman correlation tests. The training phase used a backward stepwise multiple logistic regression model retaining variables with $p<0.05$. Internal validation included 1000 bootstrap replicates for model robustness assessment.

Results: Late G2+ lymphopenia occurred in 9.2% of patients. Multivariate analysis identified significant predictors: baseline absolute lymphocyte count (ALC) (HR=0.997, 95% CI=0.996-0.998, $p<0.003$), smoking status (HR=2.774, 95% CI=1.21-6.22, $p=0.016$), and craniocaudal (C-C) extent from L5 (HR=1.016, 95% CI=1.004-1.027, $p=0.01$). Internal validation metrics included average precision (0.43), F1 score (0.4), ROC curve AUC (0.87), and McFadden's pseudo-R-squared (0.26). When acute G3+ lymphopenia was included, it remained an independent predictor (HR=4.343, 95% CI=1.894-9.956, $p=0.0005$), improving average precision (0.5), F1 score (0.4), ROC curve AUC (0.88), McFadden's pseudo-R-squared (0.31). Cut-off values for predicting G2+ lymphopenia were baseline ALC<1835.4/µL and C-C extent>12 mm. Figure 1 illustrates the risk over a 2-year period against baseline ALC, stratified by smoking status and C-C extent.

Conclusions: G2+ lymphopenia 2 years post-RT is notable in a substantial rate of patients, with baseline ALC playing a significant role. C-C extent emerged as an independent predictor, emphasizing the importance of BM- sparing techniques during treatment planning.

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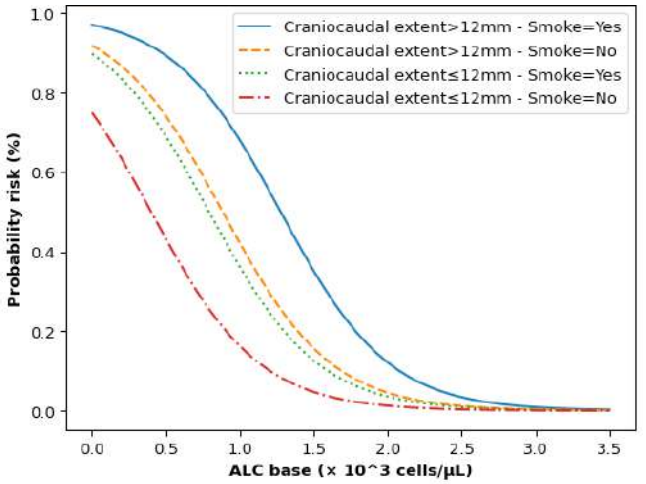

Figure1. Probability risk for 2-year G2+ lymphopenia resulted by the dichotomization of craniocaudal extent above and below the cut-off value (12mm) which maximizes Youden's index for the ROC curve.

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CLINICAL VALIDATION OF A DEEP LEARNING-BASED SEGMENTATION MODEL FOR PROSTATE CANCER RADIATION THERAPY PLANNING

Code: 124

Aims: In prostate cancer radiation therapy planning, image segmentation is vital for treatment quality, plan optimization, and radiation dose accuracy. Manual contouring is time-consuming and operator-dependent, leading to inconsistency. This study aims to validate the RayStation (RaySearch Laboratories, Stockholm, Sweden) auto-segmentation module for prostate cancer and assess the agreement between automatically and manually contoured volumes.

Methods: Computed tomography images from 25 prostate cancer patients were used. Three operators manually segmented the prostate gland (CTV), bladder, rectum, and femoral heads (OARs) to evaluate inter- observer variability. Automatic segmentation was performed using the "Pelvic Male CT" module on RayStation. Agreement was assessed using overlap metrics (Dice Similarity Coefficient - DSC) and distance metrics (Hausdorff Distance - HD, Average Hausdorff Distance - AHD, HD 95th percentile). Factors affecting agreement, such as region of interest (ROI) type and operator expertise, were tested by MANOVA.

Results: Overall, there was good agreement between automatic and manual contours (Table 1). Mean DSC and AHD values were 0.878 and 1.935 mm, respectively; no significant ROI volume differences were found. Sub-analyses showed excellent agreement for bladder (DSC = 0.952, AHD = 1.036 mm), high agreement for rectum (DSC = 0.838) with a significant volume overestimation by DL segmentation, excellent agreement for femoral heads (DSC > 0.9) with slight volume differences for right-sided ROIs, and good agreement for prostate gland (DSC = 0.76) with DL segmentation tending to overestimate volume. ROI type significantly influenced agreement ($p = 0.001$ for all metrics), while the operator did not ($p \geq 0.303$ for all metrics).

Conclusions: RayStation's auto-segmentation model demonstrated excellent agreement with gold standard contouring for OARs and CTV in prostate cancer. Implementation in clinical practice reduced contouring time significantly. However, clinicians need to review and correct potentially inaccurate segmentations impacting dose accuracy.

ROI	DSC (± SD)	HD (± SD, mm)	AHD (± SD, mm)	HD95 (± SD, mm)	Volume differences
Overall	0.878 (± 0.097)	14.683 (± 10.025)	1.935 (± 1.049)	7.543 (± 4.87)	Non-significant (p = 0.319)
Bladder	0.952 (± 0.03)	7.283 (± 9.103)	1.036 (± 0.858)	3.382 (± 4.463)	Non-significant (p = 0.707)
Rectum	0.838 (± 0.055)	21.346 (± 9.556)	2.325 (± 1.094)	9.453 (± 4.434)	Overestimation of DL contour (p = 0.003)
Femur_Head_L	0.926 (± 0.028)	14.931 (± 11.053)	1.645 (± 0.831)	7.89 (± 5.564)	Non-significant (p = 0.14)
Femur_Head_R	0.914 (± 0.025)	16.386 (± 7.767)	1.882 (± 0.601)	9.417 (± 3.956)	Overestimation of DL contour (p =0.0059)
CTV	0.76 (± 0.13)	13.468 (± 6.8)	2.79 (± 0.880)	7.574 (± 2.955)	Overestimation of DL contour (p = 0.0089)

Table 1: DSC values and distance metrics (HD, AHD, and HD95) and statistical significance level of volume differences between manual vs automatic segmentation for each ROI.

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CLINICAL OUTCOMES OF STEREOTACTIC BODY RADIOTHERAPY FOR LOCALIZED PROSTATE CANCER: A SINGLE CENTER EXPERIENCE

Code: 546

Aims: This study aimed to evaluate the clinical outcomes of patients who underwent stereotactic body radiotherapy (SBRT) for localized prostate cancer at the Radiotherapy division of the Regional Hospital "Umberto Parini" in Aosta, Italy.

Methods: Between January 2016 and December 2023, 141 patients (mean age = 74.8 ± 6.2 years) diagnosed with prostate cancer (low or intermediate risk according to NCCN guidelines) received SBRT treatment. Approximately half (51%) received short course (4-6 months) androgen deprivation therapy (ADT) before, during and after SBRT. The prescribed RT dose was 36.25 Gy delivered in 5 fractions every other day by TomoHelical IMRT (Accuray Inc, Sunnyvale, CA, USA). Clinical outcomes assessed included:
Acute and late genitourinary (GU) and gastrointestinal (GI) toxicity at 6, 12, 24, 36, and 60 months post-SBRT completion.
Survival endpoints, including overall survival (OS), cancer-specific survival (CSS), and disease-free survival (DFS).

Results: At the end of SBRT, 82 patients (58.2%) experienced GU toxicity (G1: 43.3%, G2: 14.2%, G3: 0.7%). Most toxicities resolved during follow-up, with rates of G0 toxicity at 6, 12, 24, 36, and 60 months being 70.7%, 74.4%, 76.7%, 79.1%, and 73.7%, respectively. No GU toxicity ? G2 was observed at 5 years post-treatment. Regarding GI toxicity, only 16.3% of patients experienced adverse events at the end of treatment (G1: 14.9%, G2: 1.4%), which also tended to resolve over time (G0 rates at 6, 12, 24, 36, and 60 months were 97%, 97.6%, 93.3%, 95.3%, and 94.7%, respectively). Survival analysis was performed on 94 patients with a minimum follow-up of 6 months (median: 37.3 months, range 6.7-83.7 months), revealing 7 deaths, with only one attributable to malignancy, and 5 cases of disease recurrence. Survival endpoints were as follows (Figure 1):
- OS: 100% (12 months), 93.5% (36 months), and 89% (60 months).
- DFS: 98.8% (12 months), 89.6% (36 months), and 85.3% (60 months).
- CSS: 100% (60 months) and 90.9% (72 months).

Conclusions: SBRT was associated with excellent results in terms of survival endpoints for patients with localized prostate $_{cancer,}$ with low rates of side effects.

Figure 1

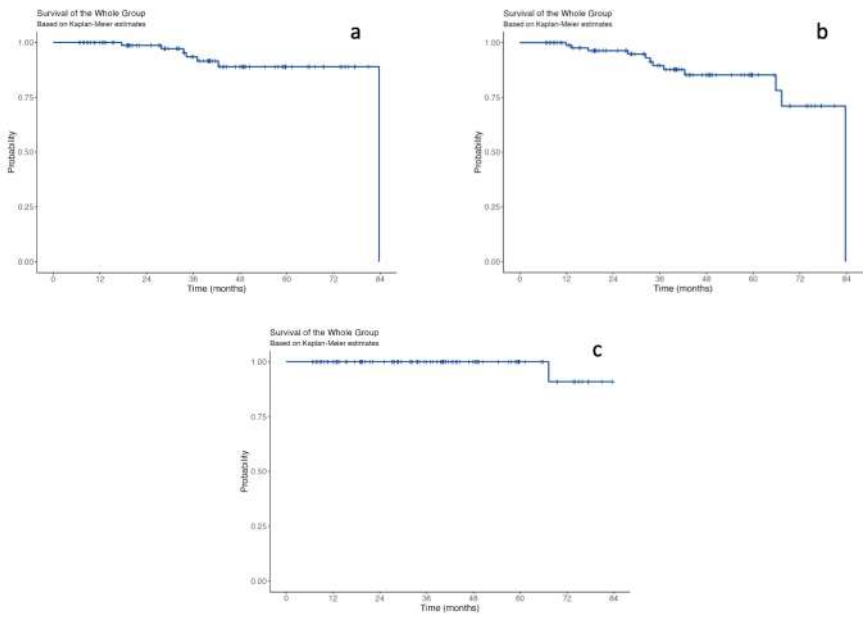

Figure 1: Kaplan-Meier curves for OS (a), DFS (b) and CSS (c)

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PATTERNS OF LOCO-REGIONAL FAILURE IN PATIENTS WITH NON-METASTATIC HEAD AND NECK SQUAMOUS CELL CANCER TREATED WITH CHEMOTHERAPY AND IMRT

Code: 249

Aims: To evaluate the patterns of failure in patients with non-metastatic head and neck squamous cell cancer (NMHNSCC), undergoing chemotherapy and intensity-modulated radiation therapy (IMRT).

Methods: We retrospectively analyzed NMHNSCC patients treated in our department from January 2021 to April 2023, matching the following inclusion criteria: age >18 years, availability of 18F-FDG CT/PET before and after the treatment, T3-4 N+ disease, adjuvant or exclusive concurrent chemoradiation therapy (cCTRT) +/- induction chemotherapy (iCT). Prescribed doses were organized as follows: CTV1 54 Gy (1.8 Gy/die), CTV2 60-62 Gy (2-2.07 Gy/die), GNV 63-66 Gy (2.1-2.2 Gy/die), GTV 66-69 Gy (2.2-2.3 Gy/die). Treatment volumes extension was determined according to international guidelines. Time of treatment, interruptions, dose prescriptions, sites of progression, and histopathological features were analyzed.

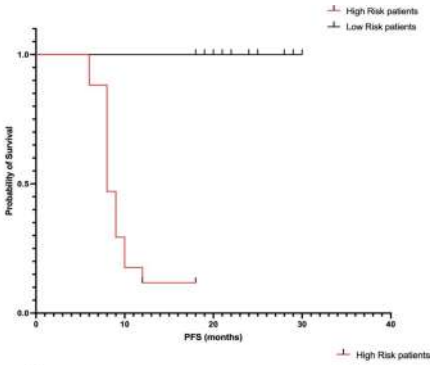
Results: From an initial number of 105 patients, 31 eligible patients were collected. Median age was 65,8 years (range 53-72 years). Median time of follow-up was 18,6 months. 14 patients (45,2%) with nodal staging ranging from N1 to N2b, with end of treatment delay (EoTD) <5 days, achieved a complete metabolic response. 12 (85,71%) of them being EBV- and 7 (50%) of them undergoing iCT before cCTRT.
2 patients (6,4%) with N2c nodal stage showed no response with persistence of disease. 15 patients (48,4%) didn't achieve complete remission andexperienced tumor progression, in areas with delivered dose ranging from 52,97 to 61,76 Gy; of these, 12 patients (70,58%) having N2c-N3 and 5 patients (33,33%) EBV+ disease; EoTD for toxicities was between 5 and 15 days, being ≥10 days in 9 (60%) of them. EoTD >5 days and PFS <10 months reduce the probability of survival, in high risk patients (with N2c-N3 and/or EBV+ disease). Overall Survival (OS) was 80,54%. Median Progression Free Survival (PFS) was 15.2 months.

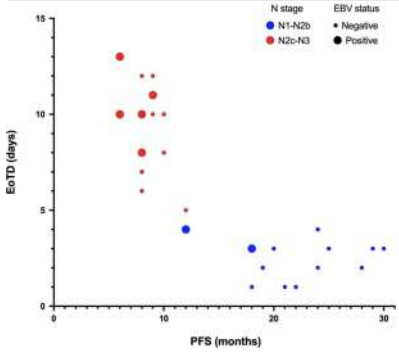
Conclusions: This study shows the role of a correctly timed radiotherapy without long delays, which could compromise the patients' clinical outcome, being worse in patients with EBV+ disease and high tumor burden. It was also confirmed that patients, not achieving complete remission, experience disease progression in sites located outside the GTV/GNV, but still included in the low/intermediate risk CTV (CTV1/2). Thus, patients with tumor progression after chemoradiation should be included in clinical trials testing immunotherapy, alone or with chemotherapy.

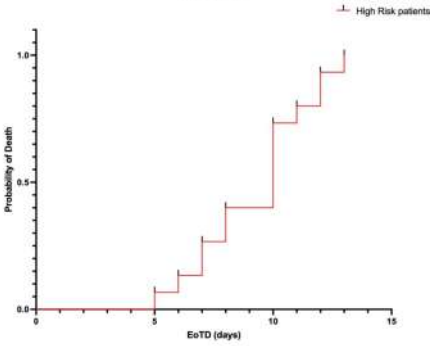
N stage	N1-N2b	N2c-N3
EBV + patients	2	5
EoT Delay (days)	<5	5-15
Patients with disease progression	3 patients	12 patients
Stable disease	/	2 patients

Legenda:

- EoTD = End of Treatment Delay
- PFS = Progression Free Survival







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PROSTATE STEREOTACTIC BODY RADIOTHERAPY WITH A MRI DEFINED FOCAL SIMULTANEOUS INTEGRATED BOOST TO THE DOMINANT INTRAPROSTATIC NODULE

Code: 55

Aims: Stereotactic body radiotherapy (SBRT) represents an effective curative option for localized prostate cancer. Although localized prostate cancer is multifocal, there is a general consensus that dominant intraprostatic nodule (DIN) is mainly responsible for disease progression after radiation therapy. The addition of a focal boost to the DIN is an emerging strategy to potentially improve tumor control in patients with organ-confined prostate cancer.

Methods: Between May 2020 and June 2023, 44 patients with clinically localized prostate cancer, having a mean age of 72 years (range 56 - 83) and with a mean iPSA of 8.6 ng/ml (range 2.7 - 44.7) underwent Cyberknife stereotactic radiotherapy treatment. According to the D'Amico definition, 10 of them (23%) had low risk, 26 (59%) intermediate and 8 (18%) high risk disease. Most of the patients (52%) had 3+4 or 4+3 Gleason Score. All patients received 37.5 Gy in 5 consecutive fractions to the whole prostate gland, having an average volume of 66 cm (range 31-138), while an integrated boost up to a total dose of 50 Gy was applied to the DIN detected on the multiparametric MRI, having an average volume of 1.58 cm (range 0.28 - 5.40). 29 patients (66%) had PI-RADS 4 lesions and 10 patients (23%) had PI-RADS 5 lesions. 6 patients (4 high risk and 2 intermediate risk disease) recived concomitant and adjuvant HRT for 12 months mean time (range 4 - 36). Real time intrafractional motion tracking was used.

Results: The mean IPSS before treatment was 15 (range 1 - 22) and no worsening was found during the acute phase. The most common GU complains were urinary urgency and aggravating nocturia, while increased stool frequency was the main GI symptom. Cumulative acute G1-2 GU toxicity rate was 27.3%. In one patient TURP was necessary for acute G3 incontinence. No GI acute toxicity G2 was observed. With a mean follow up of 16 months (range 6 - 36) mean PSA was 0.9 ng/ml (range 0 - 3.5), biochemical failure was observed in 1 intermediate risk disease patients 12 months after the treatment.

Conclusions: Simultaneously integrated boost to the DIN was well tolerated with similar acute GU and GI toxicity rates compared with historical prostate SBRT cohorts, mainly due to the more and more proven ability of current technologies to minimize treatments adverse effects. Longer follow-up is required to confirm long term results, both for tumor control and late toxicity.

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CYBERKNIFE FRACTIONATED STEREOTACTIC RADIOTHERAPY FOR UVEAL MELANOMA

Code: 52

Aims: We report our clinical experience of a hypofractionated Cyberknife radiotherapy treatment for uveal melanoma.

Methods: We retrospectively evaluated 66 patients, mean age 67 years (range 36 - 90) suffering from uveal melanoma (63 choroidal melanoma and 3 ciliary body melanoma) treated by Cyberknife, between April 2014 and December 2022. All the patients had received a

diagnosis and referral from an ophthalmologist. Cyberknife robot-controlled LINAC radiosurgery was performed delivering a mean total dose of 56 Gy (range 54 - 60) given in mean 3 fractions (range 3 - 5) of mean 18 Gy (range 11 - 20) prescribed to a mean 81% (range 79 - 85) isodose surface. All patients underwent orbit MRI with gadolinium (1 mm thickness) for coregistration with the planning CT scans. The planning target volume (PTV) included the contrast-enhancing lesion on MRI (GTV = CTV) plus 2.5 mm margins in all directions. All patients were irradiated eyelids closed, with a bandage on it, using a contention with a thermoplastic mask. For 15 patients tantalium markers were sutured to the sclera around the tumor. At presentation the mean PTV volume was 1815 mm^3 (range 100 – 5792), mean tumor base 11 mm (range 4-20) and mean thickness 5 mm (range 2-10) measured ultrasonographically.

Results: After a mean follow-up of 40 months (range 6 – 111) local control was achieved in all the patients, 6 (9%) developed and died for distant metastases. We observed a reduction of 9% in mean base and of 40% in mean thickness at the last follow-up. The most common side effects were radiation maculopathy (mostly with edema) reported in 57% of patients, cataract (26%), choroidal ischemia (34%) and radiation neuropathy (19%). 12 patients (18%) suffered of retinal detachment and 6 patients (9%) of neovascular glaucoma which required enucleation in 5 patients (8%). To reduce toxicity intravitreal anti-VEGF (+/- photodynamic therapy) and steroids 4 months after the treatment were performed to the 63.6% of patients. Visual acuity was reduced in 52 patients (79%), increased in 7 (10.5%) while in the others 7 patients (10.5%) no change was found.

Conclusions: Our results are consistent with data in literature and show a safe, minimally invasive, and well tolerated method for treating uveal melanoma. The main limitation is that it is a retrospective study. Continued accrual and follow-up are required to confirm long term results.

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BREAST CANCER RADIOTHERAPY AFTER NEOADJUVANT SYSTEMIC THERAPY: A RETROSPECTIVE EVALUATION

Code: 96

Aims: The increasing use of neoadjuvant chemotherapy (NAC) in high-risk, locally advanced breast cancer (BC) patients has resulted in treatment issues for radiation oncologists, caused by few studies in this setting of patients. The aim of this study is to evaluate patients undergoing NAC and adjuvant RT in terms of clinical outcomes and to assess the value of pathologic complete response (pCR) after NAC and the time from surgery to RT.

Methods: We retrospectively analyzed BC patients treated in our RT Unit. All patients underwent NAC followed by breast conserving surgery (BCS) or mastectomy. Whole breast RT with or without supraclavicular nodes RT was performed. Loco-regional recurrence (LRR), disease-free survival (DFS) and overall survival (OS), were measured from surgery until first event and all time to-event distributions analyzed with the Kaplan–Meier method to calculate the DFS and OS rates at 5 years. RTOG scales were used for acute RT toxicity evaluation. pCR was defined as the absence of residual invasive disease in the breast and lymph nodes. The time to start of RT was calculated as the interval between the date of surgery and the first day of RT obtaining 2 group: patients undergoing RT until and after 4 months.

Results: One-hundred and ten BC patients undergoing NAC and treated between 2014 and 2020 were retrospectively analyzed. The median age was 51 years (range=29-80). Patients, tumor and treatment characteristics are summarized in table 1. NAC was prescribed according to staging and tumor biology. After NAC, 42% of patients underwent BCS, while 58% underwent mastectomy; axillary dissection was performed in 64% of patients. All patients underwent adjuvant RT: conventional fractionation was chosen in 24%, while in 76% a moderate hypofractionation was used; 73% of patients underwent supraclavicular lymph node RT. The median follow up was 37 months (range=14-109) with a LRR of 6%. 5-years OS and DFS were 78% and 73% respectively. Time to RT 2.

Conclusions: NAC resulted effective in downstaging tumor before local treatment: about one third of our patients achieved a pCR. In this setting of patients, performing RT until 4 months could ensure a better results ment in terms of OS. More studies are needed in order to strengthen clinical guidelines.

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Table 1. Patients, tumor and treatment characteristics

Patients	**n (%)**	**Patients**	**n (%)**
Age (years)range	51 (29-80)	**Pathological Tumor Stage**	
Clinical Tumor stage		ypT0-Tis	38 (34)
cT1	7 (6)	ypT1a	12 (11)
cT2	50 (46)	ypT1b	9 (8)
cT3	28 (25)	ypT1c	18 (16)
cT4	25 (23)	ypT2	24 (22)
Clinical Nodal stage		ypT3	5 (5)
cN0	25 (23)	ypT4	4 (4)
cN1	72 (65)	**Pathological Nodal Stage**	
cN2	5 (5)	ypN0	54 (49)
cN3	8 (7)	ypN1mic	5 (5)
Clinical Molecular subtypes		ypN1a	21(19)
Positive Hormonal Receptors	29 (26)	ypN2	22 (20)
HER2+	54 (49)	ypN3	8 (7)
Triple negative	27 (25)	**Hystological Type**	
Neoadjuvant Therapy		Ductal	62 (56)
Antracyclines + Taxanes	40 (36)	Lobular	5 (5)
Chemotherapy + Trastuzumab	54 (49)	Other	5 (5)
Other	16 (15)	Not evaluable (pCR)	38 (34)
Clinical Response		**Grade**	
Complete Response	12 (11)	1	4 (4)
Partial response	63 (57)	2	39 (35)
No Response	12 (11)	3	37 (34)
Not available	23 (21)	Not evaluable (pCR-pT0)	30 (27)
Type of Surgery		**Nodal Ratio**	
BCS	46 (42)	0	55 (50)
Mastectomy	64 (58)	< 0.5	40 (36)
Axillary Dissection		≥ 0.5	15 (14)
Yes	70 (64)	**Adjuvant Therapy**	
No	40 (36)	Yes	93 (85)
BRCA 1-2		No	17 (15)
Wilde Type	23 (21)	**Radiotherapy**	
Mutate	7 (6)	Hypofractionaction	84 (76)
Not available	80 (73)	Conventional fractionaction	26 (24)

A DEEP LEARNING-BASED TOOL FOR AUTOMATIC SEGMENTATION IN BREAST RADIOTHERAPY: VALIDATION AND EVALUATION

Code: 514

Aims: In this study, MIM Contour Protégé AI™ (MIM Software Inc., Ohio), a deep learning-based tool for automatic segmentation (AS), has been evaluated in breast cancer 3D-conformal radiotherapy using both quantitative and qualitative metrics.

