Development of a Screening MRI Protocol for the Detection of Prostate Cancer: Initial Experience

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Target audience: Those interested in imaging of prostate cancer

Purpose: The current standards of care in screening of prostate cancer are serum PSA measurement and digital rectal examination (DRE). There is significant controversy about using these as screening tools[1] as both suffer from poor sensitivity and specificity. The standard 12 quadrant transrectal ultrasound guided (TRUS) biopsy based on these tests results in an overdiagnosis of non-life-threatening prostate cancer in 60% of patients[2], without significant benefit in mortality or morbidity[3]. To limit the harms of overdiagnosis, active surveillance protocols use biopsy to arrive at management decisions. However, biopsy underestimates aggressiveness of tumors in 25-30% of patients[4]. Hence, there is an interest in developing secondary screening tools as MRI to aid detection of clinically significant cancers, and improve risk stratification using targeted biopsies. The widespread use of MRI as a screening tool has been prohibitive due to cost and time constraints.We have developed a pelvic MRI protocol that reduces imaging duration to 15-20 minutes, opening the possibility of developing a cost and time effective imaging screening tool. Here, initial clinical experience in the first cohort of patients undergoing this protocol is shared, exploring whether biopsy targeted towards lesions discovered with our MRI protocol could improve detection of clinically significant prostate cancer compared to serum PSA and DRE alone.

Methods: We prospectively enrolled men in the age group of 40 – 75 years with elevated PSA or abnormal DRE without history of prior prostate biopsy. Thus far, 9 patients have undergone both imaging and biopsy. The abbreviated pelvic MRI protocol performed without contrast consisted of three sequences: three plane single shot T2 weighted (slice thickness: 4 mm, FOV: 300 mm, TR: 2000 ms, imaging time: 3 min 40 sec), axial high resolution T2-weighted TSE (slice thickness: 3mm, FOV: 160 mm, TR: 7200 ms, imaging time: 3 min 30 sec), and diffusion-weighted imaging with ADC maps (slice thickness: 3 mm, FOV: 240 mm, TR: 7900 ms, b values of 50, 600, 1000 s/mm^2, imaging time: 3 min 59 sec). Total imaging time was 11 min 29 sec, and table time varied with patient. Lesions were identified in consensus by two attending radiologists with extensive experience in prostate MR, and categorized as: no cancer, low, intermediate, or high suspicion for cancer. Region of interest (ROI) evaluation was performed for lesions and normal peripheral zone (NPZ) of prostate on ADC maps. Patients then had a standard 12 core transrectal ultrasound (TRUS) biopsy with the urologist initially blind to the MR read. After completion of the TRUS biopsy, MRI data were revealed and any suspicious lesions identified were targeted with an additional two core biopsies per lesion. Targeted biopsy results were then compared to the results of TRUS biopsy.

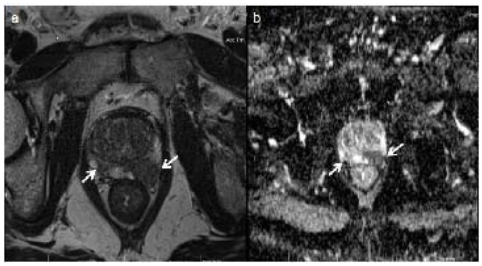

Fig. 1. Axial T2-weighted image (a) depicts a large mass in left peripheral zone with extracapsular extension and a smaller lesion in right peripheral zone. Both show decreased ADC on ADC map (b) – proven high grade tumor on biopsy

Results: Average table time for the patients was 18 min, though this is biased by the initial two patients (32 and 22 min, respectively), and averaged 16 minutes for the subsequent 6 patients. Four lesions in three patients were read as "high" suspicion for cancer (Fig. 1) and a fifth lesion in a fourth patient was read as "intermediate" suspicion. All five lesions were positive for cancer. Of these, one cancer was identified where the standard TRUS cores alone were negative and thus missed the lesion (Gleason 3+4 in 50% of the core). In a second case, targeted biopsy results upgraded the lesion from Gleason 8 to Gleason 9. Overall, standard biopsy identified 3 patients with clinically significant disease, whereas the MRI-targeted cores identified all 4 patients, yielding a 25% higher detection rate. The remaining four patients were read as low suspicion or completely negative. Of these, 3 had chronic inflammation and one was negative (matching the read). One patient with a "low" suspicion scan had low volume (5% of core, Gleason 3+4) disease in a single core.

Discussion: These very early results, while still on a small group of patients, are very encouraging. They indicate that cancer detection and performance of biopsy in detecting clinically significant lesions is improved when MRI is performed before prostate biopsy. This result is in agreement with previously reported studies[5, 6]. However,prior studies were performed with multiple parameters that included dynamic contrast enhanced MRI, with or without spectroscopy,which significantly increased the scan duration[7, 8]. Since the literature suggests that T2w and diffusion imaging are the most important in characterizing cancer, only these two sequences were included in the truncated protocol. We have found thus far that the lesions identified as "high" or "intermediate" suspicion on MRI consistently turned out to be clinically significant cancers, whereas lesions categorized as "low suspicion" on MRI turned out to be either chronic inflammation or very low volume disease. Although preliminary, the relationship between MRI read and Gleason grade seen on biopsy in our study is consistent with earlier studies[9, 10]. If this relationship persists in future as we enroll more patients and the evidence is compelling, this MRI protocol could potentially be used as a cost-effective secondary screening tool in prostate cancer management algorithms. The surgeon may choose to perform targeted biopsy only in patients with "intermediate" or "high" suspicion lesions, and choose active surveillance or follow up for patients with "low" suspicion scans. This approach is consistent to the cost-effectiveness analysis performed by Mowatt et al who reported that cost-effectiveness of MRI may compare favorably with standard TRUS biopsy if MRI can achieve a high negative predictive value for no cancer/ low risk disease, while maintaining a high confidence level for detecting intermediate/ high risk disease[11]. The biggest limitation of our study is that we have a small number of patients thus far. Secondly, in this preliminary study, imaging data were used for cognitive needle guidance to the tumor location, and real-time imaging guidance was not used to perform thetargeted biopsy. In the near future, an improvement to this technique will include targeted biopsy either with MRI-ultrasound fusion guidance, or in-gantry MRI guidance.

Conclusions: Our early experience with a fast pelvic MRI protocol improved the detection of clinically significant prostate cancer over PSA and DRE alone, with upstaging of Gleason Grade in one patient and diagnosis of cancer in another patient that would have been otherwise missed with the standard TRUS biopsy. The results, while preliminary, indicate that a fast screening protocol MRI, which is not cost prohibitive and time-constrained, could be used to diagnose cancer and improve risk stratification using targeted biopsy. Further work is needed on a larger number of patients to determine if addition of this novel MRI protocol to PSA and DRE could increase the accuracy of detecting clinically significant prostate cancer, while eliminating "false positives" and decreasing biopsy frequency.

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