Probabilistic Connectivity Mapping Using the Asymmetric Uncertainty of Diffusion Tensor Imaging

Y. Lu[1], Z. Ding[1], J. Qi[1], J. C. Gore[1], A. W. Anderson[1]
[1]Institute of Imaging Science, Vanderbilt University, Nashville, TN, United States

Introduction

Noise and partial volume averaging cause errors in estimating the major eigenvector, which is commonly used as the local fiber orientation, thus making fiber tracking uncertain. Previous studies [1,2] assumed a symmetrical distribution of the directional uncertainty and hence a univariate normal distribution of the fiber orientation probability. In the present study we used perturbation theory to analyze and compute more rigorously the directional uncertainty, which is generally distributed asymmetrically. The fiber orientation probability was modeled instead as a multivariate normal distribution. A stochastic streamline method and a new probabilistic measure were employed for fiber tracking and assessing the connectivity of the human brain.

Methods

1. *Calculation of the directional uncertainty*: According to perturbation theory, if the matrix elements of the perturbation matrix $\tilde{V} = \tilde{D} - \tilde{D}_0$ ($\tilde{D}$ — the measured diffusion tensor, $\tilde{D}_0$ — the true tensor) are small, the eigenvalues and eigenvectors can be expanded in a power series: $\lambda_i = \lambda_{i0}+\lambda_{i1}+\lambda_{i2}+ \dots$, $\mathbf{v}_i = \mathbf{v}_{i0}+\mathbf{v}_{i1}+\mathbf{v}_{i2}+ \dots$, i = 1,2,3. The first-order correction $\mathbf{v}_{11}$ to the major eigenvector $\mathbf{v}_1$ projected onto other two eigenvectors $\mathbf{v}_2$ and $\mathbf{v}_3$ is expressed as [3,4]: $\mathbf{v}_{10}^T\mathbf{v}_{11}=0$, $\mathbf{v}_{20}^T\mathbf{v}_{11} = \mathbf{v}_{20}^T\tilde{V}\,\mathbf{v}_{10}/(\lambda_{10}-\lambda_{20}) \approx \mathbf{v}_2^T\tilde{V}\,\mathbf{v}_1/(\lambda_1-\lambda_2)$, $\mathbf{v}_{30}^T\mathbf{v}_{11} = \mathbf{v}_{30}^T\tilde{V}\,\mathbf{v}_{10}/(\lambda_{10}-\lambda_{30}) \approx \mathbf{v}_3^T\tilde{V}\,\mathbf{v}_1/(\lambda_1-\lambda_3)$. The covariance matrix Σ of this kind of correction is then expressed as:$\Sigma = [(\mathbf{v}_{20}^T\mathbf{v}_{11})^2\,(\mathbf{v}_{20}^T\mathbf{v}_{11}).(\mathbf{v}_{30}^T\mathbf{v}_{11})\ ;\ (\mathbf{v}_{30}^T\mathbf{v}_{11}).(\mathbf{v}_{20}^T\mathbf{v}_{11})\ \ (\mathbf{v}_{30}^T\mathbf{v}_{11})^2]$. Using principal component analysis, the two principal axes of variance of this projection are σ_1 along $\mathbf{n}_1$ and σ_2 along $\mathbf{n}_2$ as shown in Figure 1.

2. *Modeling of the fiber orientation probability*: A multivariate normal function was used to model the fiber orientation probability at each voxel: $p(\mathbf{v}) = 1/(2|\Sigma|^2)*\exp[-0.5*(\mathbf{v}-\mathbf{v}_1)^T\,\Sigma^{-1}(\mathbf{v}-\mathbf{v}_1)]$, where $\mathbf{v}$ is a random unit vector, $\mathbf{v}_1$ is the major eigenvector, Σ is the 2-by-2 covariance matrix of the first-order correction to the major eigenvector, $(\mathbf{v}-\mathbf{v}_1)^T$ is the transpose of $(\mathbf{v}-\mathbf{v}_1)$, Σ^{-1} is the inverse of Σ , and $|\Sigma|$ is the determinant of Σ.

3. *Connectivity mapping*: a). Stochastic streamline fiber tracking: The fiber-tracking process is essentially a stochastic line propagation: $\mathbf{s}_{i+1} = \mathbf{s}_i + \mathbf{r}_i*\alpha$, where $\mathbf{s}_i$ is the position vector, i the discrete step index, α the step size, $\mathbf{r}_i$ is a random vector distributed with the probability $p(\mathbf{v})$.

b). Connectivity assessment: A new scalar measure was employed to assess the connectivity between a target point and the seed point. The connectivity is defined as the square root of the product of the two measures φ_1 and φ_2, where φ_1 is the averaged m^{th} root of the probability product of the m points of a tract, φ_2 is the number (n) of tracts passing through the target point divided by the total number of tracts (N). φ_1 shows the likelihood of a tract, and φ_2 indicates the likelihood that the target point lies on a tract, i.e.:

$$\varphi = \sqrt{\varphi_1 * \varphi_2} = \sqrt{\frac{1}{n}\sum_{j=1}^{n}\sqrt[m]{\prod_{i=1}^{m} p(i,j,v)} * \frac{n}{N}} = \sqrt{\frac{1}{N}\sum_{j=1}^{n}\sqrt[m]{\prod_{i=1}^{m} p(i,j,v)}}.$$

Given a seed point, for each iteration, a putative fiber pathway was tracked using certain termination criteria (e.g. large curvature, low FA value, etc.). After a number of iterations (5,000 in this study), a connectivity map between other points in the whole brain and the seed point was obtained.

