3D High Resolution Diffusion-Weighted MRI at 3T: Preliminary Application in Patients undergoing Active Surveillance Protocol for Low-Risk Prostate Cancer

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Target Audience – MR scientists, MR engineers, Urologists, and Radiologists specializing in pelvic imaging

Introduction – For prostate cancer, diffusion-weighted (DW) MRI in combination with T2-weighted MRI improves the accuracy of tumor detection and localization [1-4]. Recently, DW MRI has been proposed for noninvasive monitoring of low risk prostate cancer (lrPC) in patients on active surveillance (AS-PC) for possible grade progression (e.g. Gleason grade 3 to 4) or increase in tumor volume [5-7]. Although conventional single shot (SS) DW echo planar imaging (EPI) may be adequate for evaluating bulky tumors typically managed with radical surgery, accuracy and sensitivity is limited for monitoring low volume / low Gleason grade tumors seen in AS patients because of limited spatial resolution and poor image quality [8]. To address this technical challenge, we developed a novel 3D High Resolution DW MRI sequence using a diffusion-prepared balanced steady-state free precession (bSSFP) approach using multi-shot imaging to achieve sub-millimeter spatial resolution and reduce susceptibility-related artifacts [9].

Methods – In a group (N=8) of healthy volunteers, we compared the proposed technique (TE_{prep}=60ms, FA=90°, 48 segments, 5 Kaiser ramp-up, centric encoding, parallel imaging R=2, low res (LR): TR_g/TR/TE = 2000/3.0/1.44ms, 2 shots; high res (HR): TR_g/TR/TE = 1200/3.5/1.74ms, 4 shots) with SS DW EPI (TR/TE=4700/80ms, parallel imaging R=2, low res: NEX=13 and high res: NEX=7) at two matched spatial resolutions (LR: 2.1x2.1x3.5mm^3; HR: 0.9-1.3x0.9-1.3x3.5mm^3). We statistically tested (unpaired two-tailed student t-test) differences in mean trace apparent diffusion coefficient (ADC) values of the peripheral (PZ) and central zones (CZ). All diffusion sequences encoded 3 orthogonal DW directions at 2 b-values (300 and 600 ms/um^2) and a b0 image (7 measurements, 7.5 minutes). Image quality was scored and statistically tested on a 5-point scale accounting for susceptibility artifacts, geometric distortion, and visibility of anatomy[10] relative to a T2-weighted turbo spin echo (TSE) (0.5x0.5x3.5mm^3, TR/TE=4800/125ms). The proposed technique was also compared with SS DW EPI in a group (N=9) of AS-PC patients at the same two spatial resolutions mentioned above. The four diffusion scans were integrated into a routine clinical pelvic MR scan that included T2-weighted TSE and dynamic contrast enhanced (DCE) T1-weighted gradient-recalled echo (GRE) scan (1.3x1.3x3.5mm^3, TR/TE=3.02/1.09ms, temp res = 40s). Two hours following imaging, a standard 12-point biopsy was performed blinded to the imaging results and acted as gold standard. Accuracy of identifying biopsy-confirmed lrPC lesions was reported citing mean contrast-to-noise ratio (CNR). Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and area under the receiver-operator curve (AUC) of the pelvic MR protocol (low ADC in DW MRI, hypointense in T2w, and elevated k_{Trans} or fast early wash-in in DCE) using SS DW EPI or the proposed technique was compared with biopsy in identifying regions positive for lrPC. The MRI reading was blinded to biopsy.

Results – For healthy controls, the proposed technique at both spatial resolutions yielded mean ADC values that were not statistically different than those in SS DW EPI in the PZ (LR: 1.67±0.3 (population mean±SD) vs 1.73±0.4 um^2/ms, p = 0.34; HR: 1.66±0.2 vs 1.69±0.4 um^2/ms, p = 0.22) and CZ (LR: 1.26±0.5 vs 1.31±0.5 um^2/ms, p = 0.27; HR: 1.22±0.4 vs 1.27±0.5 um^2/ms, p = 0.18). Image quality scores were statistically better for the proposed technique at both spatial resolutions (LR: 3.4±0.6 and 2.1±0.5, p < 0.05; HR: 3.7±0.5 and 2.9±0.9, p < 0.05). The proposed technique had no statistical difference in image quality between the two spatial resolutions (p = 0.42), while SS DW EPI yielded statistically significant difference (p < 0.05). For AS-PC patients, all (N=16) but one lrPC lesion (94%) were delineated by the proposed technique at low and high resolution with mean CNR=3.2 and 2.2, respectively. In contrast, SS DW EPI detected less lesions for both low (69%) and high (81%) resolutions with lower mean CNR=1.3 and 1.8. T2w TSE was able to detect 93.7% of the lrPC lesions with mean CNR=2.8. DCE was only able to identify 40% of the confirmed lrPC lesions with mean CNR=1.8. Sensitivity, PPV, NPV, and AUC of the clinical MR protocol using the proposed technique (94%, 54%, 97%, 0.80) was significantly higher (p < 0.05) than the protocol using SS DW EPI (63%, 48%, 82%, 0.67). Specificity was lower for the proposed technique (65.8%) compared with SS DW EPI (71.1%).

