Quantitative Assessment of Traumatic Spinal Cord Injury with Diffusion Tensor and Magnetization Transfer MRI

S. A. Smith[1,2], V. Belegu[3,4], B. A. Landman[5], B. A. Chodkowski[1,2], J. A. Farrell[2,6], P. C. van Zijl[1,2], and J. W. McDonald[3,4]

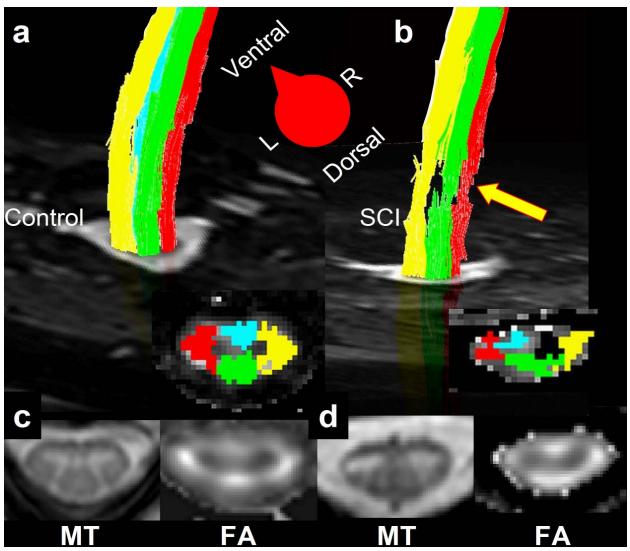
[1]F.M. Kirby Center, Kennedy Krieger Institute, Baltimore, MD, United States, [2]Russell H. Morgan Department of Radiology and Radiological Science, Johns Hopkins University, Baltimore, MD, United States, [3]International Center for Spinal Cord Injury, Kennedy Krieger Institute, Baltimore, MD, United States, [4]Department of Neurology, Johns Hopkins University, Baltimore, MD, United States, [5]Department of Biomedical Engineering, Johns Hopkins University, Baltimore, MD, United States, [6]Program in Molecular and Computational Biophysics, Johns Hopkins University, Baltimore, MD, United States

Introduction: Lesions in the spinal cord contribute to functional deficits in patients afflicted with pathologies of the central nervous system (CNS) such as spinal cord injury (SCI) and even multiple sclerosis (1). In traumatic SCI, the neurological location of the injury and the American Spinal Cord Injury Assessment Score (ASIA) are used to describe the clinical severity of the injury. However, the ASIA scale is not a continuous, linear scale and may not be specific for prognosis or identification of the potential for recovery. MRI of the spinal cord is difficult because of pragmatic barriers: 1) the spinal cord is small, (1-1.5 cm in diameter) and the internal structures damaged in SCI are even smaller (3-5 mm); and 2) physiological motion (CSF flow and respiration) can lead to artifacts (i.e. image blurring) in high-resolution imaging. Furthermore, while conventional MRI of chronic SCI easily shows the etiology, is hindered by the lack of visual clues to the morphology of the damaged tissue (due to poor contrast between white matter, gray matter). Consequently, SCI is difficult to directly quantify with conventional MRI due to a lack of straightforward correlation with functional deficits. Thus, a spinal cord MRI protocol that can examine the structural integrity of the cord, in a tract-specific, quantitative fashion, would be helpful in the clinic.

Methods: MRI Acquisition: Six healthy volunteers and one chronic, traumatic SCI patient (C4-5 ASIA D) were studied after signed, informed consent. All studies were approved by the local institutional review board. Scans were performed on a Philips 3T MRI system with body coil excitation and a 16 channel neurovascular coil for reception. The imaging volume was centered at the thyroid cartilage and covered the superior aspect of C2 to the inferior aspect of T2. Diffusion tensor imaging (DTI) of the cervical cord was performed using a multi-slice spin echo with single-shot EPI. Five averaged minimally weighted (b_o) and 16 diffusion weighted volumes (b-value = 500 s/mm^2, non-collinear directions optimized, *a priori*, to sample a prolate tensor such as is found in the spinal cord) were acquired. Other parameters were: TR/TE = 6.2s/63 ms, nom. resolution = 1.5x1.5x3 mm, 40 slices, 3 averages, and scan time = 2 min. per average. Magnetization Transfer (MT) weighted imaging was performed using a 3D GRE sequence with multi-shot EPI (factor = 3, TR/TE/α = 110 ms/13 ms/9°) with a 24 ms, 5-lobed sinc-gauss MT prepulse of 8.5 µT, at 1.5 kHz off-resonance. A reference scan was acquired without MT preparation. MT sequences were obtained over the same field of view as DTI, but with a nominal resolution of 0.7x0.7x3.0 mm, 40 slices, 2 averages, and total scan time = 7.5 min. **Data Analysis**: All images were coregistered to the initial b_o using a two step, sequential procedure implemented in AIR to correct for different distortion patterns between MT and DTI acquisitions: 1) 3D rigid body alignment, and 2) slice-by-slice, 3 degrees of freedom (1 rotational, 2 translational) 2D rigid body transformation. After coregistration, the diffusion tensor was estimated. Fractional anisotropy (FA), mean diffusivity (MD), transverse diffusivity ($\lambda_\perp$), and longitudinal diffusivity ($\lambda_{||}$) were calculated. Additionally, the MTCSF (magnetization transfer normalized by CSF) was calculated slice by slice (2). From the DTI datasets, the lateral and dorsal columns were reconstructed by selecting ROIs on the MTw images where excellent anatomical differentiation is seen (**Fig 1c**). These ROIs were used to seed the fiber tracts (thresholds: FA = 0.2, turning angle = 60°) analyzed in DTIStudio (3). These 3 tracts served as ROIs to obtain quantitative metrics of each column of the cervical spinal cord.

