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Visualising the proximal urethra by MRI voiding scan: results of a prospective clinical trial evaluating a novel approach to radiotherapy simulation for prostate cancer

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Original Article

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Abstract

Background: Delineating the proximal urethra can be critical for radiotherapy planning but is challenging on computerised tomography (CT) imaging.
Materials and methods: We trialed a novel non-invasive technique to allow visualisation of the proximal urethra using a rapid sequence magnetic resonance imaging (MRI) protocol to visualise the urinary flow in patients voiding during the simulation scan.
Results: Of the seven patients enrolled, four were able to void during the MRI scan. For these four patients, direct visualisation of urinary flow through the proximal urethra was achieved. The average volume of the proximal urethra contoured on voiding MRI was significantly higher than the proximal urethra contoured on CT, 4·07 and 1·60 cc, respectively ($p = 0·02$). The proximal urethra location also differed; the Dice coefficient average was 0·28 (range 0–0·62).
Findings: In this small, proof-of-concept prospective clinical trial, the volume and location of the proximal urethra differed significantly when contoured on a voiding MRI scan compared to that determined by a conventional CT simulation. The shape of the proximal urethra on voiding MRI may be more anatomically correct compared to the proximal urethra shape determined with a semi-rigid catheter in place.

Introduction

Delineating the proximal urethra for radiotherapy planning is commonly done for the treatment of prostate cancer. With the growing use of high-dose per fraction treatment paradigms such as stereotactic body radiation therapy and the dose escalation of magnetic resonance imaging (MRI)-detected prostatic lesions, this practice may become increasingly critical. Higher urethral dose with such treatment approaches is associated with increased toxicity including urinary frequency or dysuria.[1–3] Interest is growing in the use of urethra-sparing radiation therapy for prostate cancer; however, results from these approaches have been conflicting.[4–6] In part this may be due to challenges in accurately contouring the proximal urethra.

Identifying the proximal urethra can be challenging on computerised tomography (CT) scan alone, and the geometric centre of the prostate has been used as a surrogate.[7,8] However, the geometric centre has been shown to vary significantly from the Foley catheter-defined urethra.[9] Accurately contouring the proximal urethra often relies on Foley catheter insertion, retrograde urethrogram or using the geometric centre of the prostate. Drawbacks to these approaches include patient discomfort and possible distortion of normal anatomy from catheter placement.[9,10] We hypothesised that we would be able to visualise and contour the proximal urethra by using a MRI scan to delineate urine flow during voiding. We believed that during the act of voiding urine would fill the potential space in the proximal urethra and that this flowing urine would be observed during an MRI scan. By visualising the urine flow and proximal urethra non-invasively, we expected that this non-invasive approach would be preferable to invasive methods due to greater patient satisfaction and reduced risk of infection and trauma compared to current methods for visualising the prostatic urethra. Our aim was to determine if it was feasible to visualise the proximal urethra using a non-invasive novel technique.

We prospectively trialed a novel non-invasive technique to allow visualisation of the proximal urethra during simulation scanning using a rapid sequence MRI protocol to visualise the urinary flow of patients voiding during the MRI scan.

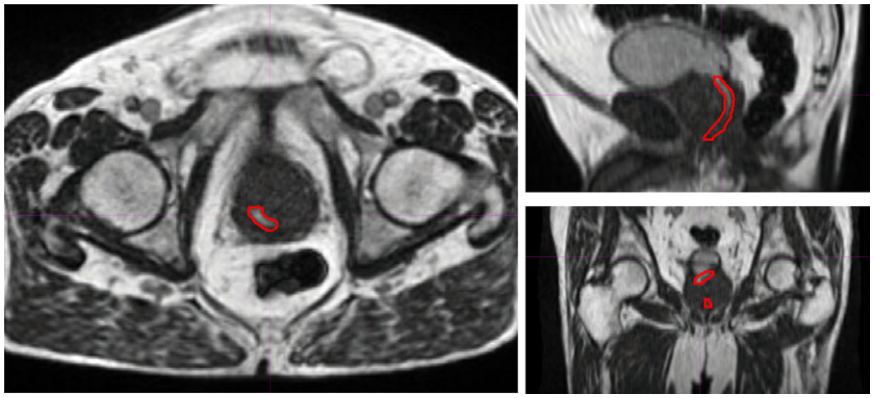

Figure 1. MRI showing the visible proximal urethra during voiding, contoured in red, with increased signal intensity shown as urine passes from the bladder through the urethra.

