Novel Measure of Fiber Integrity based on Q- Ball Imaging and the Tensor Distribution Function avoids Problems with Fractional Anisotropy Measures

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Introduction: Diffusion tensor imaging (DTI) is powerful tool for investigating white matter micro-structure and fiber integrity, but it cannot resolve more complex diffusion geometries, such as fiber crossing. To tackle this, we recently introduced the tensor distribution function (TDF) [1] to reconstruct multiple underlying fibers per voxel, from high-angular resolution diffusion images (HARDI). TDFs represent the diffusion profile as a probabilistic mixture of tensors. Here we argue that white matter integrity, measured using the fractional anisotropy (FA) derived from standard DTI, is an imprecise concept as it is influenced by the number of dominant fiber directions, the anisotropy of each component fiber, and partial volume effects from neighboring gray matter. DTI-derived FA correlated poorly with true individual fiber anisotropy, computed from a more precise TDF model of the underlying fibers. FA is incorrectly diminished when fibers cross, and may be sub-optimal for detecting developmental or disease processes that affect myelination. We show how to compute FA more accurately from a full diffusion gradient set (Figure 1), by (1) directly fitting a unit-mass density on the full 6D manifold of symmetric positive definite tensors (Eqns. 2-3), (2) deriving a tensor orientation density (TOD; Eqn. 4), and (3) computing TDF-averaged eigenvalues using the TOD as a weighting function (Eqns. 5-6); (4) deriving FA from the weighted eigenvalues (Eqn. 7).

Methods: First we defined DTI-FA based on the diffusion tensor eigenvalues ($\lambda 1$, $\lambda 2$, and $\lambda 3$), estimated using MedINRIA software (Figure 1, Eqn. 1). Then, we computed the TDF at each point as in [1]; to allow numerical optimization in 4D rather than 6D, we assumed fiber tracts were cylindrical with two equal smallest eigenvalues, excluding planar-shaped tensors, i.e., $\lambda 1 \geqslant \lambda 2 = \lambda 3$ for each individual tensor. From a tensor distribution function P, we computed each fiber's eigenvalues from their expected values. To more accurately assess anisotropy, we defined two new measures in the TDF framework: (1) FA-1, calculated from the eigenvalues of the first dominant fiber, and (2) TDF-FA, computed by voxelwise TDF-averaged eigenvalues (see Figure 1 for formulae).

Results: TDFs were computed from 94-direction human brain HARDI data (4 Tesla; 1.8x1.8x2mm voxels; b=1159s/mm2). As more than one fiber direction may be present, we examined how well conventionally-defined DTI-FA correlated with either the dominant fiber's FA (FA-1) or the overall TDF-averaged FA (TDF-FA). Correlations were only moderate (0.431 for DTI-FA vs. TDF-FA, 0.252 for DTI-FA vs. FA-1) when both gray and white matter were included; correlations were much weaker (0.206 and 0.294 respectively) when we only considered the white matter. Even so, the two more precise measures, TDF-FA and FA-1, correlated well with each other (0.893 for GM and WM, 0.835 for WM only).

Conclusions: In white matter, DTI-FA, as it is commonly defined based on the single-tensor model, correlates poorly with the true individual fiber anisotropy. Our improved TDF-FA measures exploit the full information in the diffusion gradient set. To maximize statistical power, DTI researchers may benefit from our framework which assesses the number of dominant fiber directions in each voxel, their corresponding eigenvalues, and anisotropy. The TDF framework is ideal for achieving these goals.

References: [1]. Leow AD et al. *The Tensor Distribution Function*, Magnetic Resonance in Medicine 2008, in press.

$$\begin{cases} DTI-FA=\sqrt{\frac{3}{2}\left(\frac{(\lambda_1-<\lambda>)^2+(\lambda_2-<\lambda>)^2+(\lambda_3-<\lambda>)^2}{\lambda_1^2+\lambda_2^2+\lambda_3^2}\right)} \\ <\lambda>=\frac{\lambda_1+\lambda_2+\lambda_3}{3} \end{cases} \quad \text{Eq(1)}$$

$$S_{calculated}(q)=\int_{D\in\overline{D}} P(D)\exp(-tq^tDq)dD \quad \text{Eq(2)}$$

$$P^*=argmin_p\sum_i(S_{obs}(q_i)-S_{calculated}(q_i))^2 \quad \text{Eq(3)}$$

$$TOD(\theta)=\int_\lambda P(D(\lambda,\theta))d\lambda \quad \text{Eq(4)}$$

$$\begin{cases} \lambda_1^1=\frac{\int P(D(\theta^*,\lambda))\lambda_1 d\lambda}{\int P(D(\theta^*,\lambda))d\lambda} \\ \lambda_2^1=\frac{\int P\left(D(\theta^*,\lambda)\right)\lambda_2 d\lambda}{\int P(D(\theta^*,\lambda))d\lambda} \\ \theta^*=argmax(TOD(\theta)) \end{cases} \quad \text{Eq(5)}$$

$$\begin{cases} \overline{\lambda_1}=\int_{\mathrm{D}\in\mathrm{D}} \mathrm{P}(\mathrm{D})\lambda_1 \mathrm{dD} \\ \overline{\lambda_2}=\int_{\mathrm{D}\in\mathrm{D}} \mathrm{P}(\mathrm{D})\lambda_2 \mathrm{dD} \end{cases} \quad \text{Eq(6)}$$

$$\begin{cases} FA-1=\sqrt{\frac{3}{2}\left(\frac{\left(\lambda_1^1-<\lambda^1>\right)^2+\left(\lambda_2^1-<\lambda^1>\right)^2+\left(\lambda_2^1-<\lambda^1>\right)^2}{{\lambda_1^1}^2+{\lambda_2^1}^2+{\lambda_2^1}^2}\right)} \\ <\lambda^1>=\frac{\lambda_1^1+\lambda_2^1+\lambda_2^1}{3} \\ TDF-FA=\sqrt{\frac{3}{2}\left(\frac{(\overline{\lambda_1}-<\bar{\lambda}>)^2+(\overline{\lambda_2}-<\bar{\lambda}>)^2+(\overline{\lambda_2}-<\bar{\lambda}>)^2}{\overline{\lambda_1}^2+\overline{\lambda_2}^2+\overline{\lambda_2}^2}\right)} \\ <\bar{\lambda}>=\frac{\overline{\lambda_1}+\overline{\lambda_2}+\overline{\lambda_2}}{3} \end{cases} \quad \text{Eq(7)}$$