Purpose: Multi-parametric MRI has established high diagnostic performance in evaluating MIBC compared with CT [1]. However, radiotherapy planning is reliant on CT data. Improving soft tissue definition should make visualisation of key target areas easier, allowing greater accuracy and reproducibility in volume delineation. However, experience of MRI in radiotherapy planning is limited. This study aims to establish the inter-observer variability of target volume definition for bladder radiotherapy using MRI prior to any education/consensus meeting.
Methods: MRI scans of 3 patients with MIBC were contoured by 8 members of the bladder cancer MDT (4 clinical oncologists, 2 radiologists, 2 radiotherapy radiographers). Participants were given case vignettes and guidance on GTV and CTV definitions, but were not coached on MRI interpretation. Participants were blinded to each other's volumes. GTV and CTV contours were completed on T2- and outer bladder wall (oBW) contours completed on T1-weighted imaging; diffusion-weighted images were available for reference. Once all contours were completed a Simultaneous Truth and Performance Level Estimate (STAPLE) was created for each structure set to facilitate inter-observer comparisons. Tests for variability were carried out using ADMIRE research version v2.0 (Elekta AB, Stockholm, Sweden).
Results: In total, 72 contours were completed. The median DICE coefficients for GTV, CTV and oBW were 0.78 (IQR 0.69–0.84), 0.94 (IQR 0.74–0.95) and 0.95 (IQR 0.94–0.96), respectively. The median Cohen Kappa was 0.75 (IQR 0.67–0.81), 0.91 (IQR 0.90–0.92) and 0.92 (IQR 0.90–0.93), respectively, and the median Hausdorff distance was 10.20 (IQR 6.98–16.4), 8.55 (IQR 6.52–11.16) and 7.80 (IQR 6.71–10.19), respectively.
Conclusion: MRI target volume definition shows good concordance between bladder MDT experts. Greatest variance was seen for GTV delineation. Ongoing work will involve developing MRI-based radiotherapy consensus contouring guidance for MIBC.

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Re-planning Bladder Cancer Radiotherapy: Should we be Moving to Adaptive Radiotherapy?

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Purpose: Variation in organ shape and position significantly compromises target coverage despite typically large margins for bladder radiotherapy [1]. Adaptive radiotherapy (ART) strategies can be employed to reduce normal tissue dose and therefore toxicity [2]. With the increased time burden for bladder PTV revision mid-treatment we sought to identify the indications for re-plan and assess bladder size and position interfractional changes compared with planned volume, to identify whether ART introduction would be beneficial.
Methods: This retrospective study collected data on the last 5 radical bladder RT patients. Reasons for re-plan were collected. Bladder volumes were contoured on daily cone beam CTs (CBCTs) and verified by a second reviewer. Subsequent daily bladder volume and interfractional translational shift data were analysed. The selected patients were also audited as compared with London Cancer Bladder Radiotherapy guidelines [3] for comparing timing of radiotherapy from decision to treat and completion of baseline investigations prior to radiotherapy treatment initiation.
Results: 5 patients underwent radical radiotherapy for bladder cancer with stages between T2a and T4 disease. All were treated using volumetric modulated arc therapy with daily CBCT and soft tissue match. 3/5 patients were re-planned: 2 due to changes in CTV position falling out of original PTV and 1 due to increasing CTV not covered by original PTV. 2/5 had conventional fractionation (66 Gy in 33 fractions) and 3/5 were hypofractionated (55 Gy in 20 fractions) and did not receive concurrent chemotherapy due to comorbidities. Large interfractional treated bladder volume variations existed (largest variation 168.5 ± 26 ml).
Conclusion: High re-plan rates support the transition to adaptive strategies. However, large intra-patient variations in bladder volume and translational shifts in this small study reinforce the importance of proper bladder preparation.

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Immunogenic Effects of Radiotherapy for Bladder Cancer

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Purpose: Radiotherapy (RT) is an important part of the management of many patients with bladder cancer (BC), albeit with radical or palliative intent [1]. As well as directly cytotoxic effects, RT can exert immunogenic changes in the tumour microenvironment [2]. RT may cause tumour cells to undergo 'immunogenic cell death' and upregulation of cell-surface proteins in the tumour microenvironment leading to tumour-specific immune responses [3]. We aim to determine if RT exerts immunostimulatory effects in murine bladder cancer cell lines. We also developed a murine orthotopic tumour model more characteristic of *de novo* human tumours [4,5] to determine immunogenic changes occurring *in vivo*.
Methods: A murine vaccination study was employed to determine immunogenicity of cell death after RT. Western blotting and flow cytometry determined immune phenotypic changes in response to RT *in vitro*. To generate an orthotopic model of murine BC, MBT2 cells were inoculated intravesically into C3H/Hen mice. Ultrasound monitoring was used to measure tumour growth.
Results: Mice inoculated with BC cells irradiated with a single fraction of 16 Gy prior to implantation demonstrated a survival advantage after subsequent re-challenge with viable cells. RT led to upregulation of immunostimulatory surface proteins ICAM1 ± CD80, MHC I and Fas but not calreticulin or HMGB1, in a dose- and time-dependent manner after treatment in MB49 or MBT2 cells *in vitro*. Bladder tumours were visible on ultrasound 10–15 days after inoculation and showed reproducible growth with a >80% take rate.
Conclusion: RT induces immunogenic effects on murine BC cells, including upregulation of various tumour cell surface proteins. Future work will evaluate the importance of these changes for efficacy of RT. Successful generation of an orthotopic model of murine BC will allow determination of RT-induced immune changes within a representative tumour microenvironment. This information may help determine therapeutic strategies to enhance the efficacy of RT for patients with BC.

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