Mapping axon radius in the human corpus callosum using dual spin-echo diffusion MRI

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Intended Audience: Diffusion MRI researchers and those interested in the estimation of physical microstructure parameters

Purpose: There has been a considerable amount of recent interest in the use of diffusion MRI (dMRI) as a tool to estimate physical microstructure parameters such as axon radius and density (e.g. [1,2]). In this work we demonstrate, for the first time, microstructural parametric maps based on *in vivo* human imaging using an optimised dual spin-echo (DSE) dMRI pulse sequence. This is the primary dMRI sequence available on many modern clinical scanners, due to its advantage of being robust to eddy-current induced distortion effects, but has not been used for microstructural diffusion imaging before.

Methods: The arrangement of field gradient pulses in the standard DSE sequence was redesigned for microstructural imaging purposes using the active imaging optimisation framework, which aims to maximise the expected precision of a set of tissue model parameters [3]. The tissue model in this case was a simple representation of white matter, consisting of a series of parallel impermeable cylinders embedded in a homogeneous extracellular substrate. This same model has previously been used with the simpler Stejskal–Tanner dMRI sequence [2], and a theoretical extension to the DSE sequence has also been described [4], but no *in vivo* data have previously been shown using DSE. The final optimised acquisition consisted of four pulse arrangements, for each of which 90 noncollinear gradient directions were applied, along with 9 $b = 0$ images. Data were acquired using this scheme from two volunteers, a 42 year-old male and a 31 year-old female, on a Siemens Trio 3 T scanner using 35 mT m^{-1} maximum gradient strength. Final voxel dimensions were 2.3 mm isotropic. Scan time was approximately one hour.

Initial estimates of the tissue model parameters were derived from a standard least-squares diffusion tensor fit where possible. Final parameter estimation was then performed within a single midsagittal slice of each subject's corpus callosum using a Markov chain Monte Carlo approach to sample from the joint posterior distribution over all parameters. A Metropolis–Hastings sampler was used, with a multivariate Gaussian proposal distribution whose covariance matrix was estimated and tuned through a pilot sampling phase. A burn-in of 5000 steps was run, after which 50 samples of each parameter were obtained at intervals of 100 steps. All priors were uninformative. A Rician noise model was used, and a data pooling approach was taken to obtain a better estimate of the noise level in each image voxel [5]. An isotropic diffusion compartment was included in the fitting model to allow for partial volume effects with cerebrospinal fluid.

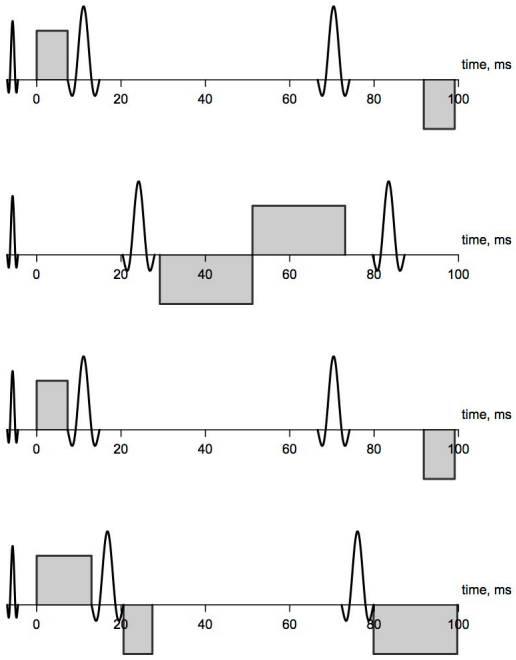

Fig. 1: *Illustration of the set of four optimised pulse sequences used in our DSE-based acquisition protocol. The first and third arrangements are identical.*

Results: Fig. 1 shows the optimised set of four pulse sequences which comprised our acquisition, with b-values of 422, 620, 422 and 2378 s mm^{-2}. (The first and third arrangements are in fact identical.) Echo time was 119 ms in each case, and the time between the onset of the first and last pulses varied between 22 and 92 ms. Note that although the DSE sequence provides the basic template, only a subset of the four usual pulses actually appear in each arrangement. The active imaging optimisation framework produced this mixture of high and low b-values, and of long and short diffusion times, without special constraints being applied to enforce these characteristics.

Parametric maps of axon radius are shown in Fig. 2. These values were obtained by taking the median of the sampled axon radii at each image voxel. In line with previously reported dMRI experiments, the axon radius estimates obtained are higher than those suggested by data derived from microscopic study of postmortem brains [6], a fact explained by tissue shrinkage during fixation on the one hand, and the limitations of our simple tissue model on the other. Nevertheless, a tendency for axon radii to be highest in the midbody and in the most posterior part of the splenium of the corpus callosum—and lowest in the genu—is common to both, particularly for our second subject (lower figure).

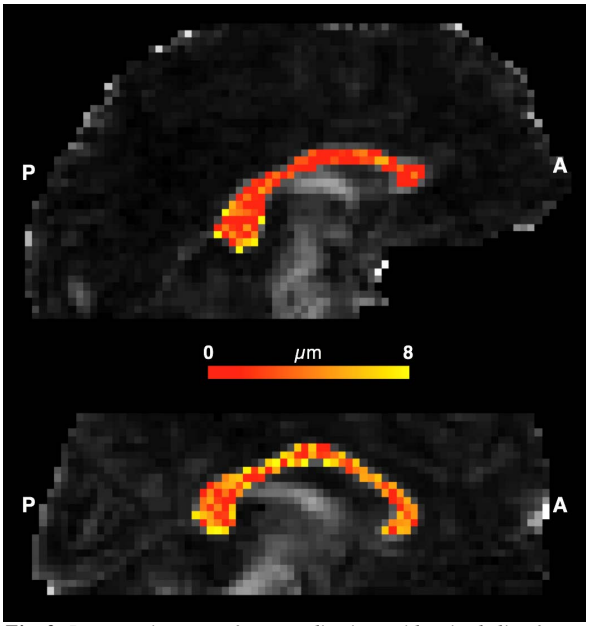

Fig. 2: *Parametric maps of axon radius in a midsagittal slice for each subject, based on the median sampled value in each voxel. The background image is fractional anisotropy in each case.*

Discussion & Conclusion: We have demonstrated *in vivo* microstructural parametric maps using the common DSE diffusion MRI sequence and clinical gradient strengths (35 mT m^{-1}), for the first time. This represents a significant step towards wider applicability of microstructural dMRI techniques. Future work will investigate the reproducibility of the results.

References: [1] D. Barazany et al., *Brain* **132**:1210 (2009); **[2]** D.C. Alexander et al., *NeuroImage* **52**:1374 (2010); **[3]** D.C. Alexander et al., *Magn Reson Med* **60**:439 (2008); **[4]** J.D. Clayden et al., *Lect Notes Comp Sci* **5636**:264 (2009); **[5]** J.L.R. Andersson, *NeuroImage* **42**:1340 (2008); **[6]** F. Aboitiz et al., *Brain Res* **598**:143 (1992).