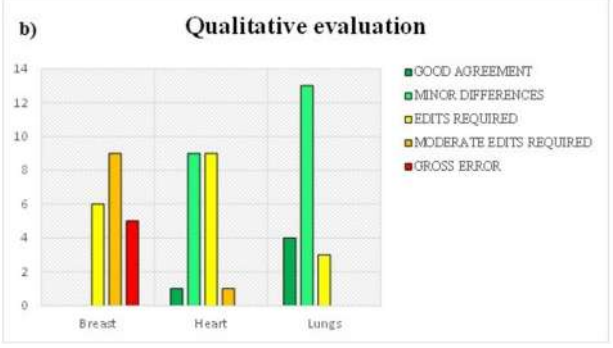
Methods: A retrospective analysis was performed on a mono-institutional cohort of 20 patients treated for breast cancer. Included anatomical structures were the left and right breast (LB and RB), heart (H), and left and right lung (LL and RL). The selected patients presented a large breasts volume variability: [123.0 – 1200.2 cm^3] for LB and [103.3 – 1152.8 cm^3] for RB. The 20 automatic structure sets were compared to the corresponding 20 manual Ground-Truth (GT) sets according to the Dice Similarity Coefficient (DSC) and Hausdorff Distance. Furthermore, MIM AS times were registered and manual correction times needed by a radiation oncologist (RO) to correct a complete structure set were collected. Simultaneously, RO performed a qualitative evaluation (QE) using a 5-degree scale (good agreement, minor differences, edits required, moderate edits required, gross errors).

Results: AS times resulted in a median value of 1.5 min per structure set and RO's manual corrections required a median time of 16.3 min. QE confirmed excellent results in both LL and RL recording no need for relevant edits in 17 out of 20 cases, accordingly to geometric evaluation which resulted in a median DSC of 0.98 for both lungs. H, LB, and RB showed DSC values lower than 0.80 (**Figure 1a**), although, H registered a better QE assessment, as reported in **Figure 1b**.

Conclusions: These preliminary results showed that the use of deep learning-based software in AS would allow for faster RT

Figure 1 – a) MIM performance in terms of Dice Similarity Coefficient and Hausdorff Distance. Median values and ranges are reported. Bold: not clinically acceptable. **b)** Qualitative evaluation of MIM contours performed by a radiation oncologist.

a)	**Dice Similarity Coefficicent**	**Hausdorff Distance**
Left breast	**0.74** [0.61 – 0.90]	45.88 [24.38 – 80.43]
Right breast	**0.73** [0.59 – 0.83]	51.95 [29.16 – 73.12]
Heart	**0.78** [0.61 – 0.86]	41.44 [31.23 – 60.21]
Left lung	0.98 [0.97 – 0.98]	25.33 [15.88 – 36.99]
Right lung	0.98 [0.96 – 0.99]	21.56 [16.30 – 45.70]



workflow thanks to very good performances in contour correctness and their significantly reduced segmentation times. However, breast AS is affected by differences, especially, in cranio-caudal definition. To further validate MIM AS capabilities, an on-going study is collecting results for other structures to be included in breast volumetric modulated arc therapy, and additional QE by other ROs.

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COMPREHENSIVE EVALUATION OF THREE DEEP LEARNING-BASED TOOLS FOR OARS AUTOMATIC SEGMENTATION IN CERVICAL CANCER RADIOTHERAPY

Code: 524

Aims: In this preliminary study, 3 automatic segmentation (AS) deep learning-based (DL) models were evaluated in OAR contouring in cervical cancer (CC) treatment, MVision (MV), LimbusAI (LI) and MIM (MM).

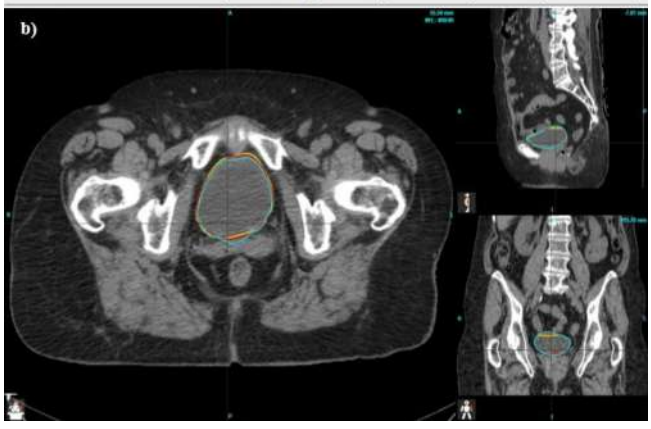
Methods: A mono-institutional consecutive series of 20 CC structure sets (SS), consisted in bladder, bowel bag, rectum, left and right femoral heads, were retrospectively selected to be auto-segmented by MV, LI and MM and compared, setting manual contouring as the Ground-Truth. AS times have been registered. Performances have been tested by comparing the resulting 60 sets by means of the Dice Similarity Coefficient (DSC) and the Hausdorff Distance (HD). The Wilcoxon-Mann-Whitney test has been performed to assess statistical significance ($p<0.05$).

Results: The median CC AS time per structure set was 0.7 min, 1.1 min, and 2.5 min for MV, LI, and MM, respectively. Geometric results are summarized in **Figure 1a**and an example of bladder AS is reported in **Figure 1b**. Rectum and bladder AS performance resulted comparable for all DL algorithms, which moreover had excellent DSC values for femoral heads contouring. Performances in bowel bag AS showed a dependence on cranial extension with statistically significant differences ($p<0.05$).

Conclusions: An on-going study is collecting AS correction times and qualitative scores to validate AS results. Female pelvis segmentation is known to be a difficult task, due to the high variability of the filling organs sizes. DL excellent performances in OAR contour correctness and their significantly reduced segmentation times would allow for faster RT workflow and high-quality treatments, possibly automatizing its running in the background. To further validate the capabilities of the DL models, an extension to other districts and a multicenter study are necessary.

Figure 1 – a) Comparison of automatic segmentation tools performance in terms of Dice Similarity Coefficient and Hausdorff Distance. Median values and ranges are reported. Bold: not clinically acceptable. **b)** A comparison example of cervical cancer automatic segmentation of bladder. *Legend: Yellow=MVision, Red= Limbus, Light Blue=MIM.*

a)	Dice Similarity Coefficient		
	MVision	LimbusAI	MIM
Bladder	0.95 [0.89 – 0.98]	0.94 [0.79 – 0.98]	0.94 [0.85 – 0.98]
Bowel bag	0.88 [0.74 – 0.94]	**0.79** [0.55 – 0.91]	0.89 [0.83 – 0.93]
Left femoral head	0.95 [0.81 – 0.97]	0.94 [0.77 – 0.95]	0.96 [0.76 – 0.97]
Right femoral head	0.95 [0.84 – 0.97]	0.95 [0.90 – 0.96]	0.95 [0.91 – 0.97]
Rectum	0.86 [0.11 – 0.93]	0.83 [0.75 – 0.92]	0.85 [0.69 – 0.94]
	Hausdorff Distance		
	MVision	LimbusAI	MIM
Bladder	13.31 [5.15 – 25.82]	13.82 [5.90 – 53.02]	13.18 [8.96 – 54.42]
Bowel bag	33.07 [25.96 – 80.92]	48.19 [26.47 – 118.29]	33.46 [24.21 – 44.04]
Left femoral head	16.24 [6.36 – 179.46]	15.98 [9.16 – 186.08]	15.15 [8.77 – 170.88]
Right femoral head	16.35 [6.77 – 55.28]	15.45 [6.70 – 58.62]	14.82 [6.94 – 52.89]
Rectum	23.81 [6.99 – 51.84]	23.32 [8.68 – 37.10]	19.89 [8.80 – 48.07]



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CONE BEAM COMPUTED TOMOGRAPHY AUTO- SEGMENTATION FOR PROSTATE CANCER RADIOTHERAPY: A DEEP LEARNING-BASED RESEARCH TOOL

Code: 278

Aims: A novel research tool on automatic segmentation (AS) of Cone Beam Computed Tomography (CBCT) images of male pelvis is available in Limbus Contour (LI) (v1.6.0-CBCT Limbus AI Inc, Regina, Canada). A geometric, time- based, and clinical qualitative evaluation was conducted for contouring the prostate (P), seminal vesicles (SV), rectum (R), bladder, and left and right femoral heads (LFH and RFH).

Methods: A mono-institutional consecutive series of 10 SBRTp patients was retrospectively selected. In addition to rectal micro-enema and bladder filling with 150 cc of saline solution, the selected patients were simulated and treated with a 16 French Foley catheter. The structure sets were LI auto-segmented and compared to manual Ground-Truth (GT) after retrieving selected CBCT images (120 kVp, 360° acquisition, 1mm-thick slices). A clinical AS validation was performed on a structure-based basis by recording LI time and radiation oncologist (RO)'s correction times. Furthermore, a qualitative evaluation (QE) was conducted using a 5 degrees-score (good agreement, minor differences, edits required, moderate edits required, gross errors). The 20 sets (10 LI vs 10 GT) were compared according to the Dice Similarity Coefficient and Hausdorff Distance.

Results: Manual contouring, LI AS, RO's manual correction registered a median time of 82.0, 1.1, and 41.5 min, respectively. As reported in **Figure 1a**, AS showed very good geometric results in P, R, B, LFH, RFH, while SV showed lower DSC values. QE showed a good agreement for femoral heads in 8 out of 10 cases, R and B required some edits, in 4 out of 10 SV moderate edits have been necessary. Although the registered high DSC values,all P structures showed gross contouring errors that required segmentation from scratch (**Figure 1b**).

Conclusions: A prostate SBRT offline evaluation with LI showed satisfactory DSC values. A strict institutional preparation protocol and soft tissue-bone interface contrast resulted in the best segmentation results for the rectum and femoral heads. The bladder catheter produced some inaccuracies, registering also the lowest DSC: air bubbles in the bladder caused an inaccurate cranial-anterior wall delineation. The errors in prostate and SV contouring, however, highlighted the need to improve CBCT image quality: an improved image pre-processing or reconstruction algorithm can allow more accurate segmentation.

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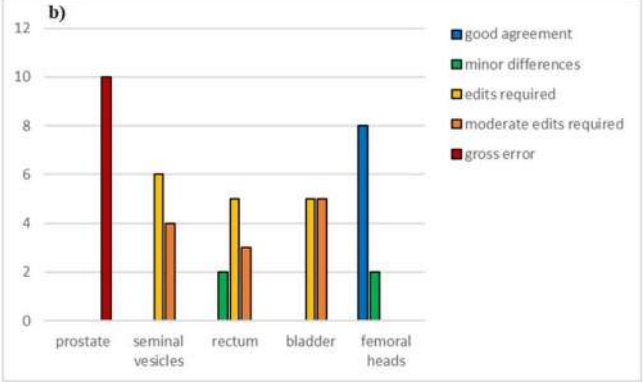
Figure 1 – a) Limbus performance in terms of Dice Similarity Coefficient and Hausdorff Distance. Median values and ranges are reported. Bold: not clinically acceptable. **b)** Qualitative evaluation of LI contours performed by a radiation oncologist.

a)	Dice Similarity Coefficient	Hausdorff Distance
Bladder	0.90 [0.45 – 0.95]	15.66 [10.95 – 34.81]
Rectum	0.84 [0.75 – 0.91]	20.52 [12.52 – 48.15]
Prostate	0.87 [0.72 – 0.88]	10.84 [7.66 – 14.37]
Seminal vesicles	**0.67** [0.54 – 0.77]	11.44 [7-08 – 15.19]
Left femoral head	**0.85** [0.79 – 0.92]	33.01 [20.26 – 42.15]
Right femoral head	**0.84** [0.78 – 0.87]	33.84 [27.21 – 43.05]



ULTRA-HYPOFRACTIONATION WITH SIMULTANEOUS INTEGRATED BOOST: LESS IS MORE?

Code: 503

Aims: Whole-breast irradiation (WB) following breast-conserving surgery (BCS) is recommended in some cases to enhance loco-regional control. Previous research has demonstrated that including a tumor bed boost improves local control, although it doesn't seem to affect overall survival. However, this approach may increase the risk of cosmetic issues. Furthermore, recent studies suggest that an ultrahypofractionated treatment schedule of 5 fractions over one week is non-inferior in terms of locoregional control and toxicity profiles. Nonetheless, the use of simultaneous integrated boost (SIB) in this context has been insufficiently investigated. This study focuses on the application of hypofractionation schemes coupled with SIB, in the context of whole breast radiotherapy (WB) with 2 different regimens.

Methods: Eligible patients had histopathological confirmed unifocal breast cancer planned for whole breast irradiation plus boost radiotherapy to the tumor bed. The study included two groups: Group 1 (60pts) received a total dose of 40.05 Gy to the WB and 47.55 Gy to the tumor bed in 15 fractions of 3.17 Gy, while Group 2 (20pts) received a total dose of 26 Gy to the WB and 29 Gy to the tumor bed in 5 fractions. Radiotherapy could be administered using either three-dimensional conformal radiotherapy (3D- CRT) or volumetric modulated arc therapy (VMAT). The primary study objectives were feasibility, safety, acute and long-term toxicities.

Results: We analyzed 80 patients treated by WB plus SIB, between November 2020 and December 2023, with a median follow-up time of 20 months. Acute and late toxicities, particularly fibrosis, were assessed according to the Lent/Soma scale. Acute toxicity was acceptable in both groups, with mild skin erythema observed. 37 (61.6%) pts and 4(6%) pts developed skin toxicity grade 1 and 2 respectively in group1; 9 pts (45%) 1 pts (5%) in group2. No other acute toxicities were observed. Regarding late outcomes, the rate of grade 1 breast induration underneath the SIB region was 2% in group 1 and 3% in group 2, respectively

Conclusions: In conclusion, the integration of hypofractionation with a SIB in WB presents a promising avenue for improving treatment efficiency without compromising efficacy. Hypofractionated (15fx)+SIB confirm to be a safe treatment without significant side effects, Ultra-hypofractionated (5 fractions over one-week)+SIB seems to be feasible and well tolerated, too. Although longer follow-up is necessary to confirm these results in this subgroup.

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HOLD YOUR BREATH SAVE YOUR HEART? MONOINSTITUTIONAL ANALYSIS AND OUTCOMES

Code: 519

Aims: Radiation therapy (RT) for left-sided breast cancer (LBC) carries a risk of cardiac toxicity, which is known to be dose-dependent. This study aimed to evaluate the effectiveness of RT using the moderate deep inspiration breath-hold (mDIBH) technique with the assistance of the Active Breathing Coordinator (ABC) in reducing cardiac exposure, specifically the mean heart dose (MHD) and doses to the left descending coronary artery (LAD). The study also assessed the feasibility of this technique across various doses and treatment volumes.

Methods: Data from LBC patients (stages 0-III) undergoing RT with ABC/mDIBH were collected prospectively. Inclusion criteria: left-sided RT eligibility, mDIBH tolerance, willingness for device training, and 20-second breath-hold ability. Primary endpoints: heart/LAD dose reductions, procedural success rates across different treatment schedules and target volumes, and a subgroup comparative dosimetry analyses.

Results: A cohort of 207 LBC patients (stages 0-III) was enrolled between November 2020 and July 2023. Of these, 195 underwent RT with ABC, achieving a procedural success rate of 94%. RT doses varied from ultrahypofractionated 26 Gy in 5 fractions(fx), to conventional 50 Gy in 25fx and standard 40 Gy in 15fx. In the ultrahypofractionated regimen, the Heart Dmean was 0.73 Gy, while the LAD mean and max doses were 1.83 and 5.49 Gy, respectively. In the conventional fractionation scheme, the Heart Dmean was 2.84 Gy, with LAD Dmean at 5.25 Gy and LAD Dmax at 11.68 Gy. Finally, in the standard fractionation scenario, the Heart Dmean was 0.90 Gy, while the LAD mean and max doses were 2.29 Gy and 8.98 Gy, respectively. Comparative analysis with free-breathing plans showed a significant reduction in MHD from 1.23 ± 0.64 Gy (free-breathing) to 0.90 ± 0.32 Gy (mDIBH) ($p < 0.0143$). Notable LAD sparing was also observed, with decreases in Dmax from 20.63 ± 12.42 Gy (free-breathing) to 8.98 ± 5.10 Gy (mDIBH) ($p < 0.0001$) and in Dmean from 4.64 ± 4.55 Gy (free-breathing) to 2.29 ± 0.86 Gy (mDIBH) ($p < 0.0073$). Among patients receiving 50 Gy with breast reconstruction (20 patients), the mean heart dose was 1.347 Gy, indicating significant dose sparing.

Conclusions: This study confirms the efficacy of mDIBH with the ABC device in reducing cardiac exposure during RT for LBC. It's a preferred approach for cardiac sparing, demonstrating feasibility and safety across treatments. Only 5% of patients faced ineligibility due to device issues or hearing impairment.

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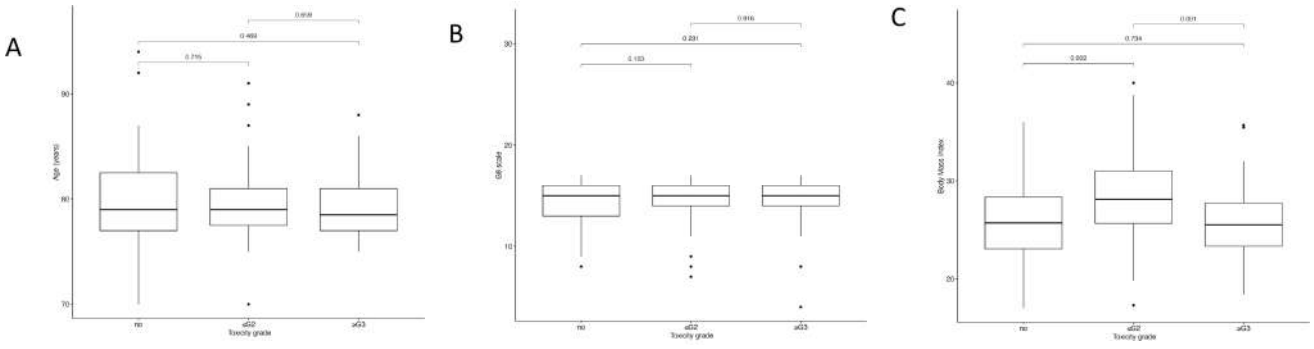
BODY MASS INDEX (BMI), G8 SCALE AND ACUTE RADIOTHERAPY (RT) TOXICITY: RESULTS FROM A MONO-INSTITUTIONAL EXPERIENCE

Code: 568

Aims: The impact of age, Geriatric 8 (G8) scale, and Body Mass Index (BMI) on Radiotherapy toxicity in elderly patients is still unclear. To estimate the correlation between BMI, G8 with Acute toxicity in an observational prospective cohort of cancer patients ≥ 75 years old undergoing Radiotherapy.

Methods: Elderly patients with cancers were evaluated by a dedicate Onco-Geriatric Team before starting RT course. Demographic, BMI with Interquartile (IQR) evaluation, and G8 were recorded at baseline. At the end of RT treatment course, acute RT toxicities were collected by Radiation Oncologists using RTOG scales. Wilcoxon test was used to verify the correlation between BMI, G8 and acute toxicity grade.



Results: 154 patients were enrolled, median age was 79 yrs (M 60% ; F 40%). At baseline, median BMI was **26** (IQR 23 - 28), **28.12** (IQR 26 - 31), and **26** (IQR 23 - 28); median G8 was **15** (IQR 13 - 16), **15** (IQR 14 - 16), **15** (IQR 14 - 16); median age was **79** (IQR 77 - 83), **79** (IQR 78 - 81), and **79** (IQR 77 - 81) in patients with no acute toxicity, ≤ G2, and ≥ G3 acute toxicity, respectively. The Wilcoxon test showed no correlation between G8, age and any grade of toxicity. On the other hand, median BMI was higher in patients with ≤ G2 acute toxicity compared to patients without acute toxicity (p-value = 0.002). Patients with ≥ G3 acute toxicity showed a median BMI lower than patients with ≤ G2 acute toxicity (p-value = 0.001) (See figure 1 A - B - C).

Conclusions: Age and frailty, such as identified by G8 scale, were not relevant for significant acute toxicity (≥ G3). BMI, as part of the multidimensional Onco-Geriatric assessment, could be used as a prognostic indicator to predict RT toxicity and compliance in elderly cancer patients.

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IS RAPIDPLAN A SUITABLE TOOL FOR PLANNING QUALITY ASSURANCE IN PROSTATE CANCER?

Code: 200

Aims: RapidPlan (RP) is a knowledge-based planning process implemented in the Varian Eclipse treatment planning system. The model estimates the DVHs of the organ at risk (OAR) to generate optimization objectives customized for the geometry of each new patient. In this analysis, a RP model was created and validated to evaluate the plan quality made with RP compared to plans created in a manual way for prostate cancer. The scope of this study is to determine if the use of RP is indicated as a planning QA tool and able to reduce the variability between users.

Methods: The RP model was fed with the planning data of 46 prostate Volumetric Modulated Arc Therapy (VMAT) plans. The patients were chosen as their plans were considered to be dosimetrically optimal. All plans were optimized for the VMAT technique, with two 6MV arcs. Inverse planning used the PO optimizer; the final calculations used AcurosXB. The dose prescription was 67.5 Gy (prostate lodge) and 52.5 Gy(nodes) to PTV_high and PTV_intermediate, respectively, in 30fractions. An overlap on the bladder and rectum was generated with a dose prescription of 66Gy to reduce acute toxicity.The model was validated on 10 cases of new patients by comparing RP model plans against manual clinical plans optimized according to the clinical dose constraints to OAR, including the rectum, bladder, femoral heads, penile bulb, cauda, and bowel. The variability between planners was assessed on a set of 10 new patients: for each of them 4 different planners created 2 plans, one with and one without RP.

