In Vivo 3D Single-Shot Echo-Planar DWI at 7T for Mapping Tissue Microstructure using Mean Apparent Propagator (MAP) MRI

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Synopsis

A number of advanced diffusion models have demonstrated great promise for mapping tissue microstructure in *ex vivo* studies with high resolution and fidelity using a wide range of diffusion weightings, but the increased acquisition time (days) is not feasible *in vivo*. In this study we have addressed some basic DWI acquisition pitfalls by using 3D single-shot EPI on a high-field (7 Tesla) pre-clinical MRI system, and adapted one of the most promising diffusion modeling techniques, mean apparent propagator (MAP) MRI *in vivo* to derive information about rat brain microstructure within a reasonable time frame.

Introduction

Magnetic resonance (MR) diffusion tensor imaging (DTI) is a non-invasive imaging technique that uses information of magnitude and direction of water molecule diffusion within a voxel to infer features of tissue structure on macro and micro levels.[1] Furthermore, DTI appears to be very promising for identifying markers of trauma-related tissue changes following injury.[2] In recent years, however, a number of more sophisticated diffusion models have been proposed that may offer improved markers of post-traumatic abnormalities (e.g. DKI, NODDI and MAP-MRI).[3-6] It would be advantageous to translate these newer approaches for pre-clinical use in animal models of traumatic brain injury to identify potential biomarkers and test the effects of novel therapeutic strategies.

Diffusion weighted images (DWIs) have poorer image quality and resolution compared to other conventional MR images, especially at very high diffusion weighting, required for newer theoretical methods. DWI artifacts like eddy-current distortion, RF noise, and subject motion, and those arising from the use of faster image acquisition techniques such as echo planar imaging (EPI), including susceptibility-induced distortion, all reduce DWI quality. While more advanced DW techniques show great promise for mapping tissue microstructure in *ex vivo* studies, [5,6] where high-resolution and high-quality DWIs need to be acquired over a wide range of diffusion weightings, these requirements can increase scan time to several days, which is clearly not feasible for pre-clinical studies and certainly not for clinical translation.

In this study we have addressed some basic DW imaging acquisition pitfalls by using 3D single-shot EPI on a high-field, high-gradient pre-clinical MRI scanner, and adapted one of the most promising diffusion modeling techniques, mean apparent propagator (MAP) MRI [6] *in vivo* to derive information about rat brain microstructure and cytoarchitecture within a reasonable time frame.

Methods

MRI experiments were conducted using a 7T Bruker Biospec 70/20 (Bruker Biospin, Billerica, MA) equipped with high-performance actively shielded gradients (660 mT/m) with integrated shim coils. A birdcage RF transmit coil in combination with actively decoupled 4-channel RF receive array coil was used. Four female Sprague-Dawley rats weighing 250-300 grams were scanned 4 times over 10 days to assess repeatability. A single-shot 3D EPI sequence was used to acquire DWIs: TR=800 ms, TE=40 ms, FOV=22.4×22.4×28.5 mm^3, matrix=128×64×48, resolution=280×280×750 μm^3, δ=5 ms and Δ=12 ms. 14 non-collinear diffusion directions were used for DTI, with b-values=0, 800, and 1600 s/mm^2. For the MAP-MRI acquisition, 32 and 56 diffusion directions were used with b-values=3200 and 4800 s/mm^2, respectively. Two sets of data per each diffusion volume with opposite phase encoding directions (blip-up/blip-down) were acquired (to correct susceptibility-induced EPI distortion using DR-BUDDI [7] approach). A total of 260 DWI volumes were acquired *in vivo* within 2 hours. The data were processed using TORTOISE [8] (NICHD, NIH) for DWI corrections and DTI fitting and custom IDL tools for MAP-MRI fitting according to (6) (implementation of Alan Barnett, NICHD, NIH).

Results and Discussion

There are many practical problems to address when acquiring DWIs for *in vivo* imaging applications, particularly for MAP-MRI and other methods requiring large b-values. Our goal was to obtain high-SNR high-quality and high b-value DWIs within a reasonable acquisition time. We chose a single-shot 3D EPI (to reduce motion and drift-related artifacts) with 4^{th}-order ghost correction (diminishing the effect related to the oscillation of the readout gradient) to increase SNR and decrease repetition time, providing high-quality DWI data while shortening the overall acquisition time.

