Gy and 67±14 Gy, respectively. Crude incidences for CTC G≥3 and G≥2 were 1,4% (n=17) and 11% (n=126), respectively. Crude incidences for EORTC Very much and ≥Quite a bit were 6,1% (n=53) and 18% (n=160), respectively. Incidence of CTC G≥1 persisting events was 15% (n=168), while for EORTC persisting ≥Quite a bit events was 4,8% (n=42).

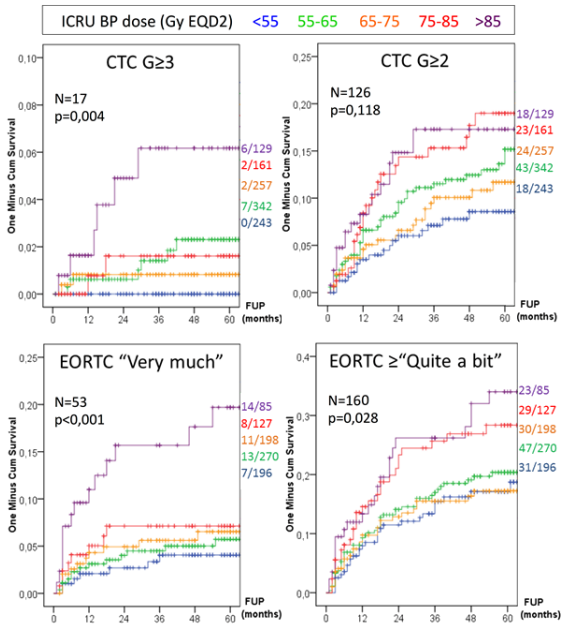
Table 1 shows the Hazard Ratios (HR) for significant factors (p≤0,05) in MVA. ICRU BP dose was a risk factor for CTC G≥2, G≥3 and for EORTC "Very much" (incidence). In addition, ICRU BP dose was borderline significant for persisting CTC G≥1. Bladder D_{2cm3} was significant in UVA only for CTC G≥3. Baseline incontinence and body-mass-index were significant risk factors for most CTC and EORTC scores. Age was significant in UVA, but correlated with ICRU BP dose and was not included in MVA. Since concomitant chemotherapy did not significantly increase incontinence in UVA, this parameter was not tested in MVA. Smoking was a risk factor for EORTC scores. The impact of ICRU BP dose is confirmed by Fig.1 showing Kaplan Meier (KM) curves for CTC (G≥3; G≥2) and EORTC (Very much; ≥Quite a bit).

Table 1: Factors tested for physician assessed (CTC) and patient reported (EORTC) urinary incontinence. Hazard Ratios (HR) are shown only for variables that were significant in MVA.

Variables	CTC ≥3 (n=17)	CTC ≥2 (n=126)	CTC G≥1 persisting (n=168)	EORTC Very Much (n=53)	EORTC ≥Quite a bit (n=160)	EORTC Quite a bit persisting (n=42)
	HR(95%CI)	HR(95%CI)	HR(95%CI)	HR(95%CI)	HR(95%CI)	HR(95%CI)
Baseline incontinence (B) *Yes vs. No*	17,96 (4,764-67,72)	5,184 (2,826-9,506)	3,713 (1,612-8,550)	4,126 (1,872-9,096)	3,943 (2,376-6,544)	10,47 (4,645-23,59)
Age (M) *years*	ns	Correlation with ICRU BP dose*	Correlation with ICRU BP dose*	Correlation with ICRU BP dose*	Correlation with ICRU BP dose*	Correlation with ICRU BP dose*
BMI (M)	ns	1,048 (1,019-1,079)	1,066 (1,035-1,098)	1,072 (1,032-1,115)	1,072 (1,047-1,098)	1,073 (1,023-1,125)
Smoking status (B) *Yes vs. No*	ns	ns	ns	2,069 (1,200-3,567)	1,615 (1,168-2,235)	ns
Ureter stenosis (B) *Yes vs. No*	ns	3,238 (1,819-5,764)	ns	ns	ns	ns
Chemo cycles (B) *4-8 vs. 0-3*	ns	ns	not tested in MVA**	ns	not tested in MVA**	ns
EBRT tech. (B) *IMRT vs. 3DRT*	0,101 (0,013-0,771)	ns	ns	ns	ns	ns
EBRT pr. dose (M) *Gy*	1,357 (1,123-1,640)	ns	ns	ns	ns	ns
Bladder D_{2cm3} (M) *Gy*	Correlation with ICRU BP dose§	ns	ns	ns	ns	ns
ICRU BP dose (M) Gy	1,039 (1,011-1,067)	1,013 (1,000-1,025)	ns	1,025 (1,006-1,044)	ns	ns

