

# Acute in vivo DTI predicts chronic neurological disability in rats suffering traumatic spinal cord injury

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## Introduction

Traumatic damage to spinal cord results in severe functional deficit. Since the injury occurs radically, acute non-invasive diagnosis is essential for efficient clinical intervention and yet there is a lack of accuracy in current clinical diagnosis. Rodent has been used as animal model for contusive injury reporting promising results from fundamental mechanism of injury to effective treatment. Recent work suggests that *in vivo* MR-diffusion measurements can detect lesion on spinal cord white matter with appropriate histology validation (1 -3). In this study, in vivo full tensor diffusion measurement was conducted for acute contusion injured rat cord using a custom-made passively decoupled volume and surface coil. Relatively high spatial resolution of DTI maps was achieved at field strength 4.7 T close to clinic. The acquired DTI maps (anisotropy, axial and radial (parallel and perpendicular to spinal cord) diffusivity) provide detailed structural information of spinal cord white matter for both control and injury enabling acute non-invasive evaluation of injury.

## Methods

Fourteen female sprague-dawley rat weighing 150 – 175g received contusive injury at T9 vertebrae level with impacting displacement from 1.0 mm to 1.5 mm. Acute *in vivo* DTI was performed covering epicenter at a 4.7 T magnet utilizing respiratory gated spin-echo diffusion-weighted sequence and passively decoupled volume (12-cm inner diameter, RF excitation) and saddle type surface coil (2.5 cm x 2.0 cm, signal receiver). The overall set up is similar to that described previously (4). All images were obtained with acquisition parameters of TR 2.5 sec (gated acquisition), TE 38 ms,  $\Delta$  18 ms,  $\delta$  7 ms, slice thickness 1.5 mm, field-of-view 2.0 cm x 2.0 cm, data matrix 128 x 128 (Image resolution, 157  $\mu$ m x 157  $\mu$ m x 1500  $\mu$ m), total data acquisition time ~ 1.0 hrs, (Gx,Gy,Gz) = (1,1,0), (1,0,1), (0,1,1), (-1,1,0), (0,-1,1), and (1,0,-1), and b = 0 and 1.0 ms/ $\mu$ m<sup>2</sup>. The neuro-function of injured rat was longitudinally assessed. The correlation between DTI parameters and neuro-function was examined by statistical analysis.

## Results and Discussion

High spatial resolution (78  $\mu$ m x 78  $\mu$ m x 1500  $\mu$ m after zero-filling) in vivo diffusion weighted images were acquired for full tensor within one hour. The tensor analyzed diffusion maps revealed anisotropic characteristic of rat spinal cord (Fig. 1). In general, white matter anisotropy is three folds of gray matter while axial diffusivity of white matter is six times of radial diffusivity. The white matter anisotropy and radial diffusivity (perpendicular to spinal cord) were preserved largely at acute phase providing manual ROI for total ventrolateral white matter where axial diffusivity (parallel to spinal cord) sensitively reflected traumatic injury enabling segmentation for normal appearing (or spared) white matter from traumatic damage (Fig. 1). The extent of normal appearing white matter was segmented by using normal axial diffusivity as threshold and the normalized volume showed good correlation to injury severity (impacting displacement) and endpoint (3 weeks after on set) neuro motor function (Fig. 2).

## Conclusion

Acute in vivo DTI derived axial diffusivity reflected injury severity enabling quantitative segmentation of normal appearing white matter. The quantified normal appearing white matter volume had accurate correlation to endpoint neuro motor function showing potential of axial diffusivity as biomarker in contusive injured spinal cord white matter.

## References

1. Kim *et al.*, MRM, 2007. 2. Deo *et al.*, MRM 2007. 3. Loy *et al.*, J. Neurotrauma, 2007. 4. Kim *et al.*, Neurobio. Dis., 2006.

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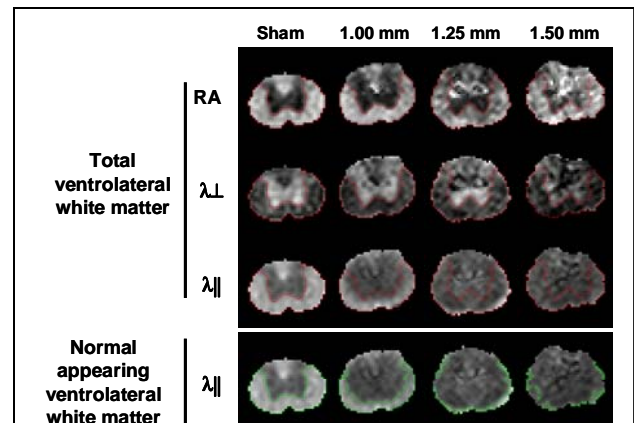


Fig. 1 Region of interest (ROI) analysis is done for total ventrolateral white matter (red line) and normal appearing white matter (green line). Two distinct regions, bright and dark, are clearly seen from total ventrolateral white matter. Normal appearing white matter could be accurately segmented using normal axial diffusivity as threshold.

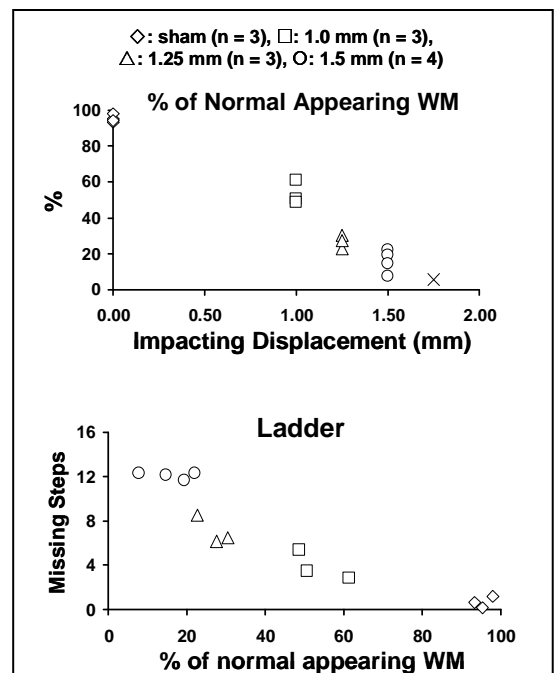


Fig. 2 The normal appearing white matter volume show linear decrease tendency ( $r = 0.95$ ,  $p < 0.001$  for Pearson-product linear correlation) with increase injury severity (impacting displacement). They also show excellent linear correlation to neuro motor function (deficit in horizontal ladder walk, at 3wks),  $r = -0.91$ ,  $p < 0.001$ .