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Estimating the Principal Diffusivities (Eigenvalues) of the Effective Diffusion Tensor

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INTRODUCTION

Diffusion tensor MRI (DT-MRI) provides a means to measure the degree of diffusion anisotropy in tissues quantitatively (\bar{I}). In theory, the most informative parameters with which to characterize diffusion anisotropy in a voxel are the three principal diffusivities (or eigenvalues) of the diffusion tensor, \underline{D} : λ_1 , λ_2 , and λ_3 (1). In normal tissues, differences among them may be indicative of a particular architectural motif (2, 3), while in certain disease states, it is reasonable to expect that changes in their magnitude and time course would have diagnostic value (4). In practice, noise in DWIs biases the principal diffusivities. For example, if one determines the largest, intermediate, and smallest principal diffusivity in each voxel, then their respective ROI-averages: $\langle\lambda_1\rangle$, $\langle\lambda_2\rangle$, and $\langle\lambda_3\rangle$ will be biased so that $\langle\lambda_1\rangle$ overestimates and $\langle\lambda_3\rangle$ underestimates their (true) population means (5). ROI averaging of the sorted eigenvalues makes isotropic media appear anisotropic, and generally leads to an overestimate of the degree of diffusion anisotropy, e.g., as measured by $\langle\lambda_1\rangle/\langle\lambda_3\rangle$, at all SNRs (5).

THEORY:

We evaluate a new method designed to improve the estimate of the eigenvalues of \underline{D} within an ROI. First, we determine functional ROIs within an image by segmenting all the voxels (regardless of position) according to their diffusion and relaxation characteristics. Useful features in clustering these voxels are the three scalar invariant quantities, I_1 , I_2 , and I_3 , where

$I_1 = \lambda_1 + \lambda_2 + \lambda_3$; $I_2 = \lambda_1\lambda_2 + \lambda_2\lambda_3 + \lambda_3\lambda_1$; and $I_3 = \lambda_1\lambda_2\lambda_3$ and the T2-weighted signal, $A(\underline{h}=\underline{Q})$. The three scalar invariants do not depend on the order of the eigenvalues in a voxel so, by design, I_1 , I_2 , and I_3 are not susceptible to the sorting bias previously discussed (5). Once the functional ROIs (clusters) are identified, we then average the three scalar invariants within each cluster: $\langle I_1 \rangle$, $\langle I_2 \rangle$, and $\langle I_3 \rangle$. Then, we use these quantities to specify the characteristic equation for each cluster:

$$\langle\lambda\rangle^3 - \langle I_1 \rangle \langle\lambda\rangle^2 + \langle I_2 \rangle \langle\lambda\rangle - \langle I_3 \rangle = 0.$$

Finally, we solve the characteristic equation for its three real roots, which are written in order of decreasing magnitude: $\langle\lambda_1\rangle$, $\langle\lambda_2\rangle$, and $\langle\lambda_3\rangle$. In this way, the eigenvalues are not sorted within each voxel before ROI averaging; rather their sorting is deferred until the last step. Thus, no systematic bias is introduced, while significant noise reduction is expected through cluster averaging.

METHODS:

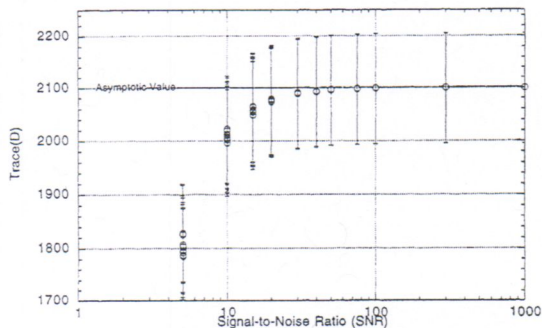
Monte Carlo simulations of Diffusion Tensor MRI studies were first undertaken recently, and have proven useful in understanding the origin of subtle experimental artifacts in DT-MRI studies (6). Here Monte Carlo simulations help us to test whether the use of scalar invariants as statistical parameters improves the estimation of the eigenvalues within an ROI. As described previously (6), we synthesize noisy DWIs using diffusion tensors that are representative of ones we measured in different regions of normal human brain (3) as well as *b*-matrices and MRI parameters that are identical to those used in this study, to calculate a set of noise-free complex DWIs. Then, to each DWI we add complex Gaussian noise (7). From the noisy magnitude images, we estimate \underline{D} in each voxel (8) and then calculate the eigenvalues and eigenvectors of \underline{D} , and their statistical distributions within an ROI.

RESULTS AND DISCUSSION

Figure 1 shows the ROI-averaged scalar invariant $\langle I_1 \rangle$ vs. SNR for different levels of diffusion anisotropy ranging from 1:1:1 to 10:1:1. One interesting finding is that $\langle I_1 \rangle = \langle \text{Trace}(\underline{D}) \rangle$ underestimates its true (asymptotic) value at all SNRs but its percentage error at any SNR is virtually independent of the degree of diffusion anisotropy of the tissue. This is not the case for $\langle I_2 \rangle$ and $\langle I_3 \rangle$ which depend both upon SNR and the degree of tissue anisotropy. This result suggests why there may be differences in reported values of $\langle \text{Trace}(\underline{D}) \rangle$ by different groups, and how measurements of $\langle \text{Trace}(\underline{D}) \rangle$ using different imagers with different SNRs could potentially be reconciled and compared quantitatively (e.g., in a multisite study).

Although a bias still exists (i.e., the sample and population means are unequal) in $\langle I_1 \rangle$, $\langle I_2 \rangle$, and $\langle I_3 \rangle$ it is now due exclusively to background (thermal) noise. At high SNRs (i.e., above 50) their bias and variance are low. At lower SNRs, their bias generally grows slowly and their variance remains symmetrical about their means. This is not the behavior seen with ROI-averaged eigenvalues (5). Nonetheless, the distributions of the roots of the characteristic equation are sensitive even to small biases in $\langle I_1 \rangle$, $\langle I_2 \rangle$, and $\langle I_3 \rangle$, and overall, performance of the new method represents only a marginal improvement.

One disadvantage of any ROI-averaging scheme is that ROIs will contain different numbers of voxels, so uncertainties will vary between them. In human brain, cortical tissue has the most diverse diffusion characteristics (3), and thus the estimates of its principal diffusivities may be the most unreliable.



CONCLUSIONS

Bias introduced by sorting the eigenvalues of the diffusion tensor can be completely eliminated in ROI averages by sorting the scalar invariants of \underline{D} instead. Nevertheless, while conceptually appealing, this approach is still susceptible to MRI noise.

Monte Carlo simulations of Diffusion Tensor MRI studies continue to prove useful in understanding the origin of experimental artifacts due to noise in MRIs.

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