SHORT PAPER SESSION H2

H2.1 Benefit of dedicated Radiotherapy Clinical Trial Education sessions to Cancer Research Network Staff

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Background
Dedicated education sessions focused on radiotherapy (RT) and RT clinical trials are not delivered routinely to staff involved in clinical trials across the cancer network. The project was undertaken to assess any benefit in delivering a RT education session by evaluating changes in non-RT staff knowledge following a half day educational session on these topics.

Methods
A baseline survey was distributed via email prior to attendance and made available for completion upon arrival to the education session. A post-session survey was then circulated by email after the session. The baseline survey asked for self-reported RT knowledge and RT trials knowledge, graded as none, little or a lot, as well as the identification of which of the four session topics (RT basics, delivery, techniques, data) participants felt they needed a better understanding of. The post-session survey asked if RT knowledge and RT trials knowledge had stayed the same, slightly or greatly improved; and identify if their knowledge had improved in any of the four session topics.

Results
Twenty two baseline surveys were completed. Of those 90.0% reported having little or no knowledge of RT and 72.7% knew little or nothing about RT clinical trials. 77.3% reported needing a better understanding in all four of the session topics.
Twelve participants completed the post-session surveys. 100% of those felt both their knowledge of RT and RT clinical trials had improved slightly or greatly.

Conclusion
A dedicated RT education session enables non-RT staff to enhance their knowledge on RT and RT clinical trials.

H2.2 Can radiological response to 1st line chemotherapy predict the response to Immunotherapy as 2nd line in patients with advanced or metastatic oesophageal squamous cell carcinoma?

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Background
Oesophageal squamous cell carcinoma (SCC) accounts for 90% of oesophageal cancer and has a poor prognosis. Patients with unresectable locally advanced or metastatic SCC, 2nd line nivolumab is the standard of care based on the results of phase III ATTRACTION-3 trial, demonstrating better overall survival (OS) and a favourable toxicity profile compared with chemotherapy. We audited the outcomes of patients treated with nivolumab and investigated if radiological response to 1st line chemotherapy correlated with nivolumab outcomes.

Methods
We retrospectively identified patients who had received nivolumab following chemotherapy between 2022 and July 2024. Demographic data, toxicity, baseline serology and, radiological response was collected from electronic medical records. Radiological response was defined using the RECIST criteria. Statistical analysis was conducted using SPSS.

Results
Data from 19 patients was collected. Median age was 68. 47% were male, 63% had metastatic disease, 47% had immunotherapy toxicity and, 42% progressed on first line chemotherapy. The median OS from the start of nivolumab between patients who responded/progressed radiologically to 1st line chemotherapy was 11 months (95% CI:4.7-17.3) and 5 months (95% CI:0-10.5) respectively (p=0.043). First line response to predict nivolumab response was not significant (p=0.085), however, the duration of 1st line chemotherapy control was associated with better response to nivolumab (p=0.036).

Conclusion
We observed a better median OS with nivolumab when patients had a good radiological response to 1st line chemotherapy. Duration of 1st line control was associated with a better response to nivolumab. Larger patient cohorts are required to further validate these findings.

Table

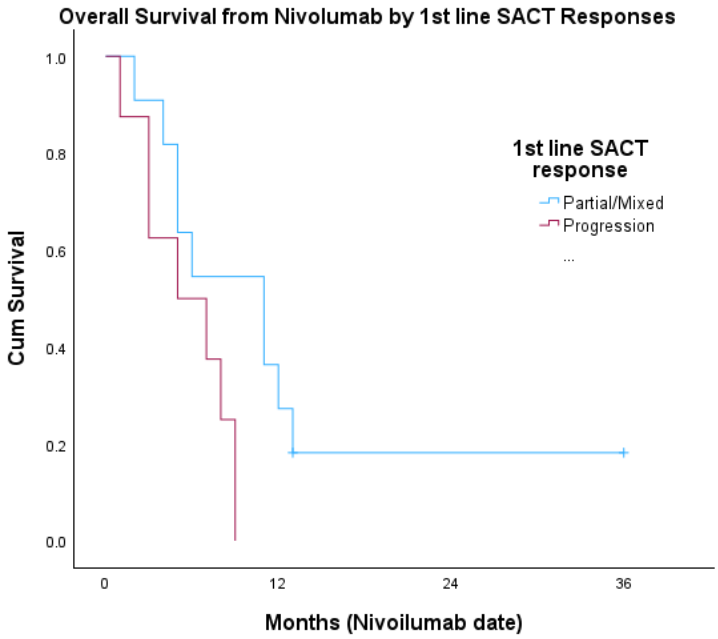

Figure 1| Kaplan-Meier curve showing the overall survival of patients treated with nivolumab second line from the start of nivolumab treatment separated by whether they had a response to 1st line chemotherapy (p=0.043).

