

## Diffusion Tensor Imaging Detects Injury to Medial Longitudinal Fasciculus

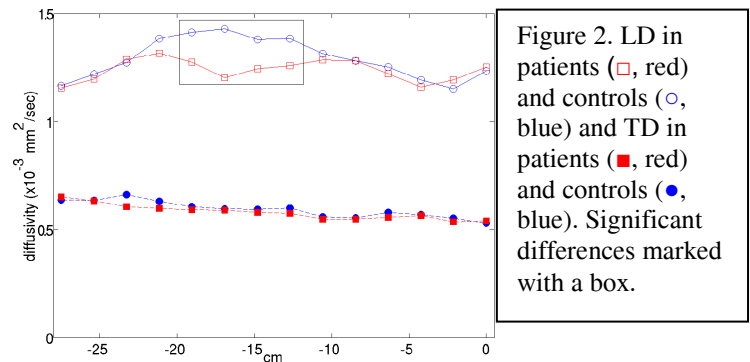
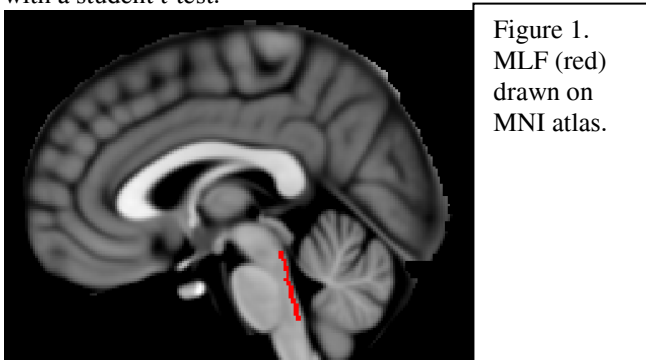
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**TARGET AUDIENCE:** Researchers and clinicians studying imaging-function correlates in multiple sclerosis (MS), particularly with regard to diffusion tensor imaging (DTI).

**PURPOSE:** To test the hypothesis that DTI can detect injury to the medial longitudinal fasciculus (MLF) in the context of MS-induced internuclear ophthalmoplegia (INO). Conventional imaging identifies MS pathology but is limited in quantifying injury. Quantification is confounded by the weak correlation between lesions and clinical concomitants, the clinico-radiologic paradox. DTI provides quantitative measures of tissue injury while injury to the MLF in MS provokes a well-characterized ocular motor disorder, INO. INO can be confirmed at the bedside and objectively with high precision infrared oculography<sup>1</sup>. The tight relationship between the MLF and ocular motor function provides a unique opportunity to couple a disease-related pathophysiologic signature with advanced imaging metrics of CNS tissue injury. However, as the MLF is small compared to typical spatial resolution for DTI, it is unclear if DTI has sufficient sensitivity to detect injury associated with INO.

**METHODS:** 11 healthy controls and 32 patients with chronic INO were studied under an IRB-approved protocol. All imaging was performed on a 3 T Philips Achieva with standard 8-channel head coil (Philips Healthcare, Cleveland). DTI was acquired at high spatial resolution with cardiac pulse triggering, covering brainstem (1x1x2mm voxels, 20 slices, 30 diffusion-weighting gradients with  $b=700$  sec/mm<sup>2</sup>, one  $b=0$ , NEX=2). After motion correction, the diffusion tensor and measures of tissue integrity (longitudinal diffusivity (LD), transverse diffusivity (TD), mean diffusivity (MD) and fractional anisotropy (FA)) were calculated for each voxel with a free water fraction correction for partial volume averaging with surrounding cerebrospinal fluid spaces<sup>2</sup>. The MLF was drawn by hand on the Montreal Neurological Institute (MNI) template (figure 1) and coregistered to DTI space using FSL<sup>3</sup>. The median of each tissue integrity parameter was taken in each slice. Values in corresponding slices were compared between patients and controls with a student t-test.



**RESULTS:** Figure 2 shows the mean, across subjects, of LD and TD at positions below the inferior edge of the red nucleus. Significant differences (boxed) were found at levels from 12 to 19 mm below the inferior edge of the red nucleus ( $p < 0.02$ ) for LD. No significant differences were found in TD or FA. Significant differences in MD ( $p < 0.05$ ) are driven largely by changes in LD.

**DISCUSSION:** Significant differences are found in LD, a proxy for axonal integrity<sup>4</sup> at levels corresponding to crossing pontine fibers. The lack of differences found in TD, a proxy for demyelination, is surprising given that MS is a demyelinating disease. These findings may either reflect a pattern of injury specific to INO or the relative sensitivity of the measurement to different tissue integrity parameters.

**CONCLUSION:** We find that DTI is capable of detecting injury to the MLF relating to INO despite the small size of the pathway. Future work will focus on correlations with high precision measurements of oculography<sup>1</sup> towards characterizing the association between imaging and functional measures of disability.

### REFERENCES

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