MRI-guided adaptive radiotherapy for prostate cancer: When do we need to account for intra-fraction motion?

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ABSTRACT

A shift of the daily plan can mitigate target position changes that occur between daily MR acquisition and treatment for MR-linac radiotherapy, but increases the session time. We demonstrated that our workflow strategy and decision-making process, to determine whether a subsequent shift is necessary, is appropriate.

Introduction

Magnetic resonance image guided radiotherapy (MRgRT) delivered with the Unity MR-Linac (Elekta AB, Stockholm, Sweden), utilises an integrated 7MV flattening filter free (FFF) Elekta linear accelerator (linac) and a Philips 1.5T Magnetic resonance imaging (MRI) scanner, enabling online adaptive radiotherapy and real-time imaging \cite{1}.

Patients with low and intermediate risk prostate cancer were treated with radical radiotherapy on the MR-Linac within the Prostate Radiotherapy Integrated with Simultaneous MRI (PRISM) \textsuperscript{-} trial (NCT03658525). Two online workflow planning strategies were used, ‘Adapt to Shape’ (‘ATS’) and ‘Adapt to Position of the ATS’ (‘ATP-of-ATS’) \cite{2}. In ATS a new plan is created online by creating new contours on the initial daily MR image (MR\textsubscript{session}) and for ATP-of-ATS a subsequent modification or ‘shift’ (adjustment of the treatment field apertures) of the daily ATS plan is performed to correct for motion \cite{3}. Intra-fraction motion, resulting from bladder filling, patient movement, or rectal changes may occur during the MR-Linac treatment session \cite{4}, which are typically longer than those on conventional linacs \cite{5,6}. A MRI acquired immediately prior to treatment (MR\textsubscript{verification}) can determine such motion by a rigid registration with the MR\textsubscript{session} image. Any intra-fraction motion can be accounted for, by performing an ATP-of-ATS at the expense of further increasing session time.

Although ATS strategies have been demonstrated to be acceptable \cite{7}, there have been reported cases where ATP-of-ATS would have improved dosimetry, albeit in only 4% of fractions \cite{8}. The additional time needed to perform ATP after ATS for all fractions would impact patient throughput and increase the potential for further intra-fraction motion. We have investigated whether criteria implemented to perform ATP-of-ATS was appropriate and evaluated the predicted dosimetric benefits, if any, of using an ATP-of-ATS compared with ATS only.

Methods

This study was approved by the Royal Marsden NHS Foundation Trust audit committee. The first seven patients consented to the PRISM MR-Linac Trial (NCT03658525) for prostate cancer treatment with daily MRgRT, treated between October 2018 and March 2019 were included. Patient preparation and treatment planning parameters and procedures have been previously described \cite{3}.

Treatment planning was performed using the Monaco Treatment Planning System (TPS) (Elekta AB, Stockholm, Sweden, v5.40.00). The primary clinical target volume (CTV), Prostate CTV, was defined as the prostate plus proximal 1 cm of seminal vesicles (SV) with an elective CTV (‘SV CTV’) consisting of the proximal 2 cm of seminal vesicles exterior to the prostate. The primary Planning Target Volume (PTV\textsubscript{6000}) was a 5 mm left, right, superior, inferior, anterior and 3 mm

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The frequency of using an ‘ATP-of-ATS’ was determined. Overall daily plan compliance was determined by permitting two variations in the clinical goals, following strategies implemented for trials such as the PACE C (NCT01584258) [10] (Table 1), with 14/16 passing clinical goals deemed an acceptable online plan if failed clinical goals were approved by a clinician. Clinical goal compliance for treated and alternative workflows was assessed for all fractions.

Results

Of the seven patients treated between October 2018 and March 2019 five patients were included with 94 fractions available for analysis. The workflow described was not implemented for the first treated patient and another patient excluded due to bladder voiding during the workflow for over half the fractions. Six fractions were unable to be analysed because of disruptions to the MRLinac workflow for example bladder voiding (n = 4) and software issues (n = 2). Patients included were allocated numbers 1–5.

‘ATP-of-ATS’ was used for treatment in 25 % (23/94) of fractions, with ‘ATS’ used for treatment in the remaining 75 % (71/94). Of the 23 fractions treated using ATP-of-ATS, the majority (22) were spread evenly between three patients. ATS-treated fractions achieved equivalent predicted clinical goal compliance of 95 % and similar rates of overall plan acceptability (92 % compared to 93 %) compared to the alternative workflow (Table 2). For fractions where ‘ATP-of-ATS’ was used, a greater percentage of predicted clinical goals were achieved (93 %) and a greater number of plans considered acceptable (96 %) compared to the alternative workflow where the ATS was delivered without an ATP (89 % and 70 %, respectively). Two fractions treated with ATS would have benefited from ATP-of-ATS, in terms of clinical goal compliance. No fractions that were treated ATP-of-ATS would have benefited from the alternative workflow — with ATS alone.

