Patterns of White Matter Tractography Dispersion in the Human Brain: Relation to White Matter Diffusion Properties

M. Lazar[1], A. L. Alexander[1,2]

[1]Waisman Center, University of Wisconsin, Madison, WI, United States, [2]Medical Physics, University of Wisconsin, Madison, WI, United States

Introduction: White matter tractography estimates pathways of connectivity between different brain regions from the directional continuity patterns in the three-dimensional diffusion tensor field of the human brain. The precision of a connectivity pathway is sensitive to the DTI measurement noise, which can lead to errors in the fiber direction estimates (1, 2). Theoretical studies and simulations showed that the uncertainty associated with a fiber tracking result may be characterized by a two-dimensional distribution with standard deviations, s_1 and s_2, which depend inversely proportional on the eigenvalue contrasts $\Delta\lambda_{12}=\lambda_1-\lambda_2$ and $\Delta\lambda_{13}=\lambda_1-\lambda_3$, and principal axes, which are estimated by the diffusion tensor medium and minor eigenvectors ($\mathbf{e}_2$ and $\mathbf{e}_3$) (1,2). These dependences imply that the dispersion pattern of a tract is anisotropic (i.e., $s_1>s_2$) in white matter structures characterized by cylindrically asymmetrical diffusion (i.e., $\lambda_2>\lambda_3$) and dependent on $\mathbf{e}_2$ and $\mathbf{e}_3$orientations. However, these relationships between the diffusion properties of a tract and associated tract dispersion have not been demonstrated in the human brain. Previous studies (3,4) showed that most of the brain white matter is characterized by cylindrical asymmetry. This cylindrical asymmetry is associated with tract specific orientational patterns of secondary ($\mathbf{e}_2$) and tertiary ($\mathbf{e}_3$) diffusivity. The goal of this study was to investigate the relationship between the orientational patterns of white matter tractography dispersion and orientational patterns of medium and minor tensor eigenvectors in measured diffusion tensor data in the human brain.

Methods: Diffusion Tensor Imaging: DTI images for two subjects were obtained on a 3T MRI scanner using a cardiac-gated single-shot spin-echo EPI pulse sequence with diffusion-weighting gradients applied in 12 uniform distributed encoding directions. The acquisition for each encoding direction was repeated eight times. Thirty-nine axial slices were acquired. The original voxel size was 0.94x0.94x3 mm^3. The total imaging time was around 30 minutes. Image misregistration from motion and eddy current distortion was corrected using a 2D affine registration algorithm in AIR (5). Field map correction was subsequently applied to correct for EPI distortions resulting from B_0 inhomogeneities. White Matter Tractography: Fiber trajectories were estimated using the tensorline algorithm (6). Diffusion properties such as eigenvalues contrast and tensor eigenvectors along each trajectory were recorded. A bootstrap method (7) was used to generate the fiber distributions associated with the trajectories of interest. For each seed point, 1000 tract estimates were generated. Tractography dispersion was characterized using the principal directions and standard deviations of the two-dimensional distribution of trajectories in planes orthogonal to the average tract direction.

Results: The effect of the cylindrically asymmetric diffusion on the WMT dispersion was examined for trajectories of corpus callosum, cingulum, and arcuate fasciculus. Representative results are presented here. Tract distributions of a corpus callosum and a cingulum trajectory are shown in Figures 1a and 1b, respectively. The tract distribution in planes perpendicular to the average tract direction was characterized by its standard deviations (s_1 and s_2) and principal directions in the laboratory frame (ξ_1 and ξ_2), which are orthogonal to the local tract direction, ξ_1. Such a distribution of trajectories is displayed in Figure 1c for the corpus callosum pathway (approximate position of the plane shown in (a)). The eigenvalue contrasts and the eigenvectors orientations for each trajectory are plotted in Figures 2a and b. The corresponding standard deviations, s_1 and s_2, and principal axes ξ_1 and ξ_2 describing the dispersion distribution are shown in Figures 2c and d. Vector orientations along tract trajectories are given by the color of the curves, using a RGB color mapping. Generally, for all trajectories, similar orientational patterns of the tract dispersion and secondary and tertiary diffusivity are apparent. For the corpus callosum trajectory, the largest dispersion occurs for most of the trajectory in the anterior-posterior direction, which is also the direction of $\mathbf{e}_2$. The smallest dispersion occurs in the superior-inferior direction for the medial region of the tract, and from right to left (R/L) in the lateral branches, roughly matching $\mathbf{e}_3$ orientation. For the cingulum bundle, the largest dispersion occurs primarily R/L, similar to $\mathbf{e}_2$ orientation. Note that the change in orientation of $\mathbf{e}_2$ and $\mathbf{e}_3$ in the anterior region of the tract is associated with similar change in ξ_1 and ξ_2.

