Feasibility planning study to improve local control for MIBC using therapeutic imaging and iso-toxic dose escalation

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Background

Five-year survival rates for muscle-invasive bladder cancer (MIBC) have remained around 50% since the 1980s in the UK [1]. Bladder-conserving treatments show comparable results to cystectomy [2], despite radiotherapy (RT) dose limitations due to the toxicity of uniform whole bladder RT. Dose escalation trials show promise; however, limited visibility of residual tumour on CT/ cone beam CT (CBCT) is an impediment [3]. Diffusion-weighted magnetic resonance imaging (DW-MRI) provides good visibility of volumes of high tumour burden and is increasingly used for diagnosis and as a biomarker [4]. DW-MRI could also facilitate targeting RT to aggressive areas of tumours via therapeutic imaging [5], however inherent distortions could limit positional accuracy.

Aims

• Quantify the effects of geometric distortion in DW-MRI of bladder cancer,
• Infer potential increase in tumour response from dose escalation via RT plans of simulated tumours, mimicking use of DW-MRI to inform tumour volume via MR-sim and/or an MR-linac.

Material & Methods

A phantom was designed to mimic a bladder and internal tumour on CT, T2w-MRI and DW-MRI; image distortion was corrected using FSL [8]. The Poisson model was used to re-fit clinical trials data previously modelled with the logistic model by Plataniotis and Dale [7] for RT-alone and RT + chemo to predict tumour control probability (TCP). Treatment plans were produced on a patient CT, with dose escalation to simulated tumours of differing volumes and locations within the bladder, and margins accommodating results from the bladder phantom work.

TCP was calculated for all plans and both TCP models; clonogenic cell density within the GTV was assumed to be 10²/cm³, and a range of densities tested for the uninvolved bladder wall.

Results

DW-MRI images were distortion-corrected using FSL [8] and new ADC maps created. Positions of interest (POIs) were used to mark fiducials, and their locations on T2w and ADC compared against the rigidly-registered CT in RayStation TPS.

POI agreement between CT and T2w-MRI at 3 T were within 1.2 mm at all points. The greatest uncorrected ADC POI differences were 6.3 mm, reducing to 1.8 mm for FSL-corrected images. At 1.5 T these values were 3.8 mm and 1.7 mm respectively.

A patient CT on which 18 different tumours had been simulated was used to mimic registration of CT with DW-MRI-based tumour information. Over 180 RT plans were produced with doses escalated isotoxically, using OAR constraints taken from the RAIDER clinical trial. Tumour DVHs and Poisson TCP models were used in MATLAB to predict TCP (endpoint 2 yr local control) for all dose escalated plans and a standard whole bladder plan. The highest dose escalation was possible for inferior tumours due to distance from bowel; the effect of variations in tumour volume were less significant than location.

Conclusions

• DW-MRI images of a bladder phantom which were distortion-corrected and then used to produce ADC maps showed resultant distortion below 2 mm at both 3 T and 1.5 T,
• Isotox dose escalation up to 78 Gy was feasible for some bladder tumours; this was dependent upon location with inferior tumours able to be escalated further,
• Theragnostic imaging using DW-MRI could therefore improve patient outcomes despite inherent distortion via increasing TCP using a personalised approach.

Future Work

Future work will require streamlining of the process of image distortion correction, and further testing by applying this approach within a retrospective planning study for patients imaged using DW-MRI.

References


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