*Age was significant in UVA, but showed a moderate and significant (r=0,31) positive correlation with ICRU BP dose; therefore this parameter was not included in MVA.
**Concomitant chemotherapy was not found to significantly increase incontinence in UVA; therefore this parameter was not tested in MVA.
§Bladder D_{2cm3} was significant in UVA, but showed a significant moderate (r=0,61) correlation with ICRU BP dose; therefore this parameter was not included in MVA. Bladder D_{2cm3} was independently included in another MVA model for CTC G≥3, but was not significant.
Abbreviations: (M) – metric variable; (B) – binary variable; 95%CI – 95% Confidence interval; ns – not significant; BMI – Body Mass Index; Chemo – chemotherapy; EBRT – External Beam Radiotherapy; tech. – technique; IMRT – Intensity Modulated Radiotherapy; 3DCRT – 3D Conformal Radiotherapy; EBRT pr. dose – EBRT prescription dose to the CTV; ICRU BP – ICRU Bladder Point.

Fig.1. KM curves obtained by binning the cumulative (EBRT+IGABT) ICRU bladder point (BP) dose for: severe (G≥3) CTC events (upper left panel), moderate to severe (G≥2) CTC events (upper right panel), "Very much" EORTC answers (bottom left panel), "Quite a bit" and "Very much" EORTC answers (bottom right panel)



Conclusion

ICRU BP dose, rather than bladder D_{2cm3}, is a risk factor for severe and moderate urinary incontinence. This finding emphasizes the importance of the ICRU BP, which is closely related to structures linked to incontinence (trigone, bladder neck). This provides clinical evidence for consideration of new dose constraints.

OC-0681 Deep learning auto contouring of OAR for HN radiotherapy: a blinded evaluation by clinical experts

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Purpose or Objective

Coutouring is one of the most time-consuming steps in the radiotherapy workflow. The accuracy of high precision image-guided delivery techniques is hampered by potential deviation in target and normal tissue volume delineation. Artificial intelligence can accelerate organs-at-risk (OAR) delineation and homogenize volume definition. This study aims at evaluating a commercial solution that explores an ensemble of anatomically preserving deep-learning-based networks in two radiotherapy sites with expertise in head-and-neck cancers.

Material and Methods

ART-Plan is a CE-marked solution for automatic annotation of OAR harnessing a unique combination of anatomically preserving and deep learning annotation concept. In average 6,600 samples were used for training per organ after data augmentation. Evaluation of the software was performed in two phases. In phase I, 100 patients were retrospectively selected in centres 1 and 2. For each patient, ART-Plan was used to generate full annotation of 15 OAR. Using a random selection, the contours generated from ART-Plan were blended with the ones corresponding to the clinical expert. For the whole cohort, 50% of the structures were the ones produced from the ART-Plan and the remaining ones from the expert in a random manner. Each contour was then scored by 5 experts, as A/clinically acceptable, B/clinically acceptable after minor corrections, C/not acceptable. The second phase of evaluation refers to the time gain between a fully manual delineation and one targeting to correct the outcomes of automatic contouring. This was done for 50 patients (25 patients from each centre) with respect to a full annotation of the 15 structures that were considered also in phase I.

Results

96% of all manual contours were classified as clinically relevant (75% and 21% for A and B categories respectively). Values were equal to 98% for automatic contouring (56 % and 39 % for A and B respectively). Spinal cord and oral cavity obtained better scores for automatic contouring than for manual contouring (77 % and 89 % of score A for spinal cord and oral cavity versus 65 % and 64 % for manual contouring). On the contrary, optical nerves and mandibular glands were more difficulty delineated by the automatic solution. Inter-observer variability was high between experts. Average consensus for phase I was 63% between experts ranging from 53% to 77%. The time observed to correct the automated contours was

significantly inferior to the time required to generate contours fully manually. In average, 2 minutes were needed to correct the contours after auto-segmentation versus 30 minutes for manual delineation.

Conclusion

This is the first blinded, multicentric, and random back to back evaluation of an automated engine for delineation in HN tumours. The results are highly promising suggesting that this deep-learning based method should contribute to provide clinically acceptable OAR delineation. Further evaluation is on-going to quantify the dosimetric impact of the variations observed.