Fig.1

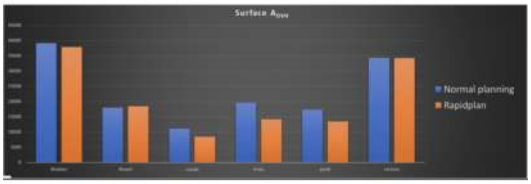
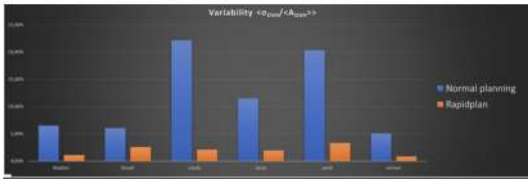


Fig.2



Results: In the validation model of 10 cases, the RP model can estimate the dose comparable to the target volume of the manual clinical plan, which evaluated values of Dmax, D95%, D98%, HI, and CI and showed comparable results. The RP model exhibited a better dose for OAR than the manual clinical plan, which is interesting to highlight suboptimal plans with a simple comparison (Fig1). Moreover the dosimetric variability of the plans made with RP is substantially reduced (Fig2). An unexpected gain was also the capacity to create automatically cold boosts in the overlap region without using a dedicated optimization structure.

Conclusions: The Varian RP KB planning can produce better OAR sparing without increasing plan complexity and was introduced as a planning QA method in our department. Moreover, the RP model can enhance the efficacy and quality of plans, reducing the variability between planners.

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MRI-GUIDED STEREOTACTIC BODY RADIATION THERAPY FOR VERY ELDERLY PATIENTS WITH LUNG CANCER: A RETROSPECTIVE ANALYSIS OF SAFETY AND EFFICACY PROFILES

Code: 281

Aims: Non-small cell lung cancer (NSCLC) is the most common malignancy of the lung. Although it is usually diagnosed at an early stage, in very elderly patients who are medically inoperable due to comorbidities, stereotactic body radiotherapy (SBRT) could be used as a potential curative option.

This retrospective analysis aimed to investigate the efficacy and safety of MRI-guided SBRT (MRIgSBRT) for NSCLC patients aged ≥75 years old, assessing the clinical impact of this approach on local recurrence (LR), progression of disease (PD) and overall survival (OS).

Methods: Data of patients aged ≥75 years old with a diagnosis of NSCLC, treated in our Institution between 2017 and 2023, were retrospectively collected. The analysis of the survival curves in terms of OS, Local recurrence free survival (LRFS) and Progression free survival (PFS) were estimated using the Kaplan- Meier method. An overall evaluation of the treatment outcomes and the toxicity profiles, assessed using the Common Terminology Criteria for Adverse Events (CTCAE scale version 5.0), was performed.

Results: With a median follow up of 16.9 months (range 0,97-66,70), the study included 39 NSCLC patients (14 females and 25 males) with a median age of 82 years old (range: 75-87) and a median Charlson score of 6 (range: 5-12). The definite evaluation of 45 lesions (6 patients have been treated on two referred lesions) was performed. The examined were treated with MRIgSBRT with a median total radiotherapy dose of 62,5 Gy (range 24-75 Gy) delivered in 5 fractions (range 3-8) between June 2017 and August 2023. The 1-, 2-, 3- year OS rates were 98%, 96% and 80%, respectively while 1-, 2-, 3- year PFS were 82%, 51%, 45%, respectively and the 1-,2-,3- year LRFS was 97,5%. The reported toxicities included acute G2 pulmonary toxicity in 4 patients (10,26%), while as tardive toxicities G1 post-actinic asymptomatic lung consolidations in 6 patients (15,38%) and G2 dyspnoeic toxicity in 1 patient (2,56%).

Conclusions: MRIgSBRT is shown to be a valid therapeutic option, both in terms of tumoral control and tolerability, in very elderly patients aged ≥75 years old with comorbidities and competing risk factors that limit their own performance status and their eligibility for other invasive strategies.

Characteristics	N (%)
Patients	39
Lesions	45
Median Age (years) (range)	82 (75-87)
Gender	
F	14 (35.9)
M	25 (64.1)
Median Follow-up (range)	16.87 (0.97-66.70)
Charlson score	
5	4 (10.3)
6	14 (35.9)
7	7 (17.9)
8	5 (12.8)
9	1 (2.6)
10	6 (15.3)
11	1 (2.6)
12	1 (2.6)
T stage	
1a	5 (11.1)
1b	13 (28.9)
1c	8 (17.8)
2	6 (13.3)
3	2 (4.4)
4	5 (11.1)
GTV (cc), median (range)	3.6 (0.4-61)
PTV (cc), median (range)	10.05 (1.9-83.9)
Histology	
Adenocarcinoma	22 (48.89)
Squamous cell carcinoma	2 (4.44)
Mixed adenocarcinoma	1 (2.22)
Unclassified NSCLC	2 (4.44)
LC-NEC and SCLC	1 (2.22)
N/A	17 (37.78)
Prescribed dose (Gy), median (range)	62.5 (24-75)
24	1 (2.2)
50	10 (22.2)
62.5	26 (57.7)
68.75	6 (13.3)
75	2 (4.4)
Fractions	
3	1 (2.2)
5	42 (93.3)
8	2 (4.5)
BED, median (range)	117.19 (36-136.07)

Table 1: Patient characteristics

GTV: gross tumor volume; PTV: planning target volume; NSCLC: non-small cell lung cancer; LC-NEC: Large cell neuroendocrine carcinoma ; SCLC: small cell lung cancer; BED: biologically effective dose

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ACUTE AND LATE TOXICITIES IN ULTRA- HYPOFRACTIONATION OF BREAST RADIOTHERAPY: OBJECTIVE EVALUATION USING SKIN ELASTICITY MEASUREMENTS

Code: 254

Aims: An ultra-hypofractionated schedule for adjuvant breast radiotherapy (RT) was proposed in the FAST FORWARD protocol, with acute and late G2 skin toxicity incidences of 36% and 12%, respectively. We report the preliminary results of a breast ultra-hypofractionated RT implemented with the automated hybrid-VMAT technique, deep-inspiration breath-hold, and the use of the LimpiAD medical device (@Aileens Pharma s.r.l.), administered as supportive care to reduce skin and subcutaneous radio-induced toxicity. In addition to clinical evaluation, skin damages were evaluated with an objective instrumental evaluation of skin elasticity using a Cutometer device.

Methods: Patients received RT as follows: 26 Gy to the whole breast and 30 Gy to the tumoral bed in 5 fractions per week after surgery. LimpiAD cream/foam BID on the irradiated gland for 21 days was prescribed as supportive therapy. Acute and late skin toxicities were evaluated subjectively at baseline, 1 month, and 6 months after treatment using the CTC-AE v.5.0 scale. At the same time, an instrumental evaluation was performed using a Cutometer® Dual MP580. This is a non-invasive instrument able to measure the skin elasticity parameters, based on the suction method, through a probe that applies a negative pressure to the skin

Results: From July 2022 to January 2024, 30 patients, stage T1–T2, N0, completed radiotherapy and were enrolled in the study. The median age was 67 (45-86) years. Four of 30 (13.3%) patients reported G2 acute skin toxicities. At 6 months, 3/30 cases (10%) of G2 late toxicity were reported. A total of 2160 measures of two parameters, R0 (the total skin firmness, mm) and Q1 (the elastic recovery, %), were recorded from the cutometer. The device was able to detect small variations in skin elasticity following RT. At 1 month after treatment, no correlation was found between measured values of R0 and Q1 and clinical evaluation. At 6 months after treatment, clinical late toxicity ≥ 2 was strongly associated with decreased R0 and Q1 values
≥ 24% ($p = 0.003$) and ≥ 18% ($p = 0.022$), respectively (Figure 1). Smaller decreases in R0 and Q1 were not clinically detected.

Conclusions: Ultra-hypofractionated whole breast radiotherapy supported by advanced treatment techniques and the LimpiAD device led to lower G2 acute and late toxicities in comparison with literature data. The cutometer represents a reliable and sensitive, noninvasive method for the objective and quantitative evaluation of skin elasticity.

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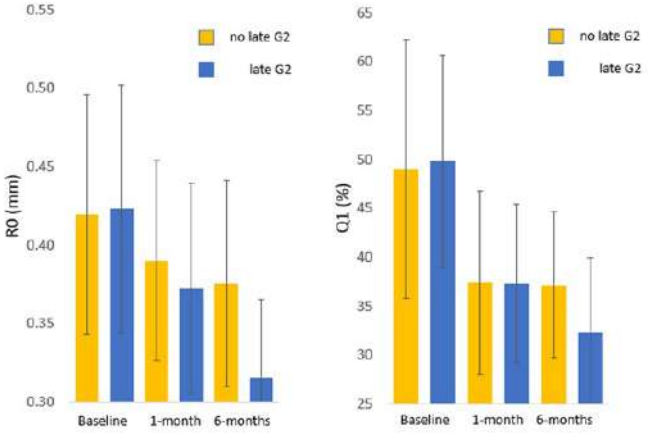

Figura 1

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OBSERVATIONAL STUDY OF HEALTH - RELATED QUALITY OF LIFE CLINICAL STUDIES IN BREAST CANCER PATIENTS REPORTED FROM 2019 TO 2023

Code: 605

Aims. In breast cancer (BC) therapies, patient-reported outcome measures (PROMs) are needed to measure outcomes that are best reported by patients The goal of this study was to identify whether the quality of life intruments and methodology has been improved over the last five years.

Methods. We searched the studies through the available literature in MEDLINE (PubMed) and Goggle scholar to identify review papers, systematic reviews of randomized or non-randomized controlled trials and observational studies on HRQoL in BC. An extra search was performed to check reviews trials and observational studies indexed in the CDSR. Current study covers all full review publications that appeared in English language biomedical journals between January 1, 2019 and June 1, 2023. Publications were screened using the PRISMA guideline.

Results. There were 32 papers that reviewed literature on instruments used to quantify quality of life in BC patients and to propose new modalities of collecting data. The EORTC QLQ-C30 health-related quality of life questionnaire is one of the most widely used cancer-specific health-related quality of life questionnaires worldwide for BC. Reviews found that specific measures including the Functional Assessment of Cancer Terapy-Breast quality-of-life (FACT-B) and the EORTC QLQ-BR23 were the frequently used specifc QOL instruments in BC patients. The EORTC QLQ-BR45 is a breast cancer-specific module updated in 2020 from the EORTC QLQ - BR23 to reflect current treatments. A number of new measures have been developed and validated, ofering promising options for assessing HRQoL in this patient population as FBSI, NFBSI-16, YW-BCI36, BCSS, QuEST-Br, QLICP-BR, INA- BCHRQoL, and two newly developed unnamed measures A systematic review aimed to identify the methodological aspects of HRQoL measurement among HER2+ metastatic BC patients and critically appraise their strengths and weaknesses. Seven HRQoL instruments (EORTC QLQ-C30, FACT-G, FACT-B, FACT-B TOI, EORTC QLQ- BR23, FACTBr, and EORTC QLQ-BN20) were identified, among which FACT-Br and EORTC QLQBN20 were used in BC with brain metastasis.

Conclusions. Interpretation of clinical outcomes should not be based solely on the presence or absence of statistically significant differences. The development of standardized best practice guidelines in BC HRQoL data collection and analysis is recommended to improve data quality to assist evidence-based clinical decision making.

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INVESTIGATING THE DOSIMETRIC IMPACT OF NON- LINEAR RESAMPLING FOR 8-BIT CTS IN TOTAL MARROW LYMPH-NODE IRRADIATION PLANS

Code: 89

Aims: Modern radiotherapy planning frequently involves co-registering CT and MRI scans. This study explores the dosimetric impact of CT non-linear resampling (from 12 to 8 bits) in total marrow lymph-node irradiation (TMLI) plans, utilizing AI-generated synthetic CTs. The aim is to assess the dosimetric and clinical implications of this approach.

Methods: Ten patients undergoing TMLI were randomly selected. CT scans, extending from the head to mid femurs, were resampled using both linear and non-linear Look-Up-Tables (L-LUTs and nL-LUT). Treatment plans were created on Eclipse TPS and calculated using AAA and AcurosXB algorithms. Dosimetric and clinical evaluations were conducted. In particular, six radiation oncologists evaluated the two resampled CT series in terms of the ability to contour the target.

Results: The nL-LUT method revealed higher discrepancies in Hounsfield Units (HU) compared to L-LUT, with average root mean square error of 10±1 HU and 6.8±0.6 HU, respectively. Despite this, the nL-LUT method demonstrated superior dosimetric agreement for both algorithms. Overall, the resampling process led to increased hotspots in the dose distributions, with the nL-LUT exhibiting smaller differences (around 0.1% for D98% and D2%) than L-LUT (0.2%). For PTV, soft tissues, and lungs, the dose variations arising from the use of resampled CTs were less significant than those resulting from a change in the calculation algorithm (up to 1.8% for D98% and D2% - $p<0.05$). The 3D gamma passing rate (GPR) indicated that relevant disagreements between dose distributions emerged only when using AAA and AXB on the same original CT (GPR(1%,1.25mm) =82±4%), while high agreement was observed using same algorithm for resampled and original CTs (GPR=99.8±0.3%) (Figure 1). Regarding the clinical assessment, L-LUT displayed pixelation in the brain (rating: 1[IQR=0]), while nL-LUT showed no discernible difference from original CTs (rating: 3.75 [IQR=1.25]).

Conclusions: The nL-LUT outperformed the L-LUT in dosimetric agreement and visual tissue discrimination. The differences in DVH statistics between original and resampled CTs were clinically acceptable. Furthermore, the clinical evaluation indicated that non-linearly resampled CTs can be employed for contouring purposes. Therefore, 8-bit CTs represent a promising option for optimizing AI algorithms for synthetic CT generation. This study was supported by GR-2019-12370739.

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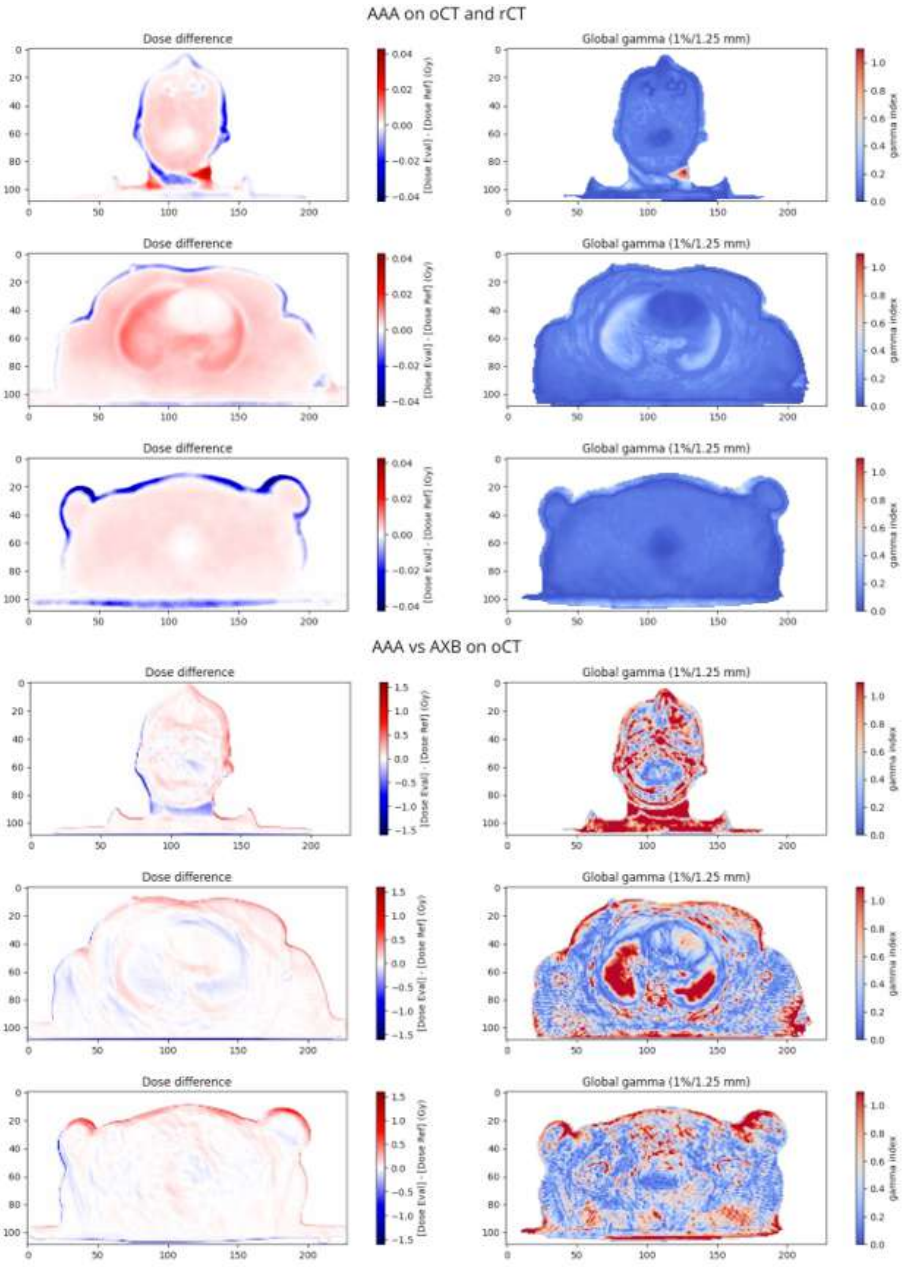

Figure 1: 3D GPR evaluation: comparison between dose distributions computed with original CTs (oCTs) vs non-linearly resampled CTs (rCTs) with AAA, and AXB vs AAA on oCTs.

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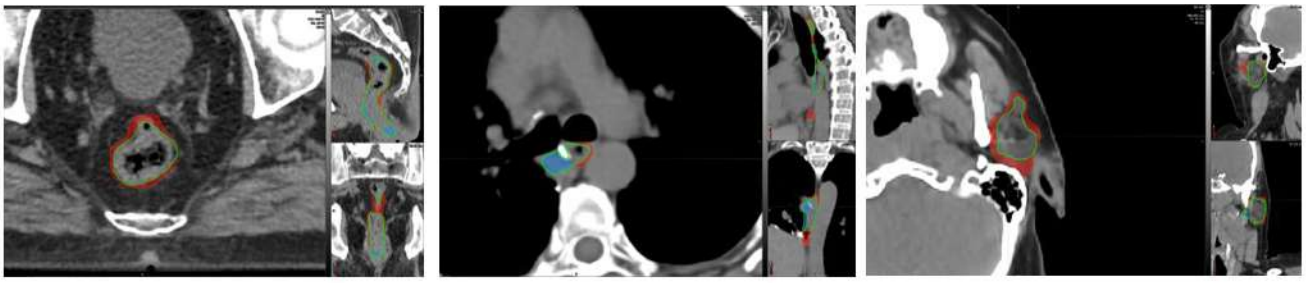
DEPLOYING DEEP LEARNING CONTOURING METHOD IN CLINICAL ROUTINE: A SINGLE CENTER EXPERIENCE

Code: 15

Aims: Today RT treatment outcomes lay in the accuracy of the radiation delivery through complex techniques such as VMAT, IMRT, SBRT which require high precision organ at risk and target definition. Manual contouring methods are very time consuming and subjected to a inter and intra operator variability. Deep Learning algorithms applied to Contouring (DLC) are becoming a practical alternative. Commercial software based on Neural Network trained on a large dataset is going to be deployed in a clinical routine soon. The aim of this work is to evaluate the impact of DLC in term of both standardization of manual contouring and time saving.

Methods: 30 patients have been enrolled for this retrospective study: The sites of the treatment were: 12 Head and neck (HN), 9 thoracic and 9 prostate treatment sites. All of the CT study set have been contoured by a radiation oncologist, and, as it as is customary in our center, they were reviewed by an expert one. In a second step, the same cases have been sent to DLC. Then, DLC contours have been edited to reach the expected results, in a blind way. The structured contoured and analyzed have been: bone mandible, parotid left and right, spinal cord, oral cavity, carina, oesophagus, great vessels, heart, lung left and right, trachea, bladder, femur left and right, rectum and prostate gland. The contouring time for each step have been recorded. The time associated to DLC is the sum of DLC and manual editing times. Each patient contoured sets have been overlapped and the differences have been analyzed using DICE and Jaccard indices. Analysis in terms of regions added and regions removed and their volumes have been carried out (Figure 1).

Results: The most evident result lays in the time sparing of DLC for all treatment site: the total mean time saved per patient contouring is 198±97 minutes For HN and thorax site, the values reach 260 and 249 minutes, respectively. The medians for the DICE and the Jaccard Index are 0.81, 0.84 and 0.66 for HN, thorax and prostate respectively.



Conclusions: This retrospective work assesses the utility of DLC in clinical routine in terms of contouring process time saving but also in terms of reduction of operators inter and intra variability.

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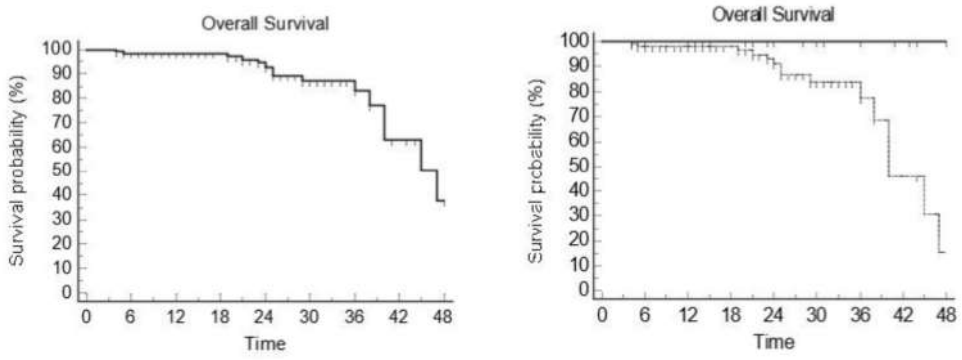
PREDICTORS OF pCR IN PREOPERATIVE RADIOTHERAPY FOR LOCALLY ADVANCED RECTAL CANCER

Code: 366

Aims: Preoperative radiotherapy(PRT),both delivered as short course(SC-RT) or long course with concomitant capecitabine (LC-CRT),is an essential component of the multimodal treatment approach for locally advanced rectal cancer(LARC).Pathologic complete response(pCR) has been associated with overall survival(OS) in RC patients(pts).Ongoing research endeavors seek to identify factors that may influence pCR



attainment in rectal cancer pts,including treatment-related timing.We aimed to study the predictive value of pCR on OS and the potential effect of time to surgery on pCR in LARC pts treated with PRT.

Methods: Clinical and treatment-related data from pts with LARC undergoing PRT with LC-CRT or SC-RT at our Centre between January2019 and March2023 were retrospectively collected.Survival analysis was performed using the Kaplan Meier method.Multiple regression was performed on variables that proved statistically significant($p<0.05$).

Results: Overall,125 pts were analyzed.Median age at diagnosis was 72 years(IQR 62-75)and 87 pts(70%) were male.Thirtythree pts(26%)were diagnosed with cT4 tumor stage and 52(42%) with cN2 nodal stage.Mesorectal fascia(MRF) and extramural venous invasion(EMVI) were reported in 24(19%) and 19(15%)pts respectively.LC- CRT was performed in 88 pts(70%),while 37(30%) pts underwent SC-RT.Nine pts(7%)received induction chemotherapy prior to PRT.All pts achieved surgical resection;median time to surgery was 9 weeks(IQR 7-11 weeks)and pCR was achieved in 27 cases(22%).At a median follow up of 24 months(range 3-51 months),13 pts died(10%).Median OS was 47 months(95% CI 40-47).Survival rates at 2 years and 3 years were 93% and 87% respectively.Among the variables analyzed(age, gender, cNstage, cTstage,induction chemotherapy,MRF and EMVI involvement,use of LC-CRT, pCR)at univariate analysis, only pCR was correlated with improved OS(median not reached versus 40 months, p= 0.021)[Fig.1].Median interval between neoadjuvant treatment and surgery did not significantly differ between pts with and without pCR(10 versus 9 weeks, NS).Lower rates of pCR were correlated with use of SC-RT(10% versus 27%, p=0.041)and cT4stage at diagnosis(3% versus 27%, p=0.0083).None of the other variables analyzed were statistically associated with pCR.

