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SHORT COMMUNICATION

Impact of dosimetric differences between CT and MRI derived target volumes for external beam cervical cancer radiotherapy

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Objectives: The use of MRI is becoming more prevalent in cervical cancer external beam radiotherapy (RT). The aim of this study was to investigate the impact of dosimetric differences between CT and MRI-derived target volumes for cervical cancer external beam RT.

Methods: An automated planning technique for volumetric modulated arc therapy was developed. Two automated planning plans were generated for 18 cervical cancer patients where planning target volumes (PTVs) were generated based on CT or MRI data alone. Dose metrics for planning target volumes and organs at risk (OARs) were compared to analyse any differences based on imaging modality.

Results: All treatment plans were clinically acceptable. Bladder doses (V40) were lower in MRI-based plans ($p =$

0.04, $53.6 \pm 17.2\%$ vs $60.3 \pm 13.1\%$ for MRI vs CT, respectively). The maximum dose for left iliac crest showed lower doses in CT-based plans ($p = 0.02$, 47.8 ± 0.7 Gy vs 47.4 ± 0.4 Gy MRI vs CT, respectively). No significant differences were seen for other OARs.

Conclusions: The dosimetric differences of CT- and MRI-based contouring variability for this study was small. CT remains the standard imaging modality for volume delineation for these patients.

Advances in knowledge: This is the first study to evaluate the dosimetric implications of imaging modality on target and OAR doses in cervical cancer external beam RT.

INTRODUCTION

Radiotherapy is a well-established treatment modality for cervical cancer. It is the primary treatment modality for women presenting with locally advanced cervical cancer and is used as an adjuvant therapy for patients who undergo surgery and have risk factors for locoregional recurrence.¹ Accurate and reliable target and organ at risk (OAR) delineation is an essential component of radiotherapy treatment planning. Interobserver variability in target delineation has been quantified and reported for many tumour sites,² including cervical cancer.^{3,4} Several studies have addressed the consequences of interobserver contouring variability on the resulting dose delivered to the patient. This has been addressed for external beam radiotherapy (EBRT)⁵⁻⁹ and brachytherapy¹⁰⁻¹² for many tumour sites. The dosimetric

impact of variations in cervical cancer target volume delineation for EBRT has only been reported by Eminowicz et al as part of the INTERLACE trial quality assurance (QA) where 21 centres delineated clinical target volume (CTV) in 2 test cases.⁹ The study reported that cervical cancer CTV delineation varied among the centres and created a larger overall CTV compared to the gold-standard CTV, leading to significant reductions in dose delivered to the planning target volume (PTV),⁹ however, these results were based on only two patients and were derived from QA exercises which may lead to biased results.

CT has long been the standard of care for radiotherapy treatment planning including delineation of target volumes and OARs. CT offers several clinical advantages for treatment planning including electron densities for dose

calculations, clear visualisation of high contrast bony landmarks, excellent spatial fidelity and displays some soft tissue contrast for delineation. However, MRI has been shown to better identify soft tissue definition and improve target volume and OAR delineation for many tumour sites.¹³ With the rapid uptake of MRI in radiotherapy planning, it is important to assess the benefit of MRI for each tumour site. The use of MRI for cervical cancer brachytherapy is well established and is superior to CT,¹² however the impact on EBRT is not well understood. As modern radiotherapy techniques such as volumetric modulated arc therapy (VMAT) are increasingly used for cervical cancer, the accuracy of delineation is crucial. Our previous work to quantify differences in delineated CTVs between CT and MRI showed significantly smaller CTV on MRI.⁴ As an extension of this previous work, we planned to quantify the dosimetric impact of the delineation variation. We hypothesised that MRI-based target volume is associated with radiotherapy plans with a better therapeutic ratio (better target volume coverage and lower OAR doses). Therefore, the aim of this pilot study is to evaluate the impact of dosimetric differences between CT and MRI derived target volumes for cervical cancer EBRT. To our knowledge, no planning study has been conducted to evaluate the dosimetric implications of imaging modality on target and OAR doses in cervical cancer VMAT.

