Assessing white matter microstructure in regions with different myelin architecture

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Purpose

Diffusion-weighted imaging, Myelin Water Fraction (MWF) and Magnetization Transfer (MTR) have been shown to be suitable for the quantification of white matter (WM) tissue changes [1]. Especially neurite density and orientation dispersion imaging (NODDI), a recently developed technique, has been suggested to be highly sensitive for microstructural WM differences [2]. The objective of this study was to assess several WM imaging protocols in their ability to detect differences in myelin architecture between the cortico-spinal tract (CST), known to exhibit unique MRI characteristics [3] based on its histological properties of larger axon diameters and thicker myelin sheaths [4], and frontal WM regions in healthy adolescents. In addition, preliminary data from patients with Metachromatic Leukodystrophy (MLD) were studied in order to explore the possibility to quantify demyelination by these methods [5].

Methods

18 age- and gender-matched healthy volunteers (median age 14.9 yrs, range 9-32 yrs) and 5 patients with MLD (median age 22yrs, range 13-32 yrs) were scanned at 3T (Siemens Skyra, 2-ch body Tx coil, 32-ch head Rx coil, examination time: 40min):

A) 2-shell diffusion-weighted EPI (64 directions with b=2000s/mm^2; 30 directions with b=700s/mm^2, TE/TR = 89/9100 ms, voxel: 2×2×2 mm^3). B) CPMG multi-SE (32 echoes, TE: 10ms-320ms, TR=5s, voxel size = 1.5×1.5×5 mm^3, 1 slice), modified to have shorter RF pulse durations and increased 180° RF profile. C) B1 mapping for each transmit channel was performed and combined using the manufacturers standard approach. D) bSSFP-based MTR images, voxel size = 1.3×1.3×1.3 mm^3) [6].

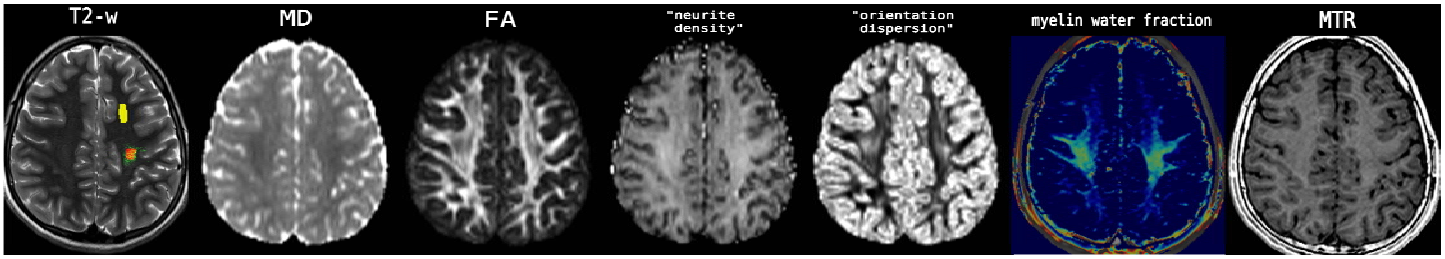

Figure 1: T2-weighted image (left) of a 14y-old healthy subject with ROI-definition in yellow (frontal) and red (CST), guided by the CST-fibres (green).

Data Analysis: mean diffusivity (MD) and fractional anisotropy (FA) were calculated using a non-linear least squares fit. NODDI-derived parameters, including intracellular volume fraction (neurite density) and orientation dispersion (ODI) were calculated based on a two-compartment model [2]. CST was tracked by constrained spherical deconvolution using the MRtrix software package [7]. MWF was fitted voxel-wise [8], in 2 steps. First all parameters including the flip angle were fitted, in the second step, the flip angle was fixed to the voxel-specific measured value, scaled to match the median value found in the first step. Number of fitted T2 points: 32; Chi^2 regularization of 1.01. ROIs were drawn onto conventional T2-weighted images with the CST overlaid (see figure 1).

Results

Figure 1 shows images of all measured microstructural imaging parameters. In the healthy controls (figure 2), MD, FA, MWF, and neurite density, but not ODI or MTR, were sensitive to differences in myelin architecture between the frontal WM and the CST ($p<0.01$). The relative standard deviations were smaller for the neurite density than for FA. The patients with MLD, where demyelination was suspected from diffuse T2-signal hyperintensity in the WM, showed significantly reduced FA, neurite density, MWF, MTR, and higher MD than the controls in the ROIs ($p<0.01$). Most striking differences were seen in neurite density, MD, and MWF.

Discussion

We found that diffusion imaging and myelin water fraction can give quantitative and sensitive information about differences in myelin microstructure. Neurite density was found to be more sensitive than FA, underlining the limitation of FA (and eigenvalues) in crossing fibre regions.

The higher myelin water fraction in the CST is in accordance with previous results [3] and, together with the increase in neurite density, might be caused by the thicker myelin sheaths and larger axon diameter with higher intracellular diffusion fraction [2]. On the other hand, in regions with demyelination, the myelin loss as well as the increase in extracellular space, lead to lower MWF and decreased neurite density.

Conclusion

NODDI and MWF parameters appear to be sensitive in the study of WM with underlying crossing fibre architecture and give additional information in MLD microstructure. These preliminary results should be replicated in a more systematic analysis of a larger cohort of this rare disease.

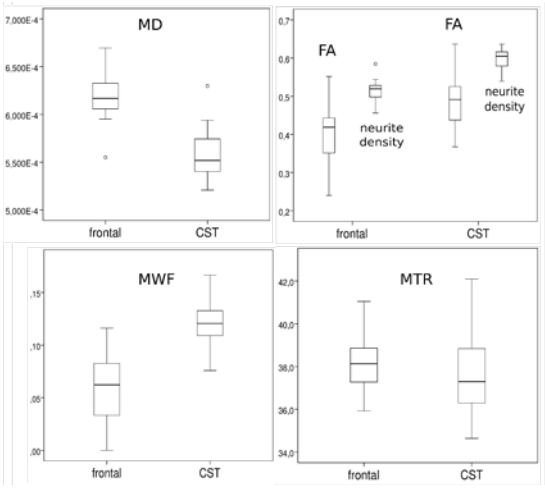

Figure 2: Measurement parameters in healthy subjects of frontal WM vs. CST.

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