# In vivo diffusion tensor derived fiber orientation failed to detect secondary axonal injury

Joong Hee Kim[1], and Sheng-Kwei Song[1]
[1]*Radiology, Washington University School of Medicine, St. Louis, MO, United States*

**Introduction**

Diffusion tensor imaging (DTI) has been employed to examine spinal cord white matter injury utilizing the derived fiber orientation, anisotropy, and diffusivity. The disconnected spinal cord white matter tracts from transection injury has been successfully detected using diffusion tensor tractography (DTT)[1]. However, DTT based on anisotropy threshold and the direction of the major eigenvector may not sufficiently reflect white matter tract integrity or functionality. For example, injured axons may still preserve its directionality and anisotropy, as seen in acute SCI[2]. In this study, we present longitudinally observed DTI of the rat spinal cord undergoing right lateral transection. The pixel-based directional diffusivities acutely localized the disrupted white matter tracts and detected secondary axonal injury where anisotropy and major fiber orientation failed.

**Materials and Methods**

Twelve female Sprague-Dawley rats weighing 200 – 250 g underwent right lateral white matter transection (n = 6) or sham operation (n = 6) at T9. In vivo DTI was performed at 3 hrs and one week after injury using respiratory gated spin echo diffusion weighted sequence using previously reported imaging setup[3,4]. The in-plane resolution of present study is 156 μm x 156 μm with 1.5 mm thickness on a 4.7 T magnet. The obtained DTI parameters maps were co-registered and averaged[5].

**Results and Discussion**

The co-registered axial diffusivity (λ||, $\mu m^2$/ms) and fractional anisotropy (FA) maps are shown in Fig. 1. For entire in vivo study, the DTI measures of contralateral white matter were comparable to those of control (data not shown). Thus, data analyses were focused on ipsilateral white matter. Two segments, epicenter (0.0 mm) and 6.0 mm rostal to epicenter, were investigated to examine temporal and spatial white matter degeneration. Acutely, only λ|| detected white matter injury localizing epicenter with significant diffusivity reduction where FA failed to identify epicenter (Fig. 1-d). The remote cord (6.0 mm) showed no difference from control. At one week after injury, most significant λ|| and FA reduction was seen at epicenter. In addition, significantly reduced λ|| and FA was seen at 6.0 mm cord suggesting diffuse axon injury. The suggested axon injury was also observed in immunohistochemical histology (data not shown). The whisker plot of major fiber orientation was observed at one week after injury (Fig. 2). A completely disoriented fiber orientation was observed at epicenter as expected from λ|| and FA. However, the remote cord (6.0 mm) showed largely preserved fiber orientation where both DTI measures (λ|| and FA) and histology showed axonal injury. The results in Fig. 1 and 2 may suggest that DTT based on diffusivity threshold would show better sensitivity to axon integrity from acute to chronic phase of injury. Another interesting finding in this study is the heterogeneously reduced λ|| and FA in the remote (6.0 mm) cord (Fig. 2 - e and f). The λ|| and FA of outer lateral white matter was reduced more than those of inner lateral tracts. Considering the fast Wallerian degeneration along neural signal transduction direction, the relatively significant λ|| reduction in outer lateral white matter suggested that ascending white matter tracts from caudal to rostral cord are populated at the outer white matter where inner tracts are mainly descending. This finding is in good agreement with previous reports[6]. In conclusion, the longitudinally observed λ|| accurately detected acute and diffuse axonal injury by providing accurate assessment of axon integrity.

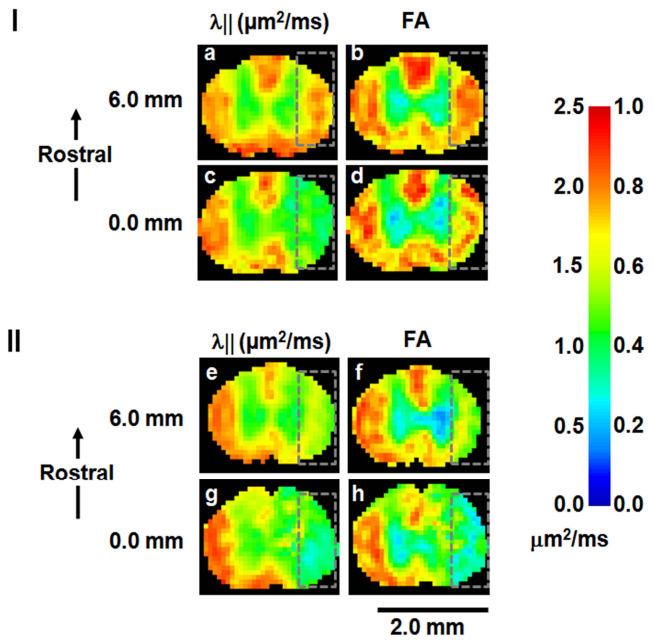


Figure 1. In vivo DTI derived axial diffusivity (λ||, $\mu m^2$/ms) and fractional anisotropy (FA) maps at 3 hrs (panel-I) and one week (panel-II) after injury. Maps were averaged from six injured rats by co-registration. Both λ|| and FA of contralateral white matter are comparable to control (data not shown) at both acute and one week after injury. In acute (panel – I), significantly reduced λ|| is well seen at epicenter (0.0 mm) where no visible difference is seen in FA map. Both λ|| and FA of ipsilateral white matter at 6.0 mm are comparable to those of contralateral (or control). In chronic (panel – II), both λ|| and FA at epicenter (0.0 mm) are significantly reduced. The 6.0 mm remote ipsilateral white matter also shows reduced λ|| and FA. The reduction is more severe at outer lateral white matter.

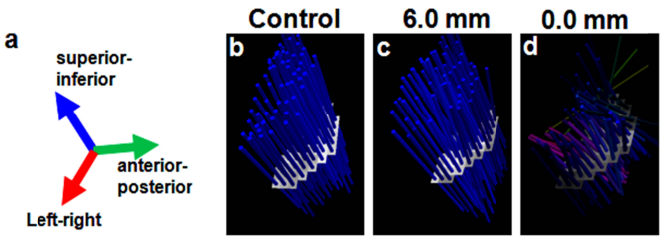


Figure 2. Whisker plots for major orientation of axon at one week after injury. The whisker plot was generated at right lateral (ipsilateral) white matter for control (b), 6.0 mm rostral (c), and epicenter (d). The overall axial diffusivity of panel b-d are 2.05 ± 0.08 (b), 1.47 ± 0.09 (c), and 1.08 ± 0.08 (d) in $\mu m^2$/ms. A statistically significant difference was seen (b vs. c, p = 0.003) and (c vs. d p = 0.003). However, the 6.0 mm cord shows largely preserved major axon orientation as control where completely disoriented major axon direction is seen at epicenter.

**References**

1. Fujiyoshi *et al.,* J. Neurosci., 27:11991-11998, 2007.
2. Loy *et al.,* J. Neurotrauma, 24:979-990, 2007.
3. Kim *et al.,* Neurobiol. Dis., 21:626-632, 2006.
4. Kim *et al.,* ISMRM Proc., 19:5604-2404, 2011.
5. Budde *et al.,* J. Neurosci., 29:2805-2813, 2009.
6. Watson *et al.,* The Spinal Cord, Academic Press, 2009.

**Acknowledgements:** This study was supported by NIH: R01 NS 047592 and R01 NS 054194.