Correlation of Histology from MR guided Transperineal Prostate Biopsy with Multiparametric MR Imaging: a Feasibility Study

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Introduction Prostate cancer continues to be the most common malignancy and third leading cause of cancer-related mortality in American men. As the US population of male "baby boomers" age, there will be an increase in prostate cancer diagnosis and an increase in the number of men presenting for therapy. Incidence is estimated to exceed 450,000 cases per year by 2015. While current treatments for localized prostate cancer are generally global treatments such as radical prostatectomy and external beam radiation therapy, for early stage tumors, organ-sparing focal therapy may provide a reasonable balance between cancer control and quality of life in a select group of patients. A necessary step in taking focal therapy into the clinical realm is to accurately delineate focal tumor. Recent changes in MR techniques and hardware are significantly improving the quality and specificity of prostate MR. The state-of-the-art is now 3T imaging using an endorectal coil and a multi-parametric MRI (mpMRI) protocol, including standard T2-weighted (T2W) sequences, diffusion weighted imaging (DWI), and pharmacokinetic parameters derived from dynamic contrast enhanced (DCE) imaging. Coupled with these imaging advances, our group has recently started an MRI-targeted prostate biopsy program using a transperineal approach at 3T. In this preliminary study, by means of image registration techniques, we were able to identify the location of the specimen collected during the biopsy, and correlate the histological analysis outcome with mpMRI. The goal of this study was firstly to develop the protocol for area-based correlation of the mpMRI with the biopsy core sample histology, and secondly to determine if MP sequences correlate with pathological outcome.

Methods

Patients and diagnostic imaging Eight patients, with an elevated prostatic specific antigen (26.6±18.8ng/ml) presenting for MRI-targeted prostate biopsy were enrolled in a prospective clinical trial approved by our institutional review board. These included patients not suitable for transrectal ultrasound (TRUS) guided biopsy due to total colectomy (n=1) or inflamed ileal J-pouch (n=1), multiple prior negative TRUS-guided biopsies (n=4), prior prostate brachytherapy and MRI focus suspicious for recurrence (n=1), and MRI focus suspicious for higher grade tumor than suggested at prior TRUS-guided biopsy (n=1). Prior to biopsy, all had undergone mpMRI (T2WI, T1WI, DWI b 0-500 sec/mm², DCE) at 3T using an endorectal (n=6) and pelvic phased array coil (n=8), which had demonstrated a dominant index lesion most suspicious for cancer. Cinetool software (GE Global Research) was applied to compute the pharmacokinetic (PK) maps using a population averaged bi-exponential arterial input function for Volume transfer constant (K^{trans}), extravascular extracellular volume fraction (k_{ep}), maximum slope (MaxS), intertistial volume (V_e) and wash out. Suspicious areas were reviewed and marked in 3D Slicer software [3] by a radiologist (K.T.) based in this preoperative image set and clinical history.

Biopsy technique and intra-procedural imaging All the patients underwent a 3T MRI guided (Siemens Verio) transperineal prostate biopsy, with the patient in the lithotomy position. A T2WI MRI covering the whole prostate was obtained using surface coils. Pre-procedural mpMRI were then fused with this intra-procedural image using a hierarchical registration method implemented in 3D Slicer. Pre-procedurally planned targets were warped to the intra-procedural configuration of the gland and were used for guidance. After needle insertion, an axial single slice T2 real time acquisition was performed to confirm needle position. In the cases when patient movement occurred during procedure and was detected based on visual assessment, needle insertion plan was updated by the interventional radiologist accordingly(K.T.).

Correlation method Location of needle tip was estimated based on the artifact in the intra-procedural single-slice acquisitions. Intra-procedural patient movement was compensated by rigid registration between the single-slice acquisition and intra-procedural prostate volume MRI. The transform produced by non-rigid registration was inverted and applied to map the location of points back to the diagnostic MRI (figure 1). Due to the inherent imprecision of needle localization from the artifact and registration errors, some residual error will always be present. To correct for this caveat, cores located closer than 10mm to each other were clustered together in our analysis.

Image Interpretation Preoperative image sets were presented for rater review (F.F., 8 years of experience in prostate MRI), according to the previously reported criteria [1]. The rater was blinded to patient's pathological results. Sequences from each patient were presented in a random order for review. The rater's confidence level for malignancy on a scale of 1 to 5 (1- definitely not present, 2- probably not present, 3- indeterminate, 4- probably present, 5- definitely present) was recorded [1], as was the presence of post biopsy hemorrhage in T1WI and image quality.

Statistics Receiver Operating Characteristic curve (Hanley & McNeil) analysis was performed for each parameter independently. Area under curve (AUC) and its *p* value are reported in the table below, as well specificity considering a positive diagnostic a score ≥3 [1].

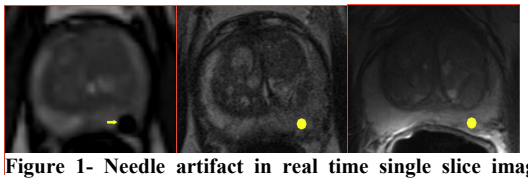

Figure 1- Needle artifact in real time single slice image (left), needle position retrospectively marked in intra operative whole prostate T2 (middle) and the same point retrospectively marked in the diagnostic T2 (right).

Results

A total of 32 suspicious areas (mean 4, range 2-6) were sampled and were grouped in 23 clusters. Images were considered poor or non diagnostic for 5, 2, 4 and 3 clusters in the images DWI b500, ADC, wash out and ve respectively. Malignancy (Gleason 3+3 and 3+4) was identified in a total of 3 cores, collected in two patients.

Conclusion and Discussion

As a result of this preliminary work, we were able to develop a workflow for correlating the core histology collected during transperineal MR guided biopsy with the diagnostic mpMRI. We showed the feasibility of such analysis by applying it to analyze the data collected for 8 biopsy patients. Our preliminary results showed that specificity is comparable to those reported in the literature [2]. AUC showed reasonable results. The current study had several limitations. First, the reference standard was biopsy and regions considered to harbor small tumors might not be sampled. Second, the bias selection to our subjects and to regions reviewed, already considered suspicious enough to be biopsied. Third, we had a small population. This study therefore demonstrates the feasibility of registering pre-operative mpMRI with intra-operative imaging, which allows for pathological confirmation of suspicious areas on mpMRI. Further large scale studies are required to determine the specificity and sensitivity of each MP sequence for prostate cancer detection.

Table 1- ROC analysis for mpMRI

Image Modality	Specificity(%)	AUC (95% CI)	p value
T2	70	0.85 (0.64-0.96)	0.01
DWI b500	80	0.62 (0.36-0.83)	0.52
ADC (0-500)	61.1	0.75 (0.51-0.91)	0.15
DCE subtraction	60	0.76 (0.54-0.91)	0.11
Ktrans	55	0.82 (0.61-0.95)	0.03
Kep	55	0.75 (0.52-0.90)	0.14
Ve	64.7	0.78 (0.54-0.93)	0.08
Wash out	70.5	0.86 (0.63-0.97)	0.03
Max Slope	55	0.77 (0.55-0.92)	0.10

References: [1] Kitajima K. Prostate Cancer Detection With 3T MRI: Comparison of DWI and DCE in combination with T2WI J MRI 31: 625-631. [2] Turkbey B. Prostate Cancer: Value of Multiparametric MRI at 3T for Detection – Histopathologic Correlation. [3] 3D Slicer http://slicer.org

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