Quantitative differentiation of prostate cancer from normal peripheral zone using Magnetic Resonance Fingerprinting (MRF) and Diffusion Mapping

Chaitra Badve[1], Alice Yu[2], Shivani Pahwa[3], Matthew Rogers[2], Yun Jiang[4], Yiying Liu[5], Mark Schluchter[5], Lee Ponsky[6,7], Mark Griswold[4], and Vikas Gulani[1,3]

[1]Radiology, University Hospitals, Cleveland, Ohio, United States, [2]School of Medicine, Case Western Reserve University, Cleveland, Ohio, United States, [3]Radiology, Case Western Reserve University, Cleveland, Ohio, United States, [4]Biomedical Engineering, Case Western Reserve University, Cleveland, Ohio, United States, [5]Biostatistics, Case Western Reserve University, Cleveland, Ohio, United States, [6]Urology, University Hospitals, Cleveland, Ohio, United States, [7]Urology, Case Western Reserve University, Cleveland, Ohio, United States

Target audience: Those interested in imaging of prostate cancer, quantitative imaging, MR relaxometry and MR Fingerprinting (MRF).

Purpose: The goal of this study was to compare T_1, T_2 relaxation times in peripheral zone prostate cancer to those from normal peripheral zone (NPZ) using MRF, and to also explore the use of combination of T_1, T_2 and quantitative apparent diffusion coefficient (ADC) measurement in separating cancer form NPZ.

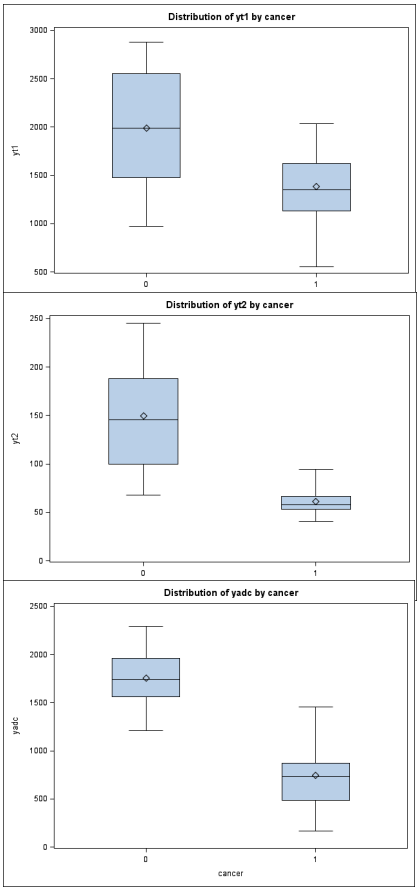

Fig. 1. Box plots of T1, T2 and ADC values in NPZ (0) and cancer (1)

Introduction: Multiparametric MRI evaluation for adenocarcinoma of the prostate is currently predominantly qualitative in nature except for diffusion (ADC) and perfusion (DCE) mapping [1]. Quantitative ADC mapping helps differentiate cancer from benign tissue and also can help in tumor grading [2]. T_2 mapping has also been explored for differentiating benign from malignant disease [3]. The utility of combination of various quantitative parameters in helping differentiate benign and malignant tissue remains minimally explored. MR fingerprinting is a technology in which MR signal evolutions are not allowed to reach a steady state, but rather take on different forms for different tissue types. These signal evolutions are matched to dictionaries of all possible signal evolutions based on potential combinations of relaxation parameters, and the match yields highly accurate maps of the relaxation parameters of interest such as T_1 and T_2 [4]. Here we explore the use of MRF relaxometry in combination with clinical ADC mapping, to differentiate cancer from benign tissue.

