Challenges in spatial correlation of multiparametric MRI sequences and pathology findings in prostate cancer staging

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Purpose: MRI is an important prognostic indicator for prostate cancer, and there is much interest in identifying a role for multiparametric Magnetic Resonance (mpMR) sequences as non-invasive biomarkers. The gold standard in determining the sensitivity and specificity for each mpMR sequence is histopathology. Gleason score, cell density and proliferation index have all been used for characterizing prostate cancer aggressiveness (*1). Establishing imaging surrogate biomarkers for this disease has tremendous potential in improved management of prostate cancer patients. Spatial correlation of individual sequences with tumor pathology requires (1) adherence to an optimized mpMR protocol to maximize tumor detection; (2) a detailed, descriptive pathological report including information on tumor number, location and grade; and (3) spatial alignment between the individual mpMR sequences. For validating prospective imaging biomarkers, comparison of the MR-based parameters between the normal and tumor areas is desired, and thus the level of detail in the biopsy/pathology report is crucial for confident discrimination of these 2 areas. When different mpMR sequences are compared, a form of inter-sequence registration needs to be considered to compensate for patient motion, inter-sequence deformation of the gland and the acquisition-related distortions. In this educational exhibit we explore the feasibility of patient-specific spatial correlation of individual mpMR sequences with routine pathology findings using our optimized clinical protocols, and demonstrate specific examples of the challenges faced.

Outline of contents: Feasibility was examined in our subject population of 27 patients, who had either diagnosed or suspected prostate cancer, and were prospectively enrolled in an institutional review board-approved study. All of these patients had a standard clinical MR imaging exam that consisted of endorectal mpMR at 3.0T (Signa HDx, GE Healthcare; air-inflated Medrad endorectal coil). The imaging sequences included T2 weighted imaging (WI), high temporal resolution dynamic contrast imaging (HTR-DCE) and diffusion weighted imaging (DWI, b=0/500 and b=0/1400). Transrectal Ultrasound (TRUS) guided or MR guided (MRg) biopsy data, or total prostatectomy routine histology data was available for correlation. As this study evaluated spatial correlation of routine clinical cases, whole mount pathology was not requested/available. The following criteria were used for identifying a sub-population suitable for spatial correlation of histology with imaging: (1) histology report detailed enough to allow for correlation with tumor location on mpMR; (2) adherence to the HTR-DCE protocol; (3) technically feasible and successful deformable registration between the sequences (to recover acquisition-related distortions on DWI by registering b0 DWI image to T2WI, which in turn were registered to T1WI and DCE) for direct voxel-wise mpMR comparison. Each case was then examined by an expert radiologist (10 years experience in prostate imaging) who outlined tumor and normal prostate tissue based on review of all mpMR sequences and histology.

Out of 27 men enrolled (mean age 58 ±7.2 years of age; mean PSA 9.46 ±9.8 SD ng/ml) 13 patients were not suitable for imaging/histology spatial correlation analysis for the following reasons: (1) insufficient level of detail in the TRUS biopsy reports (n=4); (2) negative MRg biopsy result (n=5); (3) failure of image registration (n=2); (4) non-adherence to the HTR-DCE protocol (n=2). Review of all sequences and histology by one radiologist resulted in identification of 14 definitive areas of tumor, and 4 definitive areas of normal prostate tissue, allowing for intra-patient mpMR comparison in just over half our patients (n=14), and allowing direct comparison of the MR parameters between normal areas and areas of tumor in just 4 cases, similar to figures reported by others (*2) In this exhibit, we will outline potential pitfalls in prostate mpMR-pathology spatial correlation, and present examples of different levels of detail present in prostate pathology reports, which allows for varying degrees of mpMR/histology correlation. For comparison, we will demonstrate the relative ease of correlation of mpMR sequences with whole mount pathology. We will also show examples of failures of image registration. Our goal is to make the audience cognizant of these issues when reviewing the relevant literature, or prior to conducting similar studies.