METHODS AND MATERIALS

Study population and imaging

Data from a previous study assessing the impact of MRI on target volume delineation for cervical cancer⁴ were used for this study. Study population included 18 patients with Stage IB-IV cervical cancer with a macroscopic pelvic tumour, undergoing primary radiation therapy. All patients underwent a planning CT scan with a 2 mm slice thickness in the treatment position on a Philips Brilliance Big Bore CT simulator (Phillips Medical Systems, The Netherlands). Patients underwent a bladder filling protocol prior to the planning CT to ensure a consistent bladder volume for the scans and treatment. The MRI scans were acquired on a 70 cm bore MAGNETOM Skyra 3T (Siemens Medical Systems, Erlangen, Germany) scanner with a two-dimensional axial T₂ weighted turbo spin echo using flatbed tabletop. Patients were set up in the same position as they were in for their planning CT and underwent the same bladder filling protocol they completed prior to the planning CT, unless the MRI was immediately after the CT. The imaging was scheduled to minimise time between the two scans and the aim was to image patients on the same day with both CT and MRI.

Delineation process

The delineation process, outlining comparison methods and CTV delineation results have been reported previously⁴ and is outlined briefly. Three experienced radiation oncologists specialising in gynaecological cancer independently delineated a pelvic CT and MRI data set for each patient. The following structures were delineated on both imaging data sets; gross tumour volume (GTV), uterus, vagina, cervix, parametria and lymph node clinical target volume (LN-CTV). Combined CTV contours were generated by combining all delineated contours.

Creation of gold-standard planning target volume and OARs

The PTV for each data set was generated by applying a 15 mm margin to the combined CTV. This margin was considered safe as internal target volume (ITV) was not used in this study, and bony matching was assumed for treatment verification. Probabilistic estimates for gold-standard PTVs for each image set were generated using the Simultaneous Truth And Performance Level Estimation (STAPLE) algorithm,¹⁴ and subsequently labelled CT-STAPLE PTV and MR-STAPLE PTV. This study aimed to assess differences in doses due to target volume delineations, therefore MRI information was not considered in OAR definitions and all OARs were delineated on CT data. This is to ensure that the OARs are consistent in both CT- and MRI-based plans. Delineated OARs included the small bowel, rectum, bladder, femoral heads, iliac crests and cauda equina. All OARs were defined by a radiation therapist and checked by a radiation oncologist.

Planning technique

Following image registration, both CT-STAPLE and MR-STAPLE PTVs were imported onto the respective CT data set for planning. The Pinnacle³⁸ treatment planning system (Philips Radiation Oncology, Madison, WI) has implemented the Auto Planning (AP) module, a template-based optimisation tool. An AP technique for VMAT was developed for this study, resulting in a single click optimisation solution. Two AP plans were generated for all patients; one using CT-STAPLE PTV, and another using MRI-STAPLE PTV. A prescription of 45 Gy in 25 fractions was used for all cases with the aim of meeting the dose compliance criteria adapted from EMBRACE-II protocol¹⁵ (Table 1).

Analysis

Paired *t* tests were used to analyse differences in the STAPLE PTV volumes between CT and MRI. The metrics recorded in Table 1 for each STAPLE PTV volumes were extracted and paired *t* tests were used to compare differences between imaging modality. Population mean DVHs for CT- and MR-STAPLE PTV treatment plans were generated, with Wilcoxon matched-pair sign rank probability curves calculated to indicate dose regions where statistically significant differences between mean DVHs exist.¹⁶ Conformity index (CI = V95% /VPTV) and homogeneity index (HI = [(D2% - D98%)/(D50%)]) were calculated for all plans.

RESULTS

All treatment plans were considered clinically acceptable and adhered to the hard constraints for target volumes. Overall, the mean STAPLE PTV volumes were smaller on MRI (1552.5 ± 326.8 cc) compared to CT (1603.3 ± 396.5 cc), however this difference was not statistically significant (*p* = 0.08). Table 2 shows the comparison of mean target & OAR dose metrics, and conformity & homogeneity indices. Statistically significant differences were seen between the two modalities for bladder V40Gy (*p* = 0.04, 53.6 ± 17.2 % vs 60.3 ± 13.1 % for MRI vs CT, respectively) and V30Gy (*p* = 0.04, 75.5 ± 14.1 % vs 79.7 ± 8.9 % for MRI vs CT, respectively), and maximum dose for left iliac crest (*p* = 0.02, 47.8 ± 0.7 % vs 47.4 ± 0.4 % for MRI vs CT, respectively). No significant differences were seen for other OARs.