Materials and Methods

After institutional review board approval and informed consent, we enrolled patients with prostate cancer undergoing CT simulation scans and 0·35T MRI scans on the same day. We utilised our Viewray MRIdian Linear Accelerator, which consists of a 6 MV flattening-filter-free linear accelerator integrated between two 0·35 T split superconducting magnets, for the MRI-simulation scans. Seven patients were enrolled on study and asked to urinate into a condom catheter in the supine treatment position. All patients were instructed to have a comfortably full bladder for simulation scan. Patients verbally indicated when voiding commenced and a 45 × 45 × 24 cm field of view, with an in-plane resolution of 1·5 mm × 1·5 mm and slice thickness of 3 mm, 17-second true fast imaging with steady-state free precession (TRUFI) MRI scan was obtained. TRUFI is a balanced steady-state free precession sequence, yielding a T2/T1-weighted contrast.[11,12] Patients additionally underwent a CT simulation scan with or without a Foley catheter in place, per current institutional standard. The MRI and CT images were fused together, based on anatomic registration with a focus on the prostate. The proximal urethra was defined between bladder neck and the base of the pubic symphysis and contoured separately on the voiding MRI scan and CT simulation scan. The proximal urethra-segmented volume between MRI and CT contours was compared and the Dice coefficient was calculated as a measure of spatial agreement.

Results

We prospectively enrolled seven patients with prostate cancer. Of these, four were able to void in the supine position during the MRI scan. For these four patients, direct visualisation of urinary flow through the proximal urethra was readily achieved. A representative scan showing the clearly defined proximal urethra during voiding is shown in Figure 1.

Of the four patients who were able to void in the supine position, one underwent CT simulation with Foley catheter and four underwent CT simulation without catheter placement. For the four patients without Foley catheter, the proximal urethra on CT was contoured as the geometric centre of the prostate, as previously discussed.[7,8] The average volume of the proximal urethra contoured on voiding MRI was significantly greater than the average proximal urethra volume contoured on CT (4·07 versus 1·60 cc, respectively; $p = 0·02$). The Dice coefficient averaged 0·28 (range 0–0·616). Representative images of patients with and without a Foley catheter, as compared with voiding MRI scan, are shown in Figures 1c and 1d. The voiding urethra tended to be non-central, larger and more curvilinear, as compared to the CT-defined urethra.

Discussion

In this small, proof-of-concept prospective clinical trial, the volume of the proximal urethra differed significantly when contoured on a voiding MRI compared to the volume determined on conventional CT simulation. This is the first study comparing the three-dimensional position of the voiding urethra to that of a CT scan-defined urethra.

The Foley catheter-defined urethra was defined as 'ground truth' in the Groupe Européen de Curiethérapie/European Society for Radiotherapy and Oncology recommendations.[13] However, there is a growing body of evidence that this may not accurately encompass the urethra in external beam treatments where a Foley catheter is not used for each treatment. Dekura et al. found that the urethral position was significantly different when using a soft guidewire as compared to when a Foley catheter was in place.[10] Additionally, Litzenberg et al. found that removing a Foley catheter could cause a significant change in the rotation of the prostate.[14] In our study, we found minimal overlap between the voiding MRI urethra and the CT-defined urethra. The location of the MRI-voiding proximal urethra is likely more anatomically correct and suggested a more curved shape compared to the shape determined with a semi-rigid catheter in place (Figure 2).

Foremost among the limitations of this study is the small number of patients and the lack of multiple participants undergoing CT simulation with Foley catheter in place. This prevents us from drawing firm conclusions; rather, our observation of changes in the urethra positing between CT scan with Foley catheter and voiding MRI scan is hypothesis generating. Four patients underwent CT simulation where the urethra was defined as the geometric centre, which is a common practice for defining the proximal urethra.[7,8] In these patients, we noted similar patterns of increased size, increased curvature and non-central location of the proximal urethra defined on MRI voiding scan, as compared to the geometric centre urethra using CT imaging. Another limitation of this study is the fact that three of the seven patients enrolled were unable to void under trial conditions, this may be due to patient discomfort of urinating in a public space or while supine.

