Efficient Mapping of Diffusion Tensor Distribution in a Live Human Brain

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Synopsis

Electron microscopy of nervous tissue reveals a multitude of compartments separated by plasma membranes where the diffusion of water may be hindered. Diffusion tensor distribution (DTD) MRI assumes each voxel consists of an ensemble of diffusion tensors described by a tensor variate probability distribution function (i.e., DTD). We assume the DTD to be the maximum entropy normal tensor variate distribution (NTVD) whose samples are constrained to be positive definite (CNTVD). A family of metrics and glyphs which aim to disentangle the size, shape, and orientation heterogeneities of diffusion processes present within a voxel is derived from the estimated DTD. In this study, we show in vivo results obtained in the living human brain using a new DTD framework on the Connectome scanner using 300 mT/m gradients and a novel time efficient and concomitant field free pulse sequence which allowed shorter echo time for a given b-value.

Methods

Assuming Gaussian diffusion in microscopic water pools within a voxel, the MR signal is given by the Laplace transform of DTD which is approximated using a Monte-Carlo method by drawing samples from CNTVD with a given second order mean and fourth-order covariance tensors. This approximation is used to estimate the CNTVD moments by iteratively fitting the acquired data to a multitude of models in decreasing order of parsimony from DTI to DTD using a nonlinear least-squares routine. The symmetric and asymmetric parts of the estimated CNTVD covariance tensor are visualized using glyphs to reveal the kurtosis and micro-structural information captured by higher rank b-tensors respectively.

Results and Discussion

The µODF glyphs shown in Figure 3 accurately captures the splaying and crossing fibers of corona radiata and internal capsule, respectively. The reduction in FA caused by the complex fiber configurations in these and other regions are recovered in the µFA map and described using large orientation and shape heterogeneities in the Vshape and Vorient maps shown in Figure 4. The size differences within fiber tracts were revealed in the Vsize map which were also highlighted in the ADC skewness map in Figure 5. This may be reflective of a skewed axon diameter distribution (ADD) in white matter. The asymmetric part of the covariance tensor is non-vanishing in many parts of the brain highlighting the need for multiple diffusion encoding measurements to capture the microstructure beyond what diffusion kurtosis imaging (DKI) can provide.
It should however be noted that the DTD model found no significant heterogeneity in the corpus callosum despite the axon diameter differences reported in other studies. This is likely due to the microvoxel size in DTD set by the gradient strength (~12 μm) being about an order of magnitude larger than the diameters of axons being probed (<1 μm).

Conclusion
A new experimental design and analysis technique is introduced to make an unbiased estimate of a DTD in each voxel, which is assumed to be the maximum entropy CNTVD. Various scalar parameters and glyphs are introduced to disentangle size, shape, and orientation heterogeneities within a voxel. This method was able to capture heterogeneity present within normal brain tissue and represents a significant advance in the study anisotropy and heterogeneity in brain microstructure.

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References

Figures
Diagram of the new time efficient and concomitant field free multi-band dPFG EPI-MRI pulse sequence used for DTD data acquisition. The two pairs of diffusion gradient pulses with equal durations, δ, are sandwiched on either side of the 180° RF pulse and separated by the diffusion time, Δ. The amplitudes and orientations of the two independent gradient pulses were calculated numerically to yield the desired rank-1 and rank-2 b-tensors.
Experimental design for DTD MRI using 216 diffusion encoding b-tensors, shown using ellipsoids (top left), with uniform distributions of b-values (top right), shapes, characterized by the ratio of the two non-zero eigenvalues of rank-2 b-matrix (bottom left), and orientations (bottom right).

Orientation dispersion measured in the brain described by comparing the macro and micro ODFs in select regions of interest highlighted in the direction encoded color (DEC) and $S_0$ maps. The kurtosis tensor obtained from the symmetrized form of the covariance tensor and the extent of microscopic anisotropy information captured by the higher rank b-tensors given by the asymmetric part of the covariance tensor are shown using glyphs. The spaying and crossing fibers in the corona radiata and internal capsule absent in the macro ODF is correctly captured by the micro-ODF glyphs.

In vivo DTD results with the human brain showing the estimated parametric maps. Several regions of interest (ROIs) were provided to highlight the new microstructural information provided by DTD MRI. The reduction in FA in the blue and red ovals with complex fiber configurations are recovered in the mFA map and identified as regions with high orientation and shape heterogeneities in the $V_{shape}$ and
V\textsubscript{one} maps. The size heterogeneity in highly aligned white matter tract shown by the yellow oval is revealed in the V\textsubscript{size} map.

Map of the distribution of apparent diffusion coefficient (ADC) quantified by its first four moments. The skewed fiber diameter distribution in several white matter tracts highlighted by yellow arrows is identified on the standard deviation and skewness maps.