Table 1. Plan compliance criteria

		Hard constraints	Soft constraints
Target	Planning target volume	V95% > 95%	
		Dmax < 48.2 Gy	
Organs at risk	Small bowel	Dmax < 48.2 Gy	V40Gy < 250cm ³
			V30Gy < 500cm ³
	Bladder	Dmax < 48.2 Gy	V40Gy < 75%
			V30Gy < 85%
	Rectum	Dmax < 48.2 Gy	V40Gy < 85%
			V30Gy < 95%
	Femoral heads	Dmax < 50 Gy	
	Iliac crest	Dmax < 50 Gy	V40Gy < 35%
			V30Gy < 50%
	Cauda equina	Dmax < 48.2 Gy	

Dmax, maximum dose; Gy, Gray; Vx, the percentage of the volume receiving more than x% of the prescribed dose.

Table 2. Mean dose metrics, conformity & homogeneity indices for CT- and MRI-based plans

		CT		MRI		
Structure	Metric	Mean	SD	Mean	SD	p-value
Planning target volume	V95% (%)	99.5	0.4	99.5	0.3	0.34
	Dmax (Gy)	46.9	0.3	47.0	0.3	0.26
Small bowel	V40Gy (cm ³)	350.8	160.9	352.0	178.0	0.45
	V30Gy (cm ³)	493.2	184.7	502.6	207.0	0.25
	Dmax (Gy)	47.6	0.5	47.8	0.6	0.19
Bladder	V40Gy (%)	60.3	13.1	53.6	17.2	0.04*
	V30Gy (%)	79.7	8.9	75.5	14.1	0.04*
	Dmax (Gy)	47.8	0.6	47.7	0.6	0.15
Rectum	V40Gy (%)	67.7	16.3	61.3	22.6	0.14
	V30Gy (%)	85.5	8.9	83.5	8.4	0.21
	Dmax (Gy)	47.6	0.7	47.6	0.5	0.36
Left femoral head	Dmax (Gy)	44.6	1.1	44.5	2.0	0.37
Right femoral head	Dmax (Gy)	43.0	1.8	43.4	2.2	0.07
Left iliac crest	V40Gy (%)	25.2	4.6	25.9	5.5	0.22
	V30Gy (%)	43.9	4.8	43.1	5.1	0.20
	Dmax (Gy)	47.4	0.4	47.8	0.7	0.02*
Right iliac crest	V40Gy (%)	23.5	3.2	22.9	4.4	0.19
	V30Gy (%)	41.5	4.1	40.7	4.5	0.15
	Dmax (Gy)	47.3	0.5	47.5	0.4	0.07
Cauda equina	Dmax (Gy)	37.7	5.5	37.8	7.3	0.46
Conformity index (ideal = 1)		1.2	0.1	1.2	0.1	0.46
Homogeneity index (ideal = 0)		0.1	0.0	0.1	0.0	0.36

Dmax, maximum dose; Gy, Gray; SD, standard deviation; Vx, the percentage of the volume receiving more than x% of the prescribed dose.

*Significant p-value

Figure 1. Mean dose–volume histogram for planning target volume and organs at risk for all 18 patients. Red line is CT plan and blue line is MRI plan. The grey line is p -value curve, while the dashed grey line shows the $p = 0.05$ threshold.

Mean population DVHs are shown in [Figure 1](#) for the PTV and OARs. No significant difference between the population mean DVH curves was observed for PTV, small bowel, rectum, left femoral head, iliac crests and cauda equina. For bladder, the MRI-based plan displayed significantly lower population mean between 10 and 12 Gy. For the right femoral head, a significant difference was observed in the interval from 10 to 14 Gy and 43 to 45 Gy, in favour of the MRI based plans.

