

Diffusion Tensor Imaging as a Predictor of Experimental Spinal Cord Injury Severity and Recovery

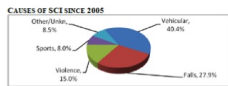
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INTRODUCTION: Traumatic spinal cord injury (SCI) remains a significant contributor to patient morbidity with limited functional recovery linked to the extent of axonal damage. The ability to ascribe quantitative measures to axonal pathology using magnetic resonance (MR) is a novel strategy that may further characterize SCI-mediated axonal injury. Furthermore, the establishment of relationships between functional recovery, imaging studies, and in vitro axonal histopathology may provide insights into understanding neuronal recovery and guide post-injury treatment strategies aimed at maximizing regenerative potential.

Spinal Cord Injury - Background

- Incidence
 - 40 cases per million population
 - 12,000 new cases per year
 - Prevalence
 - Approx. 265,000 persons living with SCI
 - Affects primarily young males
 - Etiology
 - Motor vehicle crashes
 - Falls
 - Violence
 - Sports
 - Hospitalization
 - Median days in ICU = 12
 - Median days in rehab unit = 37
 - Lifetime costs
 - \$ 1.4 – 4.3 million (including hospitalization / rehabilitation, lost wages / productivity)
- CAUSES OF SCI SINCE 2005**

Cause	Percentage
Falls	27.9%
Voluntary	20.4%
Violence	15.0%
Sports	8.0%
Other/Injury	8.5%



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Current SCI Imaging

- **Magnetic Resonance Imaging (MRI)**
 - Allows for evaluation of cord parenchyma, vertebral column and surrounding soft tissue structures
 - Conventional imaging limited in its ability to provide details concerning aspects such as fiber tract integrity, extent of secondary pathology, etc.
 - Efforts to overcome these limitations have focused on complementary techniques to evaluate more specific pathology



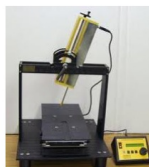
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METHODS: To examine these concepts, female Sprague-Dawley rats underwent laminectomy at T6-7 followed by traumatic spinal cord contusion of differing severities along with sham-injured animals that underwent laminectomy without contusion. Over a 4-week post-injury timeframe, locomotor scores were obtained and hindlimb kinematic functional data was collected. Ex vivo diffusion tensor imaging (DTI) was then performed to generate tractography and determine fractional anisotropy (FA), a numerical measure of relative white matter integrity, at the injury epicenter and at specific intervals rostral and caudal to the injury site. Corresponding immunohistochemistry for markers of axonal integrity and scar formation was also performed. Functional and imaging data were brought together to look for relationships between these parameters.

Hypothesis / Experimental Design

- DTI may be applied to SCI evaluation and provide information regarding injury severity and potential recovery
 - Establish imaging, locomotor, and histopathological correlations following experimental traumatic SCI
 - Rat T6-7 laminectomy followed by contusion injury
 - Mild / Moderate / Severe / Control
 - 2 and 4 week BBB locomotor scores
 - Hindlimb kinematic data collection
 - Ex vivo DTI
 - FA / Tractography
 - Histology for parenchymal pathology
 - Axonal integrity / glial scar
- 



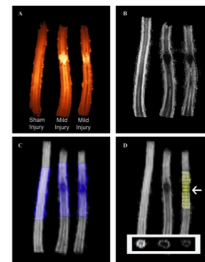
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Please attend the oral presentation on Tuesday 10/22 at 2:45 PM at the Trauma and Critical Care Subsection for a more complete discussion.

RESULTS: All injured animals showed some recovery of locomotor function while hindlimb kinematics revealed graded deficits consistent with injury severity. While standard T2 MR sequences illustrated no difference in syrinx sizes and conventional spinal cord morphology adjacent to contusions despite different injury severities, corresponding FA maps indicated graded white matter pathology within these adjacent regions. Positive correlations between locomotor (BBB score) and imaging (FA values) parameters were also observed within these adjacent regions, most strongly within the caudal segments.

Results

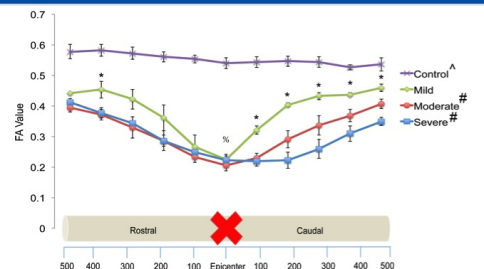


Colormetric T2 weighted images (A) and FA maps (B) for sham-injured and two mild injury spinal cords. 500 μ m rostral and caudal to the injury epicenter (shaded regions in Panel C) were outlined for analysis. These regions were subdivided into 100 μ m increments from which axial projections were used to generate FA values (panel D).

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Results



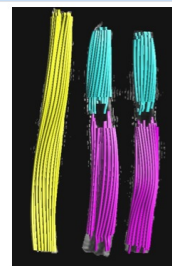
FA value vs Location as a function of injury severity. There were no significant differences between moderate and severe FA values at any location (*). Similarly, there was no significant difference in FA value between injury groups at the injury epiconter (%). Mild injury FA values were significantly different from moderate / severe values, especially within the caudal segment (*). All injury values were significantly different from control values (*). ($p < .05$)

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CONCLUSION: These findings suggest that DTI may augment current imaging modalities used to evaluate SCI and contribute to the development of clinically relevant algorithms predictive of traumatic SCI severity and potential recovery.

Results



Tractography of the sham-injured control and mild injury spinal cords seen in early images. Control fibers are linear and continuous throughout the parenchyma. Injured cords demonstrate loss of white matter continuity through the syrinx although spared tissue at the periphery indicates preserved white matter. To overcome low FA values at the injury center, fibers were traced starting from the rostral (blue) and caudal (purple) ends of the spinal cord.

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Conclusions

- **Locomotor assessments**
 - All injured animals showed a trend towards improved hindlimb function with only moderate injury achieving statistical significance
 - No difference was observed between moderate and severe injury groups
- **Hindlimb kinematics**
 - Graded deficits noted for each injury severity
 - Middle swing foot position relative to hip with most significant differences
- **DTI Results**
 - T2 sequences show “normal” parenchyma immediately adjacent to injury epicenter
 - No difference in spared tissue area between injury groups
- **FA values**
 - All injured animals with values less than control despite conventional T2 morphology suggests evolving white matter pathology
 - Unable to discern pathologic severity at injury epicenter
 - Stepwise increasing values moving away from injury epicenter in a graded fashion suggests sensitivity able to discern mild from moderate / severe injury

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Conclusions

- Correlation between locomotor and imaging studies
 - Positive correlations noted at all locations
 - Weakest at injury epicenter (consistent with FA inability to distinguish injury severity)
 - Strongest in caudal segment
- Tractography
 - Linear fibers noted within observed parenchyma
 - Centrally located fibers stop abruptly at lesion
 - Peripherally located fibers pass through spared tissue surrounding lesion
 - Histology confirms axons traversing spared tissue surrounding lesion with preserved architecture at more remote sites
 - Traversing fibers appear swollen consistent with injury
- Incorporation of DTI into overall SCI analyses may offer an additional non-invasive methodology capable of providing information regarding relative severity of perilesional white matter pathology and prognosis for potential locomotor recovery following trauma
- Existing technology is in place to move forward with clinical applications

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