Results and Discussion: **Fig. 1a,b** shows 3D reconstruction of the fiber tracts (red, yellow – lateral columns, green – dorsal columns, and blue – ventral columns) in the cervical spinal cord in a healthy volunteer (**a**) and patient with chronic SCI (**b**). Note the poorly reconstructed fibers of the dorsal and lateral columns in the patient (**Fig 1b**, arrow). At C4 in the healthy volunteer (**Fig. 1c**), excellent GM/WM contrast is seen in the MTCSF images and FA is high (bright) in WM regions. In the SCI patient (**Fig 1d)**, at C4, the epicenter of the lesion, less GM/WM differentiation is seen in the MTCSF image, and a hypointensity is apparent in the lateral and dorsal columns on the FA map. Analysis of the quantitative metrics in the lateral and dorsal columns is shown in the plots (control – black, SCI patient, red). FA is seen to drop focally at the epicenter of the lesion in all columns and returns to approximate the control value both rostral and caudal to the lesion. MTCSF, however, in the patient shows a substantial and diffuse elevation in all slices rostral to T1 indicating a more extensive abnormality. It has been suggested that MT imaging is sensitive to macromolecular content of tissue (i.e. changes in myelin content in the CNS) (4). In contrast, FA reports on the diffusion anisotropy, which is due, in part, to the presence of axonal and myelin barriers to diffusion. It is interesting to note the pattern of focal FA abnormality coupled in overall fashion with diffuse MTCSF abnormality in this particular patient. Our data suggests that that diffusion metrics and MT measures may be sensitive to different pathological processes present in chronic SCI. One possible interpretation is that there is a disruption of tissue proximal to the lesion site and concomitant diffuse, distal oligodendrocyte death with subsequent dysmyelination (5) causing altered, yet surviving, function. Interestingly, this particular patient presents with bilateral weakness (though not loss of motor function) concomitant with deficits in peripheral sensation (though the sensory system is intact). This preliminarily suggests that a many axonal connections have been maintained above and below the lesion, and due to altered function, some degree of distal demyelination, which is in accord with the MRI findings presented here.

Conclusion: A combined DTI and MT approach may allow a quantitative assessment of the structural and connective integrity of spinal cord tissue and its relationship to function. DTI tractography and column-specific metrics may be particularly useful in revealing the microstructural evolution of SCI in vivo. **References: 1)** Gass A, et al. Ann. Neurol. 36(1); 1994. **2)** Smith SA, et al. MRM 54(1); 2005. **3)** Jiang H, et al. Comput. Meth. Prog. Biomed. 81(2); 2006. **4)** Schmierer K, et al. Ann Neurol 56; 2004. 5) McDonald JW and Belegu V. Neurotrauma 23; 2006 **Grant Acknowledgement**: NIH/NCRR-P41RR15241



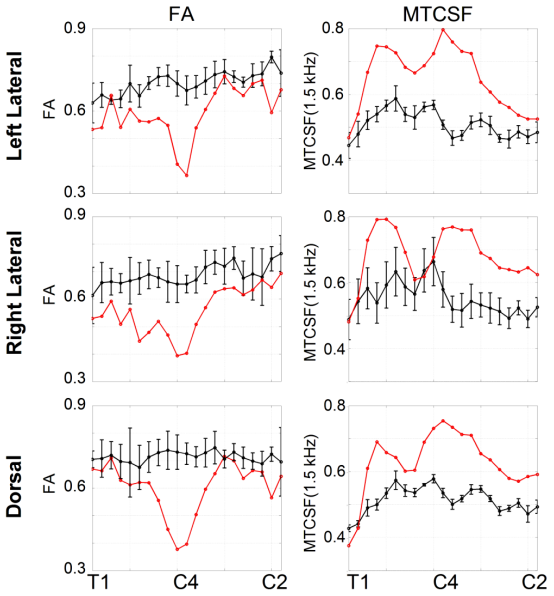


Figure 1: (a,b) 3D reconstruction of fiber tracts (dorsal – green, lateral – red, yellow, and ventral – blue) in cervical spinal cord of a healthy control (**a**) and SCI patient (**b**). **(c,d)** MTCSF and FA maps at C5 in control (**c**) and at the epicenter of the lesion in SCI (**d**). Plots represent tract-wise MTCSF and FA mean +/- STD (patient – red, control – black). Note the focal drop in FA in all columns with diffuse elevation in MTCSF representing the extent of SCI pathology.