Correlation of ADC and T2 with cell density in prostate cancer at 3.0T

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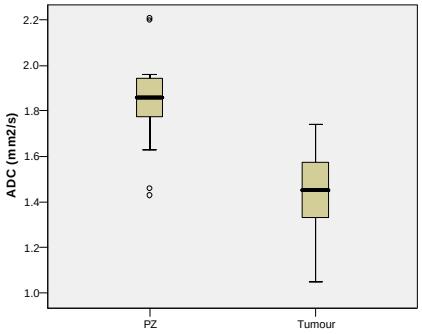
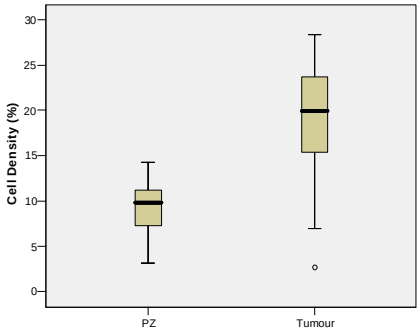
Introduction Prostate cancer rates have risen dramatically over the last few years, with a particularly marked increase evident in the under 65 age group [1]. MRI is increasingly used as a diagnostic tool in prostate cancer but, despite its excellent soft tissue contrast, high spatial resolution and dynamic contrast enhanced imaging has a diagnostic accuracy of only 70%. With the advent of 3.0 Tesla clinical scanners and improved receiver coils it is now feasible to obtain additional functional information, including metabolite concentrations, and the ADC and T2 of water within reasonable scan times. Notwithstanding the increasing use of DWI in prostate cancer [2-4] there has been little work examining the relationship between ADC and T2 values and histopathological details such as cell density. This work aims to assess the diagnostic potential of these MR parameters via correlation with pathological data obtained from whole mount radical prostatectomy specimens in a group of patients recruited over a 3 year period. While additional staining including CD31 (which reflects microvessel density) and HIF-1α (related to hypoxia) will also be performed, this initial work concentrates on comparing cell density determined from hematoxylin and eosin staining with ADC and T2 values obtained from MRI.

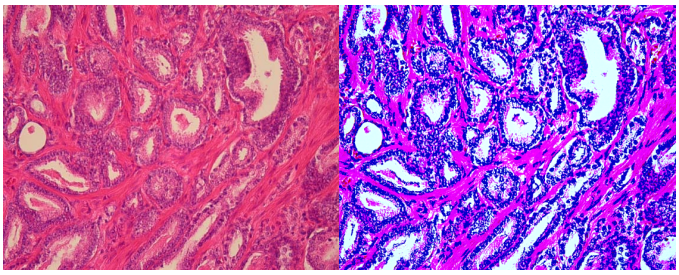
Methods To date, 65 patients have been recruited with 16 proceeding to radical prostatectomy. MRI was performed on a 3.0 Tesla scanner using a multi channel pelvic phased array. After conventional T2 weighted imaging, images at 4 echo-times (30-120 ms) were acquired using a multiple-echo fast spin-echo sequence to allow quantification of T2. Diffusion imaging was then performed using a spin-echo EPI sequence with *b*-values of 0 and 500 s/mm^2. Patients then proceeded to radical prostatectomy if this was deemed appropriate based on the combined clinical and imaging results. After surgery radical prostatectomy specimens were coated with standard marking ink and fixed in buffered formaldehyde. Specimens were then sliced at 5 mm intervals in a plane perpendicular to the long axis of the prostate to ensure correspondence with the MRI slices. An initial 3 nm microtome section from each slice was then whole mounted and stained with hematoxylin and eosin so that an experienced pathologist could outline regions of tumour appropriately. Five randomly positioned areas from within the most representative sections of tumour and normal peripheral zone were then digitally photographed at a 20× field and analysed using 'in-house' developed MATLAB software. This software utilises adaptive histogram thresholding to segment the darker stained cell nucleus thus providing an automated estimate of cell density. ADC and T2 values were then determined from the MR data using the whole mounted specimens as reference.

Results ADC values were significantly lower (p=0.001) in regions pathologically determined as tumour (1.44±0.19 mm^2/s) compared to regions assigned as normal peripheral zone tissue (1.84±0.22 mm^2/s). Similarly T2 values were also significantly lower (p=0.001) in tumour (108±22 ms) compared to peripheral zone (139±23 ms). The average cell density over the 5 fields was significantly higher (p=0.001) in tumour compared to normal peripheral zone tissue (19.2±7.2% vs. 9.0±3.4%). Boxplots demonstrating the ADC and cell density results are shown alongside.

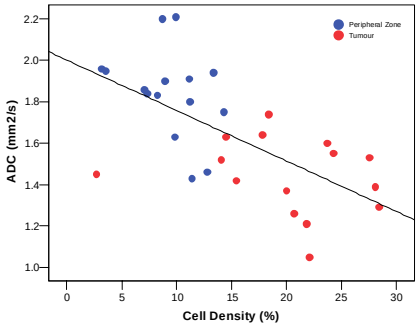




Example 20× images of a region of prostatic carcinoma before and after adaptive histogram thresholding are shown below (left and right respectively). Cell nuclei are highlighted in blue.



ADC values were found to correlate well with cell density regardless of tissue type (r=-0.678, p<0.0005) whilst T2 values correlated less well with cell density (r=-0.412, p=0.024). Reduced ADC values were evident with increasing cell density (see right).



Discussion ADC and T2 values have been successfully correlated with cell density as determined using automated thresholding of hematoxylin and eosin stained whole mount specimens. The increase in cell density evident in areas of prostatic tumour reflects the decrease in available extracellular space resulting in reduced ADC values. T2 values are also reduced since T2 is essentially a measure of the extracellular volume fraction. This work has demonstrated that ADC and T2 measurement may provide important pathological information in prostate cancer.

[1] JR Toms ed. – Cancer Stats Monograph, London CRUK 2004:p55-62. [2] MA Haider *et al* (2007) *American Journal of Roentgenology* 189:323-328. [3] A Tanimoto *et al* (2007) *JMRI* 25:146-152. [4] M Pickles *et al* (2006) *JMRI* 23:130-134.