Fig. 1 displays estimated delivered dose for a fraction where the patient demonstrated gross intra-fraction motion. For this fraction the patient was treated with an ‘ATP-of-ATS’ workflow (Fig. 1, left) with D95% of CTV Prostate predicted to be 57.2 Gy (>57.0 Gy) when scaled to twenty fractions. Had the alternative workflow been used (ATS, Fig. 1, right) D95% of CTV Prostate was predicted to be lower at 54.7 Gy.

For Patient 1, as identified on reference planning imaging, the bowel often abutted the primary target (CTV Prostate) on the MR_verification. This meant that for 13 fractions during online plan optimisation the target coverage was intentionally compromised to ensure cumulative OAR doses over the entire treatment course remained within constraints. Therefore, to ensure intentional target compromise (and corresponding predicted clinical goal failures) did not influence the interpretation of the data, the results were analysed with data for Patient 1 removed. For ATS-treated fractions there was no predicted dosimetry benefit had the alternative workflow been used, with total clinical goal compliance and overall plan acceptability being higher for the ATS-treated plan compared to alternative ATP-of-ATS workflow. For fractions where ATP-of-ATS was used, a greater percentage of predicted clinical goals were achieved (96 %) and a greater number of plans considered acceptable (100 %) compared to the ATS alternative workflow (92 % and 81 %, respectively) (Table 3). With Patient 1 removed from the analysis, 100 % of clinically delivered workflows passed with at least 14/16 clinical goal compliance (Table 3).

Discussion

We have shown that visual assessment of the prostate on the MR_verification with MR_session-defined PTVs overlaid, is an effective decision-making tool to determine the necessity of a ATP-of-ATS. The workflow strategy of using an ‘ATP-of-ATS’ where the CTV was not covered by the PTV at verification has been reported, but the frequency and impact of doing so not described [11]. We found that for fractions treated with the ‘ATP-of-ATS’ workflow, a greater percentage of clinical goals were achieved, and a greater number of daily plans deemed acceptable, compared to an ATS workflow. Conversely, there was no
appreciable difference in these metrics between the two workflows for fractions where ATS-only was used, indicating that for these fractions a subsequent ATP-of-ATS adaption would have prolonged the overall session time, by approximately 5–10 min, without a predicted dosimetric benefit.

The CTV prostate D95% constraints for the clinically treated plan were met in all but one fraction in four of the five patients. A retrospective assessment of this fraction indicated that the visible prostate on the MR\textsubscript{verification} was outside the MR\textsubscript{session} defined PTV so that although an ATS strategy was used for this fraction, ATP-of-ATS, which would have been predicted to improve target coverage, would have been appropriate in this case.

The online challenges of ATP-of-ATS must also be considered. Performing an ATP-of-ATS further extends the already prolonged treatment session, increasing the likelihood of additional motion\cite{12,13}. An alternative would be to always perform an ATP-of-ATS, to streamline the workflow and exclude the decision-making process. However, we have shown ATP-of-ATS is only necessary in <30 % of fractions and was not necessary in all patients. One patient did not require ATP-of-ATS and another only required ATP-of-ATS for one fraction.

Other centres have reported an ATS only workflow to be effective, with no excursion of the prostate beyond the PTV reported, in 20 patients receiving 5 fractions with 3 mm PTV margins\cite{7} and only required in 4 of 100 fractions in 5 patients receiving 20 fractions with 5

16 (21 %) 
96 %  
100 % 
98 %  
ATS

patient 1 removed, results from remaining 75 fractions

APPENDIX

Conclusion

We have demonstrated that our workflow strategy decision-making process, verifying if the visible prostate was within the corresponding PTV was appropriate to determine whether a subsequent ATP-of-ATS workflow is necessary for any given fraction. The dose calculated on

Table 3
Clinical goal compliance for clinically treated and alternative workflows (Patient 1 removed) e.g. for the ATS clinically delivered workflow, the offline alternative is ATP-of-ATS.

| Patient 1 removed, results from remaining 75 fractions | 
|---|---|---|---|---|---|---|
| Total clinical goals achieved | Plans which pass at least 14/16 clinical goal compliance | Clinically delivered workflow | Fractions Treated | Online treated | Offline alternative | 
| Online treated | 
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the image immediately prior to delivery was used as a surrogate for delivered dose to quantify the process.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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