Non-Gaussian Diffusion in the Rat Spinal Cord In Vivo with Phase and Susceptibility Corrected Segmented EPI

Elizabeth Zakszewski[1], Nathan Skinner[2], Shekar Kurpad[1], Brian Schmit[3], and Matthew Budde[1]

[1]*Neurosurgery, Medical College of Wisconsin, Milwaukee, Wisconsin, United States,* [2]*Biophysics, Medical College of Wisconsin, Milwaukee, Wisconsin, United States,* [3]*Biomedical Engineering, Marquette University, Milwaukee, Wisconsin, United States*

TARGET AUDIENCE: Investigators looking to improve image quality and characterization of experimental spinal cord injury with diffusion-weighted imaging.

PURPOSE: As an improvement to diffusion tensor imaging (DTI), measures of non-Gaussian diffusion signal behavior in the central nervous system have improved the sensitivity to neural injury. Specifically, diffusion kurtosis imaging (DKI) has demonstrated increased sensitivity to acute axonal damage in various injuries such as traumatic brain injury and cerebral ischemia. DKI may also be important for characterization of injury in experimental spinal cord injury. However, imaging of the rodent spinal cord is challenging and prone to artifacts. Herein, we describe several technical approaches to improve image quality in diffusion weighted imaging using mutlishot echo-planar imaging (EPI) of the rat spinal cord, with the goal of measuring non-Gaussian diffusion using DKI or other models. In addition to previously described methods of respiratory gating and cord stabilization[1], post hoc techniques including automated EPI phase correction[2], reverse-blip EPI susceptibility correction[3], non-local means filtering (NLMF)[4], and weighted least squares fitting provide a considerable improvement in image quality.

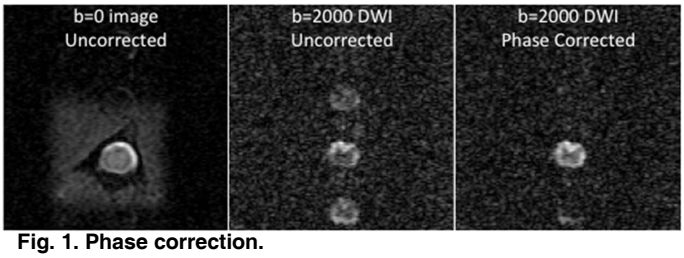

Fig. 1. Phase correction.

METHODS: Anesthetized rats were positioned in a custom head holder and ear bars and placed in a 30 mm diameter litzcage coil. A 4-shot, partial Fourier spin-echo, diffusion weighted EPI sequence (TR/TE = 1500/27.8 ms) was used with an in-plane resolution of 200 um^2 (25.6 mm^2 FOV; 128^2 matrix), partial acquisition factor of 1.3, and 4 saturation bands to suppress non-cord signal. Fourteen, 0.75 mm thick slices with a gap of 0.75 mm were acquired for spatial coverage from C1 to C5. Diffusion weighting used a multi-shell scheme with 15 directions at each of 4 b-values (250, 500, 1000, 2000 s/mm^2) with a duration (δ) of 8.25 ms and separation (Δ) of 12.5 ms along with 15 non-diffusion weighted images (b=0). Total imaging time was approximately 1:15 hrs, depending on respiratory rate.

The complex k-space data was corrected for phase errors induced by motion and diffusion weighting using an iterative phase correction algorithm[2]. The resulting magnitude images were smoothed with a non-local means algorithm[4], and corrected for susceptibility effects using the "topup" routine in FSL[3]. The diffusion tensor and kurtosis tensor were fit in Matlab using weighted least squares to obtain maps of fractional anisotropy (FA), mean kurtosis (MK), mean diffusivity (MD), along with axial and radial diffusivity (AD, RD) and kurtosis (AK, RK).

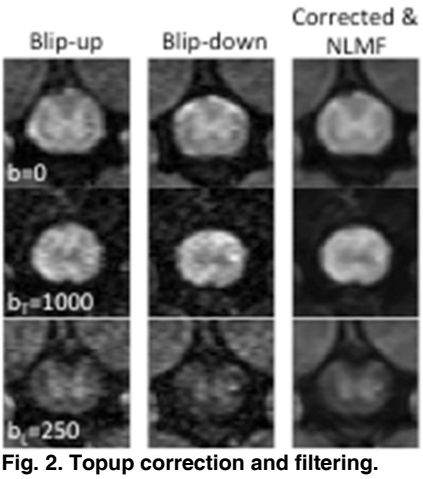

Fig. 2. Topup correction and filtering.

RESULTS: The automated phase correction procedure removed much of the EPI ghosting artifacts in the DW images, despite almost no ghosting in the uncorrected non-diffusion weighted images (Fig. 1). The procedure required approximately 10 minutes to complete for the full dataset of 1890 images. Correction of susceptibility distortions and non-local means filtering (Fig. 2) further improved the quality of the individual images, wherein clear contrast is evident between the white and gray matter with diffusion weighting applied perpendicular (middle row) or parallel (bottom row) to the spinal cord axis. With these improvements, high-quality DTI and DKI maps were obtained from healthy animals. The maps exhibited high FA and RK white matter, with sufficient resolution to visualize the dorsal and ventrolateral white matter. Several voxels were not fit well with the DKI model, where constraints or non-linear fitting may improve the fitting. In 5 healthy rats, the coefficient of variations in the ventrolateral white matter were 4.0 and 16.6 % for AD and RD, respectively, and 6.0 and 16.7 % for AK and RK, respectively.

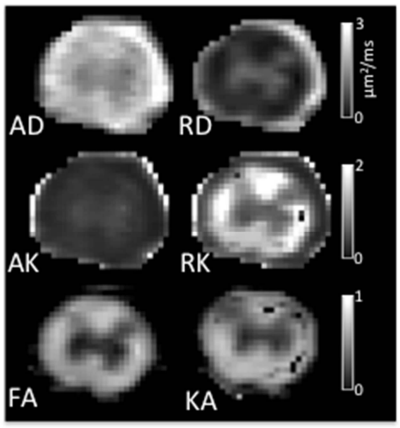

Fig. 3. DTI and DKI maps.

DISCUSSION: Along with technical improvements in the acquisition, posthoc phase correction, susceptibility reduction, and filtering enable high-quality DTI and DKI maps of spinal cord tissue microstructure. The resulting image acquisition pipeline will be valuable to investigate the natural progression of experimental models of spinal cord trauma and disease as well as noninvasive evaluation of potential therapies.

REFERENCES: **1.** Kim, JH, et al. Nature Protocols 2013; **2**. Truong, TK, et al. MRM 2012; **3.** Gallichan, D, et al. MRM 2010; **4.** Wiest-Daesslé N, et al. MICCAI. 2008.