The primary imaging optimizations that were found to be important for obtaining high-quality DWIs were: shimming of imaging region using MAPSHIM (significantly helping with field inhomogeneity), placement of saturation slices to reduce motion artifacts, decreasing the FOV, shortening TE, and measuring the k-space sampling trajectory (Figure 1). Once implemented, we were able to acquire *in vivo* high-quality and high-SNR DWIs up to b = 4800 s/mm^2 with 30 seconds per DWI volume (Figure 2).

The MAP-MRI modeling framework [6] was used to analyze 260 DWIs from rat brains acquired *in vivo* using the above-mentioned 3D EPI technique (Figure 3).

Summary

MAP-MRI subsumes DTI while providing new quantitative parameters that reflect intrinsic features of nervous tissue microstructure, in addition to those provided by DTI. For the first time in live animals, MAP-MRI-derived indices were measured and mapped and found to be of high quality, including the propagator anisotropy and non-Gaussianity, which are susceptible to noise and other imaging related artifacts. Results of this study demonstrate the feasibility of migrating a successful *ex vivo* diffusion MRI acquisition and analysis pipeline to enable *in vivo* pre-clinical studies.

Acknowledgements

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References

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Figures

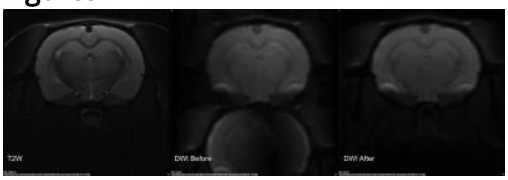

Figure 1. Rat brain T2W, single-shot 3D EPI DWI b0 before and after adjustments (Trajectories ON, Navigator ON, 4th order ghost correction ON, dynamic Ghost ON, MAPSHIM, saturation slices).

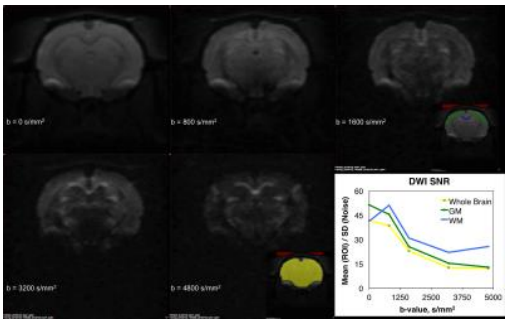

Figure 2. Representative rat brain single-shot 3D EPI DWIs at different diffusion weightings and SNR values corresponding to these images (yellow: whole brain ROI; green: grey matter ROI; blue: white matter ROI; red: noise ROI).

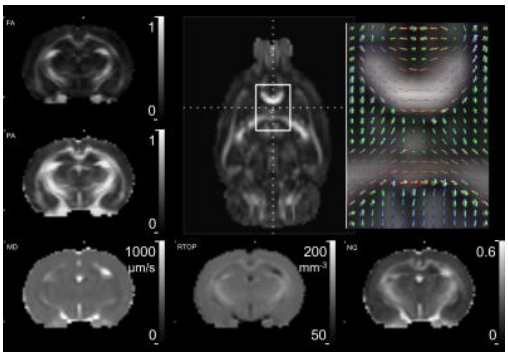

Figure 3. Representative DTI and MAP-MRI derived parametric maps. Fractional anisotropy (FA), propagator anisotropy (PA) capturing more information compared to traditional FA (especially in grey matter regions), and color glyphs illustrating the distinct fiber orientations resolved by MAP-MRI. Anisotropy in the full MAP-MRI is significantly greater than the anisotropy of DTI's Gaussian propagator. Mean diffusivity (MD), the cube root of the return-to-origin probability (RTOP), and non-Gaussianity (NG) index quantifying the dissimilarity between the propagator and its Gaussian part. NG and RTOP are very similar, and exhibit higher probability of zero displacement and higher non-Gaussianity within white matter.