Characterizing Human Brain Microstructure with Mean Apparent Propagator (MAP) MRI

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Target audience: Clinicians and basic scientists interested in translational diffusion MRI methods;

Purpose: Orientationally invariant measures such as Fractional Anisotropy (FA) or mean diffusivity (1) obtained by analyzing diffusion weighted images (DWIs) are invaluable for characterizing changes in cytoarchitecture and microanatomical organization of brain tissue during stroke, cancer, neurodegenerative diseases and aging. Recently, a novel, quantitative physical and mathematical framework was proposed for measuring the mean apparent diffusion propagator (MAP) by describing the 3D q-space signal in a series expansion of Hermite functions (2). The first term in the expansion characterizes the Gaussian displacement distribution in DTI, while all higher order terms represent orthonormal "corrections" that enable rapid convergence to the true MAP. From the series coefficients, scalar measures of zero-displacement probability, non-gaussianity and propagator anisotropy can be readily derived along the axes of the local anatomical reference frame. In this study we apply for the first time the MAP-MRI framework to measure displacement profiles of water molecules *in vivo* by analyzing a large collection of DWIs acquired in healthy volunteers using a conventional clinical scanner. We derive maps of scalar descriptors for the propagator and discuss their clinical potential. Finally, we evaluate the clinical feasibility of this technique by repeating the analysis with various subsets of the complete DWI datasets.

Methods: Three healthy volunteers were scanned on a 3T MRI scanner using a spin-echo diffusion-weighted EPI (SENSE factor of 2) sequence. The gradient pulse width and separation were $\delta=34ms$ and $\Delta=41ms$ respectively and $G_{max}=4.93G/cm$. Overall, 600 DWIs were obtained with b-values up to 6,000 s/mm^2 and multiple orientations uniformly sampling the sphere for each of the 6 b-values. Images were acquired using TE/TR=94/5800ms with full brain coverage and a 3mm isotropic resolution to ensure sufficient signal (even for high-b values) for reliable motion and distortion correction (3). After correction, the MAP MRI coefficients (up to order 6) were computed and used to derive diffusion orientation distribution functions (dODFs) as well as scalar descriptors of the propagator: return-to-origin probability (RTOP), return-to-axis probability (RTAP), return-to-plane probability (RTPP), total, parallel and perpendicular non-gaussianity indices (NG, $NG_{\perp}$, and $NG_{\parallel}$ respectively), and propagator anisotropy measures (2). To simulate a clinically feasible 15 min protocol, subsets containing only 150 of the original DWI datasets were sampled and re-analyzed.
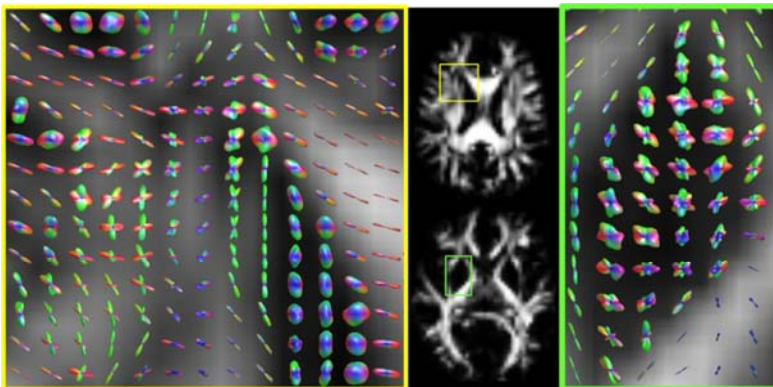

Figure 1: MAP-MRI derived dODFs in regions of low FA containing fiber crossings (yellow box) and the thalamus (green box).
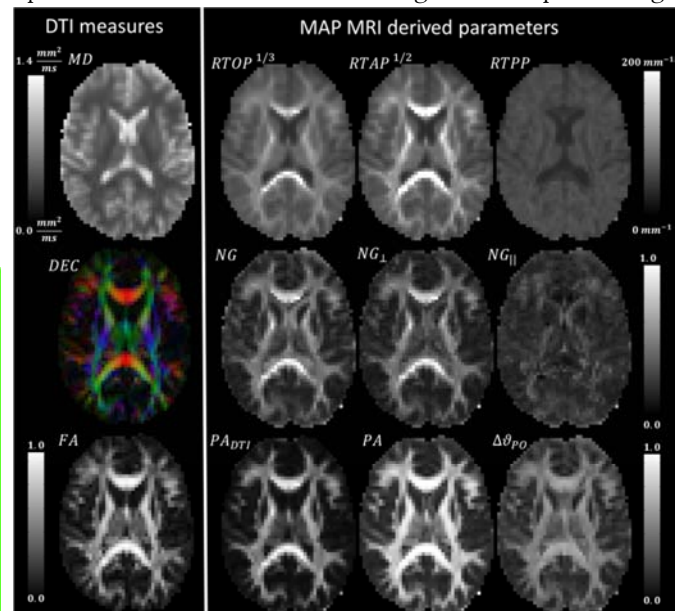

Figure 2: Comparison of DTI and MAP-MRI derived parameters. DTI: Mean diffusivity, Direction Encoded Color map and Fractional Anisotropy. MAP-MRI: zero-displacement probabilities (top row), non-gaussianity measures (middle row) and propagator anisotropy measures (bottom row).

Results and Discussion: The propagators measured using MAP-MRI revealed orientational characteristics of the rich microanatomy in regions of low FA such as fiber crossings or subcortical structures (Fig.1) despite low spatial resolution. MAP MRI derived scalar metrics showed consistent anatomical variations in all three volunteers. Large RTOP and RTAP values were observed in restricted regions of tightly packed white matter, while RTPP was similar in white and gray matter. Overall deviations from Gaussianity (NG) were larger in white matter fibers, mainly due to restriction perpendicular to the fiber orientation as indicated by large $NG_{\perp}$, while diffusion along the axial direction was relatively Gaussian ($NG_{\parallel}$). The propagator anisotropy (PA) indices quantify the dissimilarity of the propagator relative to its isotropic counterpart and can be separated in contributions from Gaussian (PA$_{DTI}$) – with contrast similar to FA – and non-Gaussian terms ($\Delta\theta_{PO}$). Scalar measures derived from subsampled datasets containing only 150 DWIs converged to within 5% error when images with b>4000 s/mm^2 were included, suggesting that MAP MRI can be accelerated sufficiently for routine clinical applications and that relatively large b-values are beneficial.

Conclusion: Our results demonstrate that the comprehensive framework of MAP-MRI can be used to analyze diffusion in the human brain and reliably derive additional quantitative indices compared to DTI for *in vivo* assessment of tissue microanatomy. Maps of these microstructural descriptors can be obtained within clinically feasible scan durations and hold great promise for accurately quantifying white matter microstructural changes in a variety of normal and pathological processes.

References: 1. Basser et al, Biophys J., 1994;66:259-267; 2. Özarslan et al., Neuroimage;78:16-32; 3. Pierpaoli et al., ISMRM 2010;#1597;