Comparison of single and multi-compartment models of diffusion in fixed prostate tissue

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

Purpose This study used high-field high-gradient diffusion-weighted (DW) MRI of fixed prostate tissue to explore the key components of an accurate biophysical model for obtaining future biomarkers of cancer and other pathology. To date, most DW-MRI studies of prostate have investigated the rate of water diffusion within tissue by considering the apparent diffusion coefficient (ADC) [1]. For example, [1] found that decrease of ADC in cancer tissue correlates with Gleason grade. It has also been suggested that ADC changes may be indicative of structural changes in lumen and ductal spaces and increased cell density [2]. However, recent evidence from imaging fixed prostate suggests that distinct diffusivity differences between epithelial, stromal and lumen spaces are likely to contribute to changes in ADC [3]. These equivocal results highlight limitations of ADC alone as a marker of cancer malignancy and motivate the development of biophysical models for estimating more specific parameters.

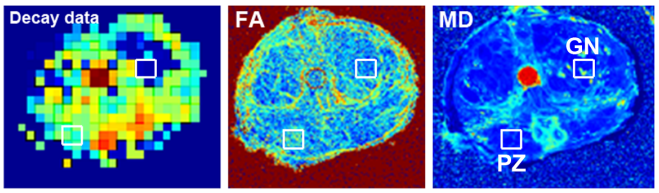

Fig. 1. Selection of decay data from peripheral zone (PZ) and a central zone glandular nodule (GN). A saline-filled tube is inserted through the urethra.

Methods We acquired DW-MRI with a rich imaging protocol and selected for modelling two tissue types having distinct diffusion properties: 1) A low ADC central zone glandular nodule (GN), and 2) an intermediate ADC peripheral zone region (PZ) (Fig. 1).

Diffusion Models We fit four diffusion models to voxels of each tissue type comparing number of compartments and restricted versus free diffusion: 1) A mono-exponential (ADC) model that assumes Gaussian diffusion and does not account for restriction; 2) A biexponential model that is a mixture of two Gaussians with two different ADCs [4]. 3) a two-compartment model with one component to characterise free isotropic diffusion in the extra-cellular space, the `Ball', and one 'Sphere' component to describe diffusion in a spherical confinement [5], i.e. isotropically restricted diffusion. We adopt the naming method for multi-compartment models of white matter from [6] and name the model 'BallSphere'; and 4) a tri-exponential model made of three Gaussians, with three different ADCs. The multi-compartment models assume different intrinsic diffusivities for each compartment.

MRI Acquisition A radical prostatectomy specimen was obtained with ethics approval and informed donor consent. The experiment acquires DW-MR images of the fixed prostate gland using a 9.4T scanner [7]. We use the pulse-gradient spin-echo (PGSE) sequence for 51 diffusion weightings: 3 diffusion times Δ=20, 40, 80ms, gradient duration δ=5ms for all Δ, and 16 equally log-spaced b values from 0.05 to 10 ms/μm^2. The diffusion gradients are placed along the three imaging coordinate axes. FOV 45×45mm, matrix size 32×32, TE= 28, 48, 88ms (we normalise the data to avoid T_2 dependence), SNR $_{b=0}$ ~ 240.

Model fitting Models were fitted to the DW-MRI data by minimising the sum of squared errors using a Levenberg-Marquardt algorithm. We chose the best-fit parameters after 1000 perturbations of the starting point to avoid local minima.

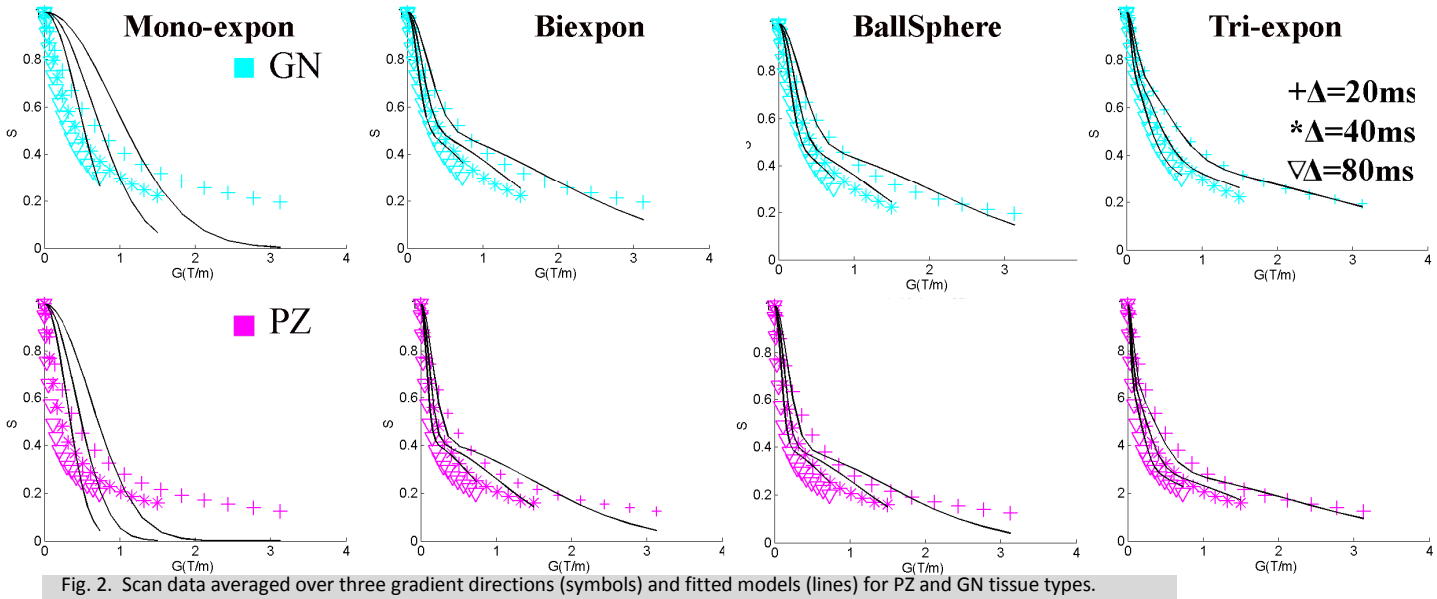

Fig. 2. Scan data averaged over three gradient directions (symbols) and fitted models (lines) for PZ and GN tissue types.

Results Fig. 2 compares data and fitted models for each tissue type by plotting the normalised signal S at all values of Δ, δ as a function of the gradient strength.

Discussion & Conclusions Our results suggest that the mono-exponential (ADC-only) model is too simple to capture the signal from either of the tissue types. The addition of the second compartment improves the fitting, but neither two-compartment models can explain the data. Visible departures appear at higher gradient strengths. The tri-exponential model is the only model tested that is flexible enough to capture the broad trends in the data, although small departures still occur. However, most likely it does so simply by virtue of additional parameters (a BallBallSphere model fits just as well), rather than providing direct biophysical insight. The result highlights the complexity of the signal even from pure tissue types and underlies the gross oversimplification of the widespread single ADC model. Future work will investigate alternative parsimonious models that explain the data e.g. by including cell-size distributions and/or permeability effects.

References & Acknowledgements 1 Vargas et al, Radiology 2011, **2** Gibbs et al, Invest. Radiol. 2009, **3** Bourne et al, MRM 2011, **4** Niendorf et al, MRM 1996, **5** Murday and Cotts, J. Chem. Phys.1984, **6** Panagiotaki et al NeuroImage 2012 **7** Bourne et al, MRM 2012

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