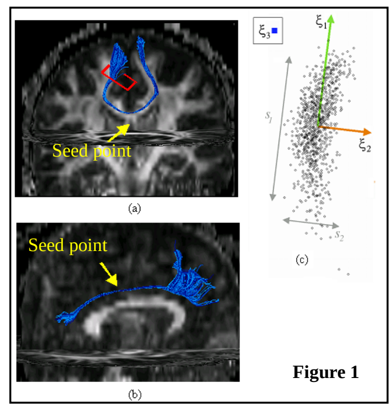

Figure 1

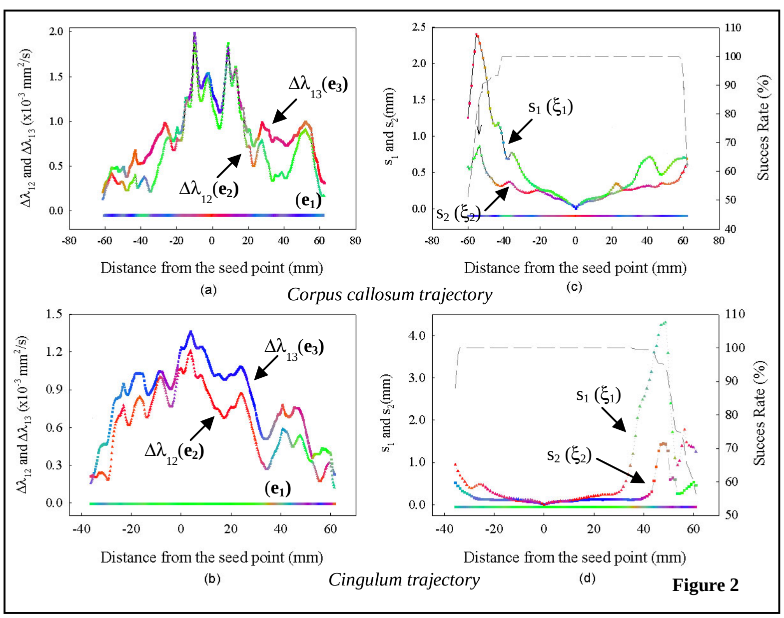

Figure 2

Discussion: One of the principal applications of DTI is estimating white matter connectivity patterns in the brain using fiber tractography. A major WMT challenge is that measurement noise and partial voluming may determine anatomically plausible but erroneous fiber trajectories and potentially lead to artifactual connectivity patterns (1, 2). Thus, the assessment of confidence intervals for WMT is essential for the proper interpretation of the results. This study demonstrates that specific patterns of orthogonal diffusivity determine specific patterns of fiber tract dispersion in white matter tractography. It is important to point out that the orthogonal diffusivity patterns are only one of the factors that influence the dispersion patterns of WMT. These patterns are also influenced by tensor field inhomogeneities (2), such as field divergence or convergence, which in some of the brain regions may dominate the shape of the tract noise-induced distribution.

Conclusion: In relatively homogeneous, cylindrically asymmetric white matter regions of the brain, white matter tractography dispersion is anisotropic, with the largest dispersion occurring in the direction of the tensor medium eigenvector and the smallest dispersion occurring in the direction of the tensor minor eigenvector. This information may be used to qualitatively estimate the dispersion patterns that are to be expected in fiber tracking (e.g., by using color maps of the medium and minor tensor eigenvectors (4)).

References: 1. Lazar M and Alexander AL. *Neuroimage* 2003; 20:1140-1153; **2.** Anderson AW. *Magn Reson Med.* 2001;46:1174-1188; **3.**Wiegell MR et al. *Radiology* 2000;217:897-903; **4.** Lazar M and Alexander AL. *Proc. ISMRM* 2004, p. 1216; **5.** Woods et al. J Comp Ass Tom 1998;22:141:154; **6.** Lazar M et al. *HBM* 2003;18:306-321; **7.** Lazar M and Alexander AL. *Neuroimage* 2004, in press.