Abstract #01557 ISMRM ABSTRACT

[USGOV] Non-parametric In-vivo Diffusion Tensor Distribution (DTD) MRI of the Human Brain

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Impact

We have developed a method which has identified various mesoscopic water pools inside each voxel not observed previously. This has the potential to detect subtle changes in tissue microstructure in disease such as traumatic brain injury (TBI), development, etc.

Synopsis

Motivation: Imaging mesoscopic water pools in live human brain is desideratum in neuroscience but challenging due to the large nominal voxel size in MRI.
Goals: To develop a method to image distinct water pools within each voxel in a clinically feasible time frame.
Approach: Map the non-parametric DTD in each voxel using marginal distributions of tensor components.
Results: Our approach detected changes in size distribution of crossing fibers of different orientation in white matter regions. It also helps with cortical parcellation by revealing the microstructural variations in white matter, soma and CSF near the cortex.

Introduction

DTD MRI has the potential to map sub-voxel mesoscopic water pools by assuming water diffusion at the mesoscale to be Gaussian characterized by the diffusion tensor distribution (DTD) [1]. Estimating the DTD from the diffusion weighted MRI (DWI) signal data is however challenging because it requires taking inverse Laplace transform (ILT) which is ill-posed. In this study, we have developed a novel method to overcome the challenges using a hierarchical approach involving estimation of marginal densities of various diffusion tensor components, extending our previous work on estimating a 2D T_1-T_2 distribution [2].

Methods

The diffusion weighted signal, $S(\mathsf{B}_m)$, under a b-tensor, B_m, from an ensemble of diffusion tensors, D_n, with probability density, $p(\mathsf{D}_n)$, is given by [3],

$$S(\mathsf{B}_m) \approx S_0 \underbrace{\exp^{-\mathsf{B}_m:\mathsf{D}_n} \Delta\mathsf{D}_n}_{\Psi_{mn}} p(\mathsf{D}_n)$$

We reduce the rank of the anisotropic Gaussian diffusion kernel matrix, Ψ_{mn}, by applying; 1) the positive definiteness constraint zeroing the DTD for diffusion tensors that do not lie on the manifold of symmetric positive definite matrices (i.e., $\mathcal{M}^+$), and 2) a hierarchy of lower dimensional marginal distributions that partition $\mathcal{M}^+$ into domains with higher density while zeroing others, thereby vastly limiting the volume of the solution space. The gradual pruning of the solution space by these constraints is illustrated for a case of 3D DTD, involving two diagonal and one off-diagonal component in Figure 1. The marginal distributions also serve as constraints in the estimation of full distribution.

The 6D DTD space is discretized into a Cartesian grid with the diagonal components of the diffusion tensor ranging conservatively from 0 to 5 $\mu m^2/ms$ to accommodate the range of ADCs expected in a live human brain. The range of off-diagonal components was set to -5 $\mu m^2/ms$ to +5 $\mu m^2/ms$ based on the Sylvester's criterion. The spectral resolution for all the components was set to 0.2 $\mu m^2/ms$, which results in approximately 2.3 billion unknowns needed to characterize the full 6D distribution without imposing any *a priori* constraints, making this problem computationally intractable.

Three sets of rank-1 (1D marginal densities), six sets of rank-2 (2D/ 3D marginal densities) and eight sets of rank-3 b-tensors (3D, 4D, 5D, and 6D marginal densities respectively) totaling 557 b-tensors with b-values ranging from 0 to 2 $ms/\mu m^2$ were used to estimate the full 6D DTD in each voxel. The b-tensor ellipsoids used for hierarchically estimating the various marginal distributions are shown in Figure 2.

The reconstruction pipeline is vetted using a synthetic voxel comprising of gray matter, white matter and CSF water pools for two different SNR. MRI data was acquired on three healthy young adults on a 3T scanner (Prisma, Siemens Healthineers) with 80 mT/m peak gradient strength and a 200 T/m/s slew rate using 64-channel coil. DWIs were acquired with a field of view (FOV) = 210 mm $\times$ 210 mm $\times$ 120 mm and 2 mm isotropic spatial resolution. The total scan time is roughly 1 hour 10 mins. The b-tensors are realized using interfused-PFG (iPFG) MR pulse sequence that can generate b-tensors of all ranks within a single spin-echo sequence [4]. The DWIs were denoised using MP-PCA algorithm [5] and registered using FSL software [6].

The estimated DTDs are visualized using 3D isocontours of the size-shape distribution defined by the space of fractional anisotropy (FA), norm of diffusion

tensor, and skewness of eigenvalues of the diffusion tensor [7]. The orientation heterogeneity is shown by the micro-orientation distribution function (μODF) glyph [4].