Urination allows for clear visualisation of the proximal urethra by MRI; however, the act of voiding may change the bladder, prostate and pelvic floor muscle positions, making fusion with a full-bladder CT scan more difficult.[10,15] To overcome this, we initially

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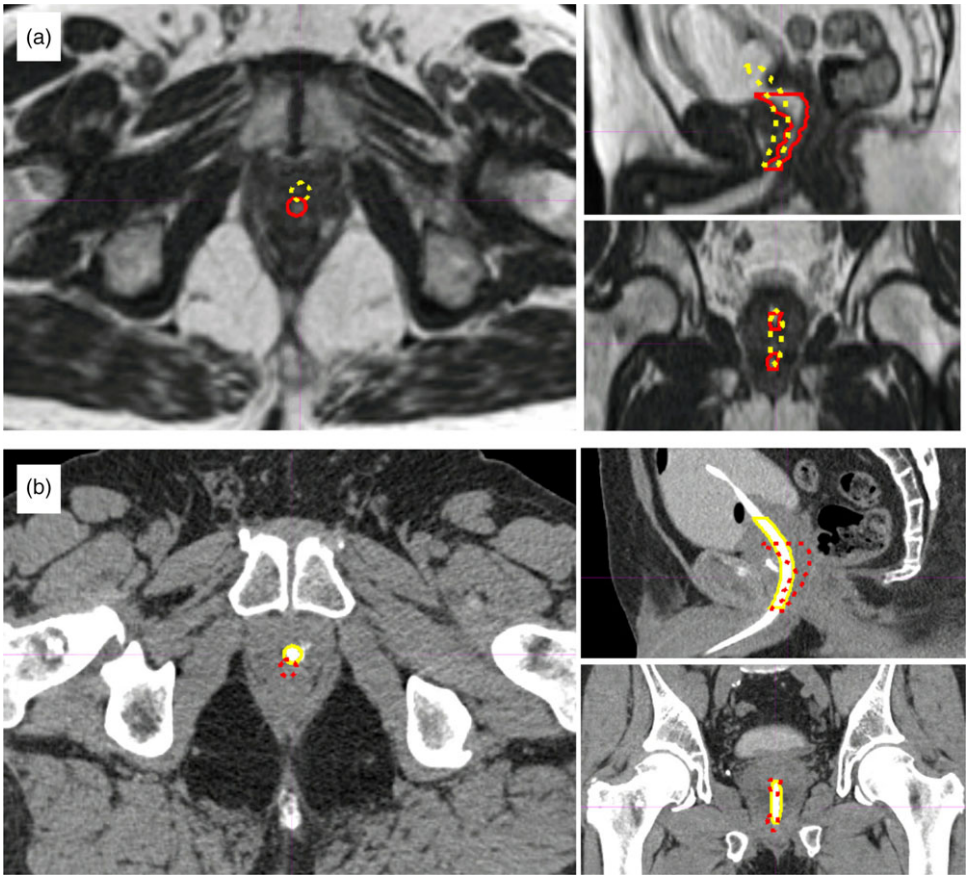

Figure 2. MRI and CT scans showing the voiding urethra and Foley catheter, with the variation in location, increased size and increased curvature of the voiding urethra appreciable. (a) The MRI scan showing the voiding urethra contoured in red with the Foley catheter contoured in dotted yellow. (b) The CT simulation scan showing the Foley catheter contoured in yellow with the voiding urethra contoured in dotted red.

complete a full-bladder MRI scan and we use the short voiding sequence MRI for defining the prostatic urethra position. In our analysis of the pre-void and voiding MRIs, we did not observe large changes in the prostate or pelvic floor musculature positioning. However, clinically we have observed such shifts in prostate and pelvic floor musculature with a Foley catheter simulation as compared to daily imaging during treatment with no catheter. This may result from pelvic floor muscle contraction secondary to discomfort from the Foley catheter during simulation and delineation of urethra by voiding MRI may overcome this challenge.

