Remedies for Anomalous Estimates of Some Tensor-derived Quantities in DTI

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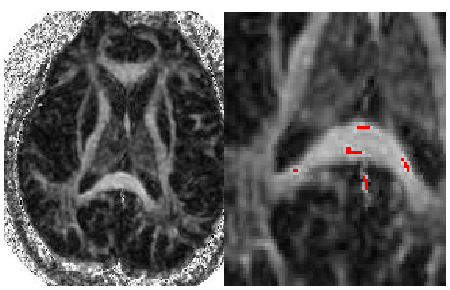
INTRODUCTION Inferences made in clinical applications will be influenced by the accuracy of the measurements of the diffusion tensor. Measurement noise can cause errors in the estimates of diffusivity and the calculated diffusion tensor measures. If the measurement errors are large enough, the estimated diffusivities can be negative and the fractional anisotropy value might be greater than unity in region of very high anisotropy. A method of constrained optimization was proposed in recent study by Wang et al. (1) to deal with the issue of positive-definiteness of the tensor matrix. In this study, we investigated the causes of negative diffusivity and fractional anisotropy anomalies. We also described and characterized a method of unconstrained optimization method which is effectively doing the same task as that of the constrained optimization method, that is, constraining the estimated diffusion tensor to be positive definite. This method uses the ideas of Cholesky factorization and it is evaluated using both measured human brain DTI data and Monte Carlo simulations.

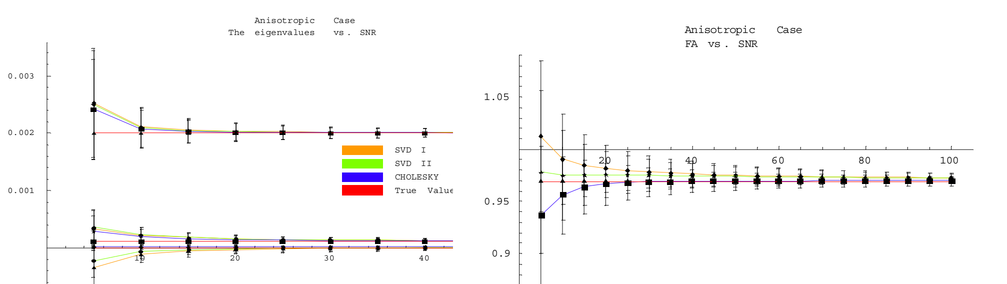
METHODS For each diffusion weighted image, we have $S_i = S_0 \exp(-b(\mathbf{g}^i)^t \cdot \mathbf{D} \cdot \mathbf{g}^i)$, with $i = 1,..., N$. Using the matrix method, it can be shown that $\mathbf{y} = \mathbf{X\beta}$, where $\mathbf{y} = [\ln(S_1/S_0) \ \cdots \ \ln(S_N/S_0)]^t$, $\boldsymbol{\beta} = [D_{xx} \ D_{yy} \ D_{zz} \ D_{xy} \ D_{yz} \ D_{xz}]^t$, and $\mathbf{X}$ is a matrix whose components are functions of the diffusion weighting b and components of the unit gradient direction vectors. Ordinary least squares can be used to obtain estimated diffusion tensors but the result obtained might not be positive definite. The necessary and sufficient condition for the tensor to be positive definite is that any of its principal submatrices has positive determinant (2). The proposed unconstrained optimization problem has the following form: $f(\boldsymbol{\rho}) = \frac{1}{2}\|\mathbf{y} - \mathbf{X} \cdot \mathbf{J}(\boldsymbol{\rho})\|^2$ where $\boldsymbol{\rho} = [R_0 \ R_1 \ R_2 \ R_3 \ R_4 \ R_5]^t$ and $\boldsymbol{\beta} = \mathbf{J}(\boldsymbol{\rho}) = [R_0^4 \ \ R_1^4 + R_3^2 \ \ R_2^4 + R_4^2 + R_5^2 \ \ R_0^2 R_3 \ \ R_1^2 R_4 + R_3 R_5 \ \ R_0^2 R_5]^t$. Thus, the constrained problem is reduced to an unconstrained function minimization with the transformation given above. This transformation is related to the Cholesky factorization. Furthermore, it can be shown that the solution of the constrained problem is equivalent to that of the least squares method when the tensor matrix is positive definite. Given the tensor matrix $\mathbf{D}$, FA can be written as $\sqrt{\left(\frac{3}{2}[1 - \frac{1}{3}\frac{Tr(\mathbf{D})^2}{Tr(\mathbf{D}^t\mathbf{D})}]\right)}$. The fractional anisotropy anomaly can be shown to imply the following relation $\lambda_1\lambda_2 + \lambda_1\lambda_3 + \lambda_2\lambda_3 < 0$. The method used for Monte Carlo simulation is similar to (3) and it is used to assess the statistical properties of the proposed method. Comparison with the least squares solution is made**.** There are three methods used in the comparison. The third method is very similar to the least squares method but with an additional condition, that is, the components of $\mathbf{y} = [\ln(S_1/S_0) \ \Lambda \ \ln(S_N/S_0)]^t$ will be bounded to be less than zero. This method will be denoted as SVD II in the Results section. The ordinary least squares method via SVD and the proposed method via Cholesky decomposition will both be denoted as SVD I and CHOLESKY, respectively. The $\boldsymbol{\beta}$ used in the simulation was {0.002,1.2e-4,1.5e-6,0,0,0} m^2/s.

RESULTS The set of encoding directions used in this experiment has twelve directions. The width, spacing, and amplitude of the diffusion gradient pulses were 25 msec, 36 msec, and 30 mT/m yielding a b value of 1113.91 sec/ mm^2. Other imaging parameters were TR = 4.68 sec, TE = 79.5 msec, field-of-view (FOV) = 240 × 240 mm^2, slice thickness = 4mm, and 3 NEX for averaging. Figure 1 is the FA map from human brain data, figure 2 is obtained from simulation data.



A B

FIG. 1(A) FA map (B) The magnified region of FA map. Areas in which the tensor matrix is not positive definite are indicated in red.



A B

FIG. 2.(A)This plot consists of the distribution of the estimated eigenvalues against SNR and (B) the estimated FA value against SNR by the three different methods of estimation.

DISCUSSION The aim of this study is to show that seemingly acceptable FA maps may have regions of negative diffusivity and to provide a simple method for solving this problem. The key factors of this issue are measurement noise, image distortion, either eddy-current-induced or subject motion, and the conflict of models in fitting the DTI tensor using the SVD method in regions with very high anisotropy. The data obtained via the proposed method showed that the problem of negative diffusivity can be corrected. The results, especially in the directionality of the major eigenvectors, are consistent with the SVD method. The simulation results showed that the proposed method produced less bias in eigenvalue estimation as well as the FA value estimation in the case of very high anisotropic diffusivities. The idea of Cholesky factorization and the shift of viewpoint in looking at this factorization as a type of coordinate transformation are keys to constructing the proposed method. We would like to note that the bias in eigenvalue estimates in Figure 2A is due to systematic sorting bias. This was pointed out by Pierpaoli and Basser (3). Figure 2B shows the presence of bias in FA estimates though this bias is not due to sorting but due to the way the FA is defined, i.e. its distributional property. The condition in which the FA value is greater than unity implies that the tensor matrix contains at least one but not more than two negative eigenvalues. Negative diffusivity does not imply that the FA is greater than unity.

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