Conclusions: Achievement of pCR following PRT was correlated to better OS in LARC pts.Use of LC-CRT was associated with improved rates of pCR,while cT4 tumors may benefit from treatment intensification to increase pCR rates.Time to surgery was not correlated to pCR.

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NEOADJUVANT CHEMORADIATION WITH VMAT FOR RECTAL CANCER: CORRELATION BETWEEN THE USE OF SIMULTANEOUS INTEGRATED BOOST (SIB) AND PATHOLOGICAL RESPONSE TO TREATMENT

Code: 88

Aims: Neoadjuvant chemoradiation followed by total mesorectal excision (TME) is the standard treatment of locally advanced rectal cancer. The purpose of this study is to verify the correlation between the use of VMAT with Simultaneous Integrated Boost (SIB) and pathological response to treatment.

Methods: Patients submitted to neoadjuvant chemo-radiotherapy (CT-RT) were the object of this retrospective analysis. Radiotherapy treatment plan was based on simulation CT-scan and image registration of a staging MRI. The clinical target volume 2 (CTV2) included the whole mesorectal space and regional lymph nodes. The SIB was delivered on GTV and corresponding mesorectum (CTV1). Radiotherapy was delivered with VMAT technique and associated with capecitabine. Patients underwent TME 8-10 weeks after the end of CT-RT and the pathological response was assessed following the Dworak criteria.

Results: We considered a series of 97 patients with stage III rectal cancer submitted to preoperative CT-RT with VMAT-SIB between 2017 and 2023. This group was compared with an historical series of 49 patients treated between 2016 and 2020 with the same radiotherapy without SIB. Median age was 61 years. All patients (n=146) received a prescribed dose of 50 Gy in 25 fractions to the whole mesorectal space and local nodes. Ninety-seven patients (66.4%) also received a SIB on GTV and corresponding mesorectum to a total dose of 55 Gy. At the restaging MRI, performed 4-6 weeks after the end of CT-RT, a complete response (CR) was observed in 27 patients (18.5%), while a partial response (PR) was observed in all the remaining patients (n=119, 81.5%).
Acute toxicities (p=0.5) were similar between the 2 subgroups, with no toxicities ≥ G3 registered in either group of patients. Late toxicities were no significantly different in the 2 subgroups, nor were the perioperative complications.
After surgery a pathological complete response (pCR, score 4 according to Dworak tumoral regression scale) was reported in a total of 39 patients (26.7%). In particular a pCR was reported in 30/97 SIB patients (30.9%) compared to 9/49 non-SIB patients (18.4%), The difference was not statistically significant (p= 0.107).

Conclusions: In our study a higher rate of pCR in locally advanced rectal cancer was observed in patients submitted to preoperative chemoradiation with VMAT-SIB, compared to patients who did not receive SIB. Acute and late toxicities were comparable in both groups.

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CONCOMITANT SIB-IMRT/VMAT COMBINED WITH SISTEMIC THERAPY FOR LA-HNSCC IN REAL LIFE DAILY CLINICAL PRACTICE: UPDATING OF A MONOINSTITUTIONAL EXPERIENCE

Code: 475

Aims: To evaluate, in daily practice, clinical outcome, feasibility and acute toxicities in locally advanced squamous cell head and neck cancer (LAHNSCC) received Simultaneous Integrated Boost (SIB) with IMRT or VMAT technique and sistemic therapy.

Methods: We retrospectively analized 72 patients (pts), stage III-IVa of LAHNSCC, who received mentioned above combined radical treatments in our Radiotherapy Unit from January 2017 to January 2024 65 pts had concomitant chemotherapy (11 high dose cisplatinum, 43 weekly cisplatinum, 11 carboplatinum-5Fluorouracil) and 8 pts, unfit for platinum delivery, were treated with cetuximab. For planning, according national and European guidelines, we identified differents treatment volumes reflecting different risks of holding disease and consequently that required different treatment doses: High-Risk (HR) volume (primary tumor GTV-CTV and positive neck nodes GTV-CTV), Intermediate-Risk (IR) volume (optional) and Low risk volume (elective nodal drainages). The median radiation dose was 69.96 Gy (66,03–70) to the HR volume. Acute toxicities assessed according RTOG scale.

Results: The main toxicities recorded were skin toxicity/mucositis, hematological toxicity and dysphagia. No one experienced G4 toxicity. 45 pts recorded G2 skin toxicity/mucositis and 15 pts G3 (3 of them treated with cetuximab). 10 pts had G2 haematological toxicity and 8 pts G3 (resolved with leukocyte growth factors). 37 pts recorded dysphagia > G1 (7 pts G3). It was necessary to recur to artificial nutrition (PEG or TNP) for limited period of time in order to complete the treatment. Patients with baseline dysphagia or with a 5% reduction in body weight were immediately referred for a nutritional visit. At the time of this abstract 2 patients are still undergoing treatment. One patient died during the treatment to other cause. Complete response was observed in 56 pts (80%) who have completed treatment, a partial response in 8 pts, while 6 pts had a disease progression in the following 3-6 months.

Conclusions: Concomitant SIB-IMRT/VMAT-chemotherapy/cetuximab is confirmed to be effective and safe for patients with LA-HNSCC and can be used in real-life daily clinical practice. In our experience, a timely nutritional assessment of patients remains essential in order to complete the combined treatment.

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HYPOFRACTIONATED PROTON THERAPY FOR PRIMARY INTRAHEPATIC CANCERS: TIME FOR A PIVOTAL ROLE? A SYSTEMATIC REVIEW AND META-ANALYSIS

Code: 332

Aims: Hypofractionated proton therapy (PT) is gaining an increasing crucial role in the treatment of primary intrahepatic lesions (PIC), especially for hepatocellular carcinoma (HCC).
However, significant inhomogeneities in terms of indication, fractionation schedules, efficacy and safety of this therapeutic strategy is reported. The present work aims to provide a critical literature review on the topic, highlighting eventual associations between treatment schedules and oncological outcomes and toxicities.

Methods: This systematic review and meta-analysis complied with the PRISMA recommendations. Inclusion criteria were: 1) curative-intent hypofractionated (≥3 Gy (RBE)/fraction) PT for PIC, 2) report of the clinical outcomes, 3) availability of full-text. The bibliographic search was performed on the NCBI Pubmed, Embase, Scopus and Web of Science in July 2023.
For each included study the BED was calculated (α/β = 10 Gy for PIC) and a BED cut-off of 100 Gy was used as a threshold for stratifying selected evidence within two subgroups (BED <100 Gy and ≥ 100 Gy, respectively), as recently reported in the field of stereotactic radiotherapy (SBRT) with photons in the same setting. The summary was estimated by pooling study-specific estimates with random-effects models.

Results: Fifteen studies and 1140 patients were available for the meta-analysis. The median delivered BED was 93.58 Gy(RBE). The local summary control (LC) rate was 88% (95%
CI 82%-92%). The $I2$ =82% $I^2 = 82\%$

showed significant heterogeneity between studies (**Figure 1**). Only a trend between a BED ≥ 100 Gy (RBE) and LC rates was found, but without significant differences compared with patients treated with BED < 100 Gy (RBE) (LC of 90.0% and 56.7%, respectively p=0.39). Toxicities ≥ 3 were rare and unrelated to the BED values.

Conclusions: Hypofractionated PT is a safe and effective therapy for PIC. The chance to deliver higher doses of PT could ensure better oncologic outcomes, providing a pivotal role in the multidisciplinary management of these malignancies.

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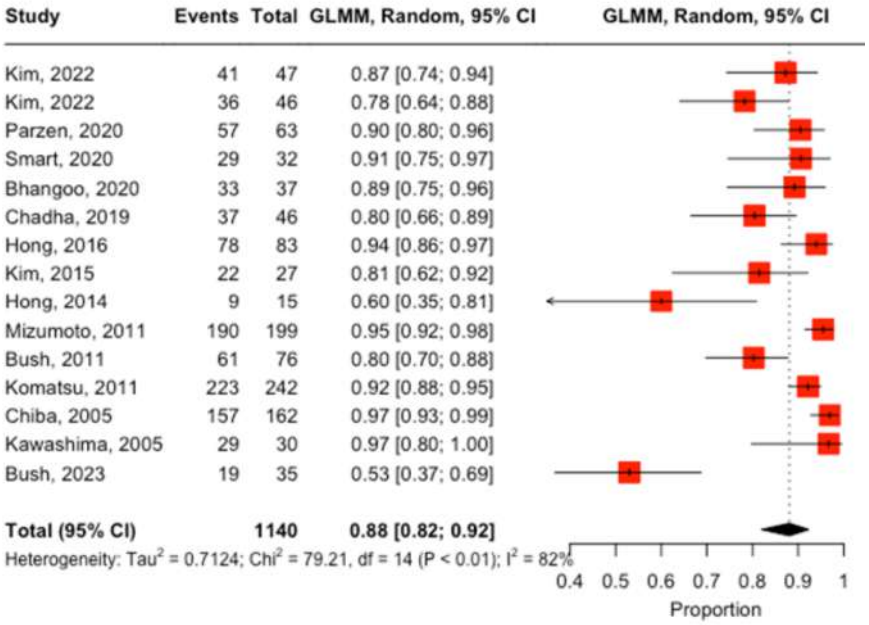

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RADIOTHERAPY AND NOVEL ANTIBODY-DRUG CONJUGATES IN BREAST CANCER PATIENTS

Code: 227

Aims: Antibody drug conjugates (ADCs) are novel drugs that combine monoclonal antibodies with cytotoxic agent, enabling the selective delivery to cancer cells expressing specific antigens. ADCs were introduced in order to overcome resistance to chemotherapy and enhance drug delivery. Trastuzumab Deruxtecan (T- DXd) and Sacituzumab Govitecan (SG) are among the last ADCs approved in clinical practice for HER2+ and triple negative (TN) metastatic breast cancer patients, respectively. There is little evidence regarding the safety and efficacy of the combination of radiotherapy (RT) with these two drugs. The aim of study is to evaluate the early toxicity of concurrent use of RT with T-Dxd and Sacituzumab Govitecan in metastatic breast cancer (BC) patients.

Methods: Patients with stage IV breast cancer undergoing a systemic treatment with T-DXd and SG, who were candidates for a radiation treatment (both palliative or curative), after being informed about the study and giving written informed consent, were enrolled in this observational study. Toxicity was assessed according to the NCI-CTCAE V5.0.

Results: From May 2023 to October 2023 a total of 23 patients treated with ADCs were enrolled in this observational study. A total of 53 radiotherapy treatments were delivered concurrently with ADCs (32 with T-DXd and 21 with SG). ADCs were delivered within 1 week or concurrently with RT. Median age was 58 years (range 33-81). Treatment description according to concomitant ADC is summarized in table 1. No patient suspended RT. Any type all grades toxicity occurred in 11 patients (47.8%). Grade >2 toxicity was observed in 2 patients (8.7%).

No grade 3 toxicity was recorded. Overall haematological toxicity was 13.3%. In T-DXd cohort one patient treated to a large femur metastasis developed grade 2 neutropenia. Also in SG cohort a patient developed a grade 2 brain radionecrosis. This patient received multiple brain SRT treatments. Toxicity details according to the type of ADCs are described in Table 2. Median duration of T-DXd was 16.6+/-10.4 months and mean duration of SG was 11.9 +/- 4.76 months. All patients treated for palliation of bone metastases (9, 39.1%) achieved pain relief (NRS pre 1.8; NRS post 0.4, p=.014)

Conclusions: RT delivered during T-DXd and SG showed mild toxicity. Longer follow-up and larger number of patients and treatments are needed to better understand the safety profile of radiotherapy delivered concurrently with these two drugs.

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EXPLORING PREDICTORS OF COMPLETE PATHOLOGICAL RESPONSE IN LOCALLY ADVANCED RECTAL CANCER: A COHORT STUDY OF NEOADJUVANT CHEMORADIOTHERAPY

Code: 284

Aims: Neoadjuvant chemoradiotherapy (CRT) followed by total mesorectal excision is the established standard of care for locally advanced rectal cancer. Despite its efficacy, identifying factors predicting a complete pathological response rate (pCR) to neoadjuvant treatment remains a subject of ongoing debate. This study sought to elucidate the determinants contributing to a complete pathological response following neoadjuvant CRT.

Methods: A retrospective cohort study was conducted, categorizing patients based on the clinical target volume, the interval between CRT completion and surgery (8 weeks), and other relevant clinical factors. Logistic regression was employed to identify independent predictors of pCR.

Results: Among the 408 eligible patients, the overall pCR rate was 25%. Univariate analysis revealed that pCR was associated with female gender ($p = 0.007$) and a time to surgery greater than 8 weeks ($p = 0.003$). Multivariate analysis confirmed that both female gender and a delay of more than 8 weeks to surgery remained independently associated with pCR (OR: 1.88, CI: 1.22-2.89, $p = 0.004$; OR: 0.45, CI: 0.27-0.74, $p = 0.002$, respectively).

Conclusions: This study identifies a delay of more than 8 weeks to surgery and female gender as factors associated with an increased likelihood of achieving pCR in our patient population. These findings underscore the importance of further prospective studies to delineate the pertinent variables for predicting pCR in the neoadjuvant setting.

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STEREOTACTIC BODY RADIOTHERAPY IN OLIGOPROGRESSIVE METASTATIC THYROID CANCER: A CASE REPORT

Code: 459

Aims: The spine is the most common site of osseous involvement in cases of metastatic thyroid cancer, especially for follicular type. Spinal metastases are associated with increased mortality and severely reduced quality of life by causing pain, vertebral fractures, and spinal cord compression. Due to the increased survival rates compared to other malignancies, optimal local control (LC) is paramount in this setting of patients to avoid long-term morbidity and neurological sequelae. Stereotactic body radiotherapy (SBRT) has the advantage of delivering a high radiation dose while preserving the surrounding normal tissue, thus providing the opportunity to improve LC and reduce the risk of side effects. This is especially important for patients already treated with iodine. Herein our case report.

Methods: A 40 years old woman diagnosed with follicular thyroid cancer and bones metastases at onset went to our observation after thyroidectomy and radioactive iodine treatments with I-131 (four cycles over two years with 7400 MBq administrated activity) followed by tyrosine kinase inhibitors therapies. Due to progression of disease, she underwent two ribs surgical removal. One year later, her Tireoglobulin level was increased. She was symptomatic for pain. Whole body scan with I-131 showed two spinal metastases: on vertebral body of D10 and on left transverse process of L3. SBRT was performed on these two targets. During treatment planning, the Radiation Biologically Effective Dose (BED) evaluation has been done considering both the contribution from SBRT and from radioactive iodine treatment.

Results: SBRT was performed with VMAT technique and 6 MV photon beams. The prescribed doses were: 30Gy in 5 fractions on D10 and 21Gy in 3 fractions on L3. Before SBRT, Tireoglobulin level was 556.9 ng/ml. At three months of follow-up, the I-131 scan and F-18 FDG PET/CT scan showed no residual activity.
Additionally, pain was reduced and the Tireoglobulin level was dropped by half. No hematological toxicities were recorded.

Conclusions: Our experience in thyroid cancer patients with spinal metastases shows that SBRT is an effective option to obtain a fast symptom relief and an optimal local control. This treatment also allows to save radioactive iodine treatments.

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LONG-TERM OUTCOMES OF RADIATION TREATMENT IN HIGH-RISK PROSTATE CANCER: A MONOCENTRIC RETROSPECTIVE STUDY

Code: 270

Aims: To evaluate the efficacy and side effects of radiotherapy (RT) in 340 patients (pts) with high-risk prostate cancer (HRPC), in terms of overall survival (OS), cancer-specific survival (CSS), biochemical- free survival, local control (LC), disease-free survival (DFS), and metastasis-free survival (MSF).

Methods: A total of 340 consecutive pts with HRPC were treated between 2009 and 2022. The pts underwent IMRT-IGRT for a total dose of 45 Gy to the pelvis, 55 Gy to the seminal vesicles, and 68.75 Gy to the prostate, administered in 25 fractions. The staging revealed that 137 pts had a Gleason score of less than 8 (40.6%), while 205 had a score of 8 or higher (60.6%). In terms of disease stage, 103 pts presented with a stage lower than T3a (30.6%), 237 pts had a stage equal to or greater than T3a (70.0%). Both acute and late toxicities were evaluated and assessed. The scoring system used for toxicity assessment was the Radiation Therapy Oncology Group (RTOG) system. The Kaplan-Meier method was employed to analyze survival outcomes.

Results: Median actuarial FUP was 70.2 months (95% CI: 60.5-80.8 months, range 2-160.5 months). Median OS was 121.5 months (95% CI: 115.1-128.2), 8-year OS: 62.4%. Median CSS was not reached, 8-year CSS: 91.4%. Median BFS was not reached, 8-year BFS: 81.5%. Median LC was not reached, 8-year LC: 94.4%. Median DFS was not reached, 8-year DFS: 81.3%. Median MFS was not reached, 8-year MFS: 89.2%. 195 pts (57.4%) experienced acute toxicity. Among these, acute gastrointestinal (GI) toxicity was recorded in 113 pts (33.2%); 91 (26.7%) G1, 22 (6.4%) G2. No cases of acute GI toxicity G3 or higher were observed. Acute genitourinary (GU) toxicity was recorded in 142 pts (41.7%); 114 (33.5%) G1 and 27 (7.9%) G2. Only 1 patient (0.2%) had G3 toxicity. 68 pts (20%) reported late effects. Late GI toxicity was recorded in 14 pts (4.1%); 9 (2.6%) experienced G1 toxicity, while 4 (1.1%) had G2. Only 1 patient (0.2%) presented G3 toxicity. Late GU toxicity was reported in 62 pts (18.2%); 40 (11.7%) experienced G1 toxicity, while 18 (5.2%) had G2 . 4 pts (1.1%) presented G3 toxicity.

Conclusions: This study demonstrates that moderate hypofractionation with a 25-fraction schedule is an effective treatment option for patients with HRPC. The treatment yielded positive outcomes in terms of survival and displayed minimal toxicity. These findings suggest that this treatment approach can be considered as a viable therapeutic choice for patients with high-risk prostate cancer.

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PROSTATE SBRT USING FIDUCIAL MARKERS AS REFERENCE IN MR IMAGE FUSION AND IGRT: A SINGLE-CENTER EXPERIENCE

Code: 423

Aims: To assess the feasibility, and early clinical outcomes of prostate SBRT, utilizing gold fiducial markers for co-registrating lower abdomen MRI with simulation CT and pre-treatment IGRT.

Methods: Between July 2022 and January 2024, twenty-five patients with prostate cancer (PCa) underwent SBRT at at a single institute.
hree gold fiducial markers were positioned in non-coplanar planes within the prostate gland. Ten days later, a simulation CT and a lower abdomen MRI were performed. Images were fused, using the spatial position of the markers, in order to delineate the target.
Fraction schedules were 42.7 Gy in 7 fractions (BED1,5=216.35 Gy) for 4 patients and 42 Gy in 7 fractions (BED1,5=210 Gy) for 21 patients.
The treatment was delivered every other day on a Linac platform using a VMAT technique. The IGRT procedure involved an initial automatic matching of the markers between the daily CBCT and the simulation CT using a dedicated software, then physicians could manually adjust the rotation and translation if deemed necessary.
Toxicity, was evaluated according the Common Terminology Criteria for Adverse Events Version 5 (CTCAE_v5) scale.

Results: Twenty-four patients had organ-confined PCa (risk class n=3 low, n=10 favorable intermediate, n=8 unfavorable intermediate, n=2 high, n=1 very high), and one patient had a single bone metastasis. Seven patients received ADT. Median age was 75 years (62-85). Fourteen patients (56%) had diabetes and/or a major cardiovascular event.
Median follow-up was 8.1 months (0.9-15.5). After one month, 2 gastrointestinal (GI) G1 and 6 genitourinary (GU) G1 side effects were recorded, respectively, among twenty-three patients. After 3 months, 1 and 7 patients respectively experienced G1 GI and G1 GU toxicity. After 6 months, 6 out of sixteen patients experienced G1 side effects (1 GI, 5 GU). No G2 side effects were recorded. Median PSA levels were 5.9 ng/ml before treatment (3.69-45), 1.20 ng/ml (0.007-4.28) at three months and 0.95 ng/ml (0.050-1.71) after six months from SBRT. Median PTV was 90.45 cc (47.56-141.21). Median PTV mean and D98% doses were 43.22 Gy (42.31-44.11) and 40.04 Gy (39.31-40.83) respectively. Bladder's median V38Gy was 4.42% (1.09-10.5) and rectal median V37Gy was 3.44% (1.57-4.28).

Conclusions: Prostate SBRT with fiducial markers has proven safe and effective, with promising oncological outcomes and no major toxicity. Long term followup is needed to confirm these findings.

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RADIOTERAPIA IPOFRAZIONATA ADIUVANTE NELLA MAMMELLA: RISULTATI DI UNESPERIENZA MONOISTITUZIONALE

Code: 417

Aims: To evaluate the treatment's tolerance and early side effects of hypo-fractionated adjuvant radiation therapy (RT) for breast cancer.

Methods: In this retrospective study, we examined patients who underwent hypo-fractionated adjuvant RT for breast cancer following a Fast-Forward regimen administering 26 Gy in 5 fractions over the course of one week, by means of VMAT technique, Monday to Friday when possible. Among those showing adequate compliance, a respiratory gating, involving simulation CT during a deep breath inspiration phase, was employed, and the treatment was delivered accordingly.
Skin toxicity was evaluated using Common Terminology Criteria for Adverse Events Version 5 (CTCAE_v5) scale. Follow-up visits were scheduled at one, three, and six months after treatment, and annually thereafter.

Results: One hundred women with median age of 68 years (46-87) were enrolled. Seventy-seven patients were Luminal A, 14 Luminal B, 5 HER2 subtype, and 4 triple-negative. Ninety-six patients received hormonal therapy and 13 chemotherapy. Fifteen patients were treated with respiratory gating technique (n=11 left breast, n=4 right breast). Median PTV was 542.94 cc (67.34-1973.68) and median PTV mean dose was 26.45 Gy (25.87-26.79). Median heart and homolateral lung mean doses were 0.96 Gy (0.5-1.91) and 3.32 Gy (1.5-4.85) respectively. Heart median V1,5Gy was 10.22% (0-57.1) and homolateral lung median V8Gy was 8.89% (2.85-18.1). Upon treatment's completion, 12 patients encountered G1 skin toxicity, while 2 patients reported G2 side effects, characterized by pruritic erythema. No further G2 toxicities were reported during the subsequent follow-up. The median follow-up period was 1.42 months (0.79-16.34). Out of 87 women, 8 skin G1 side effects were documented during the follow- up after one month. After three, six and twelve months, only one patient experienced G1 skin erythema out of 21, 12, and 7 patients, respectively.

Conclusions: Our findings show that hypo-fractionated RT for adjuvant breast cancer is feasible and safe, thus particularly appealing especially for patients living far from RT facilities like at our center, near the Italy- Switzerland border. Long term data are awaited to confirm the clinical benefit of this strategy.

