Title: Development of a Clinically Viable Microscopic Fractional Anisotropy Imaging Protocol

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Structured Abstract:

Introduction: Diffusion MRI (dMRI) is a specialized MRI technique that generates contrast based on the diffusion of water molecules. A commonly used dMRI metric to study tissue microstructure is fractional anisotropy (FA), which quantifies the voxel-scale anisotropy of water diffusion. Water diffusion is highly anisotropic in neurons due to their eccentric shape but in brain injury or disease, neuron structural integrity is often compromised, resulting in reduced anisotropy. Thus, FA is an indirect measure of neuron damage. A limitation of FA is that it is sensitive to crossing neuron fibers; if multiple axons in a single voxel run in different directions, FA will be reduced even though there is no injury or dysfunction. A more recently defined metric called microscopic fractional anisotropy (µFA) aims to quantify anisotropy independent of fiber orientation; µFA contrast comes from the difference between isotropic and linear diffusion-weighted scans. However, current protocols to determine µFA have used complicated pulse sequences, require long scan times, or use techniques that are prone to artifacts, rendering them unsuitable for clinical use. In this project, we propose a new protocol to generate full brain µFA images that is easy to implement and requires scan times of 5 minutes or less.

Methods: We developed a novel pulse sequence for µFA imaging using trapezoidal gradients and designed a basic protocol to generate full brain maps. In a preliminary test at 7T, FA and µFA images were acquired from a volunteer with MS and a healthy volunteer at 7T (TE/TR=99/6000 ms, b=2200 s/mm^2, scan time=10:00, resolution=2 mm isotropic) and later at 3T (TE/TR=99/7700 ms, b=2000 s/mm^2, scan time=4:45, resolution=2 mm isotropic). Anatomical T2-DIR images were also acquired for the MS patient to identify regions of neuronal damage called MS lesions. The mean FA and µFA were computed for MS lesions (31 in total) and contralateral normal appearing white matter (NAWM) regions in the 3T images. To optimize our protocol, we estimated the ratio of µFA to variance of µFA (SNR_µFA) to determine the optimal MRI scan parameters.

Results: In both volunteers, µFA was more homogeneous than FA in NAWM regions at both 3T and 7T. µFA within MS lesions was 8% lower than in NAWM (p=10^-5) and FA within lesions was 11% lower than in NAWM (p=0.01). Preliminary optimization work suggests the optimal b-value is ~2200s/mm^2 and the optimal ratio of linear to isotropic scans is ~1:2 to maximize SNR_µFA.

Discussion: µFA and FA were both reduced in lesions compared to NAWM, demonstrating the sensitivity of the metrics to neuron dysfunction, but greater statistical power was observed in µFA (>99%) than FA (~66%). The greater homogeneity of µFA over FA in NAWM suggests that the metric is less sensitive to crossing fibers. To validate the optimization parameters with real data, we will acquire multiple b-shell scans from healthy volunteers (b-values ranging from 0 to 2500s/mm^2).