This trial supports further investigation into delineating the prostatic urethra for radiotherapy treatment planning using non-invasive MRI imaging. Future studies may include comparison of urethral contours for a series of patients undergoing treatment simulation using a voiding MRI scan and then a Foley catheter. This may allow for more accurate image segmentation and contouring of the prostatic urethra as well as evaluation of whether and how a Foley catheter may deform this structure. Further, this could enable additional studies to evaluate approaches aimed at reducing genitourinary toxicities in these patients by more effectively constraining the dose of radiation delivered to the proximal urethra.

Conclusion

This study provides a novel non-invasive technique to allow for visualisation of the proximal urethra during simulation scanning using a rapid sequence MRI protocol to visualise the urinary flow of patients voiding during the MRI scan.

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Conflicts of Interest. The authors declare none.

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Ethical Standards. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation, the Belmont Report and with the Helsinki Declaration of 1975, as revised in 2008, and have been approved by the University of Wisconsin Institutional Review Board.

References

1. Hsu IC, Hunt D, Straube W et al. Dosimetric analysis of radiation therapy oncology group 0321: the importance of urethral dose. Pract Radiat Oncol 2014; 4 (1): 27–34.
2. Seymour Z A, Chang A J, Zhang L et al. Dose-volume analysis and the temporal nature of toxicity with stereotactic body radiation therapy for prostate cancer. Pract Radiat Oncol 2015; 5 (5): e465–e472.
3. Budaus L, Bolla M, Bossi A et al. Functional outcomes and complications following radiation therapy for prostate cancer: a critical analysis of the literature. Eur Urol 2012; 61 (1): 112–127.
4. Zilli T, Franzese C, Bottero M et al. Single fraction urethra-sparing prostate cancer SBRT: phase I results of the ONE SHOT trial. Radiother Oncol 2019; 139: 83–86.
5. Shimizu S, Nishioka K, Suzuki R et al. Early results of urethral dose reduction and small safety margin in intensity-modulated radiation therapy

https://doi.org/10.1017/S1460396921000157 Published online by Cambridge University Press

(IMRT) for localized prostate cancer using a real-time tumor-tracking radiotherapy (RTRT) system. Radiat Oncol 2014; 9: 118.
6. Vainshtein J, Abu-Isa E, Olson K B et al. Randomized phase II trial of urethral sparing intensity modulated radiation therapy in low-risk prostate cancer: implications for focal therapy. Radiat Oncol 2012; 7: 82.
7. Bucci J, Spadinger I, Hilts M et al. Urethral and periurethral dosimetry in prostate brachytherapy: is there a convenient surrogate? Int J Radiat Oncol Biol Phys 2002; 54 (4): 1235–1242.
8. Waterman F M, Dicker A P. Determination of the urethral dose in prostate brachytherapy when the urethra cannot be visualized in the postimplant CT scan. Med Phys 2000; 27 (3): 448–451.
9. Lee H K, D'Souza W D, Yamal J M et al. Dosimetric consequences of using a surrogate urethra to estimate urethral dose after brachytherapy for prostate cancer. Int J Radiat Oncol Biol Phys 2003; 57 (2): 355–361.
10. Dekura Y, Nishioka K, Hashimoto T et al. The urethral position may shift due to urethral catheter placement in the treatment planning for prostate radiation therapy. Radiat Oncol 2019; 14 (1): 226.
11. Green O L, Rankine L J, Cai B et al. First clinical implementation of real-time, real anatomy tracking and radiation beam control. Med Phys 2018; 45 (8): 3728–3740.
12. Bieri O, Scheffler K. Fundamentals of balanced steady state free precession MRI. J Magn Reson Imaging 2013; 38 (1): 2–11.
13. Kovacs G, Potter R, Loch T et al. GEC/ESTRO-EAU recommendations on temporary brachytherapy using stepping sources for localised prostate cancer. Radiother Oncol 2005; 74 (2): 137–148.
14. Litzenberg D W, Muenz D G, Archer P G et al. Changes in prostate orientation due to removal of a Foley catheter. Med Phys 2018; 45 (4): 1369–1378.
15. Rai R, Sidhom M, Lim K, Ohanessian L, Liney GP. MRI micturating urethrography for improved urethral delineation in prostate radiotherapy planning: a case study. Phys Med Biol 2017; 62 (8): 3003–3010.

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