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VALOSINB- CONTAINING PROTEIN (VCP): A PROMISING BIOMARKER IN GLIOBLASTOMA

Code: 229

Aims: Standard of care for newly-diagnosed glioblastoma (GBM) patients consists in surgical resection followed by radiation therapy (RT) with concomitant and adjuvant temozolomide chemotherapy (TMZ).
Nevertheless, the majority of patient experience recurrence, mostly within the irradiated volume, attesting a high resistance to RT. Among radioresistance mechanisms, valosin - containing protein (VCP) appears to play a leading role in different tumors types, but its significance in gliomas remain uncertain. Aim of this analysis is to investigate the role of VCP in radioresistance and its possible significance as prognostic and predictive biomarker in GBM.

Methods: The analyses included newly diagnosed isocitrate dehydrogenase (IDH) wild type GBM patients receiving surgical resection followed by RT with concomitant and adjuvant TMZ. VCP expression has been determined by immunohistochemistry evaluating VCP positive cells percentage and staining intensity. It was scored as low VCP expression (L-VCP, rating 0-3) and high VCP expression ((H-VCP, rating 4-6), and thus correlated with patient's survival.

Results: The first 25 GBM patients have been evaluated. Median age was 55 years (range 21-69); all had ECOG performance status ≤ 2. The 60% of patients received a gross total resection, 36% a subtotal one.
O6methylguanine DNA methyltransferase (MGMT) promoter was methylated in 7 out of 25 patients. Concomitant RT-TMZ was performed in 23 patients, RT alone in 2 for infective comorbidities and MGMT unmethylated status. The 44% of all tumor tissues showed H-VCP, while 56% resulted as L-VCP.
Median follow up time was 50 months (range 29-83). Median overall survival (OS) time, 6 months,1,2-year OS were 18 months (95% CI 11-21), 96% ±3.92, 68% ±9.33, 28% ±8.98, respectively. Median progression-free-survival (PFS) time, 6 months,1,2-year PFS rates were 10 months (95% CI 8-13), 84% ±7.33, 32% ±9.33, 8% ±5.43. On univariate and multivariate analysis, VCP showed a trend of significance impacting PFS. Indeed, 12-months PFS was 18.2% in H-VCP patients and 57.1% in L-VCP ones, even if a statistical significance could not be found ($p = 0.59$). Moreover, a significant correlation was found between H-VCP expression and older age ($p = 0.036$).

Conclusions: Our results suggest that H-VCP expression could be a prognostic factor in GBM, and correlation found with older age further supports this result. Additional investigations are ongoing on a larger population to clarify its significance as radioresistance biomarker in GBM.

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ASSESSMENT OF IMPACT OF PRE-TREATMENT RESPIRATORY TRAINING IN A COHORT OF LEFT BREAST CANCER PATIENTS TREATED WITH ADJUVANT RADIOTHERAPY USING DEEP INSPIRATION BREATH HOLD TECHNIQUE

Code: 303

Aims: Evaluate the impact on reproducibility and on treatment radiotherapy (RT) session time of respiratory training (TRN) in left breast cancer patients(pts) who underwent adjuvant RT using Deep Inspiratory Breath-Hold technique (DIBH-t).

Methods: We analyzed 20 pts who underwent RT for left breast cancer with DIBH-t at our Radiotherapy Department. 10 pts treated from April to December 2022 without TRN for DIBH-t and 10 pts treated from July to October 2023 with TRN. Medium age was 59.2 years for no-TRN-group (range 47-76) and 57.7 years for TRN-group (range 44-74). All pts underwent two sequential CT simulations in supine position: the first in free breathing and the second in DIBH. The impact of TRN in clinical practice was evaluated analysing the difference of a series of parameters between the 2 groups (Tab1). The useful time to process the pre-treatment images is the processing time. All these data were provided directly by ARIA software. The analysis was made using unpaired T-test, after verifying normality distributions with the Shapiro-Wilk test.

Results: From data analysis we found that for session treatment time were seen differences not statistically significant between two groups and the same was for CBCT acquisition time in BH. Instead the data showed a statistically significant difference for the following parameters: CBCT + processing time with a median time of 4.6 minutes for the TRN-group versus 7.5 minutes for no-TRN-group (P-value 0.0034); MV + processing time with a median time of 2.8 minutes for the TRN-group versus 3.9 minutes for no- TRN-group (P-value 0.0327); treatment + imaging processing time with an average difference of 1.6 minutes between the 2 groups(P-value 0.046) (Tab1). The useful time to process the pre-treatment images is the processing time. For both groups we found a progressive temporal reduction of the RT-session time during RT.

Conclusions: From our preliminary data it seems that TRN for DIBH-t RT is useful for optimizing patients' reproducibility and interpretation of daily imaging dedicated to complex treatment-planning such as CBCT. This data is indirectly confirmed by progressive temporal reduction of RT-session time during treatment for both groups of pts. While a useful reduction in the overall session time clearly did not emerge from our analysis, probably due to limited number of pts. Respiratory training in left breast cancer patients who underwent adjuvant RT using DIBH-t has become clinical practice in our Centre.

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EXPLORING FEASIBILITY OF A REMOTE MONITORING AMONG ELDERLY PATIENTS UNDERGOING RADIATION THERAPY TREATMENT

Code: 246

Aims: The pandemic era has increased the interest in remote monitoring (RM). This issue may be of particular importance in elderly patients (ELD). The aim of the study is to explore feasibility of RM among ELD undergoing radiation treatment (RT).

Methods: From 2023 December 7th to 2024 February 5th, patients aging ≥65 at time of simulation CT, were invited to wear a fitness activity tracker (FT) continuously, until the week after discharge. FT monitored blood pressure (BP), heart rate (HR), steps count (SC) and sleep activity (SA) (Figure 1a). In addition to clinical and treatment information, education, former job and familiarity with technology were collected and stored on a database. Acceptance and possible conditioning factors were evaluated.

Results: Thirty-one patients (19 M and 12 F) met the inclusion criteria. Acceptance rate was 68% (21/31). In detail, 21 patients accepted immediately, and moved on, with 2 patients, with the highest familiarity with technology, showing a particular enthusiasm; 2 patients first accepted but with hesitation, and withdrew after a week, before starting RT, reporting hassle for the accessory; 8 refused immediately, referring hassle for the accessory (5/8) and/or a psychological condition of new things rejection (4/8), and/or doubts about its usefulness (1/8). Acceptance was significantly higher in M patients (84% vs 42%, p=.02; Figure 1b). Apparently, acceptance rate was also higher among patients with medium-high familiarity with technology (80% vs 62%), education ≥high school (78% vs 64%), intellectual versus manual former job (78% vs 63%), but without reaching statistical significance. Various events occurred during RM: a patient showed frequent BP peaks; another became bedridden due to worsening clinical conditions; one had a brain stroke; a patient was hospitalized first for heart failure, then for SARS-COVID-19 infection.

Conclusions: Although acceptance among ELD is not high, RM seems to be possible in more than two third of patients. M gender seems to be associated with higher acceptance. Although currently limited to a small sample, results are promising, in the view of implementing RM in elderly patients undergoing RT.

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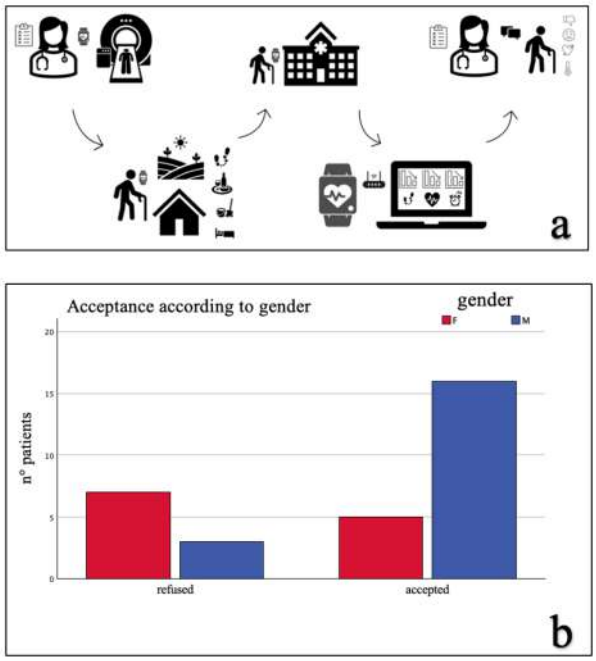

Figure 1. Workflow of data collection. The patient was asked to wear the FT at time of simulation, continuously. Data, downloaded from the FT memory to a gateway located in the hospital, will be available to the medical staff in the form of graphs and integrated with patient-reported ones (a); acceptance according to gender (b).

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MANAGEMENT ADVANTAGES OF A SINGLE CENTER WITH THE FAST AND MODERATELY HYPOFRACTIONATED SCHEMES IN POSTOPERATIVE RADIATION THERAPY FOR BREAST MALIGNANCIES

Code: 579

Aims: Starting from a 5-weeks conventional fractionation (CVF), moving on to the 3/4-weeks moderately hypofractionated (MHYPO), the shorter adjuvant (adj) radiation treatment (RT) for early-stage breast cancer (BC) after conserving surgery (CS) is represented by the FAST scheme, which reduces the treatment time (TT) to a single week. At the same time, when target volume includes elective nodes (N) with residual breast (RB), and/or chestwall (CW), the CVF can be replaced by the MHYPO scheme. In this study we evaluated the advantages in terms of both patient perception and managerial workflow, of the shortening of the treatment delivery period.

Methods: Between September 2023 and January 2024, patients (pts) requiring only RB RT have been candidates for the FAST scheme, with dose prescription (DP) of 26 Gy into 5 fractions (fx) and a 3 Gy SIB when appropriate; at same time, pts requiring adj RT on N in addition to RB and/or CW, have been candidates for the MHYPO scheme, with DP of 40 Gy into 15 fx plus a possible 8 Gy SIB. Acceptance was evaluated; a comparison with number of pts treated in the same period of the previous year in the same settings, overall treatment period variation between groups, and overall pts treated, was also carried out.

Results: 35 pts started RT with the FAST scheme, vs 20 (+75%) of last year, treated with MHYPO (Figure 1a). RT delays occurred less frequently (9% vs 80%, p<.001) with also a significant reduction (p<.001, Figure 1c) in delta between number of fx and treatment period, with a median of 0% (0-20) vs 7% (0-47). In the same period, 11 pts started RT with the MHYPO scheme, vs 9 (+22%) treated the previous year with CVF (Figure 1a). A trend was shown in RT delay rates reduction (33% vs. 89%; p=.054); a significant (p=.013) reduction of delta between number of fx and treatment period (Figure 1d) occurred, with a median of 0% (0-7) vs 8% (0-20). Patients were all compliant. Overall BC pts treated with adj purpose were 47 versus 32 of last year (+47%); overall patients treated were 234 versus 181 (+29%, Figure 1b).

Conclusions: The shorter schemes met pts' compliance, reduced RT delays, and allowed a considerable overall access increase, ameliorating the waiting list time.

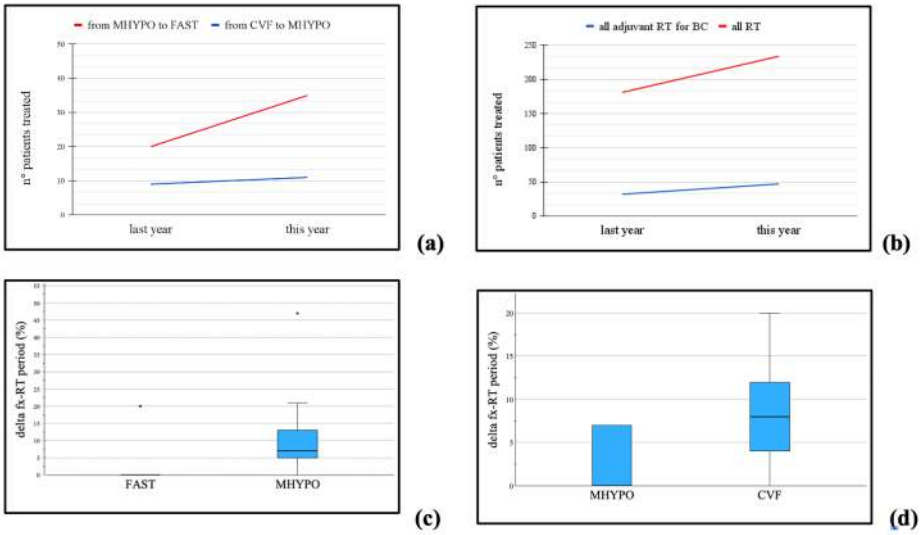

Figure 1. Variations of number of patients treated (a, b), and difference in relative treatment period between schemes (c, d).

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PATIENT-TAILORED MANAGEMENT OF POST- PROSTATECTOMY PROSTATE CANCER BIOCHEMICAL RELAPSE BY PRECISION RADIATION ONCOLOGY GUIDED BY NEXT-GENERATION IMAGING

Code: 16

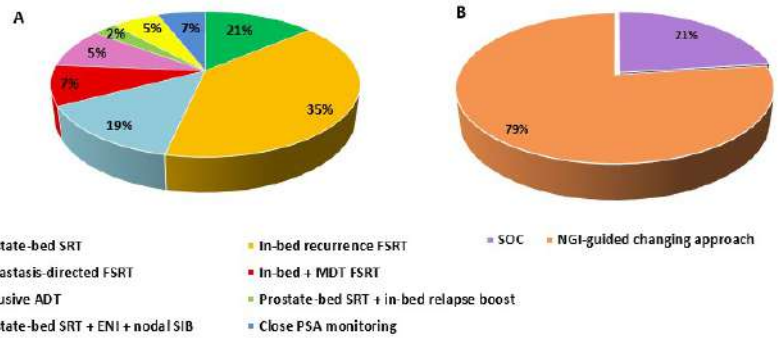
Aims: To present our preliminary experience of application of the principles of precision oncology in Radiotherapy (RT) using next-generation imaging (NGI) in the field of post-prostatectomy prostate cancer biochemical recurrence.

Methods: Data from 43 consecutive patients (pts) evaluated at our Institutional Uro-oncology Tumor Board between September 2018 and December 2023 for PSA rising ≥0.20 ng/ml after radical prostatectomy were reviewed. All pts underwent centralized 18F-Prostate-specific membrane antigen (PSMA)-PET/CT (better than 68Ga for vesicourethral anastomosis characterization) and prostate multiparametric magnetic resonance (mpMRI) (for in-bed relapse confirmation) before decision-making. This study is part of Clinical Outcome of Radiotherapy Treatment in Azienda Toscana Nord-Ovest (CORTATNO) research project funded by Tuscany Region.

Results: We found 21 (49%) in-bed local relapses, all but 3 (7%) subject to ablative fractionated stereotactic radiotherapy (FSRT) by MRI-guided dose painting, 3 (7%) of them with concurrent nodal FSRT for synchronous oligorecurrence; 1 (2%) prostate bed target volume delineation with PET/MRI-guided in-bed lesion sequential boost for irrespective healthy tissues dose constraints harboring unacceptable FSRT toxicity risk; exclusive androgen-deprivation therapy (ADT) in the remaining 2 (5%) for old age and high obstructive risk. Pelvic node and bone oligorecurrence only was detected in 8 (19%) and 2 (5%) cases, respectively: we chose metastases-directed FSRT without prostate bed salvage radiotherapy (SRT) plus ADT for all but 2 (5%) 65-year-old pts, submitted to ADT and SRT plus positive node simultaneous integrated boost and elective node irradiation. Twelve (28%) pts had negative NGI thus standard SRT was planned, but 3 (7%) refused so close PSA monitoring was applied. Changing therapeutic approach beyond the standard of care was reported in 34 (79%) of cases (Figure 1).

Conclusions: Advances in morphofunctional imaging, RT planning and delivery techniques allowed to set NGI-targeted, patient-tailored salvage treatments in nearly 75% of the analysed cohort, mostly with curative intent, or to achieve long-term disease control. Longer follow up is needed to better understand the role of precision radiation oncology in locally recurrent prostate cancer. Prospective validation of our promising findings will further clarify the true impact of NGI to maximize the therapeutic potential of RT and inform radiation decisions.

Figure 1. Next-generation image-guided decision making (A) and changing therapeutic approach beyond the SOC (B)



SOC = standard of care; SRT = salvage radiation therapy; FSRT = fractionated stereotactic radiotherapy; ADT = androgen deprivation therapy; ENI = elective nodal irradiation; SIB = simultaneous integrated boost; MDT = metastasis-directed therapy; PSA = prostate-specific antigen; NGI = next generation imaging

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RADICAL RADIOTHERAPY IN HIGH AND VERY HIGH- RISK PROSTATE CANCER PATIENTS: IS AGE A CONTRAINDICATION? AN ANALYSIS OF RADIATION- INDUCED TOXICITIES IN ELDERLY PATIENTS ENROLLED IN THE MULTICENTER REQUITE COHORT

Code: 550

Aims: The elderly population is more susceptible to aggressive prostate cancer (PCa) and is most likely to benefit from treatments with curative intent. Despite this, radical treatments are still less used in this group of patients (pts), often candidates for hormone therapy alone or just watchful waiting, even if they are fit. A possible therapeutic dilemma for these pts could be the balance between the benefits from the radical treatment of a potentially lethal malignancy and the fear of higher-than-expected treatment-associated toxicities (tox). This analysis aimed to explore whether older age impacts acute and late radio-induced intestinal (GI) and urinary (GU) tox.

Methods: We considered the radically treated high/very high-risk PCa pts enrolled in the prospective multicenter REQUITE study. According to literature data, we used a cutoff age of 75 years to define the elderly population. Proctitis (Grade?1, G?2), rectal bleeding (G?1, G?2), urinary frequency (G?1, G?2), urinary urgency (G?1, G?2), retention (G?1, G?2), urinary incontinence and hematuria (G?1) were considered as tox endpoints.

Results: Cohort: 484 pts, 152 (31%) ?75 yrs. No significant difference in the prevalence of diabetes (16.3 vs 12.5%, p=0.28, young vs elderly); for the history of cardiac diseases, a trend was found (25.9 vs 34%, p=0.06). 338 pts had 2Gy-fraction RT (60-80Gy), 146 hypofractionation (hypo) (54-75.2Gy). There was no difference in the incidence of acute tox across all endpoints, except for G?1 retention and G?1 urgency, which were increased in younger population 12.7 vs 7.9% and 40 vs 30%, respectively.
The only differences in late tox rates were for G?2 late rectal bleeding (10.5% in the elderly vs 4.5% at 2 yrs, p=0.02), G?1 and G?2 incontinence (21.2% and 10.1% in the elderly vs 15.7% and 4%, p=0.01). When stratifying for conventional/hypo, the elderly population exhibited higher tox rates in the hypo group: 21.9 vs 5.9%, p=0.005, for G?2 rectal bleeding, 12.8 vs 4.8%, p=0.05, for G?2 incontinence. For both endpoints there was no significant difference in the 2Gy- fraction group.

Conclusions: Our analysis shows that radical RT in elderly pts is a safe chance of cure in aggressive PCa, with similar GU and GI toxicity rates across different ages. Attention should be paid to dose fractionation in elderly pts to reduce the risk of G 2 late rectal bleeding and urinary incontinence.

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EARLY BREAST CANCER AND FAST FORWARD PROTOCOL: TOXICITIES AND AESTHETIC OUTCOMES IN A LARGE COHORT OF PATIENTS

Code: 540

Aims: To evaluate aesthetic outcomes and toxicities in early breast cancer patients treated with adjuvant radiotherapy using Fast Forward protocol.

Methods: We analysed all early breast cancer patients treated with adjuvant radiotherapy (RT) following conservative surgery. Toxicities were prospectively collected at baseline, during RT (acute), ≤4 weeks after RT (subacute); aesthetic outcomes at every three month after the treatment have been evaluated. Toxicities were scored according to RTOG scale. Besides, we evaluated the possible association with adjuvant chemotherapy and supportive care for skin/gland alterations.

Results: From December 2022 to December 2023 120 patients were treated, according to Fast Forward scheme; Median Age was 64 years (range 51-85); 80% of patients had histological diagnosis of invasive carcinoma no special type, 6,7% Papillar, 10% with Neuroendocrine component and 3,4% Mucinos. 41/120 patients (34.1%) were submitted to adjuvant chemotherapy. 108/120 patients (90%) received endocrine therapy.
Patients were treated with 26Gy in five fractions in VMAT technique.
Acute and Subacute toxicities were: 6,7% mastodynia G1, 8% scar pain G2, 3,4% oedema G2, 33,34% erythema associated with pruritus and burning ≤G2. No grade 3 toxicities were recorded.
Aesthetic outcomes: 8% scar fibrosis G1-2, 10.5% dyschromic skin alteration G1 and one patients showed a refractory no-cancer related inflammatory mastitis associated with peau d' orange localized in inferior quadrants. No skin/gland aesthetic alteration higher grade 3 were observed.

Conclusions: Our experience showed that FAST FORWARD protocol is feasible and well tolerated with minimal toxicities and excellent results in terms of aesthetic outcomes.

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IMPLEMENTATION OF DEEP INSPIRATION BREATH HOLD (DIBH) IN WOMEN IRRADIATED FOR LEFT BREAST NEOPLASIA

Code: 610

Aims: With PRNN funds, Radiotherapy at the San Giovanni Addolorata Hospital has acquired a True Beam Varian equipped with accessories useful for deep Inspiration breath hold (DIBH RPM Varian). During a deep breath and a subsequent apnea, the lung increases its volume to accommodate the air and the heart reduces in volume to make room for the lung by exploiting the space present in the four cardiac cavities. Evaluating the dosimetric data obtained during the implementation phase is the objective of this contribution.

Methods: From September 2023 to December 2023, 14 women who underwent breast-conserving surgery were treated with the DIBH. All received moderate hypofractionation on the left breast with a dose of 42.56 Gy in 16 fractions of 2.66 Gy and concomitant boost of 50 Gy in 16 fractions of 3.125 Gy. Depending on the anatomical complexity, 9 of them were treated with VMAT and 5 had 3D dosimetric planning. Volumetric and dosimetric data were processed with Eclipse Varian.

Results: The DIBH allows for a considerable saving of the organs at risk even in the most complex anatomies. In our series the left lung has an average value of V20 equal to 5.6 Gy, V10 equal to 20.3 Gy and V5 equal to 46.1 Gy of the left lung with the VMAT technique. The 3D technique spares the same organ more than VMAT as long as it has less complex anatomies with an average value of V20 equal to 8.6 Gy, V10 equal to 20 Gy and V5 equal to 38.4 Gy. The heart also received an average V5 dose of 5.8 Gy in VMAT and in 3D an average V5 value of 3.5 Gy. Finally, the right breast in 3D in DIBH does not receive a dose while the VMAT has an average value of 2.6 Gy and an average V5 value of 6.7 Gy.

Conclusions: Apnea reduces the movement linked to the excursion of the rib cage and moves the heart away from it by about a centimeter more than with free breathing. The small number of the analyzed sample does not allow us to draw exhaustive conclusions but offers us the indication to continue with simpler techniques when the anatomy allows it, reserving cases of more complex anatomy for VMAT.

