Potential value of diffusion weighted imaging as an indicator of tumor aggressiveness in prostate cancer

N. M. deSouza[1], S. F. Riches[1], N. J. vanAs[2], V. A. Morgan[1], C. Parker[3], S. A. Sohaib[4], and G. S. Payne[1]

[1]Section of Clinical Magnetic Resonance, Royal Marsden NHS Foundation Trust and Institute of Cancer Research, Sutton, Surrey, United Kingdom, [2]Academic Radiotherapy, Royal Marsden NHS Foundation Trust and Institute of Cancer Research, Sutton, Surrey, United Kingdom, [3]Clinical Academic Radiotherapy, Royal Marsden NHS Foundation Trust and Institute of Cancer Research, Sutton, Surrey, United Kingdom, [4]Radiology, Royal Marsden NHS Foundation Trust, Sutton, Surrey, United Kingdom

Introduction: The current selection of patients for radical treatment for prostate cancer is based on presenting T stage, PSA and Gleason score which classifies them as low, intermediate or high-risk of disease progression. However, PSA requires repeated measurement to provide a marker of the biological behaviour of the tumor, and Gleason score on biopsy is subject to sampling error. This results in the radical treatment of many patients with localised disease, who may not necessarily benefit. There is an urgent need for better predictors of biological behaviour of prostate cancer. Diffusion weighted (DW)-MRI is proving invaluable in the detection of prostate cancer [1] and provides information on the degree of restriction of water diffusion within tissues which increases as tissue cellularity increases [2]. The purpose of this study was to determine whether we could detect differences in ADC values of prostate cancer between patients classified as having low-risk lesions versus those classified as having intermediate or high-risk lesions, in order to determine its potential value as a biomarker for disease aggressiveness.

Method: Twenty-one consecutive patients with either low-risk (n=11) or high-risk (n=10) lesions referred for routine clinical evaluation in our MR centre underwent DW-MRI in addition to their standard T2W MRI. Patient characteristics for the low-risk group were : age 53-73 yrs, (mean 64.7 $\pm$ 6.9yrs.), stage T1a (n=1), T1c (n=9), T2b (n=1), Gleason Grade <=6, PSA <10 (mean 5.9 $\pm$ 2.8 ng/mL), and for the intermediate/high-risk group: age 61-78 yrs, (mean 68.9 $\pm$ 7.2yrs.), stage T1c (n=6), T2b (n=2), T3 (n=2), Gleason grade $\geq$7, or PSA > 10 mean 19.2 $\pm$ 16.3 ng/mL). A Philips Intera 1.5T scanner, with a balloon design endorectal receiver coil, was used to acquire T2W FSE images in 3 orthogonal planes, together with axial DW images with 5 b values (0, 100, 300, 500 and 800 s/mm^2). The axial T2W and DWI images were transferred offline for analysis. Software written in-house (in IDL) was used to generate isotropic ADC maps using all b values (to reflect perfusion and diffusion components) and excluding b=0 (to reflect diffusion component alone). Regions of interest were drawn on all slices of the T2W axial scans around the whole prostate, the central gland and the tumor. A region of interest was also drawn around the whole prostate on the ADC maps. ADC maps were co-registered with the T2W scans by matching the centre of mass and the whole gland outlines. ROIs from the T2W images were transferred to these ADC maps to obtain ADC values from tumor, central gland and peripheral zone (whole prostate minus central gland and tumor).

Results: Isotropic ADC values are given in Table 1 for low and high-risk patient groups for regions of tumor, non-tumor peripheral zone (PZ), and for central gland (CG). There was a significant difference in the ADC values of tumor between low and high-risk patient groups when b=0 was excluded (p=0.012; Table 1) but not when b=0 was included in the ADC calculation. The PZ and CG values in these groups did not show any significant differences between groups. There also was a significant difference in ADC values between tumor and PZ, and between PZ and CG in both groups, and between tumor and CG for the high-risk, but not the low-risk group (Table 2).

Table 1. Calculated mean ADC values of tumors in the Low-risk and High-risk groups. The p value relates to the difference in ADC values between the Low-risk and High-risk groups

	ADC tumor X10^{-3} mm^2/s		**ADC PZ X10^{-3} mm^2/s**		ADC CG X10^{-3} mm^2/s	
b-values used	0-800	100-800	0-800	100-800	0-800	100-800
Low-risk	1.49 $\pm$ 0.21	1.30 $\pm$ 0.15	1.89 $\pm$ 0.14	1.50 $\pm$ 0.09	1.66 $\pm$ 0.09	1.39 $\pm$ 0.05
High-risk	1.49 $\pm$ 0.30	1.14 $\pm$ 0.13	1.92 $\pm$ 0.21	1.56 $\pm$ 0.17	1.74 $\pm$ 0.15	1.44 $\pm$ 0.14
P value	0.984	0.012	0.71	0.32	0.17	0.31

Table 2. Significance of differences in mean ADC between tissue types for Low-risk and High-risk groups

	Tum vs. PZ (p-values)		**Tum vs CG (p-values)**		**PZ vs CG (p-values)**	
b-value fit	0-800	100-800	0-800	100-800	0-800	100-800
Low-risk	0.0001	0.003	0.029	0.074	0.001	0.002
High-risk	0.0001	0.0001	0.008	0.001	0.001	0.005

Discussion and Conclusion: In agreement with previous findings, prostate cancer has a lower ADC value than non-malignant peripheral zone [1, 3]. This study also demonstrates significant differences between the ADC values of tumors in high-risk compared with the low-risk patients, when the perfusion component is excluded. This suggests that ADC values offer potential for differentiating low-risk from high-risk prostate tumors, and that this difference is masked if the perfusion fraction is included in the ADC calculation. In addition, significant differences have been observed between tumor and CG for high-risk, but not for low-risk patients.

References: [1] Shimofusa R et al J Comput Assist Tomogr 2005; 29(2):149-153. [2] Hayashida Y et al AJNR Am J Neuroradiol. 2006;27:1419-25. [3] deSouza NM et al BJR 2007 (in press)