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Original article

Prostate cancer post-prostatectomy radiotherapy: CT vs MRI for vesico-urethral anastomosis target delineation

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ABSTRACT

Background: Vesico-urethral anastomosis (VUA) is critical to the clinical target volume (CTV) in post-prostatectomy radiotherapy (PPRT), as it is the commonest site of recurrence. Typically, this is performed on a CT alone but guidelines recommend MRI.
Objective: To evaluate the VUA spatial differences between CT (ctVUA) and MRI (mrVUA) and analyse its impact on the CT defined CTV (ctCTV) as recommended by published guidelines.
Materials and methods: We identified 34 patients with a co-registered simulation CT and T2 weighted MRI. The VUA was located on CT and MRI whilst blinded to the opposing scan. The differences were analysed using Wilcoxon's Signed Rank Test. The mrVUA coverage was investigated using three ctCTV margins of 5 mm, 8 mm and 12 mm.
Results: Median age was 63 years with 59% having pT3a disease and median Gleason score of 7. The mrVUA was coincident with the ctVUA in 12% and inferior in 88%. Median difference was 5 mm (0–10 mm) ($P < 0.0001$). Only a ctCTV margin of 12 mm would have encompassed all mrVUAs. A ctCTV margin of 8 mm and 5 mm resulted in 12% and 38% cases where the VUA was excluded from the ctCTV.
Conclusions: MRI is important for the accurate delineation of VUA for PPRT.
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Prostate cancer post-prostatectomy radiotherapy (PPRT) is used as adjuvant treatment for men at high risk of relapse or for the salvage of men who have suffered biochemical prostate specific antigen (PSA) relapse or clinical recurrence [1–6]. However, up to one third of adjuvant patients and two thirds of salvage cases will further relapse following PPRT [7].

Initial investigations to define the site of local recurrence following PSA relapse post prostatectomy used trans-rectal ultrasound guided biopsy alone. They showed that the peri-anastomotic site or VUA was the most common site of recurrence with the incidence ranging from 56 to 66% [8–10].

It is therefore essential that the VUA be accurately identified prior to PPRT to ensure adequate dosimetric coverage. Precision targeted radiotherapy with intensity modulated radiotherapy (IMRT) and image guided radiotherapy (IGRT) in prostate cancer has been shown to be important for both disease outcome and minimization of toxicity [11–13]. International guidelines and protocols stress the importance of the VUA [14–17], suggesting that it is critical to the definition of the radiotherapy clinical target volume (CTV) i.e. the volume at high risk of containing residual microscopic disease.

The guidelines recommend that axial CT slices should be used when identifying the VUA [14–17]. They acknowledge that the VUA may be more accurately identified on MRI, as the gold standard reference, [17] because of the superior soft tissue contrast. However, they concede that the utility of MRI has not been fully evaluated [15,17].

The guidelines also recommend an additional caudal CTV margin from the VUA to allow for microscopic extension [14–17]. The suggested geometric margins range from 5 mm to 12 mm. However, unless the VUA is accurately delineated this margin for microscopic disease may be compromised and consequently under-dosed.

The purpose of the study was to evaluate the utility of MRI in the accurate identification of the VUA and the impact on the CTV for PPRT relative to the recommended guidelines. Therefore, the aims of this study are

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1) To analyse the spatial differences between MRI and CT in the localization of the VUA.
2) To assess the mrVUA relative to the CT based CTV margins (ctCTV) recommended by the published guidelines.

Materials and methods

The investigation was approved as a retrospective analysis by the institutional ethics committee. The study cohort consisted of 34 eligible consecutive prostate cancer patients previously treated with post-prostatectomy IMRT/IGRT between December 2011 and October 2013 with uniform CT slice thickness.

Simulation and imaging

Patients were positioned supine with an individualized foam Alpha cradle placed on an indexed pelvic board with foot stocks. CT simulation (non-contrast) was performed on a General Electric Radiation Therapy Lightspeed Widebore® helical scanner (General Electric Healthcare, Buckinghamshire, United Kingdom) with a resolution of 512 × 512, pitch 0.75, no gap and a slice thickness of 1.25 mm. The CT origin (Z-axis 0) was centred and tattooed 5 cm superior to base of penis.

The planning MRI was performed on a 1.5 T Siemens Magneto Avanto Syngo MR B17® (Siemens Healthcare, Erlangen, Germany). The MRI sequence utilized for this study was a high-resolution 3D T2 weighted scan with a voxel size of 1 mm. This was reformatted in the axial plane and imported into CMS Focal Sim® (Elekta, Stockholm, Sweden) and co-registered with the simulation CT.