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HIGH-DOSE PROTON THERAPY IN INTRACRANIAL ATYPICAL MENINGIOMAS

Code: 228

Aims: To report clinical outcomes of high-dose active beam scanning proton therapy (PT) for intra-cranial atypical meningiomas (AM). To the best of our knolowdge this is the largest series of patients (pts) treated with PT for AM

Methods: Forty-eight pts with AM were treated with PT between April 2015 and June 2023. Median age was 56 years (range, 19-82) while KPS ranged between 70 and 100 (median 90); 29 were female (60%). All pts had histologically proven World Health Organization (WHO) Grade II tumors. In 21 pts tumor was located in the skull base. All tumors were complex in shape or in close proximity/abutting to organs at risk. All pts received PT for residual or progressive lesions after surgery. None of the pts received PT as re-irradiation. Dose prescription was 60 GyRBE (RBE: relative biologic effectiveness) in 30 fractions (2 GyRBE per fraction). CTV volume ranged from 34 to 394 cc (median, 76.5). Toxicity was assessed according to Common Terminology Criteria for Adverse Events version 4.0. Median follow-up (FU) time was 28 months (range, 6-61). Overall survival (OS) and local control (LC) were calculated using the Kaplan-Meier estimates. The log–rank test was used to compare different survival functions according to predefined stratifications

Results: Registered acute side effects include grade (G) 1 (15%) and G2 (6%) skin erythema/hyperpigmentation, G1 (17%) and G2 (58%) alopecia, G1 (44%) and G2 (6%) fatigue, G1 (4%) and G2 (4%) conjunctivitis, G1 (12%) and G2 (4%) headache, G1 (10%) and G2 (8%) nausea. G3 conjunctivitis was registered in 2% of pts. There were no further G3 or higher acute toxicities. Registered late side effects include G1 (10%) and G2 (27%) alopecia, G1 (4%) fatigue, and G1 (4%) headache. During FU 2 pts (4%) experienced symptomatic G3 radiation necrosis (diagnosed at imaging). There were no further G3 or higher late toxicities. The 3- and 5-year actuarial LC was 81% and 67%, respectively. On univariate analysis, timing of PT (adjuvant vs at progression after surgery, p=0.16) and tumor location (skull base vs other locations, p=0.27) were not significant prognosticators for LC. The 3- and 5-year actuarial OS was 100% and 67%, respectively. On univariate analysis, timing of PT (adjuvant vs at progression after surgery, p=0.31) and tumor location (skull base vs other locations, p=0.41) were not significant prognosticators for OS

Conclusions: High-dose PT is safe and effective treatment for pts with AM. Longer follow-up is necessary to confirm safety and efficacy.

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THE ROLE OF STEREOTACTIC BODY RADIOTHERAPY IN OLIGOPROGRESSIVE UROTHELIAL CANCER PATIENTS: A RETROSPECTIVE EXPERIENCE

Code: 297

Aims: Urothelial cancer is one of the most common malignancies; after relapse or disease progression, available therapeutic options are limited. The aim of our study was to evaluate the role of SBRT as a metastasis- directed therapy (MDT) to postpone the start of a next-line systemic treatment (NEST) in patients with oligometastatic urothelial cancer.

Methods: We retrospectively evaluated 10 patients (pts) and 15 lesions treated between February 2019 and December 2023. All pts experienced an oligoprogression (defined as the appearance and/or the progression of 1 up to 5 bone or nodal metastases) had ECOG Performance Status of 0-1 and received a SBRT upon oligoprogressive metastatic sites, preserving systemic treatment. SBRT was delivered under image guided radiation therapy (IGRT). The dose selection was based on the volume and localization of oligometastases. Pts were treated with a total dose of 30 Gy up to 37,5 Gy in five fractions with a biologically effective dose (BED) of at least 90 Gy using an 3 Gy / ratio. New SBRT upon new metastatic sites was also permitted. Pts receiving palliative radiotherapy were excluded. Progressive disease at > 5 metastatic sites led to a change of the systemic treatment. Toxicity was assessed by Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0.

Results: After a median follow up of 29 months a LC of 100% was achieved. No local recurrence in lesions with complete or partial response were noted. No acute and late toxicities > G1 were reported. All patients, except one, are still alive.

Conclusions: SBRT in oligoprogressive urothelial cancer as MDT during systemic treatment resulted in a feasible and effective treatment obtaining an excellent LC and delaying the start of NEST. Longer follow-up and further prospective studies are necessary to confirm our preliminary results.

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PILOT TRIAL OF LOW DOSE WHOLE BRAIN RADIOTHERAPY IN EARLY ALZHEIMERS DISEASE

Code: 384

Aims: Alzheimer's disease (A.D.) is the most common form of dementia and accounts for at least 60-80% of dementia cases. Estimated one million and 200.000 Italian people are living with dementia, and in 2050 2,3 millions of Italian will be diagnosed with A.D..Therefore, new strategies must be development to counteract this disease. One field of medicine that has obtained significant interest from researchers to potentially treat A.D. is low-dose ionizing radiation. The earliest phase of A.D. (cellular phase) happens in parallel with accumulating amyloid beta, inducing the spread of TAU pathology. For this reason various reports suggest that the brain's exposure to low doses of ionizing radiation can oppose the mechanism of accumulation of beta amyloid, neuroinflammation and cerebral vasculopathy. In the contrary recent advanced in amyloid-targeting monoclonal antibodies did not shown efficacy in stopping A.D. (Aducanumab, Lecanumab, Donanemab)

Methods: In our protocol we decided to select 4 arms: ARM 1: RT whole brain (WBI) 10 Gy in 5 fractions, ARM 2: RT WBI 10 Gy in 5 fractions and inhibitor of acetilcolinesterase drugs, ARMS 3 sham RT WBI, ARM 4: sham RT and inhibitor of acetilcolinesterase. Every arm consists of 5 patients, so total study will be of 20 patients. Patients will be esamine with neurocognitive and psychometric tests, bioumoral markers dosage, PET (Positron Emission Thomography) before and after WBI. WBI will be done with 3DCRT and we had estabilished criteria for elegibility and for exclusion. Informed consent will be administered. The follow-up is planned at 6 weeks and at 3, 6, 9 12 months with PET and neurocognitive tests and umoral markers.

Results: We will illustate the protocol of this trial and preliminary results and tolerance of WBI in active centers worldwide.

Conclusions: We propose, in this trial, the use of WBI with a low dose with the goal to slow down the evolution of A.D., and to ameliorate the patients quality of life, reducing the progression of this disease.

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A MONOINSTITUTIONAL ANALYSIS OF OUTCOMES OF SALVAGE FRACTIONATED RADIOTHERAPY FOR LARGE PITUITARY ADENOMAS

Code: 252

Aims: Gamma Knife (GK) radiosurgery (SRS) is used for the treatment of Pituitary adenomas (PA) in our institution, but large PA or those in proximity of optic pathways are referred to fractionated radiotherapy (FRT). Here we evaluate the safety and efficacy of FRT.

Methods: From 05/2011 to 08/2022 50 PA patients (pts) were treated with FRT. Patients and treatments characteristics are described in Tab.1. For 7 pts FRT was prescribed due to comorbidities. Median time between surgery and RT in pts with residual/relapsed disease was 86.9 (6.78-297.12) months. Pts were treated with 4 different EBRT techniques: 1 patient with IMRT, 22 patients with volumetric-arc therapy (VMAT), 21 with helical IMRT (Tomotherapy, TT), and 6 with robotic SRS/stereotactic radiotherapy (CyberKnife,CK). For CK treatments a total dose of 25 Gy/5 fractions (fr) was prescribed for 4 patients, 25 Gy/1 fraction for one patient, and 30 Gy/5 fractions for another patient. For the other pts, 1.8/2 Gy/fractions were delivered to a median total dose of 48.6 Gy (48.0-60.0). Median treatment volumes with IMRT/VMAT/TT techniques were: Gross Tumor Volume (GTV) 9.74 cc (2.23-56.99), Planning Target Volume (PTV) 28.6 cc (14.5-171.3) with a mean dose to the chiasm of 46.7 Gy. Median GTV and PTV with CK technique was 8.52cc (0.42-9.08) and 10.63cc (1.28-11.97), respectively, with an average dose to the chiasm of 13.1 Gy (3.1-19.4). Pts were re-evaluated with brain MRI, computerized visual campimetry, and blood tests.

Results: Median follow-up was 33 (0-122.8) months. No G3 or higher toxicities were found. One patient died for other causes (sepsis), and 5 pts were followed at other centers; 44 pts were evaluable for late toxicity and efficacy results. Only three (6.8%) patients presented progressive disease, two of them already at the first MRI evaluation. Only one patient (2.3%) died for disease progression 57 months after the end of RT, and four (9.1%) suffered a worsening of vision, with a mean interval of 39.2 (28.8-49.0) months. Hormonal control was obtained in 94.7%, and only 1/19 patients had an uncontrolled hormonal status (Secreting PRL adenoma). Tree-year overall survival (OS) was 88.5% and 5-year OS 82.6%.

Conclusions: Good local and biochemical control were obtained in pts with large PA, or in proximity of optic pathways. Late visual toxicity is acceptable, given the close relationships with the optical pathways.

Patients	50
Men	21
Women	29
Age	49,0 (10,7-88,5)
Surgery	43
Only RT	7
IMRT	1
VMAT	21
TT	22
CK	6
Secreting Adenomas	19
ACTH	8
GH	4
PRL	3
FSH	1
Mixed	3
Median Dose	48,6 Gy (25,0-60,0)
EQD2 for CK	48,0 Gy (31,2-72,9)
BED (α/β=10)	57,35 Gy (37,5-87,5)
D max Chiasma	49,7 Gy (6,5-57,8)
D mean Chiasma	47,9 Gy (3,1-56,1)

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PROFILACTIC RADIOTHERAPY FOR HIPS AND ELBOWS HETEROTOPIC OSSIFICATIONS: A RETROSPECTIVE MULTICENTRE EXPERIENCE

Code: 256

Aims: Heterotopic ossifications (HO) are a significant clinical complication, particularly in patients (pts) who had previously undergone surgical procedures on hips and elbows. These abnormal appositions of lamellar bone may limit joint mobility, also causing chronic pain. The aim of our analysis is to evaluate the efficacy and safety of prophylactic radiotherapy (RT) on elbows or hips to prevent new appositions of HO.

Methods: Between January 2015 and September 2023, 63 patients (pts) underwent RT either pre- or post- surgery to prevent HO in three different centers of the northern Italy. Among them, 35 (55.6%) were treated on the hips and 28 (44.4%) on the elbow. Average age was 55 years (range 23-82 years). Fifty-one pts were males and twelve females. Fifty-five pts had no history of previous ossifications, while 8 had experienced prior HO, six of whom were in the same location and two in a different one. The ossifications were post-traumatic, non-traumatic and neurogenic in 23, 3 and 2 pts respectively in the elbows and 12, 23 and 0 for the hips.

Results: The pre-operative RT was performed on 33 pts, with 13 receiving treatment prophylactically within 8 hours of surgery and 20 between 8 and 24 hours. Additionally, 30 pts received postoperative RT within 0 to 4 days post-surgery, with a median of 1 day. A 2D or 3DCRT plan using X-ray photons from 4, 6, 10, or 15 MV was generated respectively for 14 and 48 pts, while VMAT was used just in one patient.
The most frequently used dose was 7 Gy in a single fraction, administered to 59 pts. One patient received
7.5 Gy, another 6.5 Gy. One pt was treated firstly with 7 Gy the day before the planned surgery, but 3 Gy more were delivered a month later, because surgery was postponed due to a positive COVID-19 status. At the time of analysis, 23 patients (36,5%) were lost to follow-up. At the average follow-up period of 66,3 months (range: 4-108 months), no G2 or greater toxicity was recorded; no patient reported radiation- induced tumors occurring at the treatment site. Seven pts (11,1 %) experienced a HO recurrence to the treatment site after surgery. No difference was found in terms of recurrence when different timing of RT were compared.

Conclusions: RT for preventing HO formation seems to be well-tolerated and associated with modest recurrence rates, whether performed before or after surgery. More data and prospective studies are needed to validate the actual efficacy and the optimal timing of the treatment.

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REIRRADIATION IN RECURRENT MENINGIOMAS: A SINGLE-CENTER SAFETY AND LOCAL CONTROL ANALYSIS

Code: 405

Aims: At the current knowledge, there is a lack of standardized guidelines for recurrent meningioma (RM) even with the high probability of disease relapse. Radiotherapy (RT) plays an important role in the management of meningiomas, but its use at recurrence is still mainly guided only by clinical practice.
The aim of this study is to determine survival and safety outcomes in a cohort of patients (pts) with RM who underwent reirradiation (ReRT).

Methods: Pts treated with ReRT at our center for RM were included in the study. Data about volume of lesions at different timepoints were recorded with magnetic resonance performed as per clinical practice. Toxicity was assessed according to Common Terminology Criteria for Adverse Events version 5.0. The primary outcome was progression-free survival (PFS); secondary outcomes included overall survival (OS) and treatment-related toxicity. Kaplan–Meier curves were generated to examine the effect of several parameters on PFS; Logrank test comparison was used to determine predictors of PFS.

Results: We collected data about 22 consecutive RM pts who underwent ReRT at our center between 1995 and 2022. As first treatment, 21 (95%) pts underwent surgery. First RT course was delivered as adjuvant therapy, at recurrence and as prior treatment in 9, 12 and 1 cases, respectively. At recurrence, 36,8% of pts underwent a second surgery. Other pts characteristics can be found in table 1. We estimated the biologically equivalent doses in 2 Gy fractions (EQD2) with an a/b =2 for brain tissue and a/b = 4 for tumor. RT techniques and dosimetry are listed in table 2 and 3 respectively.
With a mean follow-up of 120 months, the mean PFS and OS observed were 22.8 and 119.1 months, respectively. PFS was longer when delivering a lower biologically effective dose (BED): 23.99 and 18.33 months if BED under or above 131.4 Gy, respectively (*p 0.81*). Furthermore, PFS was improved in pts that didn't undergo a second surgery (25.2 vs 19.0 months, *p* 0,27). Finally, the presence of alterations at magnetic resonance performed after RT, demonstrated rates of shorter PFS (13.6 vs 24.4
months, *p* 0,2). After reirradiation, we observed 2 cases of G1 acute toxicity (any kind of toxicity), 1 for G2 and 1 for G3. In chronic, we only registered 1 case of G1 toxicity and 2 cases of G2.

Conclusions: ReRT in RM can be considered as a valid and safe treatment given its low toxicity. These encouraging results need to be validated by further prospective studies.

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Table 1

Age at reirradiation	66 (59-77)
KPS at reirradiation	88,4 (70-100)
Localization: - Convexity - Falcine/parasagittal - Anterior fossa skull base - Middle fossa skull base - Posterior fossa skull base	 68,4% (n=15) 15,7% (n=3) 10,5% (n=3) 0% (n=0) 5% (n=1)
WHO grade - I - II - III - no histological confirmation	 0% (n=0) 36,8% (n=8) 5% (n=1) 57,9% (n=13)
Prior treatment - Surgery - Radiotherapy	 95% (n=21) 5% (n=1)
Surgery at progression - Yes - No	 36% (n=8) 64% (n=14)

Table 3

	1^ course RT media (range)	2^ course RT media (range)
GTV cc (range)	19,6 (6-55,5)	12,34 (0,41-33,94)
Tumor EQD2	54,9 (27,5–142,5)	32,34 (16-557,42)
Tumor BED (range)	82,3 (41,2-213,7)	131,4 (96,5-261,75)
Brain EQD2 (range)	58,8 (56-61,5)	55,4 (44,9-64)
Brain BED (range)	71,79 (20,5-123,1)	229,9

Table 2

Technique	1^ RT	2^ RT
EBRT	63%	10%
IMRT	0%	10%
multi-fraction SRS	5%	10%
single fraction SRS	32%	70%

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CYBERKNIFE- AND GAMMA KNIFE-BASED STEREOTACTIC RADIOTHERAPY FOR HEAD AND NECK PARAGANGLIOMAS: A SINGLE-CENTER EXPERIENCE

Code: 390

Aims: Head and neck paragangliomas (HN-PGs) are slow-growing tumors with a good prognosis, arising from the autonomic nervous system. The management of HN-PGs is commonly based on a multidisciplinary approach and radiation therapy plays a crucial role in the treatment strategy. The medical goal is to maximize local control while minimizing toxicity. RT has proven to be a safe and efficacious method in the management of HN-PGs, both in the upfront and post-operative setting. We report on the outcomes of a single-center cohort of patients (pts) treated with CyberKnife (CK)- and Gamma Knife (GK)- based stereotactic radiotherapy (SRT) for HN-PGs.

Methods: Consecutive pts who received CK- and GK- SRT for HNPGs in our institution between 2016 and 2022 were included. Data including age, gender, symptoms before SRS, side of radiation, history of previous operation or radiation, Fisch classification, dosimetric parameters for SRS, radiological response, changes in symptoms and treatment-related adverse events (TRAEs) were recorded. Toxicities were recorded according to Common Terminology Criteria for Adverse Events (CTCAE v5.0). Local control (LC) was defined as the absence of radiologic progression. Survival analysis were performed with Kaplan Meier method.

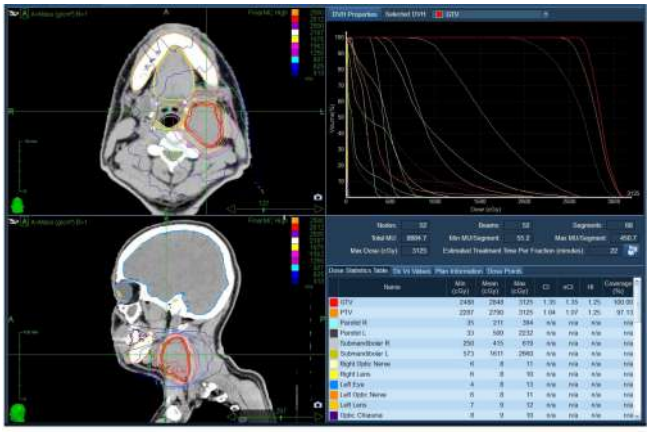

Figure 1. Treatment planning and dosimetry of a carotid body paraganglioma treated with CK-SRT.

Results: We retrospectively evaluated 19 pts treated with CK (15)- and GK (4)- SRT for temporal bone (12) and carotid (7) localization of HN-PGs (Fig.1). The most commonly adopted SRT schedules consisted of a total dose of 12-20 Gy, 24 Gy and 25 Gy delivered in 1, 3 and 5 fractions, respectively. Fish classification was available only for 8 out of 19 pts, of whom 2 were classified as Fish B and 6 as Fish C HN-PGs, respectively. At a median follow-up of 60 months [28-103 months] the LC rate was 94,7% (18/19 pts). The median age was 58 years [29-79 years] and GTV was 5,6 cm^3 [0,2 - 41 cm^3]. The symptomatic improvement has been observed in 12/19 pts (63%). Four pts had acute toxicity: grade (G) 1 dysphagia (1 pt), G2 dysgeusia (1pt), G1 esophagitis (1pt) and G3 mucositis (1pt). Only one patient experienced G1 late dysphagia.

Conclusions: The present analysis aimed to highlight the efficacy and safety of SRT for HN-PGs confirming high LC rate and low incidence of TRAEs. The optimal management depends on the site and location as well as patient's age and clinical presentation. The risk-benefit profile is different for each patient and further prospective experiences investigating larger cohorts of pts are needed.

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MANAGEMENT OF HETEROTOPIC OSSIFICATION AFTER TOTAL HIP ARTHROPLASTY: THE ROLE OF RADIOTHERAPY IN PREVENTING RECURRENCE

Code: 369

Aims: The aim of this study was to investigate the role of radiotherapy in patients who underwent surgical removal of heterotopic ossifications (HO) after total hip arthroplasty (THA), in terms of clinical and radiological outcomes, risk factors and complications.

Methods: A retrospective study was conducted, including patients who underwent surgical removal of periprosthetic calcifications after THA surgery. Patient demographics, imaging, previous surgery, clinical scores, and surgical parameters were analysed. Radiotherapy and pharmacological prophylaxis (NSAIDs and COX-2 inhibitors) were evaluated. Multivariable logistic regression analysis was used to assess the association of the presence of HO with age, sex, and all variables that differed significantly ($p<0.05$) in univariate analyses.

Results: Twenty-six patients with HO and 156 THA patients without HO (control group) were included. Patients with HO had a lower burden of comorbidities, lower BMI, and lower ASA scores than controls. Of the 26 patients with HO, 10 (38.5%) received prophylactic radiotherapy, administered as a single dose 24 hours before surgery. The total dose of 7 Gy was delivered as a single fraction to the volume defined by the extension of the prosthesis. Only one patient who underwent radiotherapy had a recurrence, while new ossifications were found in 3 patients without prophylaxis (11.5%). Logistic regression analysis showed a significant inverse association between the presence of HO and ASA scores. Surgical approach and radiographic classification improved after surgery. Radiotherapy prophylaxis and pharmacological treatment showed positive results. Complications were recorded, including local and systemic complications, but overall, patients reported physical improvement after surgery.

Conclusions: Surgical removal of HO in symptomatic patients with high-grade disease resulted in good clinical and radiographic outcomes. Radiotherapy was an effective perioperative and preventive strategy for the recurrence of HO, also in combination with NSAIDs and COX-2 inhibitors. However, additional large studies are needed to validate and further establish these findings.

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KELOIDS POSTOPERATIVE RADIATION THERAPY: EXCELLENT AESTHETIC RESULTS IN A SINGLE- INSTITUTIONAL EXPERIENCE

Code: 435

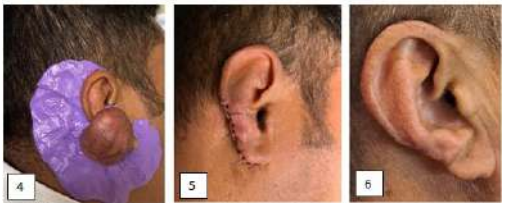
Aims: Keloids represent a benign fibroproliferative disease with a notable recurrence rate following surgical excision. The role and optimal treatment regimen of radiotherapy (RT) in these instances remain not clear. Adjuvant RT emerges as a potential option to mitigate the risk of recurrence while also preserving aesthetic outcomes. The aims of our work was to assess the effectiveness of post-operative RT following surgical intervention in cases of keloid recurrence.

Methods: We conducted a retrospective analysis of disease control, toxicity, and aesthetic outcomes associated with RT carried out on 10 keloids in 8 patients (5 females, 3 males) treated between May 2021 and July 2023. All patients had previously undergone one or more surgical interventions for recurrent keloids. RT was administered using a 6-MeV electron beam, 24 hours after the complete excision of the keloid. A personalized silicone 0.5-1 cm bolus was employed to ensure adequate radiation dose on the keloid surgical scar. Additionally, a high-density bolus (eXaSkin) was custom-made the day before surgery for keloids located in the earlobe to minimize radiation exposure to the external auditory canal and mastoid bone (Fig. 1-4 and Fig. 2-5).

Fig. 1 and 4 - Pre-operative view with personalized high-density bolus (eXaSkin)

Fig. 2 and 5 - Immediately post-surgery

Fig. 3 and 6 - 14 months follow up



Results: The median age of patients was 32 years (range 18-52), 3 out of 8 patients were Caucasian. Among the keloids, five were situated in the earlobe, two on the chest, one in the axilla, one in shoulder, and one back. Contributing

factors to keloid formation included piercing lesions (5 out of 9), surgical scars (3 out of 9 lesions), and one patient had a family history. A dose ranging between 1950 and 2100 cGy (650-700 cGy/day per fraction) was administered in three fractions beginning the day after surgery. Treatments were well tolerated without acute toxicity. The median follow-up period was 20 months (range 3-24), during which no recurrences and favorable cosmetic outcomes were observed for all patients (Figure 3-6).

