Optimizing Diffusion Tensor Imaging Protocol using *a priori* Structure Information: Experimental Validation

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Introduction

Diffusion Tensor Imaging (DTI) [1] is a Magnetic Resonance Imaging (MRI) technique that quantifies self-diffusion characteristics of water molecules, such as in the nervous system, based on mathematical models. DTI defines a classic parameter estimation problem involving a diffusion tensor with a 3x3 symmetric matrix consisting of six diffusion parameters. In this work, we validated a technique to estimate optimal experimental acquisition parameters based on the use of D-optimality [2] and appropriate *a priori* structure information [3]. We used both Monte Carlo simulations and experimental spinal cord data to demonstrate that the uncertainty in parameter estimation could be effectively reduced.

Theory

From our previous work [3], we have shown that for a non-linear least-squares estimation with additive white Gaussian noise with zero mean and σ^2 variance, the determinant of the Cramer-Rao lower bound [4] of the covariance of estimates, $\det \Sigma_{CR} = \sigma^{2M} / \det (X^T X)$, can be minimized by optimally selecting the diffusion encoding gradient directions within a spread of fiber orientations (Λ) based on *a priori* structure information. This D-optimal [2] technique has been formulated as a "minmax" problem [3] given by,

$$\Omega_{robust} = \arg[\min_{\mathbf{g}}(\max_{\{\theta_F,\phi_F\}\in\Lambda} f)], f = 1/\det(X^T X)$$

,where X is the model sensitivity matrix, $X(\Omega,\beta), \Omega = \{\mathbf{g}_i, i \in [1,N]\}$ is a set of diffusion encoding gradient directions, N is the number of observations and $X_{ij} = \eta_j(\mathbf{g}_i,\beta), \eta_j(\mathbf{g},\beta) = \partial E(\mathbf{g},\beta)/\partial\beta_j, j \in [1,M]$, M is the number of parameters. For DTI, estimation parameters β = (D_{xx}, D_{yy}, D_{zz}, D_{xy}, D_{xz}, D_{yz}) and M=6. In DTI, the observed signal can be modeled as a normalized echo attenuation, $E_i = S_i / S_0 = \exp(-b\ \mathbf{g}_i^T\ \mathbf{D}\ \mathbf{g}_i)$, where $\mathbf{g}_i$ represents the diffusion encoding gradient direction, **D** is the diffusion tensor matrix with six diffusion parameters that are to be estimated (D_{xx}, D_{yy}, D_{zz}, D_{xy}, D_{xz}, D_{yz}), b is the sensitivity factor.

Simulations

We performed Monte Carlo simulations with 20,000 realizations of the DTI signal under two different noise levels (σ = 0.1 and σ = 0.2) and with both standard and optimized gradient schemes. To verify the robustness of the scheme, the simulations were run at different angular deviations (α) from the mean fiber orientation of (0^o, 0^o) (Fig. 1). A nonlinear estimator based on the Levenberg-Marquardt (LM) algorithm was used for parameter estimation. Actual values of parameters used for simulations are D_{zz}= 1.82 x 10^{-5} $cm^2 s^{-1}$, $D_{xx} = D_{yy}$ = 9.25 x 10^{-7} cm^2 s^{-1}, $D_{xy} = D_{xz} = D_{yz} = 0$, b = 1 x 10^5 s cm^{-2}.

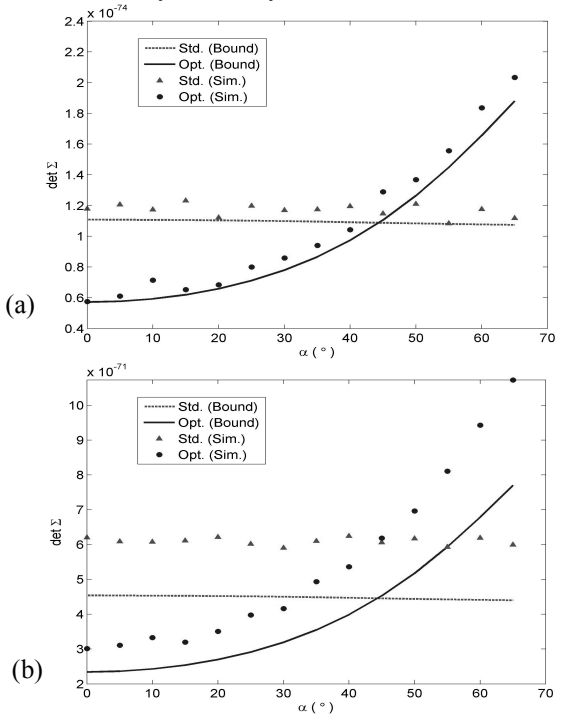

Fig. 1. Simulation results at different angular deviations: (a) σ=0.1, (b) σ=0.2.