4. *Synthetic data design*: The curves of a helix ($x = t_1\theta\cos\theta$, $y = t_1\theta\sin\theta$, $z = t_2\theta$, $\pi \le \theta \le 7\pi$, t_1 and t_2 are constants) were used to simulate fiber pathways. The tensor matrix of each point was axially asymmetric with FA = 0.9 ($\lambda_2 = 2\lambda_3$), the noise standard deviation (SD) = 0.05, the matrix size = 56*56*18.

5, *Data acquisition with in vivo data*: A human DTI data set of a healthy volunteer was acquired on a 3T GE MR scanner. The imaging field of view was 240*240mm^2. 30 slices of 4mm thick with a 256*256 matrix size were acquired at b-value = 1000s/mm^2 and the noise SD = 0.03.

Results

Figure 2 shows the profiles of the uncertainty in $\mathbf{v}_1$ for axially asymmetric tensor matrices ($\lambda_2 = 2\lambda_3$) at different FA values by simulation. It is seen that the uncertainty is larger at low FA than at high FA and this uncertainty is distributed asymmetrically. Figure 3 shows the putative fiber tracts and connectivity maps ($\varphi > 0.03$) tested with synthetic data (the seed point is shown as the blue arrow). It shows that this method can effectively reconstruct the simulated fiber pathways, and the connectivities between other points and the seed point are consistent with reality. Figure 4 demonstrates the putative fiber tracts and connectivity maps ($\varphi > 0.03$) derived from a seed point in the corpus callosum (shown as the blue arrow) of the in vivo human data. It clearly indicates the fiber bundles of the corpus callosum pass through the seed point and branch out at the optic radiation (shown as the red circle).

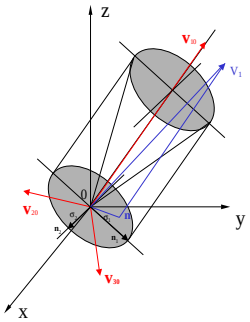

Fig.1. The projection of the uncertainty of the major eigenvector $\mathbf{v}_1$ on the plane of $\mathbf{v}_2$ and $\mathbf{v}_3$

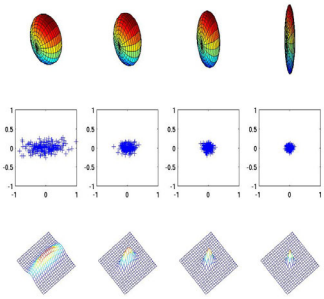

Fig.2. Simulation results. From left to right: FA = 0.6~0.9. Top row: the shape of tensor matrices; middle row: the distribution of major eigenvectors in the plane of $\mathbf{v}_2$ and $\mathbf{v}_3$; bottom row: the profiles of fiber orientation probability

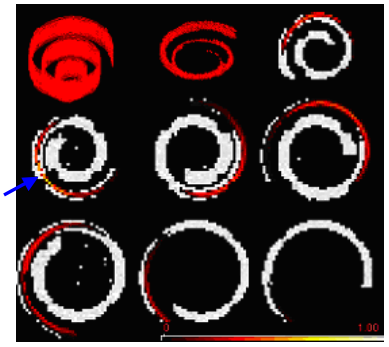

Fig.3. Results with synthetic data. From start to end, curves of the helix, putative fibers and connectivity maps at axial slices overlaid on FA maps. The color scale shows the degree of connectivity.

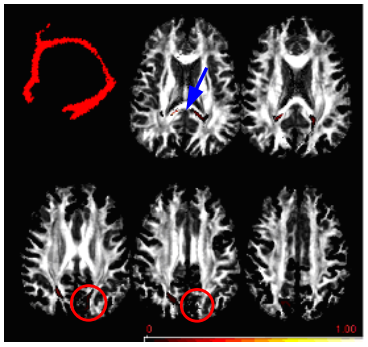

Fig.4. Results with the in vivo human data. From start to end, the putative fibers, the connectivity maps at axial slices overlaid on FA maps. The color scale shows the degree of connectivity

Discussion and conclusion

This study provides a promising new method for anatomical connectivity mapping of the human brain. More realistic models to describe the directional uncertainty and fiber orientation probability are under investigation to further improve the performance of the method. The integration with functional connectivity is also considered to provide more insight of the brain integrity.

References [1] Jones DK., MRM 2003:49:7–12. [2] Parker GJM, et al., JMRI 2003:18:242–254.
[3] Anderson AW, MRM 2001:46:1174–1188. [4] Basser PJ, Proc. ISMRM 1997:1740.