Conclusions: Adjuvant RT proved to be a viable option for reducing keloid recurrence and enhancing cosmetic outcomes. Our follow-up data confirmed these results. A multidisciplinary collaboration is essential to ensure optimal timing between surgery and radiotherapy.

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VENTRICULAR TACHYCARDIA ABLATION THROUGH RADIATION THERAPY (VT-ART) CONSORTIUM: SET-UP RESULTS OF AN OBSERVATIONAL MULTICENTRIC TRIAL VIA MATCHED PAIR ANALYSIS

Code: 597

Aims: Ventricular tachycardia ablation through radiation therapy (VT-ART) for sustained VT seems promising. Still, definitive data are lacking, and no direct comparison with standard procedures is available. Few registered trials are ongoing. Aim of this multicenter study is to evaluate efficacy and safety of VT-ART, comparing the clinical outcome of patients undergone to VT-ART to patients not having received such procedure

Methods: The two groups will not be collected by direct accrual to avoid randomization among the innovative and traditional arm: a retrospective selection through matched pair analysis will collect patients presenting features like the ones undergone to VT-ART within the consortium.

Results: The project has just been launched at the promoting Center. Currently, only the promoting Center is recruiting patients in the Consortium. The first 12 patients have been enrolled by the promoting Center. All patients were male, with a mean age at the time of the procedure of 69 years (range, 60-75). Pretreatment mean left ventricular ejection fraction was 33% (range, 22-50). All patients had at least grade 1 heart failure according to the New York Heart Association (NYHA) classification, mean grade 2 (range 1-3). Patients had previously undergone an RFCA (range 0-3) for VT on average, with a median time between the most recent RFCA attempt and the STAR session of 20 days (range 0-67). The mean CTV volume of the was 96.09 cc (range 32.50-238.50). The mean PTV volume was 135 cc (range 44 -303). For all patients, SBRT was performed with a dose of 25 Gy (80% isodose) in a single fraction. In no case did the dose administered to OARs exceed the threshold reference values. Two patients died before reaching the 3 month follow-up, due progressive heart failure. Four patients had a

dramatic reduction in arrhythmic burden. The recruitment of similar patients to the irradiate group through matched pair analysis, did found 1 matches until now: update will be provided later on. Further details about radiotherapy planning, delivery and IGRT; patient matching and clinical comparison would be reported at the congress.

Conclusions: Our trial will provide insight into the efficacy and safety of VT-ART through a matched pair analysis, via multicentric study of two groups of patients with or without VT-ART in the multicentric consortium (with subgroup stratification into dynamic cohorts). One only other Italian trial is ongoing.

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THE ROLE OF EMPATHY AND ALEXITHYMIA IN THE PROFESSIONAL QUALITY OF LIFE OF RADIATION ONCOLOGISTS AND RADIATION THERAPY TECHNICIANS: A MONOCENTRIC EXPERIENCE

Code: 467

Aims: Radiation oncology comprises many occupational profiles, including radiation oncologists (ROs) and radiation therapists (RTTs). Physical and mental well-being are crucial for these professionals as they affect performance at work and the interaction with the patients. The present study aims to explore the quality of life (QoL) of ROs and RTTs in an Italian RT department and to report data about how different factors, including personality traits such as alexithymia and empathy, may impact professional QoL.

Methods: An online survey was administered to professionals of a Radiation oncology department. Participants were asked to fill out 3 validated questionnaires, all based on a 5-point Likert scale, and dealing with professional QoL, alexithymia, and empathy: (i) Professional Quality of Life Scale (ProQoL) – 30 items divided in 3 sub-scales; (ii) Toronto Alexithymia Scale (TAS-20) – 20 items in 3 sub-scales; (iii) Interpersonal Reactivity Index (IRI) 28 items in 4 subscales. Cronbach's alpha was employed to assess the questionnaires' internal consistency and scale reliability.

Results: A total of 48 professionals completed all questionnaires. Of them, 32 (66.7%) were ROs, and 16 (33.3%) RTTs. Cronbach's alpha was

Table 1. Comparison between ROs and RTTs mean values and standard deviations for the (a) ProQOL (b) TAS-20, and (c) IRI questionnaires and their respective sub-scales.

(a)

ProQOL	Mean_total	SD	Mean_ROs	SD	Mean_RTTs	SD
Compassion Satisfaction	37.60	5.398	38.22	5.517	36.38	5.097
Burnout	25.46	4.505	25.53	4.325	25.31	4.990
Secondary Trauma Stress	21.88	4.945	22.06	4.724	21.50	5.502

(b)

TAS-20	Mean_total	SD	Mean_ROs	SD	Mean_RTTs	SD
Total	49.17	12.868	46.91	13.596	53.69	10.203
Difficulty Identifying Feelings	15.79	6.046	15.06	5.875	17.25	6.309
Difficulty Describing Feelings	14.48	5.190	13.59	5.587	16.25	3.856
Externally Oriented Thinking	18.90	4.080	18.25	4.280	20.19	3.410

(c)

IRI	Mean	SD	Mean_ROs	SD	Mean_RTTs	SD
Perspective Taking	3.48	0.534	3.57	0.546	3.30	0.478
Empathic Concern	3.58	0.457	3.68	0.470	3.38	0.368
Personal Distress	2.51	0.555	2.53	0.572	2.48	0.537
Fantasy	2.96	0.549	3.05	0.430	2.79	0.715

acceptable/good for all the questionnaires and subscales except for the IRI (sub-scale Empathic concern, α score =0.61) and ProQoL (burnout sub-scale, α score =0.63). Regarding the ProQoL, no significant differences were found among ROs and RTTs. Considering the frequencies regarding burnout and secondary trauma stress no participants were found in the high grade of risk for both scales. Nine participants (6 ROs and 3 RTTs) resulted alexithymics according to the TAS-20 overall score, and 12 borderline alexithymic (5 ROs and 7 RTTs). Finally, for the 4 subscales of the IRI questionnaire no significant differences were found. Overall mean values and corresponding standard deviations for all the questionnaires are reported in Table 1.

Conclusions: This monocentric experience results showed no intrinsic differences regarding the professional QoL between ROs and RTTs and no evidence of risk of burnout, while rates of alexithymia and distributions of empathy scores are in line with the ones observed for other radiation oncology professionals in Europe. These results underscore the importance of promoting a positive dimension of the professional work environment and could also promote other similar initiatives to point out the importance of fostering emotional competencies.

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PRELIMINARY RESULTS OF THE FIRST PROSTATE CANCER PATIENTS OF PHINRAD STUDY: PATIENTS' PERCEPTION OF RECEIVED INFORMATION IN THE RADIATION ONCOLOGY DEPARTMENT AND THEIR SATISFACTION

Code: 216

Aims: Prostate cancer (PC) is the first cancer for incidence and prevalence in men. Despite the recent impressive progresses in patients' survival, it is noteworthy to underline that up to a 30% of PC patients are reported to be dissatisfied with the information received about therapies and their toxicities. Interestingly, the counselling in radiotherapy is indicated as the worse understood and this entails confusion and anxiety, with a detrimental repercussion on patient's quality of life. Due to the lack of studies with validated instrument on this topic, the purpose of this paper is to investigate PC patients' perception of received information in the radiation oncology department (ROD).

Methods: From January 2022, we prospectively evaluated PC patients consecutive treated at our institution for a localized PC. These patients are recruited in the PHINRAD study (Prostate and head and neck cancer patients' perception of information received about disease, treatment and side effects in radiotherapy) , a monocentric prospective longitudinal cohort study designed to assess PC and head and neck patients' perception of received information after the first visit in the ROD. To assess PC patients' perception of received information and their satisfaction, the Italian version of the international validated EORTC QLQ INFO-25 questionnaire was administered.

Results: Here we present an interim analysis of the first 30 PC patients. Patient's median age was 72 years (range 53-81 years) and all patients were accompanied by a caregiver during the first visit. Median firs visit duration was 45 min (range 30-75 min). Patients diagnosed with a favourable intermediate, unfavourable intermediate, and high risk prostate cancer were 7 (23%), 13 (34%), and 10 (43%), respectively. Androgen deprivation therapy (ADT) was prescribed to 23 (77%) patients. Median EORTC QLQ INFO-25 questionnaire score was 53% (IQR1-3, 43-65%). The score in patients planned to irradiated with and without ADT was 54% (IQR1-3, 45-66%) and 49% (IQR1-3, 43-64%), respectively, (p-value: 0.61). No difference was observed in patients above or below 70 years of age (54% vs 52%, p-value: 0.91).

Conclusions: According to these preliminary data, PA patients referred to the ROD reported not to have received satisfying information; this should encourage a critical reflection among the radiation oncologists. If the trend were confirmed, an improvement of patients' informative path should be evaluated.

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QUALITY OF LIFE AND DISTRESS IN HEAD AND NECK CANCER PATIENTS ABOUT TO UNDERGO RADIOTHERAPY

Code: 536

Aims: Head and neck cancer patients undergoing radiotherapy (RT) might face psychological and quality of life (QoL) challenges, including mask anxiety, related to wearing a thermoplastic mask during the treatment. For these reasons, psychological assessment and tailored interventions are routinely offered to this population at our Radiotherapy Unit, before, during, and after RT. We present preliminary results of the psychological assessment conducted before or in the first days of RT (max within 10 days), aiming to describe QoL and distress of these patients about to undergo treatment.

Methods: During the psychological assessment, different self-report instruments are used: 1) Modified distress thermometer, to assess mask anxiety; 2) HADS, to assess psychological distress; 3) TIPI, to assess personality traits; 4) EORTC QLQ-C30 and Head & Neck Cancer Module (H&N35), to assess QoL;

Results: 38 patients have been involved until now (males=71.1%, mean age=68). The majority have been diagnosed with oral cavity cancer (28.9%), followed by laryngeal (18.4%) and oropharyngeal ones (18.4%). Most of our sample has a 4A stage tumor (34.2%), followed by 3 (21.1%) and 4B (18.4%) stage. 51.4% of patients had previous surgery and 23.7% inductive chemotherapy. 60.5% of patients are candidates for RT with curative intent, 39.5% for adjuvant RT.
Mask anxiety was very low (M=1.13, SD=2.16), with only 2 patients (5.3%) showing clinically significant scores. The total distress mean was 7.66 (SD=6.31); 18.4% of patients presented anxious symptoms and 7.9% depressive ones.
The mean QoL score was 67.1 (SD=23.3). Functioning scales means ranged from 73.2 (role) to 94.7 (cognitive). Higher symptoms reported were insomnia (M=29.82, SD=35.3) and fatigue (M=26.32, SD=33.1) in the EORTC QOLQ-C30 scale, speech (M=18.42, SD=28.6) and senses (M=15.79, SD=24.5) problems in the H&N35 module.
We performed a general linear model to assess the influence on QoL of tumor stage, chemotherapy, surgery, age, and total distress. The final general model was significant ($F_{8,28}=2.89$, $p=.018$, $\eta 2p=.45$) and QoL was significantly related to distress.

Conclusions: while mask anxiety is low, patients are about to undergo RT with psychological distress, a reduction in QoL, and some symptoms. As RT can worsen symptoms and QoL, we claim the importance of routine screening and psychological interventions for this population along and after RT. Further analysis will be presented.

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STEREOTACTIC RADIOSURGERY FOR BRAIN ARTERIOVENOUS MALFORMATIONS IN A MONOINSTITUTIONAL MULTIDISCIPLINARY EXPERIENCE

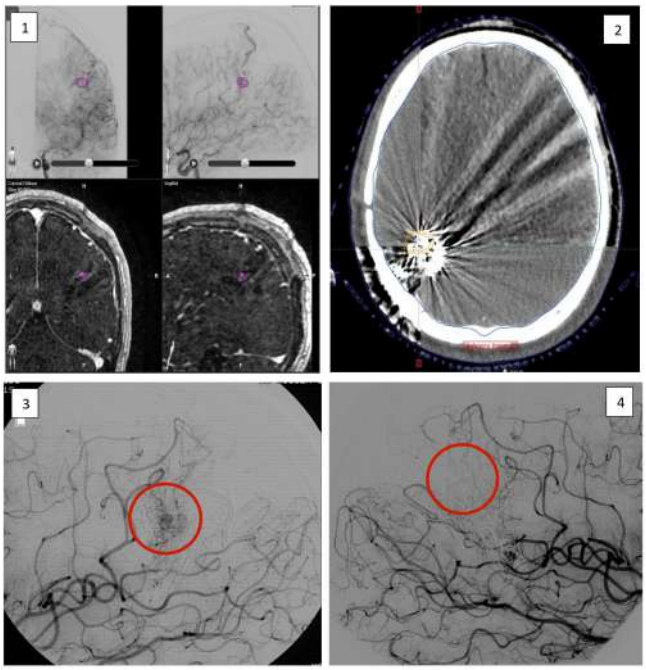
Code: 361

Aims: Intracranial arteriovenous malformations (AVMs) are congenital abnormalities characterized by an irregular tangle of blood vessels. The available therapeutic options include surgery, endovascular embolization and stereotactic radiosurgery (SRS). This study aims to assess the safety and efficacy of SRS in our experience.

Methods: A retrospective analysis was conducted on patients who underwent SRS for AVMs, following surgery and/or endovascular embolization. Pre-treatment imaging included diagnostic T1 brain MRI, cerebral angiography, angio- MRI and planning CT with thermoplastic masks. The planning CT was co-registered with MRI, angio-MRI and angiography to delineate the target volume, which encompassed the entire AVM nidus. Delineations were performed by a multidisciplinary team consisting of a radiation oncologist, neuroradiologist, and interventional radiologist using Elements Image Fusion Angio and SmartBrush software. A 1 mm margin was added to create the planning target volume (PTV). Treatment planning was conducted using the Brainlab Elements TPS and SRS was delivered using Varian True Beam STX (2.5mm MLC, perfect-pitch 6DoF, ExacTrac X-ray, OBI) with dynamic conformal arc technique employing 6MV FFF beams. Treatment outcomes and toxicities were assessed.

Results: Between 2020 and 2023, 4 patients (median age: 15 years, range: 10-23 years) underwent SRS. The median PTV was 0.85 cc (range: 0.2-1.3 cc), with a median total dose of 21 Gy (range: 20-22 Gy) delivered in a single fraction. The median average dose was 23.08 Gy (range: 21.77-24.16 Gy), with a median normal brain volume V12Gy of 2.65 cc (range: 0.3-3.5 cc). Prior to treatment delivery, CBCT was used for setup error correction, and ExacTrac X- ray images were obtained to correct intrafraction errors. Treatment was well tolerated, with no acute or late toxicities observed. At a median follow-up of 34 months (range: 12-40 months) all patients demonstrated complete nidal obliteration on MRI and/or angiography.

Conclusions: SRS demonstrates promising results in terms of safety and efficacy outcomes in the management of intracranial AVMs. Delivering optimal patient care for complex lesions such as AVMs necessitates a multidisciplinary treatment approach and specialized fusion software. The reliable presence of Elements Image Fusion Angio ensures precise and secure target delineation, proving invaluable in instances of residual or recurrent disease following MAV embolization with Onyx.



1. The contouring of the AVM nidus on angiography is reported in the angio-MRI.
2. Match CBCT-planning CT before delivery.
3. Angiography pre-SRS.
4. Angiography 1 year later SRS.

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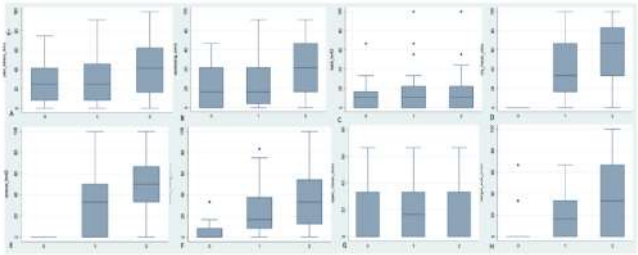
FOSAPREPITANT: A PILOT PROSPECTIVE STUDY IN THE PREVENTION OF NAUSEA AND EMESIS IN HEAD AND NECK CANCER PATIENTS TREATED WITH CISPLATIN CHEMORADIATION

Code: 371

Aims: Concurrent cisplatin-based chemoradiotherapy (CRT) is the standard treatment for head and neck squamous cell carcinoma (HNSCC). Intensity modulated radiotherapy (IMRT) may worsen the intensity of chemotherapy-induced nausea and vomiting (CINV). In this single-center prospective study we aim to report on the impact of fosaprepitant in the prevention of CINV in HNSCC.

Methods: CINV was estimated with the FLIE questionnaire. The EORTC QLQ-HN 43 was administered before treatment beginning, at week 2 and week 5. Dosimetric analysis of vomiting center structures was analysed. Nausea and vomiting items were graded according to CTCAE v.4.01.

Results: From January 2020 to December 2020, a total of 24 patients (19 male, 5 female), with a median age of 64 years at the time of diagnosis, were enrolled in our study. CRT was administered with disease- curative intent. All patients underwent helicoidal-IMRT with simultaneous integrated boost (SIB) and concomitant cisplatin chemotherapy. The worst vomiting grade was G0 for 18 patients (75%), G1 for 5 patients (21%) and G2 experienced by only one patient (4%). G2 nausea occurred more frequently in patients treated with the cisplatin schedule q21 (4/5 cases), as same as G1 vomiting (4/5), even if the patient who reported G2 vomiting underwent weekly cisplatin. No correlation was found between nausea and vomiting



center structures mean dose. According to FLIE, the mean scores of patient-reported nausea and vomiting were 27.4 and 27.7 after CRT. Significantly higher scores of pain in the mouth, swallowing, teeth domains at week 2 in comparison with baseline were observed [Fig.1].

Conclusions: Fosaprepitant in the prevention of CINV yielded a very low rate of moderate-severe nausea and vomiting.

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AUGMENTED REALITY 3D NAVIGATION SYSTEM FOR EVALUATION OF DOSE PLAN DISTRIBUTION IN RADIATION THERAPY

Code: 59

Aims: to develop and test the effectiveness of an augmented reality (AR) system for radiation therapy (RT) plan dose distribution assessment. The project is a collaboration between the IEO and the Department of Bioengineering of Politecnico di Milano.

Methods: One nasopharyngeal carcinoma patient treated at IEO with SBRT was considered. Simulation CT and the planned dose distribution were exported in DICOM files from RayStation TPS. Patient anatomy visualization in the AR environment was based on the Volume Rendering technique. The treatment plan was discretized into 2-dimensional images along the axial plane, which were subsequently aligned with the patient's anatomy. The DICOM file of the dose distribution plan was analyzed using the pydicom library for Python. The dose values range was divided into 6 levels, and a color gradient from green (low) to red (high) was assigned to each level.
The generated images were imported into the Unity3D environment with a pixel spacing parameter matching the one specified in the DICOM file. The CT scan and models of the patient's organs were also loaded using the UnityVolumeRendering plugin for Unity. Subsequently, an AR interface was developed with the Mixed Reality Toolkit (MRTK) for Unity and visualized through the HoloLens2 head-mounted display.

Results: Simultaneous visualization of simulation CT, contours (targets and OARs) and plan dose distribution in the AR environment was successfully developed. The interface offered 3D data visualization, with the ability to activate or deactivate elements via 3 graphical user interface buttons. Additionally, 2 buttons controlled the sliders, allowing users to adjust the transparency of the dose plan for better visualization of underlying structures and to visualize individual frames of the therapeutic plan.
For a more detailed analysis of isodose levels, another panel enabled the visualization of dose levels based on the dose values in Grays. The user could visualize each individual level reconstructed in 3D overlaid on CT. Screenshots of the obtained AR environment are shown in **Figure 1**.

Conclusions: An AR system for RT plan dose assessment was successfully developed. A survey will be conducted among the department to understand the usefulness of the developed system compared to the traditional 2D visualization in the TPS. Future prospects include evaluating the effectiveness of the environment in comparing rival photon-proton plans.

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IMPLEMENTING AN ELECTRONIC PLATFORM FOR A PROTON THERAPY CENTER: WHEN RESEARCH MEETS CLINICAL PRACTICE FROM THE FIRST BRICK TO FUTURE CHALLENGES

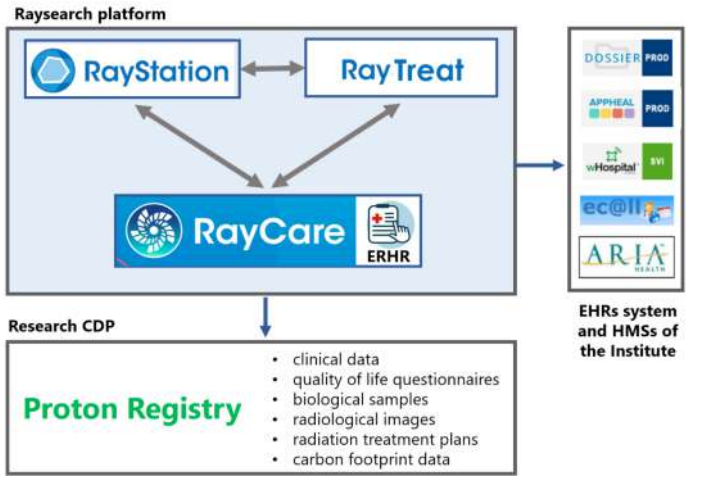
Code: 152

Aims: An electronic platform has been implemented to support clinical practice and research activities at the proton therapy (PT) center of our Institute. The present work aims to report the strategy behind this ambitious goal, highlighting the achievements and the future challenges.

Methods: Over the past two years, a dedicated multidisciplinary team of radiation oncologists, medical physicists, therapists, nurses, information technology and medico-legal officers of our Institute met on a weekly basis to develop an electronic infrastructure for PT. The project has three main goals (**Figure 1**): 1) to implement an Electronic Radiotherapy Health Record (ERHR), 2) to connect the ERHR with the already existing Electronic Health Records (EHRs) system and Hospital Management Systems (HMSs) of the whole Institute, 3) to connect the ERHR with the research platform (Clinical Data Platform - CDP) of the Institute. The Raysearch integrated system, composed of Raystation, Raycare, and Raytreat modules, has been chosen for the clinical activities.

Results: Starting from October 2022, a specific workflow for the implementation of the ERHR was designed, considering the PT patient's care pathway. For each anatomical district, different electronic clinical document templates were created for the ERHR, which almost completely replaced paper medical records. For the second goal, the Raysearch platform joined the majority of EHRs and HMSs already used at our Institute. For the third goal, the ERHR was successfully directly connected with the CDP, thus all data entered for clinical practice in the ERHR are automatically in a systematic and non-time-consuming manner transferred for research purposes. As a result, data can be collected for the POWER Registry, a study protocol registered at clinicaltrials.gov (NCT05860361) and approved by our Ethics Committee.
Since November 2023, the registry started the recruitment of the first patients treated with PT in our Institute, collecting clinical and dosimetric data, quality of life questionnaires, biological samples, and radiological images. The project is still ongoing and will promote translational research studies (e.g., radiomics studies) and encourage networking with other PT centers.

