

Evaluating prognostic biomarkers of prostate cancer behaviour: use of magnetization transfer and diffusion weighted contrast

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Introduction: Diffusion-weighted MRI (DW-MRI) is increasingly being used to aid detection of cancer within the prostate gland [1]. Restriction of diffusion within the prostate is attributed to increased cellularity within the tissues, but histological evidence for this is inconclusive. Magnetisation transfer imaging has been shown to improve tissue contrast [2,3], because in tissues with abundance of large macromolecules, their selective pre-saturation results in a decreased water signal. Investigating the correlation of apparent diffusion coefficients (ADCs and magnetization transfer ratios (MTRs) thus may offer greater understanding of underlying tissue structure in prostatic tumors. This study aimed to determine the T2 values, ADCs and MTRs and the correlation between them in normal regions of the prostate and prostate tumors.

Method: 22 men (mean age 69 ± 6 years) with biopsy-confirmed prostate cancer were studied using a 1.5T Intera MR scanner (Philips Medical Systems, Best, Netherlands) with an endorectal receiver coil, inflated with 55ml of air. 20 patients were imaged prior to any treatment and 2 patients had previous radiotherapy. Gleason scores were 5+4 (n=1), 4+5(n=1), 4+3(n=1), 3+4(n=5), 3+3(n=14); PSA ranged from 1.3 to 31.5 ng/mL (mean + SD 7.9 ± 5.9). In addition to standard 3-plane imaging (FSE, TR/TE=2000/90, 20 slices, 3mm thickness, 512x512 matrix, 140mm FOV), 12 axial slice diffusion-weighted images (TR/TE 2500/69, 3mm thickness, 200mm FOV, 128x128 matrix, 4 b-values 0,300,500,800 s/mm² in three directions) were acquired and isotropic apparent diffusion coefficients (ADC) were calculated using all b-values. An MTR sequence (FSE, TR/TE=57/5.7, 20 slices, 3mm thickness, 256x256 matrix, 140mm FOV) was acquired with and without an off-resonance magnetisation transfer pre-pulse. A multi-echo sequence (TSE, TR=3500 TE=20/40/60/80/100, 20 slices, 3mm thickness, 160mm FOV, 256x256 matrix,) was acquired and the T2 maps generated using the scanner software. The magnetisation transfer ratio (MTR) was calculated as the percentage reduction in signal between the images with and without the magnetisation transfer pre-pulse. An experienced radiologist drew regions of interest (ROI) on the images in areas of tumour (identified as hypointense signal on the T2-weighted images in a biopsy positive octant), normal central gland and normal peripheral zone. ROIs were then drawn on the ADC and MTR maps in the same location by visual matching of slices. T2 values, ADCs and MTRs for each region were compared using a paired samples t-test. Correlations between T2, ADC and MTR were examined using Pearson's correlation coefficient.

Results: Figure 1 shows a T2 map, ADC and MTR image in a patient with a right peripheral zone tumor. Differences between mean T2, ADC and MTR values between normal peripheral zone and tumor were highly significant ($p < 0.00001$, $p < 0.00001$ and $p = 0.008$ respectively, Table 1). Differences between mean T2 and MTR for central gland and tumour were not significant, but differences in mean ADC between normal central gland and tumour were significant ($p = 0.0001$). For normal peripheral zone and central gland regions considered together, there was a positive correlation between T2 and ADC ($r = 0.72$) and a negative correlation between T2 and MTR ($r = -0.67$) and ADC and MTR ($r = -0.61$), Fig. 2. For tumor regions there was a weaker correlation between T2 and ADC ($r = 0.59$, and a negative correlation between ADC and MTR ($r = -0.48$), Fig 2.

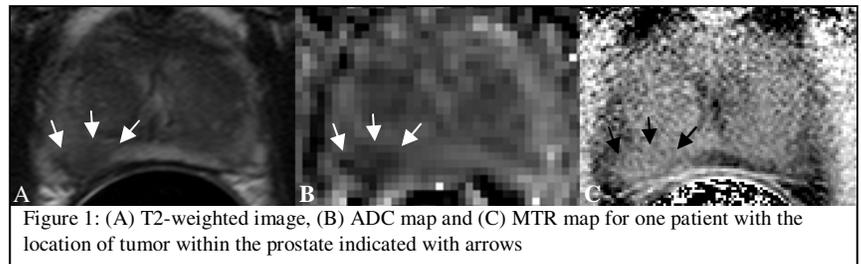


Figure 1: (A) T2-weighted image, (B) ADC map and (C) MTR map for one patient with the location of tumor within the prostate indicated with arrows

	Peripheral Zone	Central Gland	Tumor
T2 (ms)	269 ± 85	151 ± 26	145 ± 35
ADC (x10 ⁻⁶ mm ² /s)	1724 ± 235	1464 ± 170	964 ± 225
MTR	0.19 ± 0.04	0.22 ± 0.02	0.22 ± 0.03

Table 1: T2, ADC values & MTR ratios for each prostate region (mean ± SD) in 22 patients

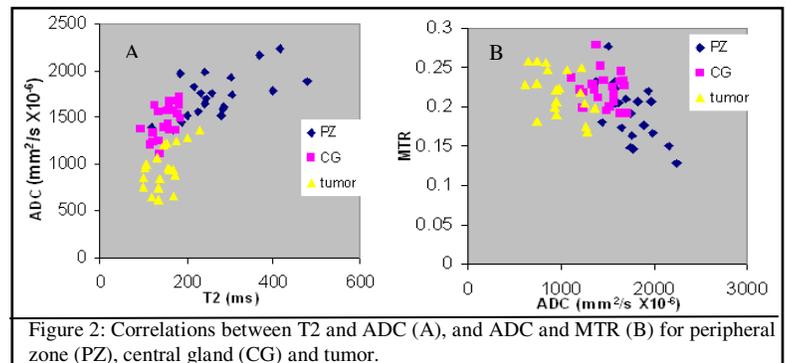


Figure 2: Correlations between T2 and ADC (A), and ADC and MTR (B) for peripheral zone (PZ), central gland (CG) and tumor.

Discussion: The correlation between T2 and ADC is in keeping with shorter T2 tissues which are less water containing showing more restricted diffusion. The weaker correlation when only tumor regions are considered, rather than normal peripheral zone or central gland reflects the smaller range of T2s within these regions. The negative correlation between ADC and MTR is weak, and suggests that regions of restricted water diffusion have higher magnetization transfer effect, possibly due to increase in large macromolecules, either within cells or in the surrounding matrix.

Conclusion: Magnetization transfer imaging in the prostate can provide new insights into structural changes within prostate cancer tissue and together with ADC warrants investigation as a prognostic biomarker.

References [1] Shimofusa R *et al* J Comput Assist Tomogr 2005; 29(2):149-153. [2] Wolfe, SD *et al*, Magn Reson Med 1989;10:135-44 [3] Henkleman, RM *et al*, NMR Biomed 200;14:57-64. **Acknowledgements:** This work was supported by Cancer Research UK grant number C1060/A5117 and also NHS funding to the NIHR Biomedical Research Centre. SR is funded by a Personal Award Scheme Researcher Developer Award from the NIHR.