Multiparametric and Ex-vivo MR Imaging in Diagnosis of Prostate Cancer: Preliminary results from a prospective trial in patients undergoing prostatectomy

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Background:

Multiparametric approaches to MR imaging of the prostate have been investigated to increase the diagnostic accuracy in the detection of prostate cancer, to include anatomical imaging at high magnetic field strength, metabolic imaging, perfusion and diffusion imaging. Various protocols have been evaluated in multiple patient cohorts, however there has been no study combining all of the above parameters to be performed in the same patient population. The gold standard for "truth" in prostate cancer research has been the comparison of imaging results to the pathology obtained through the step-sections of prostatectomy specimens. However, mapping of cancer in prostate specimen to prostate sextants in-vivo poses a significant challenge due to gland deformation between the pre-operative in-vivo imaging and ex-vivo pathology assessment.

The aim of this study was to assess the diagnostic accuracy of endorectal MR imaging at 1.5 T with a multiparametric protocol including standard T2W sequences for morphological assessment, diffusion weighted imaging (DWI), spectroscopy (MRSI), and dynamic contrast enhanced MR imaging (DCE-MRI) all performed in the same patient population. We also evaluated the feasibility of using the ex-vivo MR imaging of prostatectomy specimens for tumor co-registration between the final pathology and in-vivo imaging.

Methods:

Endorectal imaging (with Medrad coil) was performed on 1.5T GE Signa Excite and included T2W images (TR/TE 4000/90ms, slice/space 3/1 mm, FOV 14, matrix 256x192) in axial and coronal planes, DWI in axial plane (EPI TR/TE 5900/90 ms, b values 0, 500, 750, 1000), MRSI (3D PRESS CSI [1]), DCE-MRI (3D FMPGR TR/TE 14/1.3 ms, flip angle 20, slice/space 3/0 mm). 48 prostate sextants were evaluated in eight consecutive patients (age range 51-62, mean PSA level 4.4 ± 1.8 ng/ml, mean prostate volume 29.3 ± 8.2cc) with biopsy proven prostate cancer. All patients underwent radical prostatectomy with robotic assistance. Step-sections at 3-4 mm intervals along the axis of prostate were obtained for pathological diagnosis. Tumor localization was mapped on diagrams corresponding to pathology sections and was subsequently co-registered with in-vivo MRI through the use of ex-vivo MRI of the prostate specimen as an intermediate step for the correlation between pathology specimen tumor mapping and pre-operative in-vivo MRI. Ex-vivo MRI of the specimen was performed at 3T on Philips Achieva (T2W TR/TE 3700/100 ms, slice/space 1.5/1 mm, FOV 6, matrix 256x248) or 9.4T Bruker BioSpin (TR/TE 4000/37 ms, slice/space 1/0 mm, FOV 5, matrix 512x512). Accuracy of MRI, DWI, MRSI, DCE-MRI was assessed per tumor nodule identified during pathology, using criteria listed in Table 1. The study was approved by the IRB and informed consent was obtained from each patient.

Results:

Based on pathological diagnosis, 30 of 48 sextants were positive for cancer in prostatectomy specimens, Gleason score was 3+3 in 28 prostate sextants and 3+4 in 2 sextants. The dominant nodule per sextant was included in the analysis. The largest tumor nodule measured 1.7 cm and the smallest nodule 0.2 cm (mean cancer size 0.6 ± 0.3 cm). Pre-operative biopsy revealed only 16 of 30 tumor nodules (53%), with significant mis-registration of tumor localization per sextant: non-matched 20 of 30 (67%), matched 10 of 30 (33%). In per nodule/sextant analysis, diagnostic accuracy for multiparametric MRI was as shown in Table 1.

Conclusions:

MRSI and DCE-MRI demonstrate the highest specificity and PPV, while T2W and MRSI had the highest sensitivity in detecting prostate cancer. Imaging at high spatial resolution and high magnetic field strength ex-vivo improves detail of prostate gland morphology and results in visualization of 89% of tumor foci in the prostate gland detected during pathology. These results will aid in developing multiparametric models for prediction of malignancy. TRUS-guided biopsy fails to detect over 40% of tumor positive prostate sextants and biopsy results match final pathology result per sextant in less than 40%. Therefore, biopsy results should not be used as a reference for testing diagnostic accuracy of imaging techniques in prostate.

Table 1. Diagnostic accuracy for T2W, MRSI, DWI, DCE-MRI in the studied sample.

Parameter	T2W, focal nodule-like dark signal	MRSI, voxels with choline+creatine/citrate > 0.68 [2]	DWI, ADC > 1.30 * (0.99±2SD [3])	DCE-MRI, increased rate and degree of enhancement >100% from baseline
# Sextants	48	30	42	48
Sensitivity	80.64 (62-92)	70 (45-88)	61.53 (40-79)	53.33 (34-71)
Specificity	47.05 (22-72)	100 (69-100)	62.5 (35-84)	100 (81-100)
PPV	73.52 (55-87)	100 (76-100)	72.72 (49-89)	100 (79-100)
NPV	57.14 (28-82)	62.5 (35-84)	50 (27-72)	56.25 (37-73)

Note: (95% confidence interval calculated with binomial expansion), * 10^{-3}mm^2/sec,

Trace ADC maps were constructed and ROI were drawn in areas colocalized with T2 abnormal regions. In addition, areas that demonstrated a 20% decrease to normal ADC were mapped.

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References:

1. Hom JJ, et al. Prostate cancer: endorectal MR imaging and MR spectroscopic imaging distinction of true-positive results from chance-detected lesions. *Radiology* 2006;238(1):192-9.

2. van Dorsten FA, et al. Combined quantitative dynamic contrast-enhanced MR imaging and (1)H MR spectroscopic imaging of human prostate cancer. *J Magn Reson Imaging*. 2004;20(2):279-87.

3. Kozlowski P, et al. Combined diffusion-weighted and dynamic contrast-enhanced MRI for prostate cancer diagnosis--correlation with biopsy and histopathology. *J Magn Reson Imaging* 2006;24(1):108-13.