Voxel Level Radiologic-Pathologic Validation of Restriction Spectrum Imaging Cellularity Index with Gleason Grade in Prostate Cancer

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Background: Multiparametric magnetic resonance imaging (MPMRI) is a rapidly evolving non-invasive diagnostic tool that has been used to complement other emerging biomarkers in the screening, staging, monitoring, and treatment of prostate cancer (PCa). However, prostate MRI is confounded by variable sensitivity and specificity, which curtails its clinical utility. Restriction spectrum imaging (RSI-MRI) is an advanced diffusion imaging technique that shows improved conspicuity and differentiation of solid tumors compared to traditional diffusion weighted imaging. RSI-MRI can differentiate hindered from restricted diffusion, thought to correspond to the extracellular and intracellular water compartments, respectively. Prior reports show that the quantitative signal derived from RSI-MRI, the cellularity index, is associated with aggressive PCa as measured by Gleason grade (GG), and that RSI-MRI improves sensitivity to the detection of extraprostatic extension of prostate cancer. Here we evaluated the reliability of RSI-MRI to predict variance with GG at the voxel-level within clinically demarcated PCa regions.

Methods: Ten cases were processed using whole mount sectioning after radical prostatectomy. Regions of tumor were identified and demarcated by an uropathologist. The whole mount H&E stained prostate sections were scanned at high resolution (75μm/pixel). The scanned images were reconstructed into a "digital prostate map" interface and overlaid with a grid of tiles corresponding to voxel dimensions. Each grid tile was graded using the GG system. An experienced radiologist selected the slice from the presurgical T2 MR series that most closely corresponded to the plane of the histopathology section. Deformation of the histology section was corrected for by transforming the T2 and corresponding RSI-MRI slice to the size and shape of the histopathology section. The RSI-MRI cellularity index was calculated from the RSI-MRI data and presented as normalized z-score maps. In total, 2,795 tiles were analyzed and compared with RSI-MRI cellularity.

Results: Using a linear mixed-effect model with a random effect of subject, RSI-MRI cellularity index was found to distinguish between PCa and benign tumor (t=25.48,p<0.00001). Significant differences were also found between benign tissue and PCa classified as low-grade (GG=3; t=11.56,p<0.001) or high-grade (GG≥4 t=24.03,p<0.001). Furthermore, RSI-MRI differentiated between low and high-grade PCa (t=3.23,p=0.003).

Conclusions: Building on our previous findings of correlation between GG and the RSI-MRI among whole tumors, our current study reveals a similar correlation at voxel resolution within tumors. The relationship between GG and RSI-MRI means that RSI-MRI can be used as a component of active surveillance to non-invasively detect high-grade cancer and affect staging and treatment. Furthermore, because it can detect variations in tumor grade with voxel-level precision, RSI-MRI may have particular relevance for planning of focal procedures, such as MRI guided targeted biopsies and targeted radiotherapy, where identifying the area with the most aggressive disease is particularly important.

Conflict of Interest: None

Funding Acknowledgements: Department of Defense (DoD) Grant, Prostate Cancer Research Program (#W81XWH-13-1-0391), the American Cancer Society—Institutional Research Grant (#70-002), UCSD Clinician Scientist Program (#5T32EB005970-07), UCSD School of Medicine Microscopy Core, and NINDS P30 core grant (#NS047101). General Electric, Investigator Initiated Research Award BOK92325.