

Optimization of a Fast Diffusion Estimation Two-Compartment Model for Diffusion Tensor Imaging

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Target Audience: Clinicians and researchers who use quantitative diffusion tensor imaging (DTI) metrics.

Purpose: DTI as developed by Basser in 1994 [1] and still widely used today assumes that the signal attenuation due to diffusion within a voxel is caused from a single species. When this is not satisfied the single component model cannot be used. A one-tensor plus one isotropic component with fixed diffusivity model has been proposed [2] to remove CSF contamination. In that work 8 b-values with various directions were chosen a priori and used to fit the model described by $S_i = S_0[(1 - f)\exp(-b_i g_i^T D g_i) + f \exp(-b D_{iso})]$ (1), where, S_i and S_0 are the signal from the i -th diffusion and non-diffusion weighted measurements, respectively, f is the fast diffusion fraction, D_{iso} is the diffusivity of free water ($3 \times 10^{-3} \text{ mm}^2/\text{s}$), D is the tissue diffusion tensor, b_i and g_i are the diffusion-weighting amplitude (in s/mm^2) and unit gradient encoding vector, respectively. The tissue signal compartment results in the same scalar metrics of DTI. This model improves the ability to characterize tissue parenchyma microstructure in voxels with partial volume averaging and multiple diffusion components. In this work, we (1) develop a systematic and efficient approach to solve Eq. 1 including a novel weighted linear least squares method (2) determine the minimum number of diffusion b-values and gradient directions needed (3) determine what the spread of b-values needed and (4) determine how gradient directions should be distributed among the desired b-values.

Methods: This model was implemented in a straightforward and novel weighted linear least squares formulation followed by a nonlinear estimation of Eq. 1. The initial solution was obtained by fixing the f -value and then fitting for the diffusion tensor which is then the only remaining unknown. The WLLS routine was modified to allow for simultaneous fitting of an arbitrary number of f -values. Each of the f -value/tensor pairs was evaluated to determine which minimized the WLLS objective function. These values were then used as the initial point for the full nonlinear estimation. This allowed for a rapid solution without the need for any spatial constraints as has been proposed [3]. Optimal acquisition parameters were investigated through Monte Carlo simulations and human brain imaging studies. To ensure clinical feasibility the acquisition was limited to 4 b_0 and 68 diffusion weighted images. The acquisition parameters were optimized for encoding design (collinear vs noncollinear), number of shells (2-8 b-values), number of directions for each shell (with a maximum of 68 total directions), and the b-values of each shell (min 200 max 1500 s/mm^2). Monte Carlo simulations with $f = 0.2$ were performed for SNR from 20 to 80 and for different tissue diffusion tensor profiles. Repeated human brain imaging studies were performed in a healthy adult subject with the optimized protocol and a less optimized version.

Results: At a signal-to-noise ratio of 40 with 68 diffusion-weighted encoded images, most accurate estimates of fast diffusion signal were obtained with three (or more) diffusion-weighted shells (number of directions \times b-value in s/mm^2) of 12×200 , 40×650 , 12×1500 in noncollinear directions. The acquisition time for whole brain FDE-DTI with this protocol was less than six minutes and reconstruction was roughly four times that of standard DTI estimation. In the FDE-DTI *in vivo* brain studies, the optimized FDE-DTI protocol was effective at reducing the CSF partial voluming effects in the tissue DTI maps (Fig 1). The variances of f and FA estimates were lower for the optimized protocol which was predicted by simulations and seen *in vivo* (Fig 2). Using Bayesian information criteria *in vivo* results show the FDE model is globally superior to the simple DTI model for representing the measured diffusion weighted signal. The potential bias in fractional anisotropy induced by this two-compartment model was nearly an order of magnitude less than the error of using the single diffusion tensor model in the presence of partial volume effects.

Discussion and Conclusions: We determined that three nonzero b-values are optimal for estimation of FA and f -value. While it was known that one shell is insufficient without further constraints it was not intuitive that three would be an optimum number. The use of two shells stabilized the problem, but was inferior to the use of three or more shells. More than three shells adds acquisition complexity without gains in estimation accuracy. The distribution of directions within these shells was also investigated with the results that for a three shell technique the majority of directions ought to be used for the intermediate (650 s/mm^2) shell as opposed to the higher b-value. One interesting observation was that the fast diffusion fraction map appeared to reveal and remove CSF signal throughout the image volume from Gibbs ringing, thereby “cleaning up” the DTI maps. In this study, we demonstrated that the partial volume signals from CSF may be effectively minimized using the FDE-DTI model, which will result in more accurate DTI measurements in tissues adjacent to CSF spaces including the corpus callosum, fornix and cortical gray matter. This was accomplished in a clinically feasible acquisition of less than six minutes.

Reference: [1]. Basser PJ, Mattiello J, LeBihan D. *Biophys. J.* 1994;66:259–67 [2] Pierpaoli C, Jones DK. *ISMRM 2004*; p. 1215. [3] Pasternak O et al. *Magn. Reson. Med.* 2009;62:717–30.

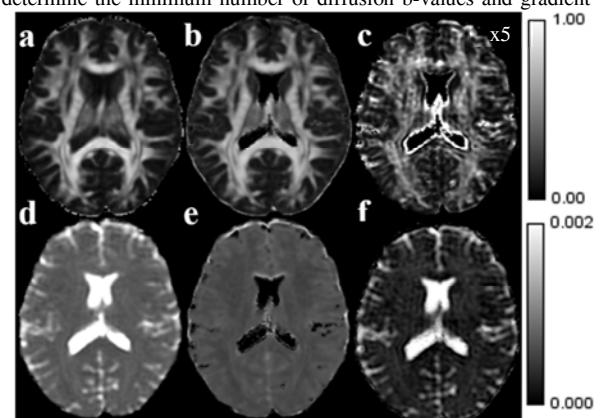


Figure 1: The top row of images show FA from DTI (a), FDE (b), and the FA increase due to fast diffusion component removal (c). The difference image was multiplied by five to maintain the same unitless scaling from zero to one for all three FA maps. The images in the bottom row show the mean diffusivity (MD) from DTI (d), the MD of the “tissue”-compartment post FDE correction (e), and isotropic volume fraction scaled from zero to one (f). All MD maps are scaled from 0 to $2 \times 10^{-3} \text{ mm}^2/\text{s}$.

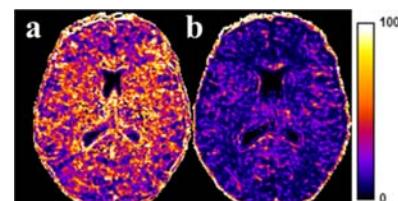


Figure 2: Relative standard error (RSE) for f using a two-shell (a) and the optimized three-shell (b) acquisitions. RSE is given as a percentage from 0 to 100.