Quantitative Tract-of-Interest Metrics for White Matter Integrity Based on Diffusion Tensor MRI Data

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Introduction We present new quantitative diffusion-tensor imaging (DTI) tractography-based metrics for assessing group differences cerebral white matter health and to conduct an initial validation of the new metrics in elderly normal controls (NC) and patients with vascular cognitive impairment (VCI), disorder characterized by T2 white matter hyperintensities.

Background: The majority of published clinical research studies using DTI have relied on region-of-interest analysis of scalar maps of anisotropy and diffusivity parameters (e.g., fractional anisotropy, mean diffusivity, respectively). ROI approaches are generally limited by the absence of directional information in the scalar parameter maps. DTI tractography provides three-dimensional models that are thought to be representative of the underlying white matter pathways.

Quantitative tractography methods can represent complex 3D geometric and integrity characteristics of white matter features with scalar measurements so that the microstructural integrity of entire tracts of interest (TOI) can be assessed. This approach has potential for helping to assess the cognitive and functional impact of disease-related injury to specific white matter pathways. However, few studies have applied quantitative tractography methods to study clinical populations. We present new quantitative tractography metrics that may have considerable utility for identifying the microstructural integrity of whole-brain white matter and specific TOI.

Method: Our quantitative tractography metrics are based on prior work in our lab in which whole-brain streamtube models (Zhang et al., 2003) thought to represent underlying white matter fibers were generated for each individual DTI dataset in our sample. We calculated five metrics from two tracts of interest (TOIs), one containing all paths in the brain and the other containing interhemispheric paths. The metrics were: 1) total length (TL, i.e., the summed total length of all streamtubes); 2) weighted total length (WTL, i.e., TL weighted for average linear anisotropy); 3) normalized total length (NTL, i.e., TL normalized by intracranial volume); 4) normalized total weighted length (NTWL, i.e., WTL normalized by intracranial volume); and 5) the number of streamtubes in the TOI (NS). The metrics demonstrate good stability ($\leq$ 2% variability) across multiple iterations of the streamtube models. We then compared these metrics in NC (n=12) and non-demented VCI subjects (n=6).

Results: The VCI group had significantly lower values ($p<.05$) than the NC group on all four length metrics with a trend in terms of the number of streamtubes (see Table 1). A similar, but somewhat less robust finding was obtained when examining the interhemispheric fibers (see Figure 1). Normalized length metrics were significantly correlated with cognitive measures known to be impacted by white matter abnormalities (i.e., executive functioning, processing speed) but they were not significantly correlated with cognitive measures thought to be sensitive to cortical disease (i.e., confrontational naming).

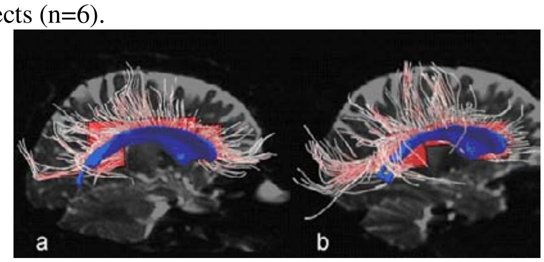

Figure 1: Interhemispheric streamtubes passing through the corpus callosum in a) a 61-year old NC and b) a 59-year-old patient with VCI. Lateral ventricles in blue.

Conclusions: These results provide preliminary evidence that these new quantitative DTI tractography metrics hold promise for examining group differences in white matter health. The correlations with cognitive test results suggest that the metrics are capturing clinically-relevant information about cognitive function. The metrics may provide a measure of white matter integrity that includes both normal- and abnormal-appearing white matter on conventional imaging. Moreover, these metrics may provide a method for tracking longitudinal changes in white matter that circumvents many of the difficulties inherent in registering DTI data collected at different time points.

Table 1: Length and number of streamtubes in whole-brain models NC vs. VCI.

	NC	VCI	F(1,15)	p
NS	5032 ± 693	4520 ± 1053	4.425	.053
TL (m)	119.5 ± 21.4	90.7 ± 17.0	15.32	.001
TWL (m)	29.3 ± 5.9	19.9 ± 3.3	16.50	.001
NTL (m)	121.6 ± 22.9	91.6 ± 23.7	17.61	.001
NTWL (m)	29.8 ± 6.1	20.2 ± 5.2	18.51	.001

References: Zhang, S., Demiralp, C., and Laidlaw, D. (2003). Visualizing diffusion tensor MR images using streamtubes and streamsurfaces. IEEE Transactions on Visualization and Computer Graphics *9*, 454-462