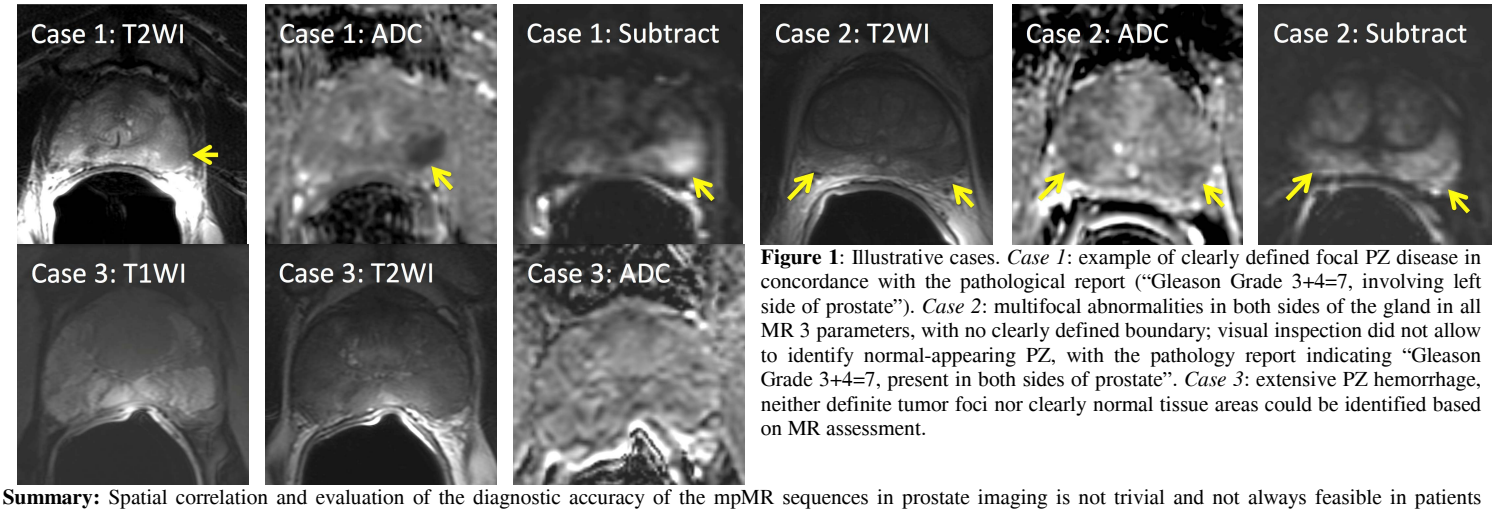

Figure 1: Illustrative cases. *Case 1*: example of clearly defined focal PZ disease in concordance with the pathological report ("Gleason Grade 3+4=7, involving left side of prostate"). *Case 2*: multifocal abnormalities in both sides of the gland in all MR 3 parameters, with no clearly defined boundary; visual inspection did not allow to identify normal-appearing PZ, with the pathology report indicating "Gleason Grade 3+4=7, present in both sides of prostate". *Case 3*: extensive PZ hemorrhage, neither definite tumor foci nor clearly normal tissue areas could be identified based on MR assessment.

Summary: Spatial correlation and evaluation of the diagnostic accuracy of the mpMR sequences in prostate imaging is not trivial and not always feasible in patients undergoing a routine clinical evaluation mpMR prostate protocol and routine histology processing. This exhibit outlines the challenges in detailed correlation of pathology findings with individual mpMR sequences in prostate cancer staging. It underscores the need for a large clinical cohort, and makes audience aware of limitations of mpMR correlation with routine histology/biopsy reports when whole mount pathology is not available. This exhibit also underscores the need for further development and validation of imaging registration technology to facilitate development of mpMR as a biomarker for prostate cancer.

*1 Rosenkrantz AB, et al. Prostate cancer foci detected on multiparametric magnetic resonance imaging are histologically distinct from those not detected. J Urol 2012;187(6):2032-8.

*2 Barrett T, et al. DW MRI in monitoring response to androgen deprivation therapy in patients with prostate cancer: a feasibility study. Magn Res Med 2012;67(3):778-85.

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