H2.3 Novel approach: Adaptive MR-guided SABR as an alternative to HDR brachytherapy boost in gynaecological cancers

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Background

Curative treatment for locally advanced cervical cancer is chemo-radiation with external beam radiotherapy (EBRT) and brachytherapy[1]. However, brachytherapy is not always feasible due to patient factors, including refusal, or technical challenges.

We investigate Adaptive MR-Guided SABR as an alternative to brachytherapy boosts. This approach adapts dose to daily anatomical variations, with superior soft tissue contrast, continuous intrafraction tracking, reduced PTV margins,dose escalation and Dmax > 150% akin to brachytherapy.

Method

Eight cases were retrospectively planned. Dose prescription was 30Gy/5#s to PTV, simultaneously boosting CTV to 35Gy. 45Gy/25# was delivered with EBRT. 0% organ at risk (OAR) recovery was assumed. Maximum PTV dose was 1 cc at 150% of 35Gy. EMBRACE-II 2cc OAR constraints were applied (bladder 90Gy, rectum/bowel 70Gy) and 0.1cc dose constraints to displace hotspots. Projected cumulative dose was calculated using α/β ratio of 5 for bladder/rectum, and 4 for bowel. Minimum cumulative EQD2 target coverage was D90% CTV≥90Gy, D90% PTVhigh≥85Gy and D90% PTV≥80Gy.

Results (Table 1, Figure 1)

Mean CTV volume was 50.4cc (range 13.1–121.7). Mean combined EQD2 D90% for CTV and PTVhigh were 93.9Gy (range 84.0-100.9) and 87.5Gy (range 83.9-91.6), respectively. Maximum (median) 2cc OAR doses to the bladder, rectum and bowel were 84.6Gy (79.3), 69.9 (69.7) and 69.5Gy (64.3),. Rectum was the dose limiting structure.

Conclusion

Adaptive MR-Guided SABR Boost has demonstrated good target coverage within OAR constraints similar to brachytherapy. This supports clinical feasibility studies with the potential of improving outcomes in patients unable to undergo brachytherapy.

Table 1 Overview of results from the eight test Gyane MRgRT boost trials. D%: dose for that specific percentage of volume. Total: summation of the base and boost treatments. CTV: clinical target volume, Px: Prescription, PTV: Planning Target Volume, EQD2: Equivalent Dose in 2 Gy per fractions, Gy: Gray, cc: Cubic centimetre, St Dev: Standard deviation

Test No	Px	Vol_CTV (cc)	D98% Boost CTV EQD2 (Gy)	D98% Boost PTVhigh EQD2 (Gy)	D98% Boost PTV EQD2 (Gy)	D90% Total CTV EQD2 (Gy)	D90% Boost PTVhigh EQD2 (Gy)	D90% Total PTVhigh EQD2 (Gy)	D90% Total PTV EQD2 (Gy)	Prescription Dose Spillage	Estimated Delivery Time (minutes)	Global D-Max (Gy)
1	30Gy/5# 35Gy CTV Boost	13.1	45.0	35.8	29.3	99.4	42.7	87.0	81.4	1.05	10.5	53.2
2	30Gy/5# 35Gy CTV Boost	27.0	40.5	35.9	27.5	93.4	43.2	87.5	79.7	1.03	11.0	54.1
3	30Gy/5# 35Gy CTV Boost	40.0	40.8	37.7	28.4	96.4	43.4	87.6	81.1	1.04	9.0	53.1
4	30Gy/5# 35Gy CTV Boost	27.9	38.4	39.3	26.4	93.2	47.3	91.6	79.9	1.07	12.0	55.3
5	30Gy/5# 35Gy CTV Boost	59.4	35.2	33.6	24.6	84.0	39.7	83.9	73.7	1.05	10.8	53.3
6	30Gy/5# 35Gy CTV Boost	31.9	49.8	38.9	28.3	100.9	44.9	89.2	87.4	1.09	8.1	51.3
7	30Gy/5# 35Gy CTV Boost	82.3	37.1	36.2	28.2	91.8	41.8	86.0	79.8	1.03	11.8	54.6
8	30Gy/5# 35Gy CTV Boost	121.7	35.9	35.1	23.6	91.8	43.1	87.3	78.4	1.06	8.7	53.6
Mean		**50.4**	**40.3**	**36.6**	**27.0**	**93.9**	**43.3**	**87.5**	**80.2**	**1.05**	**10.2**	**53.6**
St Dev		**36.0**	**5.0**	**2.0**	**2.0**	**5.3**	**2.2**	**2.2**	**3.8**	**0.0**	**1.5**	**1.2**

