Validation of a Novel Animal Model of Thoracolumbar Burst Fracture-Induced Spinal Cord Injury - The Impactor Study Phase.

Rory Petteys, MD1, Steven Spitz, MD2, Rachel Sarabia-Estrada, DVM, PhD2, Hasan Syed, MD3, Robert Rice, MD1, Daniel Sciubba, MD2, Brett Freedman, MD3.

1Georgetown University Hospital, Washington, DC, USA, 2Johns Hopkins University, Baltimore, MD, USA, 3Landstuhl Regional Medical Center, Landstuhl, Germany.


Introduction: Acute traumatic spinal cord injury (SCI) resulting from spinal fracture leads to debilitating neurological dysfunction. Researchers have made strides in understanding SCI and investigating treatments through animal modeling, but translation of this work into clinical benefit remains sparse. This may be due to interspecies differences in animal models and technical limitations of methods employed to create injury in these models. Herein, we describe the design and development of a novel model of SCI, which approaches the anterior spinal cord to accurately replicate the contusion and compression events that characterize burst fracture-induced SCI. In this study, we also describe the design, development, and validation of a novel spinal cord impactor for use in this large animal model of SCI.

Methods: This study consisted of two phases: 1) Design and development of a controlled spinal cord impactor and 2) model development and impactor testing. A custom controlled spinal cord impactor was developed that could deliver impacts from 10 to 40 N. The impactor consisted of a voice coil actuator capable of 89 N of force with a stroke length of 19mm. A voice coil was selected because it is capable of rapid acceleration with precise control of output force. Force and displacement were measured with a 25-lb button load cell and linear potentiometer respectively. Labview (National Instruments, Austin, TX) software was used to control the impact cycle and import force and displacement data (Figure 1A). Software finite impulse response (FIR) filtering was employed for all input data. In phase 1, silicon tubing was used as a surrogate for spinal cord in order to test the device; repeated impacts (5x) were performed at 15, 25, and 40 Newtons to confirm the precision of the impactor. For the second phase, ten female Yucatan miniature swine were utilized for model development. Ventral SCI was produced by creating a 1.5-cm defect in the L1 vertebral body via midline laparotomy and retroperitoneal approach to the spine (Figure 1B). The custom impactor was then introduced and animal spinal cords were impacted with loads of control (no load), 7N, 12N, 22N, 32N and 40N (Figure 1C). Neurological function was assessed for seven days after injury using the Porcine Thoracic Injury Behavioral Scale (PTIBS) and Porcine Neuro-Motor Scale (PNM). Magnetic resonance imaging (MRI) and histology were performed on postoperative day one and seven respectively.

Results: Repeated impacts in an ex vivo model demonstrated predictable results with less than 10% variability at each target force. The average duration of impact was 71.2 +/- 6.1 msec. At a target force of 40 N, the output force was 41.5 N +/- 1.7%. With a target of 25 N, the output force was 23.5 N +/- 2.7%; a target of 15 Newtons revealed an output force of 15.2 N +/- 9.3% (Figure 2). The scaled contusion loads produced graded neurological recovery from complete recovery in the 7N animal to
partial recovery in the 12N and 22N and complete injury in 32N and 40N. There was a strong linear correlation between apparent injury volume on T2 sagittal MRI and force of impact to the spinal cord ($r^2 > .99$; Figure 3).

**Discussion:** The results of this iterative experimental study, demonstrate that this novel custom designed spinal cord impactor is capable of reliably delivering precise and specified impacts to the spinal cord that range from non-injurious to complete, unrecoverable SCI. We are confident that the high-fidelity and anterior access to the spinal cord offered uniquely by this model overcome the marginal increased time and skill-set demands required to approach anteriorly. We are preparing to confirm this superiority by comparing this anterior approach to the standard posterior approach.

**Significance:** This novel animal model closely replicates the mechanism of injury responsible for burst fracture-induced SCI. Its validation holds the potential to improve understanding of the acute physiology of primary and secondary SCI, as well as serving as an excellent candidate for higher level pre-clinical testing of new and traditional SCI therapeutics, with the expectation that validly replicating the mechanism of injury will improve prediction of clinical efficacy as compared to current dorsal-approach models.