Neurite orientation dispersion and density Imaging (NODDI) in Multiple Sclerosis

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Target Audience: Clinicians, Psychiatrists, and Neuroscientists who study multiple sclerosis. MRI scientists who focus on diffusion imaging of brain microstructures.

Purpose:

Magnetic Resonance Imaging (MRI) is the preferred imaging technique to help establish diagnosis of multiple sclerosis (MS), an inflammatory demyelinating and neurodegenerative condition of the central nervous system (CNS). Conventional MRI methods used in MS diagnosis include T_1-eighted, T_2-weighted and T_2-Weighted fluid-attenuated inversion recovery (T2-FLAIR) imaging. Hyper-intense T2 or FLAIR regions in brain, known as lesions, are a hallmark of the disease. However, the underlying micro-mechanisms of these brain changes are unclear. Diffusion MRI measures water diffusion behaviors in biological systems, and is sensitive to microstructural changes in white matter (WM). The objective of this study was to perform neurite orientation dispersion and density imaging (NODDI)[1] to assess microstructural WM changes in MS. NODDI hypothesizes WM microstructures in three compartments: extracellular, intracellular and cerebrospinal fluid compartment. Information about brain microstructures, as evaluated by NODDI, may explain the microstructural changes in MS at cellular level.

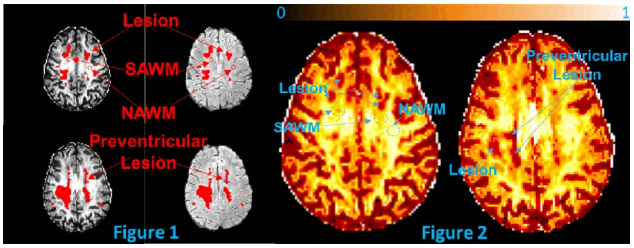

Figure 1: V_{ic} (left) and T2 flair (right) maps showing various ROIs. Figure 2: V_{ic} map showing dip in intensity on lesions, pre-ventricular lesions and SAWM ROIs as compared to NAWM ROIs.

Method:

For NODDI, diffusion-weighted (DW) imaging was performed in 6 MS volunteers on a Philips 3T Achieve TX scanner with 8-channel head coil and SENSE parallel imaging. All subjects were female, one with clinically isolated syndrome, four with relapsing remitting MS, and one with secondary progressive MS. The DW pulse sequence was a SS-SE-EPI sequence. TR was 3.59 sec. Other MR parameters were: TE = 114.24 ms, δ/Δ=46/58.4 ms, voxel size=1.75*1.75 mm^2, 40 slices with slice thickness =3 mm, SENSE factor=2. The total scan-time was about 24 min. The diffusion encoding scheme consisted of 5 b-value shells and 143 DW directions[2]. The normalized intensity in NODDI equation is given by $A = (1-V_{iso})(V_{ic} A_{ic}+(1-V_{ic}) A_{ec})+V_{iso} A_{iso}$; where V_{ic} and V_{iso} are the volume fraction of intra-cellular and CSF compartments respectively. A_{ic}, A_{ec} and A_{iso} are the normalized signal contribution from intra-cellular, extra-cellular and CSF compartments respectively. These parameters are evaluated in NODDI analysis. The extra-cellular volume fraction is $V_{ec} = (1-V_{ic})$. T2-FLAIR scans were also obtained using matrix=0.938x0.938 mm^2, slice thickness=3mm and TR of 1.1.s. The FLAIR scans were segmented using a semi-automated approach called "FLAIRSEG" [3, 4].This program uses an expectation maximization algorithm to classify each voxel in the image as lesion, normal tissue or cerebrospinal fluid. The resulting lesion masks are edited manually to ensure correct voxel classification. The T2-FLAIR and lesion masks were linearly registered to the diffusion space We studied four types of regions of interest (ROIs) in WM (Figure 1): 1) Lesions –T2-FLAIR-defined lesion located in the centrum semi-ovale; 2) Periventricular Lesions – regions of T2-FLAIR defined lesion located adjacent to the ventricles; 3) Normal-Appearing White Matter (NAWM) – regions distal to lesions showing a normal T2-FLAIR profile; and 4) Slightly Abnormal Appearing White Matter (SAWM) – regions close to lesions but with normal T2-FLAIR values. At least 3 Lesion, 3 Periventricular Lesion, 8 NAWM and 4 SAWM ROIs were chosen for each subject. Spheres of a radius of 3 mm were drawn for the ROIs and t-tests were used to compare values between NAWM and the other three types of ROIs. A p-value < 0.01 was considered significant.

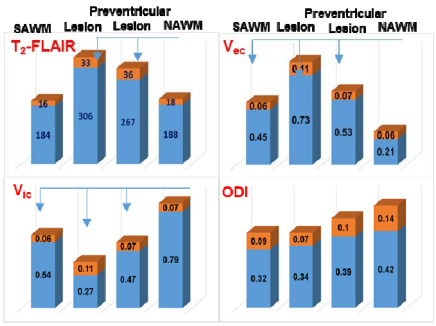

Figure 3: Bar figures for ROI's across 6 subjects. Mean values are in the blue box and standard deviations across voxels are in a orange box. The arrows show statistically significant (p < 0.01) ROI's w.r.t NAWM ROI's.

Results:

T2-FLAIR signal was, by definition, significantly higher in MS lesions compared to NAWM, but did not differentiate between SAWM and NAWM. The NODDI parameter V_{ic}, which is a measure of axonal density in WM, was significantly lower in MS lesions, periventricular lesions, and SAWM than NAWM ROIs (Figures 2 & 3). MS lesions had the lowest V_{ic} and SAWM had highest of the abnormal V_{ic} values. Orientation dispersion index (ODI) showed no statistically significant difference between any ROIs (Figures 2 & 3). As expected, the volume fraction of CSF was insensitive to any WM ROIs. Like V_{ic} , the extracellular volume fraction V_{ec} could also clearly differentiate lesions, pre-ventricular lesions and SAWM from NAWM ROIs.

Discussions and Conclusion:

Results of this study suggested that axonal density decreases in MS lesions. The decreases were most severe in established lesions that could also be identified using conventional T2-FLAIR imaging. While not detectable with T2-FLAIR, a milder, but significant decrease of axonal density in SAWM suggests the NODDI approach is more sensitive to subtle changes of WM in MS. While axonal density changed significantly, the organization of axons described by the ODI measure, had no significant changes in MS lesions compared to normal WM. The volume fraction of CSF did not significantly differ between ROIs suggesting consistent quality of the diffusion data across ROIs, especially the periventricular lesion masks. Despite limited subject number in this study, results are encouraging. A continuing study that involves more subjects is currently underway.

References: 1. Zhang et. al., Neuroimage 2012 1000-1016. 2. Wu et. al., Neuroimage 2007 36: 617-629.3. Wishart, H., et. al., Annual Meeting of the International Neuropsychological Society, Acapulco, Mexico 2010 4. Kee, E. R., et. al., Annual Meeting of the International Neuropsychological Society, Boston, MA 2011.