Conclusion – We developed a novel 3D diffusion-prepared multi-shot bSSFP technique capable of improved spatial resolution, image quality, and lesion CNR compared with SS DW EPI, while maintaining quantitative estimation of ADC. Because of these technical advances, the proposed technique yielded significantly better sensitivity, PPV, NPV, and AUC in detecting biopsy-confirmed lesions compared with SS DW EPI in a small group of AS-PC patients. By improving lesion detection, the proposed technique may allow DW MRI to potentially monitor lrPC in AS-PC.

References – [1] Bloch B, et al. Radiology (2007) [2] Lim H, et al. Radiology (2008) [3] Iwazawa J, et al Diagn Interv Radiology (2010) [4] Lawrence E, et al. Nat Rev Urol (2012) [5] Morgan VA, et al. Br J Radiol (2011) [6] Giles SL, et al. Am J Roent (2011) [7] Somford DM, et al. Invest Radiol (2013) [8] van As NJ, et al. Eur Urol (2009) [9] Jeong EK, et al. MRM (2003) [10] Husband JE, et al. Clin Radiol (1998).
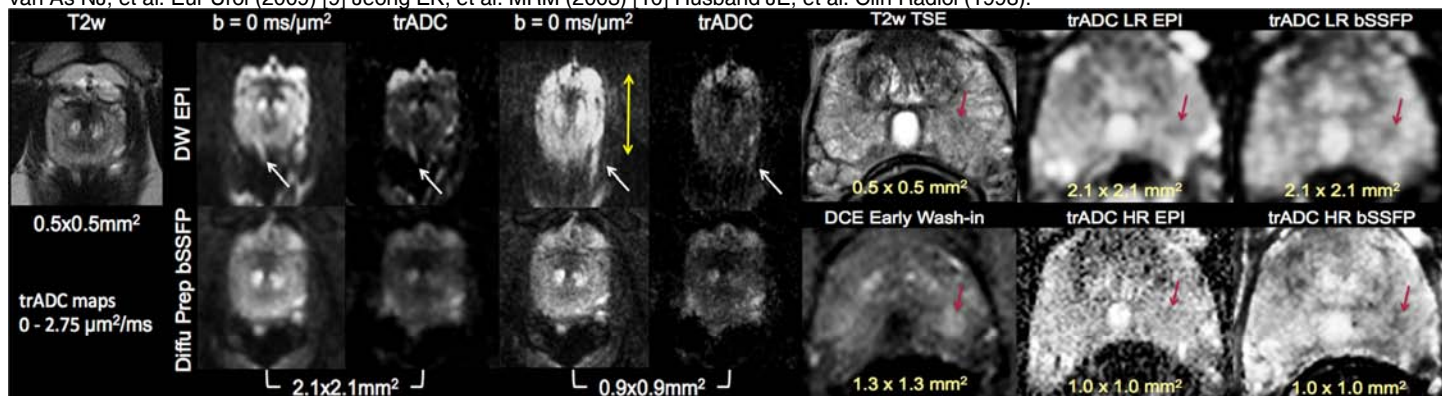
Figure 1 – Typical Healthy Volunteer. Susceptibility artifact in PZ is apparent in both low and high resolution DW EPI (white arrow). Distortion in PE direction is found (yellow arrow) in high resolution DW EPI. Proposed technique is clear of susceptibility or distortion artifacts.

Figure 2 – Typical AS-PC Patient. Biopsy (Gleason 3+3) confirmed lrPC lesion (red arrow) is depicted in the low/high res bSSFP and the low res EPI trADC maps. The high res EPI trADC map also show low intensity in lrPC lesion but at a lower CNR.