Experiments

A prescan was performed on the upper spinal cord of a 27-year-old healthy subject. The mean values of the diffusion coefficients at the white matter were estimated to be D_{zz}= 1.284 x 10^{-5} $cm^2 s^{-1}$, D_{yy} = 6.25 x 10^{-6} cm^2 s^{-1}, D_{xx} = 7.03 x 10^{-6} cm^2 s^{-1}, D_{xy} = -1.4 x 10^{-7} cm^2 s^{-1}, D_{xz} = 2.31 x 10^{-6} cm^2 s^{-1}, D_{yz} = -4.1 x 10^{-7} cm^2 s^{-1}. These values correspond to mean parallel diffusivity of 1.367 x 10^{-5} cm^2 s^{-1}, mean transverse diffusivity of 6.23 x 10^{-6} cm^2 s^{-1} and mean fiber orientation in the spinal cord region of (19.5^o,-10^o). For generating the optimized scheme

(OPT30), Λ=35° was used. The T2 and diffusion-weighted images were acquired using a spin echo EPI sequence on a 3 tesla GE Signa HDx scanner (GE Healthcare, Waukesha, WI), 8-channel head coil with 30 contiguous 3-mm axial slices, TR = 8000 ms, TE = 76 ms, matrix size =128x128, FOV = 22 cm x 22 cm, number of excitations = 2, parallel imaging acceleration factor = 2, b = 1000 s mm^{-2}, 30 diffusion encoding gradients were used (OPT30, standard MF30) and scan time per set = 8 min 32 sec.

For calculating the covariance of estimates, 5 data sets for each of the two diffusion encoding gradient schemes were collected and the data was extended to 5000 observations per scheme using a bootstrapping sampling technique. The sampling technique ensured that the mean observation of the DTI signal was not affected.

Results and Discussion

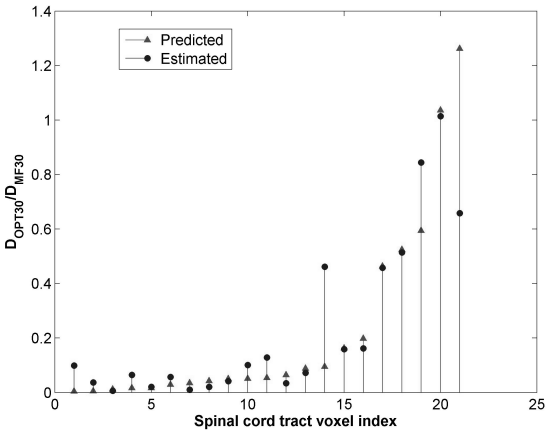

Fig. 2. Experimental results for 21 spinal cord tract voxels.

Fig. 2 shows the effect of optimized gradient scheme as compared to standard gradient scheme for 21 voxels collected in the upper spinal cord white-matter tracts. D_{OPT30} and D_{MF30} are the determinant of covariance of estimates. For the prediction, these correspond to the determinant of covariance bounds computed based on the mean values at the voxels. For improvement in uncertainty, $D_{OPT30}/D_{MF30} < 1$ and this can be observed in the voxels collected from the spinal cord tracts. For certain cases, the predicted reduction do not match the estimated and this can be due to experimental noise or voxel being on the tract boundary.

Based on our results, with our optimized scheme, the uncertainty in the estimation of diffusion coefficients was reduced when voxels have high diffusion anisotropy and a high ratio between the parallel and transverse diffusivity values. For spinal cord tracts, the axon fiber bundles have higher diffusion anisotropy than the grey matter and have a preferable orientation (superior-inferior). Thus, our optimized gradient scheme can be expected to perform better than the standard scheme which does not take advantage of the *a priori* information.

Conclusion

An optimized diffusion encoding gradient scheme was developed for Diffusion Tensor Imaging using *a priori* structure information of spinal cord tissues. These schemes were validated with both Monte Carlo simulations and spinal cord data. The uncertainty in the estimation of diffusion coefficients was reduced with the optimized scheme (OPT30) compared to the standard scheme (MF30). The scheme was optimally designed to perform within a range of angular deviation from the mean fiber direction. We also found that the reduction in uncertainty was better at higher anisotropy. Therefore, based on coarse preliminary data, a worst case situation in diffusion anisotropy can be used to design the optimized scheme, which should always perform better in regions of the tissue with a higher anisotropy. This can have implications in detecting spinal cord tract diseases such as multiple sclerosis and myelopathy that affect the diffusion anisotropy in the tract fibers. Future work includes improving the efficiency of the optimization algorithm, using a more accurate noise model, and conducting studies on more human subjects.

References

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