

Magnetization Transfer Ratio Tractometry in Multiple Sclerosis

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TARGET AUDIENCE: MR scientists developing tractography analysis tools, and clinicians studying multiple sclerosis.

PURPOSE: MR tractometry is a promising new application of diffusion tractography that associates quantitative MRI biomarkers to specific white matter pathways^{1,2}. One such biomarker is the magnetization transfer ratio (MTR), which is sensitive to the myelin content in brain white matter and is used to evaluate the level of demyelination in neurodegenerative diseases such as multiple sclerosis (MS). Combining MTR and diffusion imaging provides valuable information about the relationship between myelination and fiber integrity^{3,4}. Computing the MTR along fiber tracts can help us identify the level of myelination of different fibers in the brain, as well as understand the patterns of (de)myelination in normal-appearing white matter in MS patients and healthy controls.

METHODS: We performed MTR tractometry on three healthy controls (two females, one male, age 37.5 ± 5.5) and six relapsing-remitting MS patients (five females, one male, age 36.3 ± 9.4 , EDSS range 1-3), three of which had lesions in the cortico-spinal tract (CST). Diffusion images were acquired on a 1.5T Philips Gyroscan with 32 gradient directions (2.5mm^3 , $b_{\text{max}}=1000$, TR/TE = 8500/100ms), and a least squares diffusion tensor fit was performed to generate fractional anisotropy (FA) and mean diffusivity maps. MTR was computed from a pair of MT on/off images ($1 \times 1 \times 3$ mm, TR/TE = 35/10ms). Additionally, a PD-weighted and a FLAIR image were acquired. Lesion segmentation was performed using an automated lesion segmentation tool⁵. For each subject, both whole brain and region of interest (ROI) tract analyses were performed. For the former, whole brain streamline tractography was performed with fiber assignment by continuous tracking (FACT)⁶. Tracking was stopped if FA was less than 0.2, or the curvature from one voxel to the next was greater than 70 degrees. For the latter, tractography was used to segment the ROIs used in the analysis. The ROIs segmented were the corpus callosum (CC), CST, and arcuate fasciculus (AF), which were delineated using tract-specific waypoints drawn in standard space and transformed to native space. For the ROI analysis the FA threshold was 0.1. Tracking was initiated in all voxels in the volume and tracts that passed through the tract-delineating waypoints were retained, except for tracts passing through lesions. For both whole brain and ROI analysis, the tracts were assigned a mean MTR score, computed by averaging the MTR values in the voxels containing the tract. Histograms of the fiber MTR scores were computed, and the fibers were grouped according to their percentile ranking.

RESULTS: Figure 1 shows the fiber MTR scores for a range of percentiles in the three subject groups in different ROIs. Whole brain tractometry demonstrates fiber MTR differences between controls and patients, whereas ROI-based analyses distinguish between the two patient subgroups. Interestingly, for each subject group, the 95th percentile of fibers has similar MTR values. Figure 2 shows the 95th percentile of fibers (highest MTR score), along with the bottom 5 percent (lowest MTR score) for three subjects, representative of their respective group. While the control subject has a symmetric distribution of high MTR fibers localized in the cortico-spinal tract and the corpus callosum, the MS patients demonstrate lateralization of the high MTR fibers.

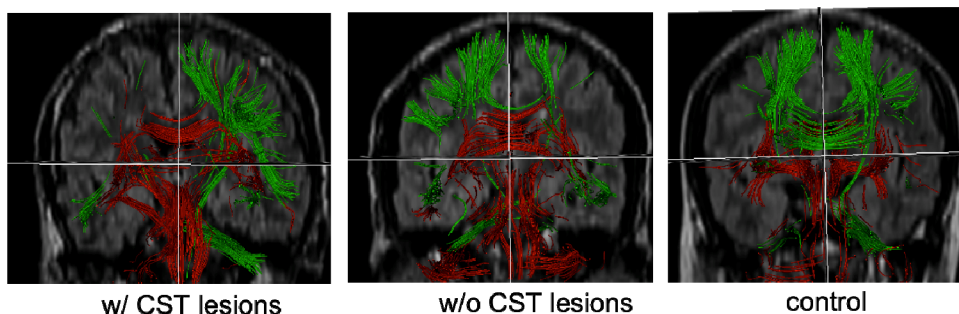


Figure 2: MS patients with (left) and without (middle) CST lesions, and a control (right). Coronal view of the 5 percent of fibers with highest (green) and lowest (red) MTR score.

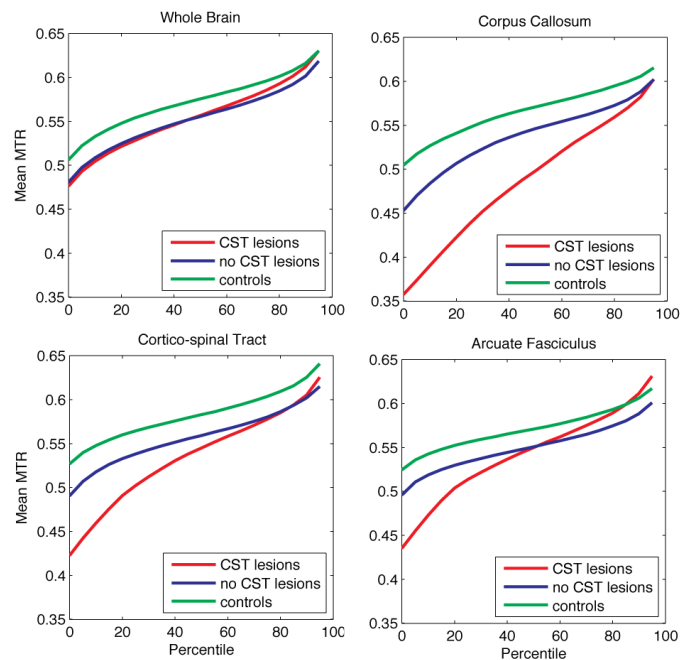


Figure 1: Mean fiber MTR in different ROIs for the three subject groups.

DISCUSSION: The decrease in MTR in the fiber tracts of patients with MS is consistent with previous studies that have combined diffusion and magnetization transfer^{3,4}. Figure 1 also confirms that normal-appearing white matter has lower MTR in MS patients compared to controls, but the most myelinated fibers have similar MTR across subject groups. This suggests that the greatest differences in demyelination due to MS are to be found in the mid-to-low MTR fibers, as evidenced by the fanning of the curves in Figure 1. Figure 2 shows that despite the similar MTR values in the 95th percentile, the clustering of highly myelinated fibers is asymmetrical in MS patients, possibly due to the MS lesion distribution.

CONCLUSION: Scoring and grouping fibers by their average MTR score gives insight in the tract-specific pattern of demyelination in MS.

REFERENCES: [1] Bells *et al.* Proc. ISMRM 19th Annual Meeting, Montreal, p.678 (2011) [2] Stikov *et al.* Neuroimage 54(2): 1112-1121 (2011) [3] De Stefano *et al.* PLoS ONE 6(4): e19452 (2011) [4] Harrison *et al.* J Neurol: 1-10 (2012) [5] Schmidt *et al.* Neuroimage 59: 3774-3783 (2012) [6] Mori *et al.* Ann Neurol 45: 265-269 (1999)