In vivo Longitudinal Diffusion Tensor Imaging of Spinal Cord Injury in Rats

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Introduction: Damage to white matter fiber tracts is a major consequence of traumatic spinal cord injury (SCI) and results in functional deficit. Diffusion tensor imaging (DTI) is a powerful modality for noninvasively following temporal changes in the fiber tract pathology. With the exception of a single abstract [1], DTI studies of SCI in rodents are limited to *ex vivo* [2], [3], which are limited to providing only a snap shot picture at a single time point. In addition, *in vivo* DTI studies of normal spinal cord, have clearly demonstrated that *in vivo* diffusion measures are quantitatively different from those of excised cords [4]. Majority of the published DTI studies of SCI focused on the anisotropic indices for assessing the tissue integrity. Recent studies strongly suggest that the individual diffusivities (eigenvalues) along the length of the cord (λ_l,) and perpendicular to it (λ_t,) provide improved pathologic specificity compared to the diffusion anisotropic indices [5]. Here we report the *in-vivo* longitudinal changes in the DTI metrics that include mean diffusivity (D_{av}), fractional anisotropy (FA), and individual eigenvalues of different white matter regions for up to 8 weeks post-injury and demonstrate regionally dependent pathologic changes.

Methods: All MR studies were performed on a 7-T Bruker scanner. A total of twelve male Sprague-Dawley rats weighing between 300 and 350 g were used in these studies and divided into two groups of six each. One group received moderately severe injury at the T7 level while the second group underwent sham operation without injury and served as the control. A 11x27 mm rectangular radio frequency coil was implanted over the site of injury and coupled inductively to an external coil of 15x30 mm in size. The BBB scores were determined every week. DTI data was acquired at two, four, six and eight weeks post injury using a multi-shot EPI sequence from 20 contiguous axial slices, each of 2 mm thick with an in-plane resolution of 200 microns and square FOV of 26.2 mm. The DTI metrics, FA, λ_l, λ_t, and D_{av}, were determined from dorsal, ventral, lateral (D-, V-, L-) white matter that are rostral and caudal to the epicenter of the injury. ANOVA with repeated measures was performed for comparing the differences between mean FA, λ_l, λ_t, and D_{av} values for all the three regions at each time point.

Results: The temporal changes of the DTI metrics 2 mm rostral and caudal to the site of injury are shown in Table 1. The FA values of injured cord are lower and D_{av} values are higher compared to the uninjured normal cord at all time points. Since the injured cord showed decreased λ_l and increased λ_t, relative to normal at all locations and at all time points, we considered an increase in λ_t and a decrease in λ_t as an indication of tissue recovery.

Rostral section: V-WM showed an increase in the FA value from day 14 to 28, followed by a decline on day 56. λ_t, initially showed a decrease, followed by an increase on day 56. L-WM showed an initial increase in FA from day 14 to 56. λ_t, continued to decline until day 56. Temporal changes were not observed in either D_{av} or λ_l in both V-and L-WM.

Caudal section: V-WM showed an initial decline in D_{av} from day 14 to day 28 followed by an increase up to day 56. λ_l remained constant until day 42, but increased by day 56. Statistically significant temporal changes were not observed in FA and λ_l. L-WM showed an increase in FA until day 42, followed by a decline by day 56. The other DTI metrics did not show any temporal changes. D-WM did not show any significant differences with time in both rostral and caudal section. The results at 4 mm caudal and rostral sections were very similar to those observed at 2 mm, except that the temporal changes in different region are smaller. At 6 mm, the DTI metrics were not statistically different from the uninjured tissue at all time points investigated in these studies.Statistically significant correlation was only observed between the BBB scores and λ_l in the L-WM in the rostral section. No correlation was observed between BBB and of the DTI metrics in the caudal section.

Discussion and Conclusions: The DTI metrics show tissue disruption in regions that appear normal on the conventional MRI, suggesting the potential of DTI in detecting subtle pathology in SCI. These studies also demonstrate that the disruption of white matter tracts is less pronounced with increased distance from the epicentre. Based on the published studies [5], demyelination increases the eigenvalue representing the transverse water diffusion, λ_t, with relatively little effect on the longitudinal water diffusion, λ_l. On the other hand, axonal damage without demyelination appears to result primarily in reduced λ_l. Taken together, our results suggest recurrence of demyelination after day 28 in the V-WM and continued remyelination in the L-WM. These results also suggest lack of axonal recovery in all the three regions of the white matter in the rostral sections. Our studies demonstrate a very heterogeneous tissue recovery in different regions of the injured cord and showed caudal-rostral asymmetry in the tissue recovery. Finally, the individual diffusivities appear to improve the pathologic specificity over the anisotropic index alone.

Rostral: V-WM

	FA	λ_t
D14	0.64 ± 0.045	0.65 ± 0.033
D28	0.70 ± 0.085	0.52± 0.030
D42	0.68 ± 0.059	0.58 ± 0.036
D56	0.65 ± 0.097	0.65 ± 0.014

[14, 28] P=0.04 [14, 28] P=0.006
[28, 56] P=0.01 [28, 56] P=0.005

Caudal: V-WM

	D_{av}	λ_t
D14	1.01 ± 0.09	0.49 ± 0.054
D28	0.95 ± 0.15	0.46 ± 0.039
D42	0.99 ± 0.12	0.44 ± 0.054
D56	1.11 ± 0.19	0.54 ± 0.068

[28, 56] P=0.04 [42, 56] P=0.02
[42, 56] P=0.04

Rostral: L-WM

	FA	λ_t
D14	0.64 ± 0.053	0.75 ± 0.056
D28	0.65 ± 0.045	0.68 ± 0.046
D42	0.69 ± 0.084	0.58 ± 0.019
D56	0.68 ± 0.047	0.61 ± 0.049

[14, 42] P=0.02 [14, 42] P=0.027
[14, 56] P=0.01 [14, 56] P=0.048
[28, 42] P=0.01

Caudal: L-WM

	FA
D14	0.66 ± 0.121
D28	0.71 ± 0.111
D42	0.72 ± 0.110
D56	0.70 ± 0.080

[14, 28] P=0.03
[14, 42] P=0.01
[14, 56] P=0.01

Table 1: The average ± mean sd at 2mm rostral and caudal to injury.

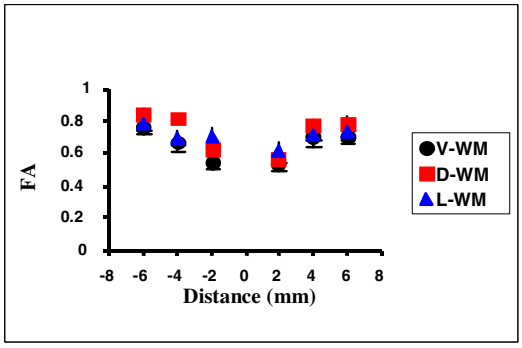

Figure 1: Spatial Variation of FA in Injured Cords

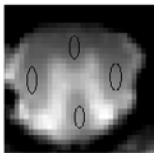

Figure 3. ROI placement in Spin echo image.

Figure 2: FA maps of Injured animal. The slice locations are shown at the bottom. Negative represents rosrtal location.

References:

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