Measuring Internal Deformation of the In Vivo Rat Spinal Cord During Traumatic Spinal Cord Injury


Introduction: During traumatic spinal cord injury (TSCI), the spinal cord is subject to deformation. The pattern of deformation is associated with the mechanism of TSCI (i.e. burst fracture, fracture-dislocation, etc.). The deformation of the spinal cord results in mechanical injury to the neural tissues and physiological dysfunction of the spinal cord. The complex relationship between the mechanism of TSCI, trauma induced in the neural tissue and the ensuing cascade of pathophysiological processes following TSCI, is currently not well understood.

In this study we aim to report internal spinal cord deformations due to the two most prevalent injury mechanisms of clinical TSCI. We utilize a novel apparatus to create either a contusion injury or a dislocation injury, at two magnitudes of severity in a rat model, inside of an MR scanner. 3D image sets are acquired of the spinal cord in the normal state and in the distressed state during the imposed TSCI. A validated image registration approach is then used to quantify the 3D internal spinal cord morphological change using voxel-wise displacement fields. We report transverse- and sagittal-plane deformation fields as well as Lagrangian finite-strain fields (normal and shear) of spinal cords undergoing TSCI; comparisons throughout the experimental design are also reported.

Methods: Adult, male, Sprague-Dawley rats (n=24, ~300g) were divided equally in a 2x2 experimental design (Table). All animals were anesthetized with isoflurane (4%, administered via nose-cone throughout the entire experiment) prior to surgical preparation. For contusion animals, partial laminectomies over C5 and C6 were performed to create a ~3mm diameter opening to the dorsal surface of the spinal cord. For dislocation animals, a facetectomy was performed at the C5/6 junction and the anterior and posterior longitudinal ligaments and the supraspinous ligament were severed. For contusion animals, a set of custom clamps were attached to vertebrae C4-C7 via the lateral notches of the vertebrae. For dislocation animals, a different set of custom clamps were attached to the cervical spine; a cranial set of clamps were attached to the C4-C5 vertebrae via the lateral notches, while a caudal clamp set was similarly attached to C6-C7. The animal was then inserted into a custom-designed MR Rig [1] and then placed into a 7T MRI scanner.

With the animal in the MR Rig, a T2-weighted sagittal scan (115x150μm in-plane resolution, 1mm slice) was performed and then followed by a T2-weighted, high-resolution transverse scan (termed ‘pre-injury’; 140x140μm in-plane resolution, 500μm slice). Once the transverse scan was completed, the pneumatic actuator of the MR Rig was activated from outside the MR scanner, producing and maintaining the desired injury mechanism in the animal. Another sagittal scan was acquired followed by another high-resolution transverse scan (termed ‘injury’).

‘Pre-injury’ and ‘injury’ image sets were segmented to isolate the spinal cord and were used as inputs for a previously validate deformable registration algorithm to produce 3D displacement fields that
mapped the ‘pre-injury’ image to the ‘injury’ image, quantifying the voxel-by-voxel transformation (Figure 1). 3D Lagrangian finite strain tensors were calculated and visualized in the sagittal and transverse plane to show lateral and dorso-ventral normal strains, as well as transverse shear strain, in the spinal cord (Figure 2).

**Results:** In the contusion injury group, higher gross injury magnitudes resulted in lateral and ventral displacement of the deeper (i.e. more ventral) tissues of the cord. For all contusion injuries, tissue beneath the point of impact seemed to be pushed, ventrally and laterally, away from the impact site (Figure 1). More severe gross injury magnitudes resulted in a greater magnitude of lateral tissue motion below the impact site, and the lateral-motion effect was also observed to occur at deeper regions of the tissue. The ventral displacement behaviour also extended rostro-caudally, largely in the dorsal portion of the cord. Higher injury magnitudes resulted in a greater range and depth, of rostro-caudal involvement. The dorso-ventral normal strain (\(e_{YY}\)) patterns in contusion injuries affected more-lateral tissues at deeper levels, subjecting more of the deep-lateral tissues to dorso-ventral compression (Figure 2). However, the tissue directly ventral to the impact site consistently experienced the highest magnitude of dorso-ventral compressive strain. In the lateral normal strain (\(e_{XX}\)) patterns in contusion injuries, a ‘band’ of tension extended ventrally, from the site of impact. Some specimens also exhibited lateral compression near the lateral edges of the cord.

In dislocation injuries, transverse-plane images show a general dorsal displacement of the spinal cord, with a region of increased dorsal displacement observed in the tissue just below the dorsal surface (Figure 1). Lateral displacement fields in the transverse-plane appeared mostly homogeneous for all specimens. Sagittal-plane images confirmed an apparent dorsal translation of the spinal cord, highly-localized at the intended epicenter of injury. The dislocation injury dorso-ventral normal strain (\(e_{YY}\)) maps indicated a region of tension in the central part of the cord that extended laterally (Figure 2). The lateral normal strain fields did not seem to exhibit a recognizable pattern. The transverse shear strain fields did not exhibit any appreciable strain or observable pattern among the animals.

**Discussion:** In current literature, the quantification of spinal cord morphology change during TSCI has either been via experimental models, or computational numerical models. In all experimental studies, measurements of spinal cord deformation are limited to a single gross linear displacement of the spinal cord impactor. This study presents the first quantification of the in vivo morphological changes of the rodent spinal cord during acute TSCI. We believe that the contribution of this work is best described as an initial ‘key foot-hold’, in an effort to quantify the internal morphological changes that the spinal cord undergoes during experimental TSCI. In vivo, experimental TSCIs have never before been visualized internally, and the capabilities shown in this study open up new avenues for experimental TSCI research. The imaged tissue states in this study do not capture the possible transient-behaviour of the cord during dynamic impact, but they are representative of what would be available, clinically, with new admits of TSCI. Considering the potential future avenues of research that have been identified through this study, we believe that the novel ability to observe and quantify spinal cord tissue morphological change during experimental TSCI is an extremely valuable contribution to the field of spinal cord injury research.

**Significance:** Heterogeneity of spinal cord injury (SCI) mechanisms in the clinical population is an important consideration when designing optimal intervention plans. This study provides insight into the different mechanical responses of the spinal cord during two clinically-relevant injury mechanisms.
Further application of these methods could help to understand the effect of SCI-mechanism heterogeneity on the lack of effective therapeutic strategies translated from experimental studies.