

## Tract-Based Spatial Statistics of Diffusion MRI in Paediatric Multiple Sclerosis

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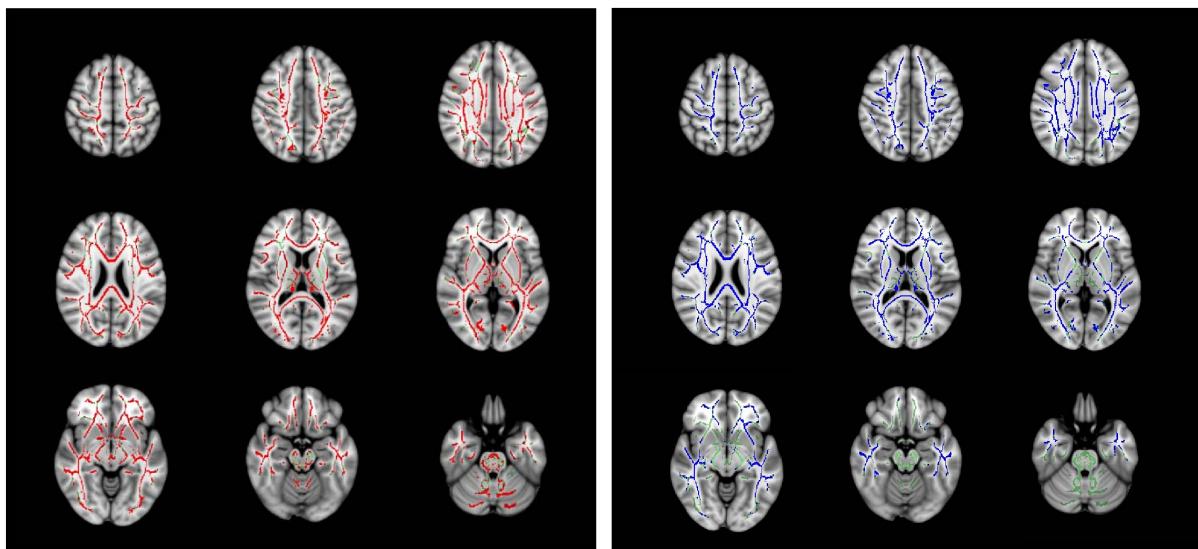
**Target audience** This study is beneficial to paediatric neurologists in showing the widespread nature of structural brain abnormalities in paediatric onset MS. This approach is readily applied to paediatric data and the method has potential to be investigated further as a prognostic marker in this patient population.

**Purpose** Paediatric onset multiple sclerosis (POMS) is known to result in a slower accumulation of physical disability over time despite the higher relapse rate than adult-onset MS [1]. However, the mechanisms associated with POMS remain unclear. In this study we aim to investigate microstructural differences between paediatric MS patients and healthy control children using tract-space spatial statistics (TBSS) [2]. We present preliminary results showing increased mean diffusivity (MD) and reduced fractional anisotropy (FA), a pattern consistent with severe demyelination, which is widespread across the white matter.

**Methods** The dataset consists of 11 children with MS aged 10.1-17.9 years (mean  $15.4 \pm 2.1$  years; 8 female) and 11 healthy children aged from 10.1 to 18.7 years (mean  $15.4 \pm 2.5$  years; 6 female). Diffusion MRI data was acquired in patients as part of their standard clinical imaging. Informed consent was obtained from children that served as controls in this study. Scans were acquired using a Siemens Avanto 1.5T clinical scanner. Echo-planar diffusion-weighted images were acquired along 60 non-collinear gradient directions at  $b=1000 \text{ s mm}^{-2}$ , with a single  $b=0$  image for normalisation. A voxel matrix of  $96 \times 96$  was used to obtain 60 contiguous axial slices with a  $240 \times 240 \text{ mm}$  field of view. The voxel dimensions were  $2.5 \times 2.5 \times 2.5 \text{ mm}$ . Other acquisition settings: TR=7300 ms, TE=81ms, gradient strength=40 mT m<sup>-1</sup>. T1-weighted images were also acquired in the same session.

Preprocessing of the data involved removal of eddy-current distortions, skull-stripping of the brain volume and fitting the diffusion tensor (DT) using FSL (<http://www.fmrib.ox.ac.uk/fsl>). The standard TBSS algorithm was used to analyse the data. To improve alignment, a study specific template was generated, to which all the subjects were registered. In addition to FA, changes in MD, axial ( $\lambda_{\text{axial}}$ ) and radial diffusivity ( $\lambda_{\text{radial}}$ ) of the DT were also investigated. As a further analysis, we correlate the diffusion measures of the patient group with the following clinical information: age at presentation, illness duration, expanded disability severity score (EDSS) and number of relapses.

**Results** Widespread significant ( $p<0.05$ ) differences were found between POMS patients and controls for all diffusion metrics. Specifically, POMS patients showed a reduced FA compared to controls (figure 1, left) and increased MD (figure 1, right),  $\lambda_{\text{axial}}$  and  $\lambda_{\text{radial}}$  diffusivities (not shown). We observe significant ( $p<0.05$ ) positive correlations between FA and age at presentation throughout the skeleton, with the strongest correlations in the corpus callosum and posterior regions of the brain. MD is significantly ( $p<0.05$ ) negatively correlated with age at presentation, but to a lesser extent. EDSS, illness duration and number of relapses are all significantly ( $p<0.05$ ) negatively correlated with FA and positively correlated with MD in similar regions.



**Figure 1** – TBSS results showing widespread significant ( $p<0.05$ ) differences between paediatric MS patients compared to healthy controls for (left) FA and (right) MD. Regions where MS patients have lower FA than controls are shown in red; regions where MS patients have higher MD than controls are shown in blue. No significant difference was found in green voxels.

**Discussion and conclusions** We present the preliminary analysis of TBSS comparing paediatric MS patients to healthy control children. Results show widespread differences throughout the TBSS skeleton in paediatric MS compared to controls for all tensor metrics. These differences are consistent with severe demyelination. Aliotta et al [3] show significant differences between patients with childhood-onset MS and adult-onset MS using TBSS. They speculate that increased brain plasticity in childhood can limit the effects of MS, which may contribute to the lower physical disability over time in POMS compared to adult onset MS. In addition to the group differences, diffusion tensor measures also correlated with clinical scores in the patient cohort. However, further work is required to clarify the precise mechanisms and trajectories of disease progression in POMS.

**References** [1] Absinta et al (2010), J Neurol Neurosurg Psychiatry, 81 (12): 1357-62 [2] Smith et al (2006), NeuroImage, 31:1487-1505 [3] Aliotta et al (2012), HBM, doi: 10.1002/hbm.221148