Results and Discussion

Simulation results are shown in Figure 3 for SNR = 200 and 1000 juxtaposed with the ground truth. The three compartments are visible in the size-shape distribution plots of ground truth and at SNR = 1000 but only tissue and CSF were clearly separated at SNR = 200 for this phantom. The μODF was accurately depicted for both simulated SNRs. The estimated DTD in select voxels in the brain are shown in Figure 4. White matter voxels (blue and magenta colored) showed two fiber populations with different size-shape distributions. We also show consecutive voxels near the cerebral cortex where two fiber populations, an isotropic tissue, and CSF compartments were captured but whose signal fraction changes as a function of cortical depth.

Conclusion

We have developed a novel method to empirically estimate the DTD using marginal distributions of various diffusion tensor components in a clinically feasible time frame. The technique is vetted using numerical phantoms and applied on live human brain. The results show various mesoscopic water pools in the live human brain not observed previously.

Acknowledgements

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References

1. Magdoom, K. N., Avram, A. V., Witzel, T. E., Huang, S. Y., & Basser, P. J. (2024). Water Diffusion in the Live Human Brain is Gaussian at the Mesoscale. bioRxiv, 2024-04.

2. Benjamini, Dan, and Peter J. Basser. "Use of marginal distributions constrained optimization (MADCO) for accelerated 2D MRI relaxometry and diffusometry." Journal of magnetic resonance 271 (2016): 40-45

3. Jian, B., Vemuri, B. C., Ozarslan, E., Carney, P. R. & Mareci, T. H. A novel tensor distribution model for the diffusion-weighted MR signal. Neuroimage 37, 164–76 (2007).

4. Magdoom, K. N., Avram, A. V., Sarlls, J. E., Dario, G., & Basser, P. J. (2023). A novel framework for in-vivo diffusion tensor distribution MRI of the human brain. NeuroImage, 271, 120003

5. Veraart, J., Novikov, D. S., Christiaens, D., Ades-Aron, B., Sijbers, J., & Fieremans, E. (2016). Denoising of diffusion MRI using random matrix theory. Neuroimage, 142, 394-406.

6. Jenkinson, M., & Smith, S. (2001). A global optimisation method for robust affine registration of brain images. Medical image analysis, 5(2), 143-156.

7. Ennis, D. B., & Kindlmann, G. (2006). Orthogonal tensor invariants and the analysis of diffusion tensor magnetic resonance images. Magnetic Resonance in Medicine: An Official Journal of the International Society for Magnetic Resonance in Medicine, 55(1), 136-146.

Figures and Tables

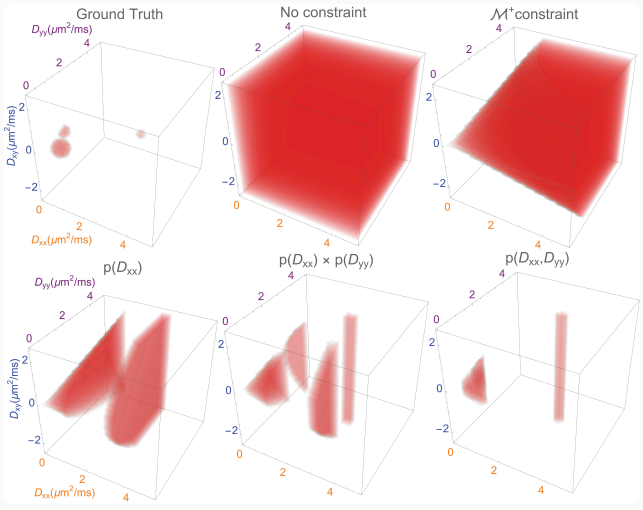

Figure 1: *The gradual pruning of the solution space by the successive application of positive definite and marginal density constraints illustrated for the estimation of p(D_{xx},D_{yy},D_{xy}). The vast 3D Cartesian grid of solution space is first reduced by the application of the $\mathcal{M}^+$constraint as shown in the figure. A further reduction in the solution space is obtained by the successive application of 1D/2D marginal density constraints for D_{xx} and D_{yy}.*

