

Online Guidance of Tumor Targeted Prostate Brachytherapy using Histologically Referenced MRI

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Introduction: Despite rationale and enthusiasm for distinguishing regions of tumor burden within the prostate gland for specific therapeutic intensity, robust methods and tools for clinical translation have not yet matured. While multi-parametric MRI can accurately identify regions of tumor-dense burden of disease within the prostate [1], its performance in delineating the boundaries of tumor targets for focal therapeutic intervention has not been determined. Here we report technical and clinical performance of a needle navigation system where pathologically referenced multi-parametric MRI guidance improved the determination of tumor boundaries, and enabled tumor-targeted HDR brachytherapy.

Methods: The navigation system utilizes a dedicated interventional MRI table (Sentinelle Medical Inc), which provides access to the perineum in a stable supine patient position within a 1.5T GE Signa scanner, and a stereotactic transperineal template assembly. The procedure involves multiparametric diagnostic imaging of the prostate gland, registration of the stereotactic system, navigation tools for needle guidance, and 3D needle verification imaging. Patients were imaged with a torso-phased array placed anterior and posterior to the pelvis and an MRI endorectal coil (MEDRAD MRInnervu) attached to the template assembly, inserted in the rectum, and locked to the table using an immobilization arm. The imaging examination included the following acquisitions: conventional diagnostic axial T2-weighted FSE acquisition (TE/TR=96/3450ms, 320x256 over 16cm); dynamic contrast-enhanced (DCE) MRI (3D SPGR, TE/TR=2/4.2ms, 256x128 over 18cm, temporal resolution 8 s, scan time 5 min during bolus infusion 3cc/s of Gd-DTPA); diffusion-weighted MRI (TE/TR=62/5575ms, 256x256 of 16cm, b=0, 600s/mm²); magnetic resonance spectroscopic imaging (MRSI) (PROSE TE/TR=130/1000, 7.5mm voxel resolution); SSFP imaging of the template system for registration (FIESTA TE/TR=1.7/5.8ms, 256x256 over 20cm), and interventional needle verification imaging (FSE TE/TR=87/3800, 320x224 over 14cm).

Patients with suspicion of local recurrence after radiotherapy were enrolled on a prospective clinical trial of 6-12 18g needle (InVivo, Germany) core MRI-guided biopsy, where an single integrated diagnostic imaging and biopsy procedure was performed under conscious sedation (propofol continuous infusion). Core samples were obtained at the boundary of tumors identified on MRI, and from all non-suspicious sextants. Those patients with visible and histologically referenced focal recurrences were eligible for tumor-targeted salvage HDR brachytherapy, each receiving two fractions (11Gy) over 14 days (Nucletron). The tumor target was defined as the shared boundary of suspicious MRI features and malignant biopsy cores mapped onto T2-weighted images using a) MRI reference coordinates where no displacement/deformation was observed, b) rigid point-based registration where displacement was present, and c) a biomechanical model-based deformable registration technique (MORFEUS) where needles deformed the prostate gland. [2] Common 3D points in the prostate were identified to confirm the accuracy of registration. Data analysis used MIPAV (NIH, Bethesda, MD) for manual segmentation and analysis of ROI volumes.

Results: Eighteen patients (age 63-83, mean 72) received MRI-guided prostate biopsy at biochemical failure 2-11 years after radiotherapy (mean 6.3 yrs), and 4 patients have proceeded to salvage HDR brachytherapy to date. Most (15/18) were found to have local recurrence, including 11 patients with confirmed focal tumor visible on MRI and amenable to local salvage. Mean absolute in-plane stereotactic needle targeting accuracy was 2.2mm (SD 0.7mm) with a small but systematic posterior bias, and biopsy core co-registration accuracy was sub-voxel. Excluding the first two patients, mean diagnostic MRI + biopsy procedure time was 80 min (55-142 min), while the mean imaging time for brachytherapy catheter insertion was 87.5min (69-100min). Tumor targets for HDR brachytherapy ranged from 1.8-4.3cc, representing 6-18% of the prostate volume. Needle core histological maps led to a change in tumor target boundary in all 4 patients, where the tumor target was enlarged in 3/4 patients.

Summary and Conclusion: Feasibility of integrating pathologically referenced multi-parametric MRI for online guidance of HDR prostate brachytherapy is demonstrated. The value of 3D imaging to document actual location of biopsy cores in reference to anatomic boundaries cannot be overstated. Online MRI needle guidance systems with accurate and responsive navigation help better define cancer features on MRI and enable tumor-targeted diagnostics and therapeutics.

References: [1] Langer, D.L. et al., *Prostate cancer detection with multi-parametric MRI: logistic regression analysis of quantitative T2, diffusion-weighted imaging, and dynamic contrast-enhanced MRI*. Journal of Magnetic Resonance Imaging, 2009. **30**(2): p. 327-34. [2] Hensel, J. et al., *The development of a Multi-Organ Finite Elements Based Prostate Deformation Registration Model Enabling the Registration of Endorectal Coil Magnetic Resonance Images (ERC-MRI) for Radiotherapy Planning*. Int J Radiat Oncol Biol Phys, 2007. **68**(5): p. 1522-8.

Figure: a) Dedicated interventional MRI table assembly providing pelvic access for stereotactic needle guidance during integrated diagnostic imaging and biopsy/brachytherapy, b) navigation software (Aegis, Sentinelle) displaying needle target (green) onto diagnostic T2 images, c) needle verification images documenting actual location of 3 biopsy needles (signal voids R and L) in reference to intended target (green), d) map of benign (green), malignant-dense (red), malignant-microfocus (pink), and indeterminate (white) biopsy cores in reference to imaging features suspicious for tumor on DCE (light blue), ADC (purple), and T2 (royal blue). In this case, the boundary of the T2-visible tumor was later revised posteriorly based on a benign biopsy core in this region, thereby reducing the target volume for salvage HDR brachytherapy.

