Monitoring prostate cancer progression with Diffusion Weighted Imaging: variability of Apparent Diffusion Coefficient measurements with ROI placement technique and time

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Introduction

Prostate cancer, particularly early stage disease, often behaves indolently. Patients with low-risk localized disease may be offered active surveillance, which involves regular monitoring with prostate specific antigen (PSA) levels and repeat biopsy at 2 yearly intervals, or sooner if there is a rise in PSA. However, PSA velocity alone is inadequate to predict the need for radical intervention, warranting repeat 10 core biopsy, which is invasive, often poorly tolerated and carries a morbidity. The aim of this study was to determine whether a change in fast and slow components of apparent diffusion coefficient (ADC) of tumor in patients on active surveillance was indicative of disease progression. In the first instance the variability in ADC measurements over the whole prostate with time and in the tumor with ROI placement techniques was investigated.

Methods

19 consecutive patients with localized prostate cancer (Stage 1 or 2a disease, Gleason 3+3, PSA <10ng/ml, <2 cores positive) managed with active surveillance underwent DW-MRI in addition to their standard T2-W MRI at baseline and after 2 years (time-points 1 and 2). MR studies were performed using a 1.5-T Intera (Philips Medical Systems, Netherlands) and a balloon design endorectal coil (Philips Medical Systems, Netherlands) inflated with 55ml of air. Hyoscine butyl bromide 20 mg was administered intramuscularly immediately prior to centering the patient in the scanner in order to reduce peristalsis. Conventional T_2-W fast spin echo images were obtained in 3 orthogonal planes (TSE 2000/90 ms [TR/effective TE], echo train length 16, 2 signal averages) with a 256x512 matrix (interpolated to 512 x 512), 3mm slice thickness, no gap and a 14cm FOV (total imaging time 12 mins). Echo-planar DW images (2500/69 [TR/TE]) with b values of 0, 100, 300, 500 and 800 s/mm^2 were obtained transverse to the prostate and parallel to the corresponding set of T_2-W images. The phase-encoding gradient was from left to right in order to minimize motion artifacts in the prostate. Twelve 4mm thick slices (no gap, 20 cm FOV, matrix 128x128) provided coverage of the prostate with an image acquisition time of 1min 24s.

Axial T_2-W and DW- images were transferred offline for analysis. Regions of interest (ROIs) were drawn in 2 ways: first on all slices of the T_2-W axial scans around the whole prostate, and the tumor (low signal intensity lesion in a sextant biopsy positive for tumor) with knowledge of the biopsy findings, but without access to the DW- data or ADC maps and subsequently on the ADC maps over a region of diffusion restriction in the peripheral zone. The radiologist had 10 years experience of prostate MRI. The centre of mass and whole gland outlines defined on ADC maps were matched with those defined on the T2-W images to correct for rigid body shifts. T2 -W ROIs were transferred onto the corresponding slices on the ADC maps. Mean ADC values (x10^{-6}mm^2/sec) from tumor, and whole prostate (minus tumor) were calculated for T2-W derived and ADC derived ROIs at both time-points.

Using the ADC derived ROIs which more closely reflect measurements in a clinical setting, the percentage change in ADC of tumor was calculated for all b values, and with only the low (0-300) and only the high (300-800) b values to reflect fast and slow diffusion components. The mean ADCs of those that progressed to radical treatment (based on PSA velocity, Gleason grade and no of positive cores) were compared to those that did not.

Results

Table 1: Variation of whole prostate of ADC with time

	0-800				0-300				300-800			
method	**T2-W**	**+/- Sd**	**ADC**	**+/- Sd**	**T2-W**	**+/- Sd**	**ADC**	**+/- Sd**	**T2 --W**	**+/- Sd**	**ADC**	**+/- Sd**
Time point 1	1400.08	+/-147.20	1419.66	+/-48.87	483.83	+/-31.79	485.18	+/-37.25	1327.04	+/-100.00	1371.32	+/-89.033
Time point 2	1403.16	+/-66.77	1405.28	+/-80.62	441.48	+/-24.02	453.13	+/-25.42	1343.04	+/-85.64	1380.24	+/-81.77
***p**	.33		.29		.03		.03		.55		.72	

***Significance of difference over time**

Table 2: Variability of Tumour ADC with ROI placement

	Time point 1 0-800		**Time point 2 0-800**	
	Mean	**+/- Sd**	**Mean**	**+/- Sd**
T2 method	1255.73	+/-73.97	1185.91	+/-45.67
ADC method	1156.68	+/-69.16	1093.70	+/-45.99
***p**	.001		.003	

***Significance of difference between method**

Table 3: Percentage change inTumor ADC in monitoring disease progression using ADC derived ROI values

	0-800	**0-300**	**300-800**
No radical treat	-2.41% +/-- 0.08	-2.16% +/-0.07	-2.17% +/-0.13
Radical treatment	-5.78% +/- 0.12	-10.26% +/- 0.13	-0.70% +/-0.14
***p**	.56	.44	.77

***Significance of difference between outcome**

Discussion and Conclusion

There was no significant change in whole prostate overall ADCs or in the slow component of ADC with time. The change in the fast component suggests a reduced perfusion component over the 2 year time period. Tumor ADCs were significantly lower using ADC derived ROIs reflecting the tighter definition of restricted diffusion lesions on the ADC maps. In this small patient group there was no significant difference in overall ADC or in the fast or slow components in patients that progressed to radical treatment compared to those that did not indicating in this preliminary work that reduction in ADC may not reliably be used to monitor disease progression.

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