DISCUSSION

This study analysed target and OAR dose differences due to imaging modality (CT vs MRI) for target volume determination. The dosimetric difference of CT- and MRI-based target volume

variability was small. However, plans generated with MRI-based target volumes resulted in lower mean dose to the bladder. This may be attributable to the overall mean STAPLE PTV volumes being smaller on MRI compared to CT. Although there was statistical significance between CT and MRI plans for bladder doses, this difference is unlikely to have a clinical impact on bladder toxicity as both plans met the bladder constraints of no more than 75% of the volume to receive a dose >40 Gy, and no more than 85% of the volume to receive a dose >30 Gy. There is limited evidence regarding dose constraints for bladder toxicities.¹⁷ The external-beam component of gynaecological cancer radiotherapy has been limited to 40–50 Gy and rarely results in severe long-term bladder sequelae.¹⁷ For several OAR metrics, lower doses were observed

for CT-based plans while for others lower doses were observed for MRI-based plans indicating no specific trend in overall doses to OARs between the two modalities. When looking at the population mean DVHs, the differences between CT and MRI plans were mostly not significant across all structures. However, as with many planning studies, the OAR DVHs are based on a single snapshot in time and the dynamics of tumour response to treatment or organ motion are not taken into consideration, both of which could result in more of the OAR moving into the high dose region as treatment progresses.

Data from a previous study quantifying the impact of MRI on target volume delineation for cervical cancer⁴ were used for this study. The previous study by Veera et al⁴ demonstrated that the dice similarity coefficient (DSC) for GTV improved from 0.77 on CT to 0.81 on MRI, $p < 0.01$, the LN-CTV DSC was 0.75 for both MRI and CT, and the combined CTV DSC was 0.81 for MRI and 0.80 for CT, $p = 0.27$. While the study found that MRI-based contouring resulted in more consistently delineated volumes when compared to CT for most CTV structures,⁴ we found that this did not have a significant impact on OAR doses and hence tumour outcomes. This may be driven by the need to include regional nodes in the treatment volumes for gynaecological cancers as most of the delineation impact of MRI is seen in the primary and surrounding gynaecological structures. Education and training interventions to support the use of MRI in radiotherapy is also necessary as MRI is increasingly being adopted into routine practice.¹⁸

Conventional treatment planning for highly conformal techniques such as intensity modulated radiotherapy (IMRT) and VMAT require multiple manual processes, with planners iteratively adjusting optimisation goals. This process is not only time-consuming, but treatment plan quality is inherently dependent on the individual skill of the planner.^{19–21} Multiple studies have assessed the efficacy of automated planning for head and neck,^{22–25} oesophageal²⁶ and prostate cancers,²⁷ and found automated planning generated plans to be non-inferior or superior to manual planning quality, while significantly reducing treatment

planning times. The use of automated planning technique for VMAT in this study ensured that plan quality and consistency is maintained for all plans, eliminating the issue of interplanner variability. This may have contributed to the consistency and minimal dosimetric differences between CT- and MRI-based plans in this study. The successful development of this AP technique for gynaecological cancer has also resulted in investigation into clinical translation of this technique in our centre.

There are limitations to the approach described in this study. This study only considered VMAT technique to assess the dosimetric impact of the two imaging modalities. There may be other dosimetric differences if the study was undertaken with a different planning technique such as IMRT or three-dimensional conformal radiotherapy. However, given the treatment planning complexity for this group of patients, there may be a preference towards VMAT. This study also did not take into account the use of ITV. PTV margins of 15 mm for the VMAT plans were used because no ITV creation (bladder full/ bladder empty planning scans) was possible at the time that the data sets were collected. These large margins may have obscured any dosimetric gains to OARs that MRI-based contouring may have provided. The OARs in this study were delineated on CT data only, therefore there may be OAR positioning differences between CT and MRI, likely due to bladder filling differences. While steps were taken to ensure patients underwent the same bladder filling protocol for both CT and MRI scans, it is possible that the bladder filling was not identical for CT and MRI. This may affect the position of the target volume and in turn impacting on the resulting dose.

CONCLUSION

The dosimetric differences of CT- and MRI-based contouring variability for this study was small. In the era of MRI-guided radiotherapy, this study is adding to the evidence to support the use of MRI by showing that CT and MRI are equivalent imaging modalities for the purposes of EBRT for cervical cancers. In clinical practice, although MRI gives better soft tissue delineation, this has minimal impact on the resultant plan for EBRT.

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