VUA identification and analysis

Following a prostatectomy, the bladder is anastomosed to the proximal membranous urethra [18–20]. The membranous urethra is normally closed by the external sphincter, both being contained within the urogenital diaphragm. Subsequently it does not contain urine. Therefore, as the guidelines recommend, the VUA was defined on the axial slice just inferior to the last slice where urine is visible, as the urine defines the bladder on both CT and MRI [14,16,17]. This was confirmed on multi-planar views. Furthermore, on T2 weighted MRI the VUA can be more precisely defined due to ability to visualize the low signal elliptic cylindrical wall of the VUA and proximal membranous urethra in contrast to the very bright signal of urine in the bladder [21].

The CT and MRI were co-registered initially using the entire pelvic bones but then refined to the region of interest that encompasses the urogenital diaphragm and VUA i.e. the bones of the ischiopubic ramus and coccyx.

The department regards the gold standard for delineation of the CTV to be the MRI for the soft tissue components not well visualized on CT i.e. the VUA, membranous urethra & urogenital diaphragm (5–10 mm) and posteriorly the meso-rectal fascia. The CT is used to define the posterior pubis, obturator internus and bladder components of the CTV as these are well seen on CT.

Following co-registration of the CT and MRI, a radiation oncologist delineated the ctVUA on the CT whilst blinded to the MRI. At a later date the same radiation oncologist defined the mrVUA on the co-registered MRI whilst blinded to the CT. All VUAs were reviewed and adjusted by a radiation oncologist and radiologist both of whom were specialized in urology.

The superior–inferior (Z-axis) coordinate i.e. vertical distance from the CT origin was recorded for both the ctVUA and mrVUA. The differences between these VUAs were calculated.

CTV analysis

Published guidelines recommend adding an inferior margin to the VUA to allow for microscopic extension beyond the VUA [14–17]. The RTOG guidelines recommend 8–12 mm [14], Princess Margaret Hospital (PMH) recommends 8 mm [17] whereas the Australasian Faculty of Radiation Oncology Genito-Urinary Group (FROGG) guidelines suggest 5–6 mm [16]. The remaining guideline from the EORTC recommends that the relevant CTV include "Centrally: the urethra-vesical anastomosis" and "Caudally: including the apex (15 mm cranially from the penile bulb)" with a 5 mm margin for high risk areas including microscopic extension, incompletely resected ECE and involved margins [15].

Statistics

The differences (ctVUA – mrVUA) were calculated for each patient. As the differences relate to the CT discrete slice thickness the median value and range was calculated. A p-value of <0.05 was afforded statistical significance between the median differences of the ctVUA and mrVUA using a two-tailed Wilcoxon Signed-Rank Test for paired samples. The mean difference for the patient population was also calculated to compare with the literature. The statistical analysis was performed using Microsoft Excel and Graphpad Prism Version 6.07.

Results

Patient cohort

The study cohort consisted of 34 patients with a median age was 63 years (range 52–72 years). Nine patients (26%) received adjuvant PPRT to a mean dose of 66 Gy and the remaining 25 (74%) received salvage PPRT for PSA relapse to a mean dose of 70 Gy. The majority had locally advanced disease with almost 60% having extracapsular extension (pT3a), whilst the median Gleason Score was 7. The apical margin was involved in 14 of the 21 patients (56%) with positive surgical margins (Table 1).

In 30 patients (88%) the vector difference between the mrVUA and ctVUA was caudal, ($P < 0.0001$). The ctVUA and mrVUA were coincident in four patients (12%). The median difference was 5 mm with a range of 0–10 mm. The mean difference was 4.82 mm with a standard deviation (SD) of 2.97 mm (Fig. 1). Notably, there were four patients (12%) with a mrVUA that was 10 mm inferior to the ctVUA (Fig. 2).

Comparison of the differences between mrVUA and ctVUA with recommended guidelines for CTV margins is shown in Fig. 3. The mrVUA was encompassed by the ctCTV in all patients when a margin of 12 mm was used. For the 8 mm and 5 mm margins the

Table 1
Prostatectomy pathological characteristics: T stage, Gleason Score and Margin Status.

Prostatectomy Tumour Characteristics (Total patients = 34)		
T Stage	Patients	%
2a	2	5.9%
2b	3	8.8%
2c	5	14.7%
3a	20	58.8%
3b	4	11.8%
Gleason Score		
7	25	73.5%
8	2	5.9%
9	7	20.6%
Surgical Margins		
Positive	21	61.8%
Negative	13	38.2%

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