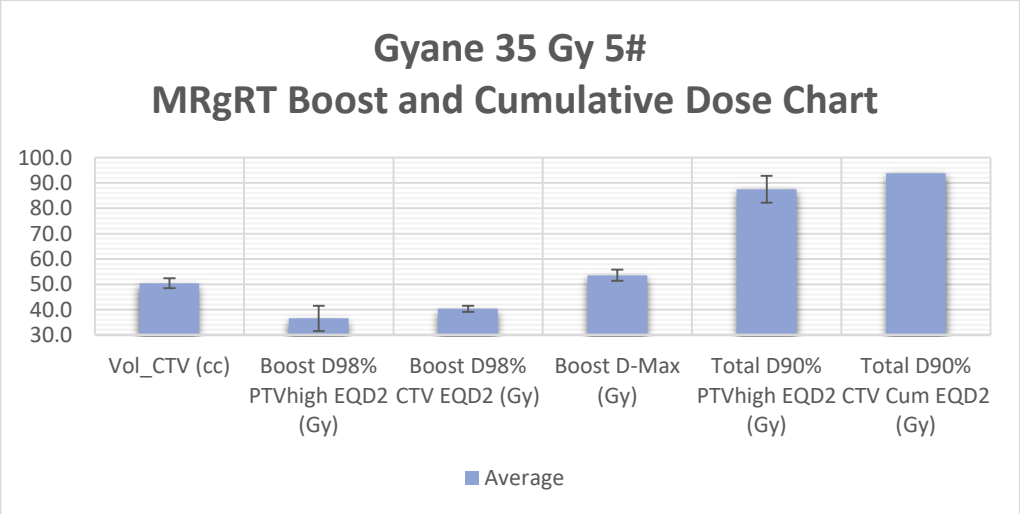

Figure 1 Mean values for boost and cumulative dose coverage for PTVhigh and CTV, as well as the standard deviations, for a total of eight test MRgRT trials.

1. Potter R, Tanderup K, Schmid MP, et al. (2021) MRI-guided adaptive brachytherapy in locally advanced cervical cancer (EMBRACE-I): a multicentre prospective cohort study. Lancet Oncol. 22(4), 538-47.

H2.4 Feasibility of soft-tissue structure registration in radiotherapy for pancreatic cancer using CBCT

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Radiotherapy (RT) for pancreatic cancer is challenging, with significant internal motion affecting image quality and IGRT verification protocols. Beyond fiducials and biliary-stent as surrogates for tissue matching, there is limited information on soft-tissue structures in decision making. Highlighting the need for further research to improve RT precision and accuracy to increase dose-escalation opportunities.

Aim

Feasibility of identifying the superior-mesenteric vein (SMV), superior-mesenteric artery (SMA), celiac axis (CA), portal vein (PV) biliary-stent (BS) on daily CBCT and quantify their variability to a region of interest (ROI)-registration

Objectives

- Determine if relevant soft-tissue structures for pancreatic IGRT can be visualised and registered on CBCT
- Quantify displacement of each soft-tissue structure from ROI match
- Quantify differential motion between soft-tissue structures associated with the pancreas

Methods

A retrospective analysis was conducted. Patients were treated with VMAT using a Varian TrueBeamTM (Varian Medical Systems, Palo Alto, CA). CBCT was acquired in breath-hold before each treatment. An automatic ROI-match was performed and checked for GTV/PTV coverage, values were recorded. Radiographer adjustments for the SMV, SMA, CA, PV, and BS, were recorded to calculate the variation.

