Biexponential modeling of diffusion in stroma and epithelium of prostate tissue

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Target audience: This work is addressed to biophysical modelers, diffusion MRI researchers and cancer imaging researchers.

Purpose: To use high spatial resolution DWI to investigate the non-Gaussian behavior of water diffusion in epithelium and stroma of fixed prostate tissue.

Introduction: Non-Gaussian diffusion behavior observed in the prostate in vivo [1,2] has also been observed in fixed prostate tissue using high spatial resolution DWI with a voxel size of 160 μm isotropic [3]. Changes in estimated partial volumes of low ADC epithelium and higher ADC stroma explained about 60% of the variation in high ADC signal fraction when multi b-value data was fitted with a biexponential model. However, the 160 μm voxel size used in that study meant that most voxels contained heterogeneous mixtures of epithelium, stroma, and lumen space. In the study presented here we obtained multi b-value data from 80 μm voxels in order to more clearly characterize the distinct diffusion properties of normal epithelium and stroma and compare these with cancer epithelium.

Methods: Three 3mm-diameter cores of prostate tissue were obtained from radical prostatectomy specimens of three patients, fixed in formalin, immersed in 0.2% v/v Magnevist, and imaged on a 16.4T Bruker AV700 microimaging system (15 mm solenoid RF coil, Micro5 gradient set) using a 3D spin echo DTI sequence with TE/TR = 28/500 ms, δ/ Δ = 2/20 ms. 80μm isotropic voxels were acquired with six gradient directions and b-values 0.50, 0.90, 1.42, 2.06, 2.78, 3.59, 4.65 ms/μm^2) with two reference images at an effective b-value of 0.335 ms/μm^2. $SNR_{b=50}$ = 40. 40μm voxels were also acquired at a single b-value of 2.70 ms/μm^2 with geometrical orientation as above. A diffusion tensor was calculated for each b-value in the 80μm data set and the mean diffusivity used to calculate a gradient direction independent normalized signal intensity at each b-value. The direction independent normalized data from each voxel was then fitted with a biexponential model of the form:

$$S_b = S_0(SF_1 \cdot exp(-D_1 \cdot b) + (1 - SF_1) \cdot exp(-D_2 \cdot b))$$

Results: Representative data are shown in Fig. 1, with manually selected regions of stroma (S1, S2), normal epithelium-rich glands (E1, E2), and a region (C1) likely to be low grade cancer based on macroscopic tissue features and previous patient biopsy results (however, not confirmed by histopathology). Table 1 shows the mean and standard deviation of the model parameters for voxels within each region of interest.

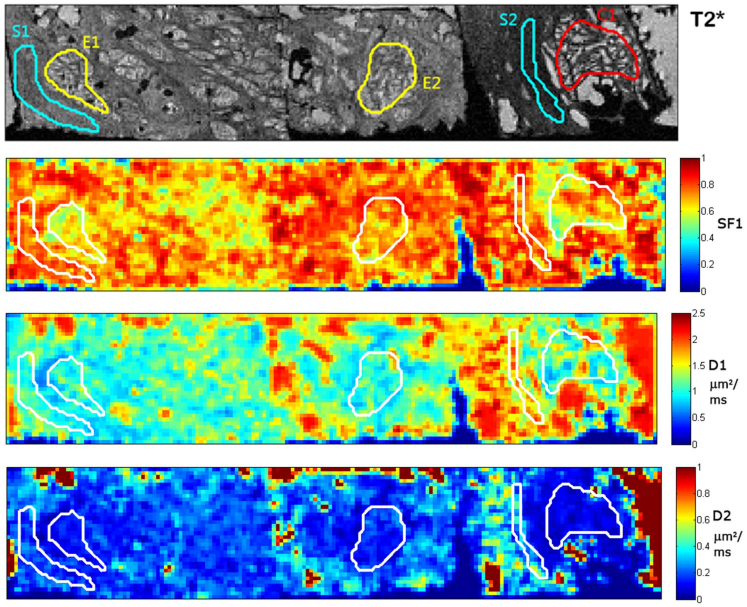

Fig.1 40 μm T_2* weighted image and 80 μm parametric maps

Discussion: The 80 μm voxel size used in this study (each voxel containing ~200 cells) is 8× smaller than that used for a previous investigation that applied a biexponential model to DWI signal attenuation in fixed prostate tissue [3]. This higher spatial resolution study demonstrates tissue-specific variations in the model parameters. Both D_1 and SF_1 were lower in epithelium-rich regions (E1, E2, C1) than in stromal regions (S1, S2). Both of these differences would lead to a lower ADC in epithelium-rich tissue than in stroma when ADC is derived from a conventional monoexponential model. As suggested previously [3], an increasing partial volume of low diffusivity epithelial cells, rather than "higher cellularity", may explain the clinical observation of decreasing ADC as prostate cancer Gleason grade increases. The lowest D_2 was found in the C1 region – suggesting a more restrictive diffusion environment in cancerous epithelium than in normal epithelium.

Conclusion: High spatial resolution biexponential modeling of diffusion in fixed prostate tissue demonstrates distinct regional variations in diffusion behavior that correlate with microscopic tissue structure features. Regions dense in glands have a higher proportion of the lower diffusivity component, and this component has lower diffusivity in the glandular regions than in regions of fibromuscular stroma.

Table 1. – Fit parameters for selected regions shown in Fig. 1 (Mean ± SD)

Region	**S1** (n=156)	**S2** (n=89)	**E1** (n=123)	**E2** (n=189)	**C1** (n=248)
SF_1	0.76 ± 0.07	0.78 ± 0.11	0.61 ± 0.06	0.71 ± 0.08	0.65 ± 0.09
D_1 (μm^2/ms)	1.23 ± 0.16	1.62 ± 0.29	0.98 ± 0.18	1.07 ± 0.21	1.15 ± 0.28
D_2 (μm^2/ms)	0.17 ± 0.07	0.27 ± 0.14	0.13 ± 0.03	0.15 ± 0.05	0.10 ± 0.10

References: 1) Mulkern, R.V., et al., J Magn Reson Imaging, 2006. 24(5): 563-568. 2) Shinmoto, H., et al., 2009 J Magn Reson Imaging. 27(3): 355-359. 3) Bourne, R.M., et al., 2012 Magn Reson Med. 68(3): 954-959.