

Use of 3D single shot echo-planar diffusion tensor imaging at 7T with a wide range of b-values for mapping tissue microstructure *in vivo*

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Introduction:

Magnetic resonance (MR) diffusion tensor imaging (DTI) is a non-invasive technique that uses information of magnitude and direction of water molecule random motion within a voxel to infer features of macro and micro tissue structure [1]. DTI holds promise for identifying markers of trauma-related tissue changes following injury [2]. In recent years, a number of advanced diffusion models have been proposed that may offer improved biomarkers of post-traumatic abnormalities (e.g. DKI, NODDI and MAP-MRI). Leveraging these newer approaches in animal models of TBI may improve identification of diagnostic biomarkers and assessment of effects of novel therapeutic strategies.

Historically, diffusion weighted (DW) images have suffered from lower quality and resolution compared to conventional MR images. Problems include distortion, low signal-to-noise ratio (SNR), low resolution, and presence of artifacts. These issues stem from faster image acquisition techniques, higher diffusion weighting, hardware, subject motion and imaging time limitations.

More advanced DW techniques have demonstrated great promise for mapping tissue microstructure in *ex vivo* studies [3-4] with high resolution and fidelity with a wide range of diffusion weighting, but the increased scan acquisition time (days) has not been feasible *in vivo*.

To overcome these challenges, *in vivo* 3D single-shot EPI on a pre-clinical MR imaging system was implemented to acquire data to be used in the mean apparent propagator (MAP) MR imaging model [4].

Methods:

MRI experiments were conducted using a 7T Bruker Biospec70/20 equipped with a high-performance actively shielded gradient (660mT/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. A single short 3D EPI sequence was used to acquire DWIs: TR=800ms, TE=40ms, FOV=22.4×22.4×28.5mm³, matrix size=128×64×48, resolution 280×280×750μm³, δ=5ms and Δ=12ms. 14 non-collinear diffusion directions were used for DTI, with b-values=0, 800, and 1600s/mm². For the MAP acquisition, 32 and 56 diffusion directions were used with b-values=3200 and 4800s/mm², 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). A total of 260 DWI volumes were acquired *in vivo* within about 2 hours. The data were processed using TORTOISE (NIH, Bethesda, MD) and MATLAB.

Results and Discussion:

There are many practical problems to address when acquiring DWI for *in vivo* applications, particularly for MAP-MRI. Our goal was to obtain high SNR quality and high b-value DWIs within a reasonable acquisition time. A single-shot 3D EPI (to reduce motion and drift-related artifacts) with 4th order ghost correction (diminishing effect related to the oscillation of the readout gradient) was chosen for the higher SNR and decreased repetition time, providing high quality data while shortening the overall acquisition time. The primary imaging optimizations that were important for obtaining high quality DW images were: shimming of imaging region using MAPSHIM, placement of saturation slices to reduce motion artifacts, a

smaller FOV, shorter TE, and measurement of the k-space sampling trajectory. Once implemented, we were able to acquire *in vivo* high quality and high SNR DWIs up to $b=4800\text{s/mm}^2$ with 30 seconds per DWI volume.

The MAP MRI modeling framework was used to analyze 260 DWIs from rat brains acquired *in vivo* using the above-mentioned 3D EPI technique. 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 index maps were generated and found to be of high quality, including the propagator anisotropy and non-Gaussianity, which are susceptible to noise and other artifacts.

Results of this study demonstrate the feasibility of migrating a successful *ex vivo* diffusion MRI acquisition and analysis pipeline to *in vivo* studies and potential for clinical translation.

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References:

1. Basser PJ et.al. 1994. Biophysical J. 66(1):259-67.
2. Hulkower MB et.al. 2013. AJNR Am J Neuroradiol. 34(11):2064-74.
3. Descoteaux M et.al. 2011. Medical Image Analysis 15(4):603-21.
4. Özarslan E et.al. 2013. Neuroimage 78:16-32.