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<table>
<thead>
<tr>
<th>Name (First, last)</th>
<th>Jane Rogers</th>
</tr>
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<tbody>
<tr>
<td>Mailing address (including province/state, country, postal/zip code)</td>
<td>4 Montgomery Close, Stratford-upon-Avon, CV37 9EU, UK</td>
</tr>
<tr>
<td>Institution/organization</td>
<td>University of Warwick</td>
</tr>
<tr>
<td>Position</td>
<td>PhD Student</td>
</tr>
<tr>
<td>Telephone (including country prefix)</td>
<td>00447722008099</td>
</tr>
<tr>
<td>Email</td>
<td><a href="mailto:j.a.rogers@warwick.ac.uk">j.a.rogers@warwick.ac.uk</a></td>
</tr>
</tbody>
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PRESENTATION TITLE
Theragnostic imaging using DW-MRI and isotoxic dose escalation for muscle-invasive bladder cancer

AUTHOR(S)
Rogers, J. A. *1,2; Sherwood, V. 2; Wayte, S. 2; Duffy, J. 1; Manolopoulos, S. M. 1,2
1University of Warwick, Coventry, UK.
2University Hospital Coventry and Warwickshire, Coventry, UK.

ABSTRACT
Theragnostic imaging using DW-MRI and isotoxic dose escalation for muscle-invasive bladder cancer

Rogers, J. A. *1,2; Sherwood, V. 2; Wayte, S. 2; Duffy, J. 1; Manolopoulos, S. M. 1,2
1University of Warwick, Coventry, CV4 7AL, UK.
2University Hospital Coventry and Warwickshire, Coventry, CV2 2DX, UK.

Purpose: Long-term survival for muscle-invasive bladder cancer (MIBC) has remained static for several decades at around 50 % in the UK [1]. Bladder-conserving treatments with trans-urethral resection followed by radiotherapy and chemotherapy show comparable results to cystectomy [2], despite standard whole-bladder radiotherapy doses being limited by toxicity (due to the large margins required to accommodate bladder filling). Partial bladder dose escalation trials using IGRT show promise, however, limited visibility of residual tumour on 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]. Therefore, theragnostic imaging using DW-MRI and an MR-linac could facilitate further dose escalation to MIBC, potentially via dose painting and/or accommodating response. However, distortion inherent in DW-MRI could limit achievable geometric accuracy. Therefore, this study quantified distortion via imaging of phantoms using DW-MRI, T2w-MRI and CT. Distortion was subsequently accommodated into treatment planning margins for simulated tumours. Doses were systematically isotoxically escalated, and the resulting increases in tumour control probability (TCP) calculated for multiple tumour locations and volumes within the bladder. The aim was to investigate individualisation of patient treatments using theragnostic imaging and biologically-adapted radiotherapy (BART) to isotoxically increase TCP, highlighting what may be achievable using an MR-linac.
Materials & Methods: Phantoms were designed to mimic MIBC, with sufficient tumour contrast for delineation across CT, DW-MRI and T2w-MRI. Effects of distortion on fiducial markers within the bladder and tumour were measured and two deformable registration algorithms were compared with rigid registration for their mitigation abilities.

Tumours were simulated in six locations within a patient bladder CT as though visualised on a registered DW-MRI. Margins inspired by the phantom investigation were used to mitigate residual geometric distortions, and the impact of dose escalation above the standard 64 Gy in 32 fractions was assessed using Poisson-based TCP models fitted to clinical trials data. Tumour clonogenic cell density was assumed to be $10^7$ cm$^{-3}$ and a range of densities investigated within the bladder wall. Feasibility of delivery and effect on TCP was assessed via dose accumulation using CBCT.

Results: Maximum residual distortions in the bladder-mimicking phantoms were found to be < 5 mm. Maximum isotoxic dose escalation to 78 Gy was possible for all inferior tumours. Superior, anterior, posterior and lateral tumours were isotoxically escalated to 70 - 72 Gy depending on location but independent of volume. Corresponding improvements in TCP were 8 – 10 % for superior tumours and 14 - 18 % for inferior tumours.

Conclusions: Theragnostic imaging using DW-MRI was investigated for BART whilst isotoxically increasing TCP. The study indicates that this approach could enable personalised radiotherapy treatment for MIBC and isotoxically improve outcomes.