Quantitative MRI in clinically relevant models of spinal cord injury

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Introduction
The type of initial mechanical injury to the cord has been shown to influence the degree of neurological dysfunction throughout the primary and secondary phases of spinal cord injury (SCI), and is therefore important to identify and track in order to guide treatment. Imaging techniques that are sensitive to damage in the white matter microstructure are attractive in characterizing the injury mechanism. Here, we investigate the ability of diffusion tensor imaging (DTI) to distinguish between three experimental rat models of spinal cord injury mechanisms – contusion, dislocation, and distraction, at various time points after injury.

Materials and methods
Sprague-Dawley rats (male, 300g) were injured at the C5/C6 level with the UBC multi-mechanism SCI apparatus. Three clinically relevant injury models were applied: contusion (direct compressive impact from an actuator tip), dislocation (dorso-ventral shearing of the spinal cord), and distraction (stretching of cord along the rostro-caudal axis). Cords were perfusion-fixed and extracted at 3 hours, 24 hours and 7 days post-injury (N=9-12 for a particular time point and injury model). DTI-EPI was acquired with a Bruker 7T preclinical scanner at 11 axial slices centered around the lesion epicentre at 50 μm in-plane resolution and 1mm slice thickness (TE/TR =38.61/2750 ms, 8 shots, 6 directions, b=1000 s/mm², NA=18, 128x128, FOV=6.4mm, 11 slices). White Matter Damage (WMD) and Damage Occurrence Ratio (DRO) maps, generated from DTI metrics, were used to compare spatial patterns of WMD between the injury models and times post-injury.

Results and Discussion
Damage classification was most robust using thresholds in the longitudinal diffusivity, which supports previous studies that show that longitudinal diffusivity is the most robust DTI metric in depicting damage in SCI. Furthermore, the spatial damage patterns from all subjects in the same group were consolidated into a "damage occurrence ratio map", which illustrates an average damage shape that characterizes the injury mechanism.

Our analysis has yielded a dataset which highlights the differences in injury pattern due to the initial mode of mechanical injury. For example, contusion produced an initial injury that emanated radially outward from the central canal, with subsequent damage along the caudal corticospinal tract and rostral gracile fasciculus; dislocation injuries showed a high level of involvement in the lateral and ventral white matter which became less apparent by 7 days post-injury, and distraction injuries were found to be less focal and more distributed rostro-caudally.

This work represents a first step in adopting the use of the primary injury mechanism as a clinical prognostic factor in SCI, which may help to inform the trialing of existing neuroprotective treatment candidates, the development of new therapies as well as personalize the management of SCI for the individual patient.

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References:
1. Choo et al., Experimental Neurology, 2008: 490-506
2. Yung et al., NeuroImage, 2019: 43-55