The Cone of Uncertainty is Elliptical: Implications for DTI Tractography

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INTRODUCTION

The diffusion tensor is always measured in the presence of background noise. Within the framework of recently proposed methods of error propagation and of 1st-order matrix perturbation for DTI [1,2], one can easily characterize the noise induced variability of the estimated tensor itself and of tensor-derived quantities, scalar or vector. Of particular interest in tractography is the uncertainty of the eigenvectors or principal directions. With this end in view, the cone of uncertainty was proposed as a local measure of tract dispersion by Basser [3] and later used by Basser & Pajevic [4] and Jones [5] as a tool for visualizing and quantifying uncertainty along the fiber tract. The cone of uncertainty is not the only measure for quantifying tract dispersion, there is another approach that based on the perturbation method, which was proposed by Anderson [6] and used by Lazar [7,8]. None of these studies provided the key geometric object relating to the local measure of tract dispersion, which is the covariance matrix of the major eigenvector of the diffusion tensor. Here we present three different methods based on the error propagation framework [1], the 1st-order matrix perturbation method [2], and the dyadic formalism [3,9], to show that the local variability in the purported fiber direction is, in general, not described by a right circular cone of uncertainty but a right elliptical cone. Consequences of this finding are discussed.

METHODS

Error Propagation Method Based on the framework presented in [1], propagation of errors amounts to finding an appropriate "coordinate" transformation between covariance structures of interest. In DTI, the diffusion tensor can be reparametrized by the eigenvalues and the Euler angles in order to construct the covariance matrix of the major eigenvector of the diffusion tensor. The eigenvectors of this covariance matrix whose eigenvalues are nonzero are then the major and minor axes of the ellipse of the cone of uncertainty.

1st-order Matrix Perturbation Method The pioneering work of Hext [10] provided a method to construct the covariance structure of the major eigenvector based on the 1st-order matrix perturbation, see Eq[4.17] of [10], but the importance of this formula has not been pointed out in previous DTI studies. Here, we suggest Hext's approach as an alternative to the other two methods proposed here for constructing the elliptical cone of uncertainty.

Dyadic Product Formalism This formalism was proposed by Basser et al.[3] to overcome the problem of bias in computing sample mean of the eigenvector. Here, we show how the cone of uncertainty can be constructed from the average dyadics. Let $\{q_{11},\cdots,q_{1N}\}$ be a sample of major eigenvectors and let $\langle q_1 q_1^T \rangle = \frac{1}{N}\sum_{i=1}^{N} q_{1i} q_{1i}^T$ be the average dyadic [3]. Further, let the eigenvalue decomposition of the average dyadics be $\langle q_1 q_1^T \rangle = \sum_{i=1}^{3} \lambda_i \psi_i \psi_i^T$ where $\lambda_1 \geq \lambda_2 \geq \lambda_3$. Then, the covariance matrix of the mean major eigenvector can be shown to be $\frac{N}{N-1}\left(\lambda_2 \psi_2 \psi_2^T + \lambda_3 \psi_3 \psi_3^T\right)$.

RESULTS AND DISCUSSION

The analysis presented above shows that the cone of uncertainty has an elliptical not circular cross section. Particularly, the 1st-order matrix perturbation method shows that the cone of uncertainty is elliptical when the two smaller eigenvalues of the diffusion tensor are not equal to each other. Only when they are equal will the cone of uncertainty have the shape of a right circular cone. Similar observations can be made based on the other two methods discussed here. Figure 1B shows the cones of uncertainty constructed from a simulated human brain data based on the error propagation method [1] and the nonlinear least squares method [11]; Figure 1A is the FA map. The implications for DTI tractography are clear. Since the medium and minor eigenvalues of most tensor estimates in the brain are generally different [12], the axial symmetry of the tract dispersion is usually broken. In streamline based or probabilistic methods [13,14], the chance of deviating away from a tract in the direction along which uncertainty is low is less likely than from deviating away from the tract in the direction along which uncertainty is high. Thus, we would predict an asymmetric spread of tracts trajectories normal to the mean trajectory in which paths tending to meander along the direction with lower variance will remain closer to the mean tract whereas tracts meandering along the direction with higher variance will exhibit more dispersion and lie farther from the mean. Generalizing the approach given in [15], we can view the tractography process as a biased random walk in which there is anisotropic diffusion of the tract trajectory normal to the mean tract. In fact, such behavior appears to have been observed in bootstrap simulations of tracts generated using a streamline following method. In Lazar et al., white matter "axial asymmetry" (i.e., inequality of λ_2 and λ_3) caused anisotropic dispersion patterns in the estimated tract trajectories [8] but a theoretical explanation was not provided for this finding.

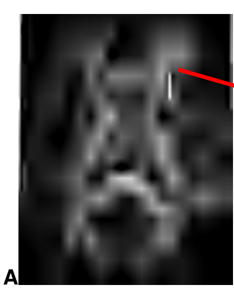
Figure 1A

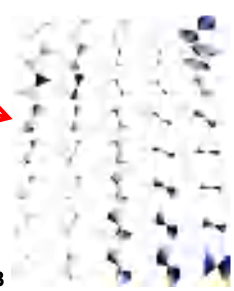
Figure 1B

CONCLUSION We have presented three independent and complementary methods to show that the cone of uncertainty is generally a right elliptical cone rather than a right circular cone. We showed that the key geometric object for constructing the local measure of tract dispersion is the covariance matrix of the major eigenvector. We have also provided the theoretical basis on which the observation of anistropic dispersion patterns in the estimated tract trajectories caused by axial asymmetric diffusion of water diffusion in white matter can now be explained.

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