Using Multiparametric MRI to Differentiate Prostate Cancer in the Anterior Aspect of the Gland

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Target audience: Urologists, radiologists and researchers studying prostate cancer.

Purpose: In recent years, active surveillance has been gaining momentum as a reasonable alternative to treatment for men with low-risk prostate cancer. It is critically important to be able to 1) evaluate the risk of disease in the entire prostate and 2) distinguish the high-risk prostate cancers from the low-risk disease. Current methods of determining the aggressiveness of prostate cancer are limited to Gleason Score grading of tissue samples obtained during a transrectal ultrasound (TRUS) guided prostate biopsy, a painful procedure, prone to sampling errors. 21% of all prostate malignancies are found in the anterior prostate (AP). Anterior tumors are not readily palpable by digital rectal exam and systematic 12-core TRUS biopsies can undersample apical and anterior areas of prostate, particularly in large glands. A TRUS biopsy can miss a clinically significant cancer up to 30% of the time[1]. Multiparametric MR (mpMRI) allows for a noninvasive evaluation of the prostate cancer. While mpMRI has been well established for identifying prostate cancer in the peripheral zone prostate tissues[2,3], its role in discriminating cancerous regions in the anterior aspect of the prostate is poorly evaluated, in part due to challenges arising from the heterogeneity and location of the disease (requiring detailed histopathology). The purpose of this study was to use a combination of semi-quantitative parameters derived from dynamic contrast-enhanced (DCE) MRI, MRSI, diffusion MR and MRI to differentiate benign and malignant tissues, and further discriminate high-risk from low-risk cancers located anteriorly, using step-section histopathology, with a percentage breakdown of Gleason grades and benign tissues, as a reference standard.

Methods: Thirty-three men with untreated prostate cancer received 3T MR scans prior to undergoing prostatectomy. Post prostatectomy, prostate specimens were processed whole-mount. During histological review, cancerous regions were outlined and graded, and the percentage of cancer estimated by the same prostate pathologist. ROIs were manually drawn on T2-weighted images based on the digitized histopathology slides, following a consensus of two readers, keeping within homogeneous regions. A total of 191 cancer ROIs were drawn. Only ROIs containing more than 50% cancer were included in the analysis. In the anterior aspect of the prostate Gleason 3+3 (n=33 regions were outlined in N=9 patients), G3+4 (n=31, N=9), G4+3 (n=23, N=6), G4+4 (n=6, N=2), and noncancerous cystic atrophy or normal regions (n=91, N=29) were identified.

MR apparent diffusion coefficient (ADC), fractional anisotropy (FA), coil-corrected[4], T2-weighted image intensity, and DCE MRI parameters: maximal enhancement slope, peak enhancement, time to peak and washout slope were calculated. Levels of prostate metabolites choline, creatine, and citrate acquired during MRSI were also evaluated. Within each individual, ROIs were grouped in accordance to tissue type and a weighted average based on ROI areas was calculated for each metric of interest. Anteriorly located cancers were 1) grouped together and compared to benign tissues, 2) separated into high-risk (G4+3 and higher) and low-risk (G3+3 and G3+4) and compared between groups and to cystic atrophy.

Results: Significant differences between benign and malignant anterior regions were observed on T2w imaging, ADC, enhancement slope, washout slope (<0.0001), max enhancement (p<0.04), time to peak (p<0.005), and choline levels (<0.05). A stepwise, logistic regression yielded significant parameters of ADC, time to peak, and (Cho+Cre)/Citrate ratio, with a combined model AUC of 0.983 for detecting benign versus cancerous regions in the anterior aspect of the prostate.

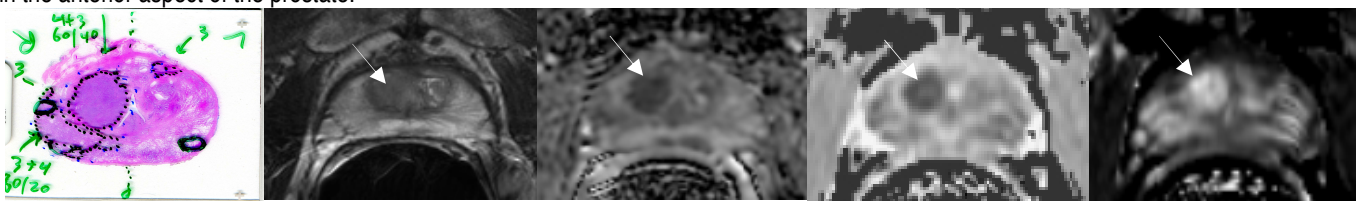

Figure 1: A clear-cut G4+3 lesion as seen on histopathology, T2 image, ADC, washout slope, and max enhancement slope. Cancer region is indicated by the arrows.

Figure1 presents an example of a high-risk cancer as seen on some of the mpMRI parameters. There were no significant differences between high-risk and low-risk cancers on any individual imaging parameters. However, a stepwise, logistic regression of washout, peak enhancement, ADC, and (Cho+Cre)/Citrate ratio yielded a combined model AUC of 0.824 for detecting high- versus low-risk cancers.

Discussion: Due to their location, anterior prostate lesions are often missed on biopsy. Mp-MRI parameters allow for a good discrimination between malignant and benign regions, with a combination yielding excellent separation (ROC AUC=0.983). Discriminating cancer regions based on cancer aggressiveness is more challenging. When distinguishing between low-risk and high-risk cancers, none of the individual parameters reached significance. However, a combination of mpMR parameters yielded a very good separation with AUC=0.824. An accurate, noninvasive evaluation of anterior prostate regions is critically important but is often impossible with traditional methods. The ability of mpMRI to discriminate between benign and malignant tissues, while providing an insight into the aggressiveness of the disease is encouraging and should be explored further.

Conclusion: A combination of mpMR measures can provide excellent discrimination between anterior cancers and benign central gland tissues. Furthermore, a combination of mpMR measures can also aid discrimination of high-grade from low-grade prostate cancers within the anterior portion of the prostate, a region that is challenging for evaluation by biopsy and standard MR methods.

References: 1-Taira et al. Prostate Cancer and Prostatic Dis. 2010. 2-Isebaert et al. JMRI 37(6):1392-401. 3-Rais-Bahrami et al. J Urology 2013; 190(5):1721-7. **Acknowledgements**: NIH R01CA148708.