MRI and Biopsy Performance in Delineating Recurrent Tumor Boundaries after Radiotherapy for Prostate Cancer

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Introduction: While multi-parametric MRI can accurately identify regions of tumor-dense burden of disease within the prostate, its performance in delineating the boundaries of tumor targets for focal therapeutic intervention has not been determined. We evaluated the performance of MRI (plus/minus guided biopsy) in delineating tumor boundaries for focal salvage therapy of prostate cancer recurrence after external beam radiotherapy.
Methods: Patients with biochemical failure after radiotherapy were enrolled in a prospective clinical trial to map sites of local recurrence after radiotherapy. An integrated diagnostic MRI and interventional mapping biopsy procedure was performed under sedation in a 1.5T scanner. Patients were imaged with a pelvic coil and an endorectal coil (MEDRAD MRInnervu) attached to a stereotactic transperineal template assembly (Sentinelle Medical Inc, Toronto). 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). The integrated biopsy procedure involved targeted radial biopsy of suspicious regions and random sextant sampling of the normal-appearing peripheral zone. Histology maps were generated by delineating and registering biopsy core regions onto diagnostic images using a point-based rigid algorithm to correct for prostate rotations and translations through the course of needle insertions. Biopsies were considered to be positive if viable tumor was present. Biopsies were considered negative in the presence of benign prostate gland tissue, prostate intra-epithelial neoplasia (PIN), or if non-viable tumor was seen and ascribed to moderate/severe radiation effect present. Two independent blinded observers reviewed diagnostic images offline and delineated tumor boundaries on each of T2, ADC, and a selected early DCE time series, which where then combined for a final tumor VOI target for focal salvage therapy. VOIs were then compared against overlaid histology maps. Boundary determination was considered accurate if all pathologically proven tumor sites were encompassed within VOIs. Data analysis used MIPAV (NIH, Bethesda, MD) for manual segmentation and analysis.
Results: Twenty-three patients have been enrolled (age 63-83, mean 72) and have received MRI-guided prostate biopsy at biochemical failure 2-11 years after radiotherapy (mean 6.3 yrs). The majority (83%) were found to have local recurrence. Of 18 patients analyzed to date, patients with <6 informative cores were excluded, leaving 15 patients for reporting. Observers performed comparably, whereby mean multiparametric MRI sensitivity, specificity, PPV and NPV for detecting tumor regions was 0.76, 0.7, 0.7, and 0.75. The best independent imaging parameter was the ADC map, with mean performance of 0.65, 0.68, 0.74, and 0.58, demonstrating a lower NPV compared with the multiparametric approach. In contrast, the tumor boundary was accurate in only 5/15 patients, improving to 8/15 patients with addition of a 5mm expansion uncertainty margin. Targeted radial biopsies improved accuracy to 14/15 patients, by excluding false positive regions (n=2), expanding tumor volumes (n=2) or both (n=2). Random sampling biopsy only contributed in 1 patient by detecting tumor not identified by MRI and targeted biopsy.
Summary and Conclusion: MRI alone is not sufficiently accurate to define boundaries for tumor-targeted salvage even with addition of an uncertainty margin. MRI-guided and targeted biopsy improved both detection and delineation accuracy for recurrent tumor regions, and changed salvage therapy planning in the majority of patients. 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 tumor boundaries on MRI and enable tumor-targeted therapy.

Figure: Case example of a patient with a false positive (left panel) and a true positive (right panel) tumor (red VOI) delineated on combined T2, ADC, and DCE images, and displayed here on anatomic T2 images. Green squares represent benign biopsy samples, and the red square represents a positive biopsy at the superior aspect of the gland. In this case, targeted biopsy improved MRI performance in determining tumor boundaries for subsequent focal salvage therapy by excluding a false-positive region.