In vivo Diffusion Tensor Imaging in Rat Model of Chronic Spinal Cord Compression

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Introduction

Although conventional MRI can identify the lesion sites in a diseased or damaged spinal cord (SC), diffusion tensor imaging (DTI) is more sensitive to subtle microstructural changes during pathology[1,2]. There were numerous studies employing DTI to differentiate pathology in various SC injury or disease models[1,3]. However, many of the studies were either performed *in situ* or in a model with traumatic injury. Cervical myelopathy, a common SC dysfunction in aged population, can be induced by spinal cord compression. In order to characterize the nature of neurodegeneration in this chronic SC disease and understand the underlying pathophysiology, *in vivo* DTI was employed to study the rat model of SC compression.

Methods

Animal Preparation Laminae of C3-C7 were exposed in 4 SD adult rats. A urethane-containing polymer was then inserted into the lateral side of C5-C6 and allowed to expand upon absorbing tissue fluid for approximately half a year before MR acquisition. ***MR acquisition*** MRI experiments were performed using Bruker PharmaScan 7T scanner. Respiration gated 4-shot SE-EPI sequence with navigator echo was used with the following parameters: TR/TE=3000/29ms, δ/Δ=3.5/17ms, slice thickness=2mm with 0.2mm inter-slice gap, FOV=30mm, data matrix=128x128, NEX=4. Diffusion encoded gradients with b=0.8ms/μm^2 were applied along 30 directions. Localization of slices is shown in Fig. 1. ***Analysis*** DTI computation and fiber tracking were performed by DTIStudio (JHU, Baltimore, mri.kennedykrieger.org) with FA threshold = 0.2, tracking was stopped if FA <0.15 or turning angle >45^0. Regions of interest (ROIs) were defined manually and measured on 4 regions of white matter (WM) in 9 slices.

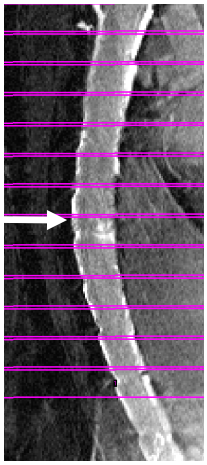

Figure 1. Localization of slices. The white arrow indicates the slice shown in Fig.2&3.

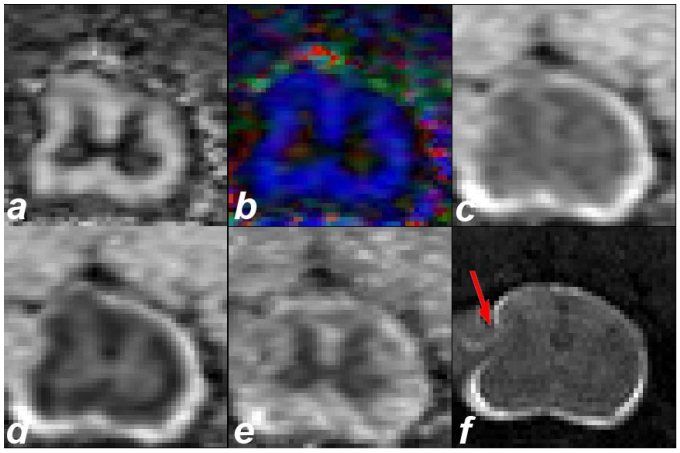

Figure 2. Different parametric maps of compressed SC. **(a)** FA, **(b)** colour coded FA, **(c)** Trace **(d)** $\lambda_{//}$, **(e)** $\lambda_{\perp}$, **(f)**PD-WI,. The arrow indicates the lesion area.

Results and Discussions

The different DTI parametric maps of a slice covering the lesion site are shown in Fig. 2, as indicated by the white arrow in Fig. 1. The water absorbing polymer compressed the spinal cord laterally as indicated by the red arrow. The ipsilesional lateral WM was compressed and distorted. However, this injury to other regions was moderate and such compression did not appear to have effect on other WM regions. A visualization of the fibers is shown in Fig.3. Fibers could be traced reasonably in different WM regions except in the ipsilesional side. ROI measurements of different DTI parameters against the distance f rom the lesion epicenter are plotted in Fig.4. Only FA in ipsilesional region showed significant difference in the non-parametric Kruskal Wallis test ($p<0.05$). FA in the ipsilesional region was significantly lower at the lesion epicenter, suggesting DTI is a sensitive metric to detect this progressive damage. Rostral-caudal asymmetry was also observed. Lower $\lambda_{//}$, $\lambda_{\perp}$ and higher FA in caudal region could be seen and they were consistent with previous studies[4]. It was proposed that such caudal regeneration was attributed to the asymmetric angiogenesis[4]. DTI is sensitive to neural degeneration and regeneration and is therefore potentially applicable in evaluation of drug treatment in SC diseases.

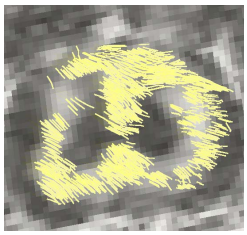

Figure 3. Fiber tracking. No fibers are seen in the lesion site.

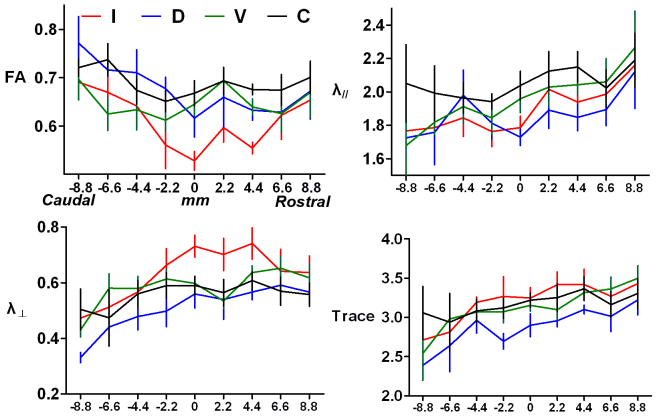

Figure 4. Average diffusion characteristic along the SC (Mean±SD). Red: Ipsilesional(I); Blue: Dorsal (D); Green: Ventral (V); Black: Contralesional (C). $\lambda_{//}$, $\lambda_{\perp}$ and Trace are listed in μm^2/ms.

Conclusion

In this study, we demonstrated the feasibility of using DTI as a non-invasive technique to obtain microstructural information from the chronic neurodegenerative SC model. With high sensitive to the subtle pathological changes, DTI could serve as a metric to monitor the disease and assess treatment.

References

1. Ellingson BM et al. JMRI 2008;28(5):1068-79 2. Ford JC et al. MRM 1994;31(5): 488-943. Kim JH et al. MRM 2007;58(2):253-260 4. Deo AA et al. J Neurosci Res 2006;83(5):801-10