Methods: 63 patients with clinical suspicion of prostate cancer were imaged for this study. Multislice MRF based on a Fast Imaging with Steady State Precession (FISP) acquisition was obtained through the entire gland [5]. Scan parameters were as follows: Slice thickness 6mm, FOV 400 mm, TR 11-13 ms, flip angle 5-75 deg, slice duration 50 sec. A linear slice profile correction was applied. T_1 and T_2 maps were generated by template matching to a dictionary of time courses constructed using Bloch simulations [4]. Region of interest (ROI) evaluation performed for lesions that were suspicious on clinical imaging and for regions of discernable NPZ on T_1 and T_2 maps as well as clinical ADC maps. Final diagnosis was determined by pathology. T_1, T_2 and ADC values were measured in 49 cancer lesions and 58 NPZ regions. Logistic regression analysis was also performed to determine the utility of these parameters, singly and in combination, in separating prostate cancer and NPZ. Among patients with cancer, 17 patients had prostate biopsy after imaging whereas the remainder of the patients had one or more biopsies before imaging. A similar analysis was also performed for these 17 pre-biopsy imaging patients to assess utility of MRF in absence of confounding effects of post biopsy changes on tissue relaxometry.

Results: The mean T_1, T_2 and ADC values for prostate cancer were 1413 ± 60 ms, 66 ± 3 ms and 745 ± 54 x 10^{-6} mm^2/s respectively. For NPZ these values were 2058 ± 77 ms, 165 ± 8 ms, and 1736 ± 37 x 10^{-6} mm^2/s respectively. The difference between cancer and NPZ was statistically significant for all three parameters ($p < 0.0001$) (Fig 1). A combination of T_2 and ADC values best separated cancer lesions from NPZ with an area under receiver operator characteristic curve (AUC) of 0.995, which had higher discriminatory power than prediction of cancer using T_2 or ADC alone (AUC = 0.978 for T_2, AUC = 0.982 for ADC) (Fig 2). T_1 alone also showed significant difference between cancer and NPZ as well as a high AUC (AUC = 0.801) but did not improve separation when used in conjunction with T_2 and/or ADC. Similar results were also seen in the smaller subset of pre-biopsy imaging group.

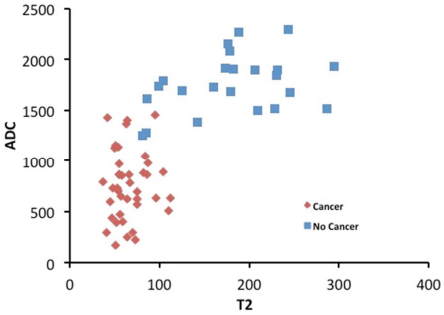

Fig. 2. Scatter plot of ADC vs T2 for separation of cancer (red) and NPZ (blue).

Discussion: MRF based T_1, T_2 relaxometry along with ADC can effectively distinguish between prostate cancer and normal tissue. This is the first study to demonstrate the utility of T_1 measurements in assessing prostate cancer. Although the exact basis of T_1 difference is not clear, it may relate to increased cellularity or atypical cellular organization in cancerous tissue. The drop in T_1 within the cancerous lesions appears to be too subtle to cause a noticeable change in the clinical T_1w image, but is clearly apparent on quantitative analysis. The reproducibility of these results in the cohort that was imaged prior to biopsy indicates that a confounding effect of biopsy related bleeding is not the cause for the observed T_1 (or T_2) changes. Decreases in ADC and drop in T_2w signal are already used clinically as indicators of cancer, and both have been independently explored for differentiating benign and malignant tissue. These results show that T_2 mapping also has strong utility in helping detect prostate cancer, and that T_2 along with ADC mapping can quantitatively separate prostate cancer from NPZ with a high discriminatory power (AUC = 0.995). Further research is required to determine the utility of quantitative T_2 and ADC in identifying prostate cancer prospectively, and to further explore the potential role of T_1 in assessing tumor pathology. MRF based evaluation has thus the potential to emerge as a rapid, completely quantitative tool for non-contrast prostate imaging.

Conclusion: MRF allows for effective separation of prostate cancer and NPZ using T_2 and ADC values. This study also found a significant difference between T_1 values in prostate cancer and NPZ, which demonstrates an unexplored potential utility of T_1 relaxometry in determining prostate malignancy.

References: 1. Ouzzane A, et al. *Urology*. (2011) 78:1356–1362. 2. Liu W, et al. *MRM*. (2011) 65:1400–1406. 3. Langer DL, et al. *JMRI.* (2009) 30: 327–334. 4. Dan M, et al. *Nature*. (2013) 187-192. 5. Jiang Y, et al. MRM, 2014. In press.

Acknowledgements: This study has received funding support from 1R01EB016728 and Siemens Healthcare