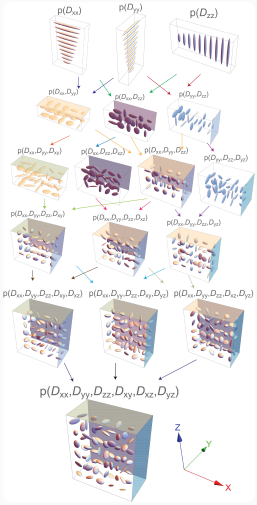

Figure 2: *Hierarchical experimental design used to estimate the 6D DTD depicted by the sampled b-tensor ellipsoids for each experiment. At the top are the rank-1 b-tensors displayed as sticks used to estimate the 1D marginal density of diagonal components of the diffusion tensor. In subsequent rows, these nD marginal distributions are used to reconstruct the appropriate (n+1)D marginal distributions shown using distinctly colored arrows ultimately leading to an estimate of the full DTD.*

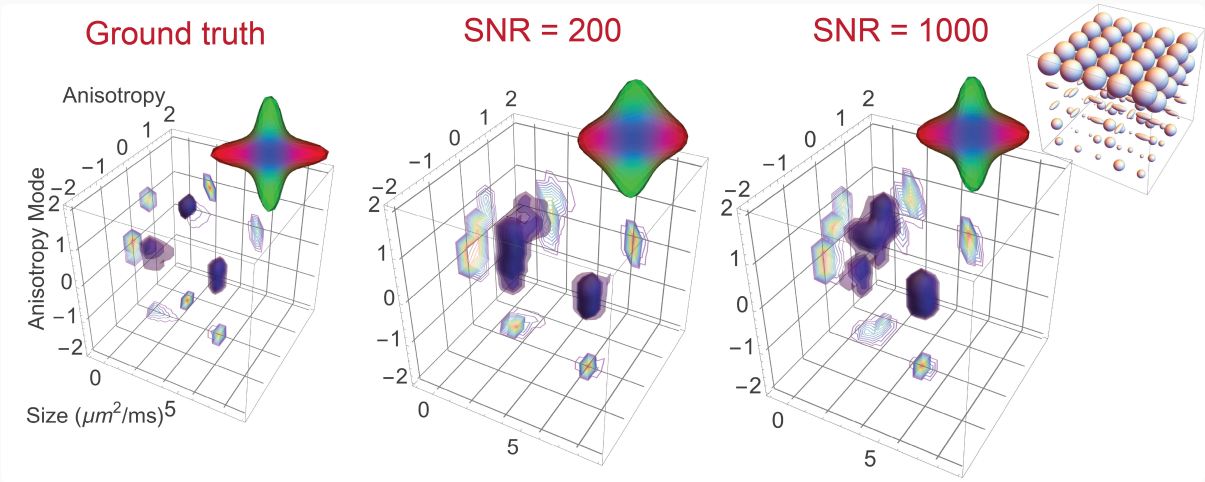

Figure 3: *A synthetic phantom depicting gray matter, white matter and CSF compartments and their reconstruction as a function of the SNR. The size-shape distribution is depicted using iso-surfaces/contours in the 3D parameter space of ellipsoid size, anisotropy, mode of anisotropy of the diffusion tensors, and the orientation heterogeneity is shown using micro-orientation distribution function ($\mu\mathrm{ODF}$). The micro-diffusion tensors comprising the voxel is shown on top right.*

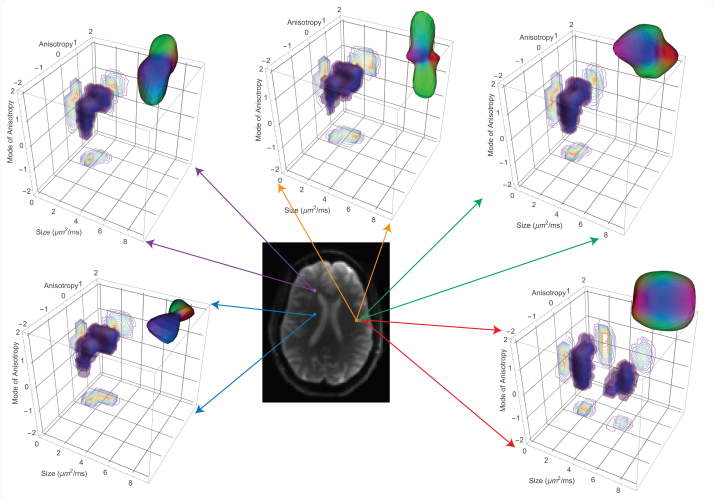

Figure 4: *Estimated DTD in select voxels in the brain. White matter voxels (magenta and blue) show different$\mu\mathrm{ODF}$and two anisotropic compartments with different sizes. A set of consecutive voxels near the cerebral cortex (orange, green and red) show two fiber populations with different orientations and size with their fraction changing as the voxels progress towards the cortex. The red voxel closest to the subarachnoid space shows CSF and an isotropic compartment.*