Correlating multi-parametric MRI with Gleason score in human prostate cancer

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Purpose: Increasing evidence suggests that hypoxia is associated with prostate tumor aggressiveness, local recurrence and biochemical failure (1). Past studies have examined hypoxia using needle electrodes or microarray expression analysis of biopsy specimens (2,3). MR imaging approaches offer insight into tumor pathophysiology and recent reports related T_2* measurements to tumor hypoxia (4,5). Ultimately multi-parametric maps are probably required and have been gaining increasing interest in assessing tumor malignancy. In this study, multi-parametric ^{1}H MRI sequences have been evaluated in patients to investigate hypoxia in prostate cancer. Blood oxygen level dependent (BOLD) MRI, dynamic contrast enhanced (DCE) MRI, and diffusion weight imaging have been intercorrelated and examined with Gleason score. In addition, histological studies have been performed post prostatectomy.

Methods: Following IRB approved consent ten men with biopsy confirmed prostate cancer (mean age 59 years, mean prostate-specific antigen (PSA) level 6.9 ng/mL and Gleason score ranged from 6 to 9) underwent multi-parametric MRI at 3T as part of their preoperative workup. Images were acquired using a 6-element SENSE body coil and endorectal coil on a 3T scanner (Achieva, Philips Medical Systems, Cleveland, OH). Dynamic R_2* maps (BOLD) were acquired using a multi-echo gradient echo sequence (TR = 65 ms, 16 echo times ranging from 1.7 to 69.2 ms, flip angle 30°), while subjects breathed air for 2 minutes followed by oxygen (15 L/min) for 5 minutes. Diffusion weighted images were acquired using a single-shot spin-echo echo-planar sequence with b values of 0, 500, 1000 s/mm^2, TE=70ms, and TR=6228ms. DCE was acquired using a spoiled gradient echo sequence (TR = 4.5 ms, TE = 2.3 ms, flip angle 15°) with 2–4 baseline acquisitions before a bolus injection of 0.1 mmol/kg gadobutrol (Gadovist, injection rate 2 ml/sec) using a power injector at a rate of 2 ml/sec and a 20 ml saline flush at the same rate. A total of 22 dynamic phases were acquired after contrast injection. All imaging analysis was performed in MATLAB using custom-written programs.

Results: Tumor lesions appeared hypointense on T_2-weighed images compared to normal prostate tissue. The apparent diffusion coefficient (ADC) was significantly lower (paired Student's t-test; $p<0.001$) in tumor ($1.26\pm0.33\times10^{-3}$mm^2/s) than surrounding normal prostate ($1.72\pm0.23\times10^{-3}$mm^2/s). Baseline R_2* values of normal prostate and tumor were found to be correlated ($R^2 = 0.88$; $p<0.001$), but the tumor R_2* (46.0 ± 20.8s^{-1}) was significantly higher (paired Student's t-test; $p<0.05$) than that of normal prostate (40.0 ± 17.8s^{-1}). Moderate correlation was found between ADC and Gleason score ($R^2 = 0.48$; $p<0.05$) in agreement with previous reports (6). ADC and R_2* were correlated ($R^2=0.51$; $p<0.05$) and trends were found between Gleason score and R_2* ($R^2=0.32$; $p=0.07$), as well as maximum intensity projection (MIP; $R^2=0.43$) and initial area under the curve (IAUC; $R^2=0.34$) calculated from DCE. No correlations were found between time-to-maximum (TTM) enhancement or contrast uptake slope and Gleason score.

Conclusion: Tumor ADC and R_2* were found to be significantly different from normal prostate and showed general inverse trends compared to Gleason score. Each has been associated with tumor hypoxia and thus the correlations are of particular interest. A multi-parametric approach promises further insights into pathophysiological information of tumor microenvironment.

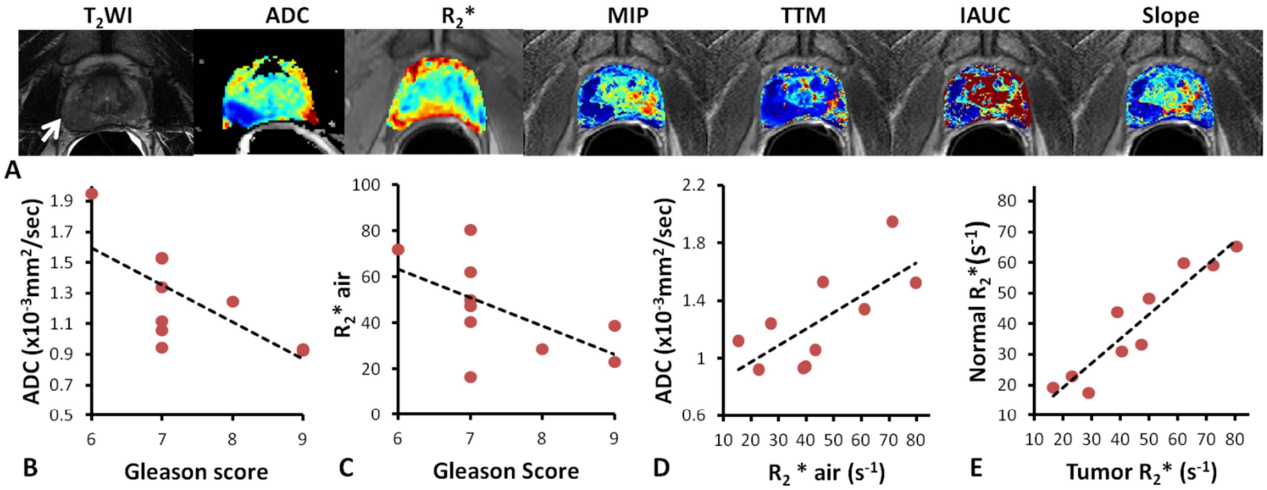

Fig. A. T_2 weighted anatomical image (tumor indicated by arrow) and multi-parametric MRI maps of one representative prostate patient (Gleason score 8). B. Correlation between Gleason score and ADC. C. Correlation between ADC and R_2* while breathing air. D. Correlation between ADC and R_2* air. E. Correlation between R_2* of tumor and normal prostate.

Reference: 1. *Int. J. Radiat. Biol.* 2006;82:699-757; 2. *Lancet Oncol* 2008;9:342-351; 3. *Int. J. Radiat. Oncol. Biol. Phys.* 2012;82:E433-E439; 4. *Int. J. Radiat. Biol.* 2009;85:805-813; 5. *Br. J. Cancer* 2009;100:644-648; 6. *Am J Roentgenol* 2011;197:1382-1390.