Diffusion-weighted MRI of the prostate for tumor detection in patients with a significant family history of prostate cancer: comparison of qualitative vs. quantitative analyses

Maysam Jafar[1], Veronica A Morgan[2], Sharon L Giles[2], Catherine J Simpkin[2], Rosalind Eeles[3], Elizabeth Bancroft[3], Elena Castro[3], and Nandita M deSouza[4]

[1]Cancer Research UK and EPSRC Cancer Imaging Centre, Institute of Cancer Research, Sutton, Surrey, United Kingdom, [2]Cancer Research UK and EPSRC Cancer Imaging Centre, Royal Marsden NHS Foundation Trust, Sutton, Surrey, United Kingdom, [3]Genetics & Epidemiology, Institute of Cancer Research, Sutton, Surrey, United Kingdom, [4]Cancer Research UK and EPSRC Cancer Imaging Centre, Institute of Cancer Research & Royal Marsden NHS Foundation Trust, Sutton, Surrey, United Kingdom

Target Audience: Radiologists, radiographers, physicists and clinicians with interest in Diffusion Weighted (DW) MRI of the prostate

Purpose: Diffusion-weighted (DW) MRI identifies prostate cancer as a focal area of restricted diffusion within the gland and has increased the sensitivity and specificity for identifying tumor when used in conjunction with conventional T2 weighted (T2W) imaging. However, in early stage disease, lesions are often small and difficult to detect, particularly if Gleason grade is low (1), making template biopsy necessary. This is invasive and carries a significant morbidity. Histogram analysis of DW-MRI data may well enable detection of small low Gleason grade tumors. The purpose of this study, therefore, was to establish the sensitivity and specificity of DW-MRI for detecting tumors within the prostate in patients with a high risk (significant family history) of prostate cancer, comparing qualitative (observer identified) with quantitative (histogram analysis) methods.

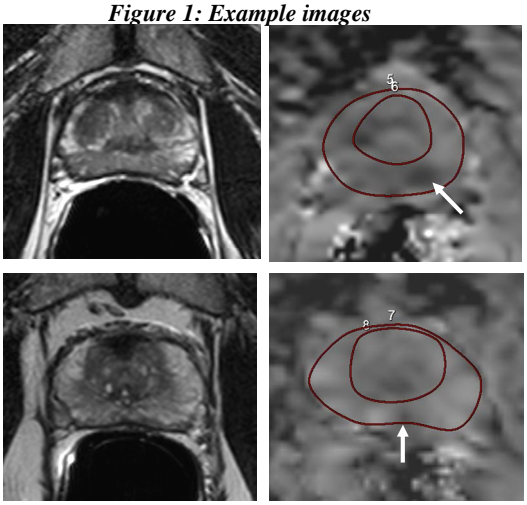
Methods: 51 patients with a positive family history of prostate cancer, defined as (a) one first degree relative with histologically or death-certificate proven prostate cancer diagnosed at <70 years, (b) 2 relatives on the same side of the family, where at least one is diagnosed at <70 years, or (c) 3 relatives on the same side of the family diagnosed at any age, were recruited. Patients were excluded if they were not between 40 and 69 years of age, had suffered a previous cancer with a terminal prognosis of less than five years, had previously been diagnosed with prostate cancer or had a negative biopsy within one year. Images were acquired at 3T using an endorectal balloon-design receiver coil, filling the balloon with 60 ml of perfluorocarbon. T2W images in 3 planes orthogonal to the prostate (FSE, TR 2500ms, TE 110ms, FOV 14 cm, slice thickness 2.2 mm, matrix 220x184, extrapolated to 256x256 were complemented by DW images in the transverse plane (single shot EPI, TR 5243ms, TE 72ms, FOV 180 cm, slice thickness 2.2 mm, matrix 80x71, extrapolated to 128x128). Images were assessed by an experienced observer using a combination of T2W and DW images and scored as positive or negative for tumor in one of 6 sextants (right apex, mid or base and left apex, mid or base), which represented the lower, mid and upper thirds of the gland respectively. Following an 8 week interval, the same observer drew regions of interest (ROIs) on every slice of the ADC maps around the whole prostate and around the central gland (CG) only using the T2W images as an anatomical reference and taking into account geometric distortion of the DW images. The difference between the whole gland and CG ROIs represented the peripheral zone (PZ). ADC values from each pixel in the PZ and CG separately produced histograms (bin width $20X10^{-6}$) from which the 10^{th} and 25^{th} centiles (C10, C25, likely to represent the low values seen in tumors), were derived. ROC curves for C10 and C25 were used to determine the sensitivity and specificity of that centile value for detecting tumor using octant biopsy as the gold standard.

Results: 28 sextants were positive in 13 patients on biopsy, all were Gleason 3 + 3. For an experienced observer sensitivity and specificity for detecting tumour in this high-risk group was 57.1% and 97.8% respectively (PPV 72.7%, NPV 95.8%) on a per sextant basis and 76.9% and 92.1% on a per patient basis (PPV 76.7%, NPV 92.1%). For histogram analyses, area under ROC curve (A_z) and cut-off centile values and their sensitivity at a specificity of 90% are given for PZ (***Table 1a***) and CG (***Table 1b***). ***Figure 1*** provides example images from (a) a patient with positive biopsy correctly assessed as positive for tumour on MRI and (b) a patient with a negative biopsy, incorrectly assessed by MRI as positive for tumour.

TABLE 1a PZ	**C10**	**C25**
A_z	0.575	0.534
Cut-off ADC($x10^{-6}$ mm^2/s)	1240.3	1508.0
Sensitivity (%)	15.4	15.4

TABLE 1b CG	**C10**	**C25**
A_z	0.660	0.694
Cut-off ADC ($x10^{-6}$ mm^2/s)	1105.5	1239.5
Sensitivity (%)	23.1	23.1

Figure 1: Example images



True Positive *(top row) showing a biopsy-proven tumor focus as an area of restricted diffusion on the ADC map (right)*

False Positive *(bottom row) showing small focus of restricted diffusion medially within the peripheral zone in a patient with negative biopsy*

Discussion and Conclusion: Detection of even low Gleason grade tumors is better with an experienced observer compared to quantitative assessment with histogram analysis because account is taken of shape, size, focality and location of areas of diffusion restriction likely to represent tumor. More complex quantitative analysis to account for ADCs in neighbouring pixels is needed. For these small lesions, centile values lower than C10 may need to be interrogated. High spatial resolution is essential for detecting small lesions with DW-MRI and is optimised by using an endorectal coil at 3T.

References: (1) Morgan et al, 2007, Acta Radiologica

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