Figure 1. Schematic representation of the project.
List of abbreviations: Electronic Radiotherapy Health Record (ERHR), Electronic Health Records (EHRs) system, Hospital Management Systems (HMSs).



Conclusions: The present work reports an example of how the collaboration between different professional figures fosters the implementation of a modern and functional infrastructure that optimizes both clinical practice and oncological research for a radiotherapy center.

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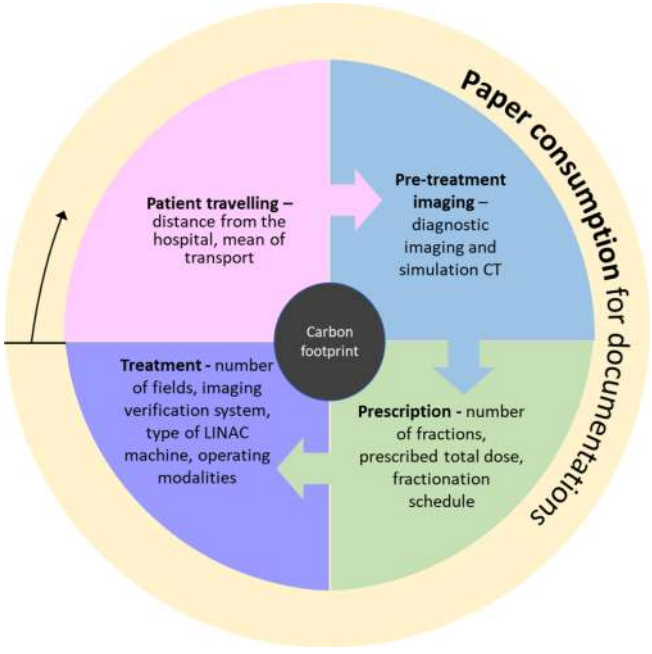
GREEN RADIOTHERAPY: A FOCUS ON HYPOFRACTIONATION. IS RADIOTHERAPY AS GREEN AS WE WOULD?

Code: 212

Aims: The concern about rising carbon dioxide (CO2) levels is increasing; in particular, healthcare has a large carbon footprint, estimated at around 5% of Europe's total carbon emissions, suggesting the importance of providing more sustainable oncology practices. Since more than half of cancer patients receive some form of radiation therapy (RT), understanding its potential environmental impact is essential. The present project aims to develop a carbon footprint score to evaluate CO2 emissions produced due to RT, focusing on hypofractionated treatments.

Methods: Patients who received an RT treatment between 2012 and 2022 at the same institution were retrospectively included. Inclusion criteria were: 1) age > 18 years; 2) any cancer histology; 3) written informed consent for research purposes. Applying advanced machine learning models, a carbon footprint score will be estimated to model CO2 emissions generated per patient at the end of RT. The score will incorporate contributions from treatment commute, pre-treatment imaging, and RT delivery/fractionation.

Results: A total of 24'617 patients matched the inclusion criteria and data are currently being extracted from patients' clinical records with data mining techniques. CO2 emissions will be modeled by: 1) average distance to a hospital from rural, suburban, and urban community settings using patients' registered data; 2) pre-treatment imaging; 3) linear accelerator (LINAC) beam-on power per manufacturing data; 4) beam- on time, estimated by average time of treatment; 5) number of fractions for patients receiving moderate hypo fractionated and ultra-hypo fractionated RT (Figure1). The development of a predictive algorithm, including ensemble machine learning techniques, will be evaluated to assess carbon footprint by creating a scoring system. Scores derived from hypofractionated treatments will be compared with those from normofractionated treatments to identify potential differences between the two groups. The established carbon footprint score will be externally validated at external centers to detect critical issues related to CO2 emissions.



Conclusions: There is an increased interest in improving the sustainability of modern radiotherapy. The results of this analysis will likely suggest where initial carbon footprint reductions could be aimed and motivate further studies on the topic. Wide adoption of these approaches can increase the sustainability of cancer treatment and might have an immediate impact on the world's ecosystem.

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MUSIC AND ANXIETY IN PATIENTS UNDERGOING RADIATION THERAPY (MUSA-RT): A PROSPECTIVE ANALYSIS

Code: 314

Aims: Receiving a cancer diagnosis can lead to emotional, physical, and social challenges that profoundly affect patients (pts), their loved ones, and caregivers. Therefore, it is imperative that current clinical care incorporates psychosocial interventions to enhance the quality of life for cancer patients. Music therapy (MT) is recognized as an effective intervention for alleviating anxiety, pain, fatigue, and other physical symptoms, thereby improving overall well-being. However, the specific role of MT in patients undergoing radiotherapy (RT) remains unclear. Our multicenter prospective study aims to assess the efficacy of MT in patients receiving RT for various malignancies by examining anxiety and stress levels during treatment using validated questionnaires (STAI-S Anxiety Scale and Symptom Distress Thermometer, SDT) at two different centers. The music playlist, primarily featuring ambient 'soundscape' music, was curated by an experienced Music Therapist with over 25 years of expertise.

Methods: Between July 2023 and December 2023, we enrolled 125 patients (60 male, 60 female), with a median age of 66 (range 28-91), undergoing radiotherapy for at least two weeks (>10 sessions) across two centers (105 in Center 1 and 20 in Center 2). The study comprised two treatment arms:
Control Arm A: 55 patients without Music Listening (ML)
Experimental Arm B: 70 patients with ML: Patients listened to a designated ML playlist during each RT session.
Weekly assessments were conducted using the STAI-S and SDT questionnaires, as well as the EORTC QLQ-C30 before and after RT treatment. Baseline data, end-of-treatment scores, and variations (Delta) were analyzed between the different arms using Chi-Square and T-Analysis, with significance set at $p < 0.005$.

Results: At baseline, no significant differences were observed in STAI-S, SDT, or EORTC QLQ-C30 scores between the two groups ($p > 0.05$). However, at the end of RT, patients in Arm B (ML) exhibited lower SDT scores (p: 0.034) compared to Control Arm A. Additionally, patients in Arm B (ML) demonstrated a significant decrease in both STAI-S (p: 0.013) and SDT (p: 0.029). No significant differences were noted for the EORTC QLQ-C30 questionnaire.

Conclusions: The potential use of ML during radiotherapy treatment warrants further exploration in patients undergoing RT. We anticipate that a comprehensive analysis upon completion of enrollment will provide deeper insights into the benefits associated with this approach.

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PROMOTING COLLABORATION BETWEEN PROTON THERAPY CENTERS: FOSTERING LEARNING CURVE AND NETWORKING

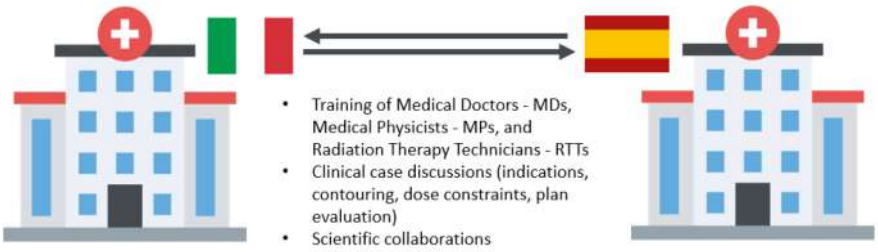
Code: 204

Aims: Proton therapy (PT) is gaining an increasingly crucial role for the treatment of several oncological diseases. However, peculiarities of this technique make the learning and starting work phase challenging for a new PT center (PTC). The present work aims to report an example of how the collaboration between two European PTCs fosters the learning curve and promote networking.

Methods: A collaboration agreement has been defined between a new opening PTC and an experienced one, with the same PT equipment to easily share protocols and procedures. The project had three main goals: 1) to promote observership periods of different professional figures (Medical Doctors - MDs, Medical Physicists - MPs, and Radiation Therapy Technicians- RTTs) between the two PTCs for educational purposes; 2) to share the clinical indications and PT treatment plans to support the learning curve during the start-up phase; 3) to foster networking between the two PTCs.

Results: The collaboration started in May 2023. For the first goal, different observership periods have been organized as follows: 1 resident (3 months), 3 senior MDs (1 week), 4 MPs (2 weeks) and 4 RTTs (1 week) from the new opening PTC to the experienced one. Similarly, 2 MPs (4 weeks) and 1 RTT (1 week) from the experienced PTC attended the new opening PTC for local support and training. In particular 2 expert MPs supervised the acceptant phase and commissioning of the PT machine before the beginning of clinical activity. For the second goal, online meetings have been scheduled twice a week since clinical activity began (November 2023). Thirty clinical cases, half of which reirradiations, have been discussed, with a focus on dose-volume constraints. Fifteen treatment plans have been revised with recommended changes regarding the entrance of the PT fields, optimization parameters and robustness evaluation. For the third goal internal guidelines for the clinical practice and study protocols have been presented by both PTCs. Two clinical studies are actually under evaluation.

Conclusions: The present work reports an example of how the collaboration between PTCs fosters either learning curve and networking in this challenging scenario. As a great number of PT facilities are planned to be opened in the next few years this approach can be used as a successful strategy by the future opening PTCs. The collaboration is still ongoing and will promote a mutual improvement both for the daily clinical activity and the research field.



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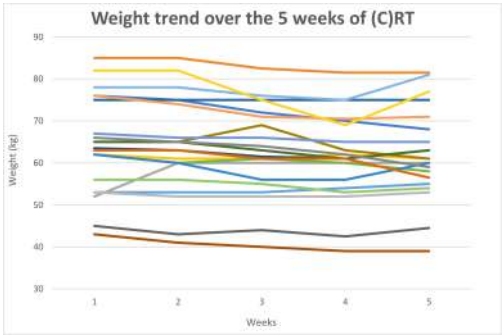
EFFICACY OF AN EPIGALLOCATECHIN GALLATE, PROPOLIS AND HYALURONIC ACID BASED MOUTHWASH IN PREVENTING RADIATION-INDUCED MUCOSITIS IN LOCALLY ADVANCED HEAD AND NECK CANCER

Code: 388

Aims: To evaluate the efficacy of a mouthwash (fructose, PVP, Propolis, Epigallocatechin gallate, hyaluronic acid, sodium xsal, aroma, sodium benzoate, potassium sorbate, water, green tea 95%, EGCG, b-caryophyllene, fluid extract of Syzygium aromaticum), in preventing radiation-induced mucositis in locally advanced head and neck cancer patients.

Methods: Patients were treated with concurrent chemoradiotherapy (CRT) or radiotherapy (RT) alone. Patients were randomised to receive the mouthwash from the start of CRT/RT or, alternatively, from the onset of symptoms until the first follow-up visit. They were clinically assessed weekly for mucositis using CTCAE(version 5.0) and weight monitoring. Three weeks after the end of RT, patients were also evaluated. Afterwards, continued with clinical- instrumental controls.

Results: To date, 21 patients have been enrolled. The median age was 69.4 years. Thirteen patients (61.9%) received the mouthwash at baseline and eight (38.1%) at the onset of symptoms. Grade 2 toxicity occurred in 6/21 patients (28.6%) and was detected in the third week of treatment:1 patient started using the mouthwash and the remaining 5 started using it when mucositis developed. One patient experienced grade 3 toxicity. Seven patients (33.3%) required the addition of antifungals between the second and third week of treatment:42.9% used the mouthwash from the first (C)RT fraction and 57.1% used it at the onset of symptoms. Two PEG patients had a mean weight gain of 4.3 kg. Eighteen (85.7%) patients lost an average of 2.3 kg: the group who used the mouthwash from the start lost an average of 1.1 kg, compared to 3.7 kg for those who started treatment at the onset of symptoms. Two patients kept their weight stable. One patient had to discontinue (C)RT for 15 days due to a bacterial pneumonia that required hospitalisation. At clinical follow-up 3 weeks after the end of (C)RT, 4 patients presented with grade 2 mucositis: 3 had started mouthwash at the start of (C)RT. Twenty (95.2%) patients had no clinical or endoscopic evidence of locoregional recurrence at quarterly and six-monthly instrumental follow-up, without signs of mucositis. One patient had a cardiac death one week after completion of treatment.



	Grade 1	Grade 2	Grade 3
Week 1	0	1	0
Week 2	2	1	0
Week 3	14	1	0
Week 4	11	6	1
Week 5	10	9	0
Week 6	11	8	0

Table 1. Appearance and progression of mucositis in relation to the week of treatment.

Conclusions: Although there appeared to be no difference at 3-6months endoscopy, patients who used the mouthwash from the start of treatment had better weight control and less mucositis. The mouthwash was well tolerated and delayed (C)RT-induced mucositis, allowing continued treatment of locally advanced head and neck cancer.

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EQUINE CATALASE IN MANAGEMENT OF RADIATION- INDUCED ORAL MUCOSITIS: A PRELIMINARY MONOISTITUTIONAL EXPERIENCE

Code: 399

Aims: The pathophysiology of radiation-induced Oral mucositis (RIOM) is a multifactorial process, due to the release of reactive oxygen species and inflammatory cytokines.
It appears clinically as hyperemia and ulceration of the oral mucosa, and it can cause significant oral pain, dysphagia, dysgeusia, weight loss, and decreased quality of life. It may need interruptions in cancer therapy and hospitalizations, and it causes significant economic costs of medical care.Topical agents reduce the severity of OM lesions and pain intensity in patients receiving radiotherapy.
This study aims to evaluate the efficacy of a topical product containing equine catalase in reducing symptoms, weight loss, and radiotherapy interruption due to RIOM in patients with oral cavity cancer.
Equine catalase (EC) is an antioxidant that splits hydrogen peroxide into oxygen and hydrogen, increasing the concentration of oxygen at the site of inflammation and promoting repair.

Methods: Between January 2022 and December 2023, 32 patients with oral cancer underwent radiotherapy in our institute. All patients had weekly clinical assessments and weight monitoring. Toxicity was assessed using the RTOG scale. RIOM often occurs during the 3rd, 4th, or 5th week of radiotherapy. Patients with G2-G3 RIOM were treated with topical EC, directly applied on mucositis areas twice a day.

Results: 11 patients developed G2-G3 RIOM. 10 of them received weekly cisplatin-based concurrent chemotherapy. 7 patients received postoperative treatment (60 Gy in 30 fractions to the oral cavity), while 4 patients received radical treatment (70 Gy in 35 fractions to the oral cavity).
For all patients, the RTOG grade of mucositis about each week of treatment and time of introduction of EC are shown in Figure 1. All patients experienced a reduction in RIOM-related symptoms. In 9 patients, equine catalase improved or stabilized the grade of mucositis within two weeks from the start. Weight loss was 0-13% of baseline (2 patients G0, 2 patients G1, 7 patients G2). 8 required non-oral nutrition, 3 patients received oral nutritional supplements. All patients completed radiotherapy within the scheduled time without interruption. No adverse events related to equine catalase were observed.

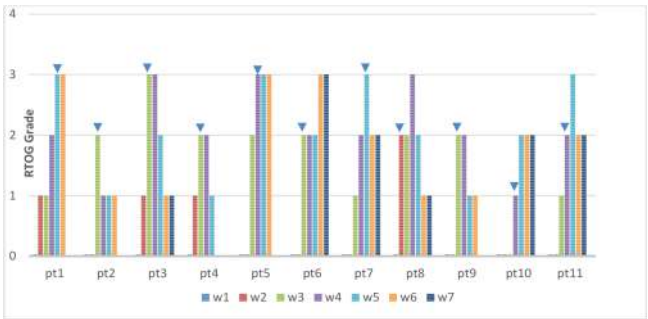

Fig. 1: RIOM RTOG grade in week (w) 1-6, in all patients (pt).

▼: time of equine catalase introduction

Conclusions: EC is well tolerated and helpful in avoiding radiotherapy discontinuation due to RIOM in patients with oral cavity cancer. Even in severe mucositis, it appears to reduce symptom intensity, oral feeding pain and to be useful in preventing severe weight loss (>G3).

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ADJUVANT VS. NO ADJUVANT IN PATIENTS TREATED WITH OPEN PARTIAL HORIZONTAL LARYNGECTOMY (OPHL): LONG-TERM TOXICITIES AND FUNCTIONAL OUTCOMES

Code: 447

Aims: Assessment of toxicity, quality of life and swallowing impairments in patients who underwent partial laryngectomy with or without postoperative treatment.

Methods: 20 patients had adjuvant treatment and 20 patients had surgery alone. These patients had an open partial horizontal laryngectomy (OPHL I, II or III) with ipsilateral or bilateral neck dissection. Adjuvant treatment was administered according to national guidelines.
Patients were analyzed by a team of a Radiotherapist, Otolaryngologist and Logopedist. Collected data involved toxicities such as Dysphagia and Xerostomia (using CTCAE 5.0 scale), evaluation of QoL via The Revised University of Washington Quality of Life (UW-QOL-R) and EORTC QLQ-H&N35 scales.
The UW-QOL-R was evaluated using two modalities: a questionnaire made up of 3 items assessing general QoL aspects and a second one involving specific aspects of daily life like swallowing, pain, social life, etc.
The EORTC QLQ-H&N35 is used for assessment of various domains like pain, sensory or social problems; 35 items, higher scores indicate more problems. An evaluation through fiberoptic endoscopic evaluation of swallowing (FEES) was also performed and the adapted penetration-aspiration scale (OPHL-PAS) has been used to score presence and degree of penetration/aspiration. OPHL-PAS score test was conducted using 4 consistency (liquid, semiliquid, semisolid, solid) giving each of them a score between 1-8.
Patients were divided in 2 major groups (Adjuvant vs No adjuvant) and 3 subgroups: Adjuvant RT, Adjuvant CHRT, Surgery. Pattern and difference in terms of toxicity have been compared with T-test for independent samples for the 2 major groups and with ANOVA analysis for the 3 subgroups. We considered as significant a p-vaue <0,01.

Results: Patients who needed adjuvant therapies had a higher disease stage in both T and N staging.
These adjuvant treatments had a influence on various aspects of UW-QOL-R and EORTC QLQ H&N35, particularly evident in areas such as xerostomia ($p<0.001$), dysphagia (p:0.003), and salivation ($p<0.001$), while no significant impact was observed on OPHL-PAS.
In case of CHRT, a significant deterioration was observed across all parameters, indicating a significant decline in swallowing function. Additional details can be found in Table 1. No Grade 3 toxicities were recorded.

Conclusions: PORT does not seem to worsen chronic morbidity and QoL. However, attention must be paid to patients who receive a CHRT as mean values are generally higher than the other subgroups.

	Adjuvant Treatment		No Adjuvant Treatment
	RT	CHRT	
OPHL 1	8	3	8
OPHL2a	5	3	12
OPHL3	0	1	0
General UW-QOL-R, mean value	6.5	7.3	6.3
UW-QOL-R, mean value	17.8	19.4	13.8
EORTC QLQ-H&N35	57.5	56	49.7
PAS-OPHL, worst score	8	8	7

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NARRATIVE MEDICINE, NARRATIVE PRACTICE, AND THE CREATION OF A CONNECTION BETWEEN PATIENTS AND DOCTORS

Code: 111

Aims: In 2015, the Italian National Institute of Health published guidelines for Narrative medicine (NM) in clinical practice. NM is a clinical intervention methodology that relies on practical communication skills. Through narration, different perspectives can be acquired, understood, and integrated by all parties involved in the disease and treatment process. A prospective study evaluated the effectiveness of a systematic narrative approach in clinical practice for oncological patients. The study aims to promote narrative skills among physicians and change their perspective towards patient care.

Methods: Cancer patients or their caregivers, if the patient is unable to participate, will receive an email invitation from their doctors (radiation oncologists or medical oncologists) and psychologists to access a web platform (DNM-Digital Narrative Medicine Società Benefit Srl, DNMLAB).
On the web platform, patients have access to specific lists of narrative stimuli, including story-sharing interventions. The stimuli consist of brief, unfinished sentences encouraging patients to discuss themselves.
In addition, there are several questionnaires available that can be completed to assess an individual's quality of life as well as their levels of anxiety or depression (QLQ C-30, *Hospital Anxiety Depression Scale (HADS),* pseudo-posttraumatic stress disorder (pseudo-PTSD).

Results: From March 2022 to December 2023, 40 patients were enrolled; 28 were female and 12 were male, with a median age of 47 (30-65 years old). All patients begin their journey in narrative medicine during oncological therapy, whether radiotherapy or chemotherapy. Writing through a web channel was comfortable and well-tolerated. They completed the entire treatment schedule without delays, highlighting a solid commitment to their health and recovery.
Treatment sessions were conducted in a safe and trustful environment, where patients knew the referring doctor and the psychologist were reading their writing. Globally, regarding the analysis of questionnaires, there has been an improvement in the levels of anxiety and depression (HADS). Patients who were followed up showed slightly decreased levels of distress and symptoms of pseudo-PTSD, such as sleep disturbances.

Conclusions: The findings indicate that integrating patients' narratives with clinical data is valuable. However, the success of the intervention largely depends on the participation of the entire care team and a well-organized healthcare system.

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CLINICAL BENEFIT OF DAILY SUCROSOMIAL IRON SUPPLEMENTATION IN CANCER PATIENTS UNDERGOING CONCURRENT RADIOCHEMOTHERAPY: A MONO-INSTITUTIONAL OBSERVATIONAL STUDY

Code: 594

Aims: Anaemia is a blood disorder consisting of the reduction of haemoglobin (Hb), haematocrit or the red blood cell count. It represents a frequent complication in cancer patients, affecting their performance status (PS) quality of life (QoL) and influencing adherence to anticancer regimens. To prevent moderate and severe anaemia in patients undergoing radio- chemotherapy (RCT), we performed an observational study on 35 patients affected by solid tumours, performing RCT treatment with daily Sucrosomial® oral iron supplementation.

Methods: We selected 35 patients affected by solid tumours (median age 64.8 years old) with Hb levels ranging from 11-13.9 g/dl performing long-course RCT treatment with 60 mg of Sucrosomial® oral iron supplementation daily. Patients were affected by tumours of the brain, gastrointestinal tract, genitourinary tract, lung, breast, head and neck district and skin. Out of the total, 31 patients performed conventionally fractionated radiotherapy and 4 patients performed moderately hypofractionated radiotherapy. Each patient has been clinically and haematologically evaluated at baseline (T0), after 15 days (T15), 30 days (T30) and 60 days (T60) from the beginning of the treatment. The primary endpoint is Sucrosomial® oral iron formulation efficacy to prevent moderate and severe anaemia; the secondary endpoint is patients' benefits in terms of QoL; the tertiary endpoint is the tolerability of Sucrosomial® iron supplementation.

Results: Sucrosomial® oral iron demonstrated good ability in supporting patients undergoing long-course RCT and preventing moderate and severe anaemia, with median Hb levels at T0, T15, T30 and T60 being 12.4 ± 0.9 g/dl, 12.2 ± 1.1 g/dl, 11.8 ± 1.4 g/dl and 11.6 ± 1.4 g/dl, respectively. In terms of QoL, all patients reported a benefit in self- reported fatigue and its impact on daily activities and function, according to the Functional Assessment of Chronic Illness Therapy-Fatigue Scale. Moreover, in all patients, Sucrosomial® oral iron support allows to administration of full and timely doses, without the necessity to use intravenous iron supplementation or blood transfusion, positively impacting health care costs. The tolerability of oral iron supplementation was excellent, and no adverse events were reported.

Conclusions: Sucrosomial® oral iron supplementation represents a valid strategy to support patients undergoing long-course RCT, improving their QoL and positively impacting healthcare costs.

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