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Testing for and Exploiting Microstructural Symmetry to Characterize Tissues via Diffusion *Tensor* MRI

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INTRODUCTION

In Diffusion Tensor MRI, a diffusion tensor, $\underline{D}$, that characterizes molecular diffusive transport, is estimated in each voxel (1). In some anisotropic tissues (e.g., in nerve white matter (2, 3) and in skeletal muscle (4, 5)), it has been explicitly assumed that diffusive transport is cylindrically symmetric (i.e., the diffusion ellipsoid is a surface of revolution about the fiber-tract axis). In asymmetric anisotropic tissues, assuming this *a priori* (while reducing the number of independent elements of $\underline{D}$ from six to four), is unjustified, whereas in isotropic tissues, it requires us to characterize four diffusive transport parameters when a single scalar diffusion coefficient would suffice.

We propose a) determining the degree of symmetry of diffusive transport in each voxel *a posteriori*, rather than assuming it *a priori*, and b) using this quantity as a novel MRI parameter indicating tissue structure and/or physiologic state. Specifically, we show how to test the hypotheses of cylindrical symmetry (transverse isotropy) and spherical symmetry (isotropy) sequentially in each voxel using asymmetric, cylindrically symmetric, and isotropic models of diffusive transport.

METHOD

To test feasibility, one can simulate a series of DTI experiments, generating sets of synthetic DWIs with different levels of Gaussian background noise (6) of media whose diffusion tensors are representative of asymmetric, cylindrically symmetric, and isotropic tissues. For each DTI "experiment" we estimate the degree of diffusion symmetry in each voxel. We use the same experimental parameters in Monte Carlo simulations as in our previous *in vivo* monkey studies (7): 14 (128 x 256) axial DW 2D-FT spin-echo images with diffusion gradients applied in 7 non-collinear, oblique directions (8). Imaging parameters are: TE=80ms, Δ=40ms, δ=19ms, TR=2sec, na=2, FOV=80mm, st=2mm, max. gradient=3.25 G/cm.

To treat background noise explicitly, we introduce a new non-linear relationship between the synthesized, noisy T_2-weighted signals, $A(\underline{b})$, each element of the diffusion tensor, D_{ij}; the b-matrix calculated for each DWI sequence (9), b_{ij}; and the r.m.s. background noise level, N:

$$A(\mathbf{b}) = \sqrt{A(0)^2 \exp\left(-2\sum_{i=1}^{3}\sum_{j=1}^{3} b_{ij}D_{ij}\right) + N^2} \qquad [1]$$

In general, Eq [1] contains eight independent parameters to estimate--six independent diffusion tensor elements: D_{xx}, D_{xy}, D_{xz}, D_{yy}, D_{yz}, and D_{zz}, as well as A(0) and N. Assuming cylindrical symmetry, these six D_{ij} can be rewritten in terms of four independent parameters: $D_\perp$, $D_\parallel$, ϕ, θ (see (2)) as well as A(0) and N. Finally, assuming diffusion isotropy, Eq [1] reduces to a three-parameter model:

$$A(\mathbf{b}) = \sqrt{A(0)^2 \exp\left(-2\left(b_{xx}+b_{yy}+b_{zz}\right)D\right) + N^2} \qquad [2]$$

where the D is the scalar diffusivity.

From the synthesized DWIs, all free parameters can be estimated in each voxel using the Levenberg-Marquardt algorithm, and optimal χ^2 and F-statistics are calculated for each model. To test the null hypothesis of cylindrical symmetry, we estimate $\underline{D}$ using this constraint. If the F-test tells us to reject this hypothesis for the given background noise level (10), we retain the asymmetric diffusion tensor representation, Eq [1]. Otherwise, we test the second null hypothesis of diffusion isotropy. We then estimate D using Eq [2]. If the F-test again tells us to reject this hypothesis, we retain the cylindrically symmetric model of diffusion in that voxel. Otherwise, we adopt the simple isotropic model.

RESULTS and DISCUSSION

It is often possible to estimate N independently in real DWIs by using measurements of $A(\underline{b})$ in regions in which there are no spin-labeled species (e.g., outside the head). This can reduce the number of free parameters to estimate by one from a series of DWIs.

In isotropic tissues, we expect that the effective scalar diffusivity, D, estimated from Eq [2] equals $\langle D \rangle$ = Trace($\underline{D}$)/3, estimated from Eq [1], although the variance of D should be significantly smaller than that of Trace($\underline{D}$)/3. In general, using fewest independent parameters that can be justified always reduces parameter uncertainty. Also, quantities derived from these estimated parameters (e.g., anisotropy ratios) will also be less biased and noisy.

Microstructural characteristics such as a non-uniform distribution of fiber-tract directions in a voxel, and partial volume contamination, as well as measurement noise tend to make asymmetric media appear more symmetric. In addition, decreasing SNR will always favor models in which diffusion appears more symmetric (i.e., isotropic).

Finally, it is informative to produce color plots of the degree of diffusion anisotropy in each voxel in which Red, Green, and Blue correspond to 2, 1, and 0 independent axes of diffusion symmetry, respectively.

CONCLUSION

The degree of symmetry of diffusive transport is a new MRI feature that we estimate in each voxel and use to elucidate and monitor structural and/or physiological characteristics of tissues in health and disease. We propose that in each voxel, translational diffusion be described by the simplest model (i.e., one having the fewest free parameters) for the experimental conditions (in particular, the background noise) and the experimental design (e.g., number of acquisitions, range of b-matrix values, ...). These also limit the degree of diffusion asymmetry we are able to ascertain in any DT-MRI experiment. Issues of experimental noise and design must be carefully considered when deciding whether a tissue (e.g., nerve white matter (2, 3) or skeletal muscle (4, 5)) is cylindrically symmetric, or whether tissue (e.g., cardiac muscle (11, 12)) is not.

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