Method for Parameterizing Clinical Diffusion Measures Along Probabilistic Fiber Pathways

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Introduction

Tissue microstructure measurements specific to a tractography-defined white matter fascicle may serve as a clinically relevant measure in multiple sclerosis (MS) (1). One problem is substantial variability along a fascicle, particularly if it includes regions near cortex and deeper in the brain. We present a methodology for segmenting a fascicle identified by probabilistic tractography and demonstrate its use in the transcallosal motor pathway of healthy subjects and MS patients. Using this method, tissue microstructure measurements can be made in a piecewise manner in order to reduce the overall variance and improve sensitivity to local differences.

Algorithm

Probabilistic tractography generates maps of track counts that can be interpreted as anatomical connectivity (AC). Figure 1A shows AC between voxels in a coronal slice (red-yellow) and bilateral hand motor cortices (not shown). The algorithm (fig. 1B) defines a curve along the high-intensity "center track" and parameterizes tissue microstructure along the center track. First, an imaging plane (P1) and its neighbor (P2) are selected. The centroid of AC in each plane (C1, C2) and the vector between these points are calculated. The vector is extended (red arrow) to define a new plane (P3). The vector from the centroid of P2 to the centroid of P3 (C2, C3) is extended and the process repeated. The centroids define the center track (fig. 1C). Values of tissue microstructure are calculated in the plane associated with each centroid and weighted by AC. To avoid overlap due to intersecting planes and ambiguity from multimodal connectivity patterns, calculations are limited to a user-defined radius around the tip (T) of each extended vector.

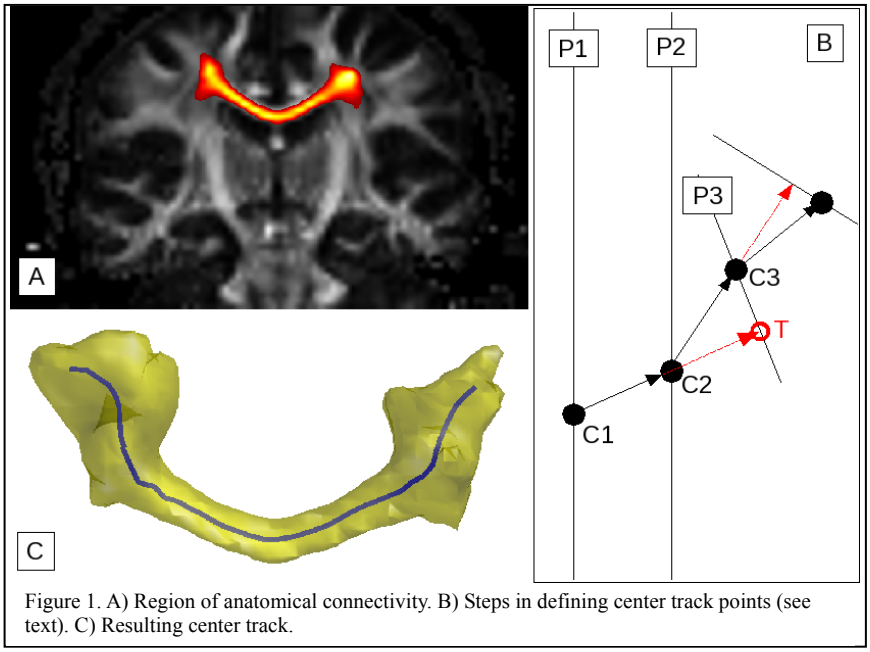

Figure 1. A) Region of anatomical connectivity. B) Steps in defining center track points (see text). C) Resulting center track.

Methods

Eighteen MS patients and 18 age and sex-matched controls were examined in a protocol approved by the local institutional review board. Anatomical T1-MPRAGE, fMRI response to bilateral finger-tapping and HARDI (2) were acquired on a Siemens TIM Trio (Siemens Medical Systems, Erlangen). Probabilistic tractography between bilateral hand motor cortices mapped the transcallosal motor pathway (1). The number of tracks in each voxel was defined as AC to the motor cortices. Longitudinal diffusivity (LD) and transverse diffusivity (TD) were calculated from the diffusion tensor (3) in each voxel. LD and TD have been found to relate to axonal integrity and demyelination (4) and are therefore used to quantify tissue integrity. A white matter mask, generated from the anatomical image and coregistered using FSL (5), was applied to exclude diffusivity measures from CSF and gray matter. The center track algorithm was implemented in MATLAB (the Mathworks, Natick). The center track initiated at the midsagittal slice and propagated to the right, and the third and fourth points of the right branch were used to initialize the left. The user-defined radius was set to 10mm. Track counts, LD and TD were calculated in each plane by trilinear interpolation. Weighted means of LD and TD in the plane associated with each centroid were grouped into three regions defined by anatomical landmarks: corpus callosum and the region from corpus callosum to left and right superior corona radiata. Values from patients and controls in each of the three regions and all regions together were compared by a t-test with a significance level of p=0.05.

Results

A center track was identified in all controls and all but one patient. A general trend of higher variance in the corpus callosum was found for LD and TD. Table 1 summarizes TD in patients and controls. Although the variances tended to be higher in the corpus callosum, differences in values were higher there, leading to a significant difference in TD ($p < 0.03$). No differences in LD were significant.

	PATIENTS	CONTROLS	p
RIGHT	0.57 (0.07)	0.55 (0.03)	0.35
CC	0.62 (0.14)	0.54 (0.05)	0.03
LEFT	0.57 (0.14)	0.54 (0.03)	0.33
ALL	0.59 (0.12)	0.54 (0.03)	0.1

Table 1. Mean (standard deviation) of TD (10^{-3}mm^2/sec) in entire pathway (ALL), corpus callosum (CC) and regions from CC to left and right superior corona radiata (LEFT, RIGHT).

Discussion

The algorithm presented is conceptually simple and may be used in conjunction with nearly any probabilistic tractography method. For the case under consideration, segmenting the white matter pathway reduces variability with commensurate increase in statistical power. As opposed to atlas-based approaches, this method uses a region defined by a subject-specific mapping of white matter fascicles. This subject-specific approach is important when considering patients with substantial atrophy. Although the algorithm was designed to map pathways with an intensity maximum with the topology of a simple curve, the generic concept of segmenting white matter pathways according to the track count intensity may be extended to more complicated cases.

References: 1. Lowe, M.J. et al. Neuroimage 32, 1127-1133 (2006).
2. Tuch, D.S. et al. Magn Reson Med 48, 577-582 (2002).
3. Basser, P.J. et al. Biophys. J 66, 259-267 (1994).
4. Budde, M.D. et al. Magn Reson Med 57, 688-695 (2007).
5. Smith, S.M. et al. Neuroimage 23 Suppl 1, S208-219 (2004).