Results

11 patients, with 65 data sets were reviewed, and displacement of 300 (100%) soft-tissue structures from the ROI match were quantified. Patient demographics are available in Table 1.Mean displacement values (cm) are available in Table 2.

Conclusion

Our analysis indicates feasibility of soft-tissue registration in pancreatic RT. Due to the variability, further work on larger data sets would be required to support the use of surrogate soft-tissue registration.

Table 1. Patient Demographics

Demographic	**Number (%)**
Gender	
Male (M)	9 (69.2)
Female (F)	4 (30.8)
Total	13
Age (in years)	
Range	44 – 77
Mean	60
Median	58
IQR	9
Variance	80.9
SD	9
Tumour location	
Head (H)	12 (92.3)
Tail (T)	1 (7.7)
Biliary stent (BS)	
Yes	8 (61.5)
No	5 (38.5)
Dose (Gy)/fractionation (#)	
30Gy/5#	7 (53.8)
35Gy/5#	3 (23.1)
50Gy/5#	3 (23.1)

Table 2. Mean (SD) displacements of soft-tissue structures from ROI, in cm.

		Displacement from ROI mean (SD) in cm				Paired t-test (significance $p \leq 0.05$)	
Registered structure number of patients with structure (n)	**Total number of structures within data sets (n)**	**Translation**					
		VRT		**LNG**		**LAT**	
SMA (n= 13	n = 65	0.09 (0.12)	0.03	-0.11 (0.19)	0.05	0.10 (0.10)	0.54
CA (n = 13)	n = 65	0.13 (0.13)	0.76	-0.05 (0.15)	< 0.001	0.11 (0.15)	0.90
SMV (n = 13)	n = 65	-0.02 (0.13)	< 0.001	-0.04 (0.15)	< 0.001	0.07 (0.14)	0.26
PV (n = 13)	n = 65	0.04 (0.11)	< 0.001	0.00 (0.16)	0.01	0.05 (0.11)	0.02
BS (n = 8)	n = 40	-0.12 (0.13)	< 0.001	-0.05 (0.14)	0.09	0.07 (0.11)	0.30
Total	300						

H2.5 Genome-wide transcriptomic response of whole blood after X-ray exposure

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Background
Ionizing radiation (IR) is used in radiotherapy (RT) across a wide dose range, from 0.5 Gy for benign conditions to ≥2 Gy for malignancies. In both cases, IR induces cell death and modulates inflammatory responses within the highly radiosensitive hematologic system, and this impact remains a key clinical concern. These effects may contribute to challenges in multimodal therapy concepts as in combined radio-immunotherapy, particularly in achieving systemic (abscopal) responses. Therefore, understanding the IR-induced transcriptional response in peripheral blood is crucial for optimizing RT's immunomodulatory effects and improving clinical outcomes.
Methods
Whole blood from two male and one female donor was exposed to 0, 0.5, 1, 2, and 4 Gy of X-rays and incubated for 2 and 6 h. RNA was extracted and sequenced using the Illumina platform. Differentially expressed genes (DEGs) were identified while accounting for donor and time effects (FDR < 0.05).
Results
We found extensive gene expression variability attributed to strong inter-donor variation and time post-exposure. The degree of gene regulation was both time and dose-dependent where higher doses and longer incubation stimulated more DEGs. Lower doses (≤1 Gy) activated DNA damage responses, while higher doses (≥2 Gy) triggered proinflammatory pathways such as T cell proliferation (GO:0042098) and B cell activation (GO:0042113). Notably, we identified 34 previously unrecognized radiosensitive genes, including GPN1, MRM2, G0S2, and PTPRS.
Conclusion
This first genome-wide RNA-seq study of ex vivo X-ray-irradiated human blood identified novel radiosensitive genes and pathways, providing insights into RT-induced immune modulation and potential biomarkers for radiation exposure assessment.