OC-0682 CBCT dose prior to radiotherapy causes up to 15 times more cell death than predicted

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Purpose or Objective

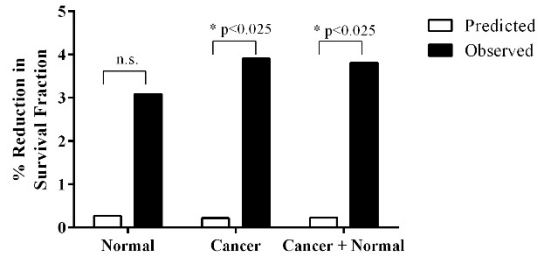
Cone Beam Computed Tomography (CBCT) is now routinely used in radiation therapy. Prostate, brain, lung and head and neck cancers are frequently subjected to CBCT to determine the position of the target volume for each treatment fraction, enabling a range of adaptive protocols to be clinically implemented. The aim of this study is to determine whether the CBCT dose alone provides a sufficient measure of the biological effects of pre-treatment imaging in radiation therapy.

Material and Methods

Four human cancer cell lines from lung (NCI-H460), prostate (DU 145), head & neck (CAL 27) and brain (Hs 683) and one normal prostate cell line (PNT1A) were exposed to a 6 MV photon beam, produced by a Varian Novalis-TX linear accelerator, to a prescribed dose that is predicted to result in 50% survival. For half the samples, a prior imaging dose was delivered using the on-board CBCT. The CBCT dose was measured to be 0.66 cGy, less than 1% of the therapeutic dose. The clonogenic assay was used to determine survival. The experiments were designed to achieve high statistical power by using an exceptionally large sample size (n=129).

Results

In this study of five cell lines, an additional CBCT imaging dose was found to significantly reduce mean cell survival relative to the survival following the treatment dose alone ($p<0.05$). The reduction was in the order of 15 times greater than that predicted for the CBCT dose. Individual cell lines did not show a statistically significant difference.



Conclusion

There are two key findings. First, CBCT preceding radiation therapy causes a measurable reduction in cell survival. We recommend that at a minimum, the dose from imaging be evaluated and recorded in the patient record, creating an opportunity to correlate the sequence and magnitude of imaging dose with patient outcomes. Second, the reduction in survival was found to be much larger (~15 times) than predicted from the dose response curves of the individual cell lines. This finding can be attributed to a combination of three effects: low dose hyper-radiosensitivity, the increased RBE of keV energy photons and the radiation induced bystander effect (RIBE) stimulated by CBCT, sensitizing the cells to the subsequent therapy dose. Of these effects, the last is likely to make the biggest contribution to the over response. Recognition of this phenomenon provides an opportunity to incorporate the imaging dose in the treatment plan for an enhanced therapeutic outcome.

Acknowledgements

This work was funded by:

- Faculty of Health Sciences, The University of Sydney, Seed grant
- Prostate Cancer Foundation Australia
- Tour de Cure

OC-0683 RTTs at the helm: moving towards RTT-led MR-guided radiotherapy

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Purpose or Objective

Adaptive Magnetic Resonance-guided radiotherapy (MRgRT) requires a multi-disciplinary approach and significant clinical resources. To facilitate sustainable MRgRT delivery models, specific magnetic resonance linear accelerator (MR-Linac) based competencies must be developed such that therapeutic radiographers (RTTs) can undertake MRgRT predominantly independently. This work describes the implementation of a protocol-driven 'clinician-lite' MRgRT workflow following the identification of MRgRT-based skills and competencies.

Material and Methods

The implementation of an MRgRT service from the ground-up required the recognition of the new knowledge, skills and competencies needed for safe, efficient MRgRT. To determine the parts of the pathway that could be devolved to RTTs and the skills required to do this, a needs assessment and informal survey of the inter-disciplinary team were undertaken. Competence in these skills was achieved using a mixed-methods educational approach that included tutorials, workshops, focused self-directed reading, and end-to-end workflow testing. The MRgRT pathway was critically evaluated by relevant professionals to encourage multidisciplinary input and discussion, allowing an iterative development of the RTT-led workflow. Starting with the simplest online adaptation strategy 'adapt-to-position' (ATP), which consists of a virtual couch shift and online re-planning, clear guidelines were established for the delivery of radical prostate radiotherapy following a 'clinician-lite' protocol.

Results

The enhanced RTT skills identified for MRgRT delivery, developed and practiced throughout the implementation period, included MRI safety and screening, MR image acquisition, MRI-based anatomy, multi-modality image interpretation and registration, and treatment plan