Title: Reliability of NODDI in the Rat Brain at 9.4 Tesla.

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Structured Abstract:

Purpose: Neurite Orientation Dispersion and Density Imaging (NODDI) is a novel diffusion MRI method that may improve upon the specificity of Diffusion Weighted MRI (DWI) by probing unique diffusion patterns within three separate microstructural environments: intra-neurite, extra-neurite, and cerebral spinal fluid (CSF) compartments. Such detailed reconstruction of in-vivo neurite morphology may offer unique information regarding neural health. While much work has been done in the development of NODDI in human imaging, the use of NODDI in pre-clinical models is still relatively new. Due to the common use of rodent models in pre-clinical imaging, the purpose of this work was to determine the reliability and utility of NODDI in a rat model at 9.4 Tesla.

Methods: 8 Adult Male Sprague Dawley Rats (age 102 days at time of initial scan, weight 323g) underwent our scan-rescan protocol (time between scans 7 days). We chose a NODDI diffusion encoding scheme utilizing a multi-shot Echo Planar Imaging (EPI) acquisition pulse sequence (slice thickness = 0.5mm, 0.250 x 0.250 mm in plane resolution, 31 total slices, TE = 36 ms, TR=5.0s, 4 shot EPI acquisition, 2 averages). We used a two-shell diffusion protocol (Shell one: 72 directions, four b-value = 0 and b-value = 2000 s/mm2 with parameters: G = 298 mT/m, Δ = 17 ms, δ = 4.5 ms, TR = 5.0s; Shell two: 36 directions, four b-value = 0 and b-value = 1000 s/mm2 with parameters: G = 149 mT/m, Δ = 17 ms, δ = 4.5 ms, TR = 5.0s). This sequence resulted in a total imaging time of 96 minutes. Images were pre-processed using fMRI Software Library (FSL, v.5.0.10, Oxford, UK). EDDY was used to correct for eddy current induced distortions as well as susceptibility-induced distortions. The NODDI Matlab toolbox (available from the UCL Microstructure Imaging Group) was then used to produce maps of Orientation Dispersion Index (ODI), Neurite Density Index (NDI), and Isotropic Volume Fraction (IsoVF). Statistical analysis focused on two common techniques: Mean Region of Interest (ROI) analysis, and whole brain voxel-wise analysis. ROI analysis focused on 4 separate and relevant regions of interest (Thalamus, Corpus Callosum, Dentate Gyrus, and Hippocampus) as well as whole brain White and Grey Matter. In both the ROI and voxel-wise analysis cases the scan-rescan reproducibility and reliability was characterized through the coefficient of variation (CV).

Results: Coefficient of Variation (CV) maps for Orientation Dispersion Index (ODI) and Neurite Density Index (NDI) showed high precision and repeatability both between and within subject, for all analysis techniques. Furthermore, it was found that small biological changes (<5%) may be detected with feasible sample sizes for these metrics. Contrary to that, Isotropic Volume Fraction (IsoVF) was found to have low precision and repeatability, necessitating very large sample sizes ($n > 50$) for biological changes to be reflected in this metric.

Conclusions: This study indicates NODDI to be a useful tool within the preclinical research setting and shows the ability of ODI and NDI to detect subtle microstructural changes at 9.4 Tesla.