A Simple, Robust, and Accurate Contusion Spinal Cord Injury Device for the Mouse Characterized by Diffusion MRI

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Introduction

Rodent models of spinal cord injury (SCI) have been widely employed to study morphological and pathophysiological change of the injured cord for developing new therapeutic interventions (1). The consistency of injury is crucial to minimize the variability of the resulting tissue damage and to isolate the effects of experimental parameters on the evaluation of interventions. Efforts have been devoted to evaluate the injury severity by measuring biomechanical parameters and its correlation with the biological outcomes, including histology and behavior (2, 3). These conventional methods have limitations to evaluate the injury in acute phase (behavioral scores) or serially (histology). Magnetic resonance imaging (MRI) is noninvasive and sensitive to morphological and physiological changes in living tissues. The apparent diffusion coefficient (ADC) derived by diffusion measurement has been used widely to investigate central nervous system pathology (4). In the present study, we report the design of a modified electromagnetically driven impact device for generating rodent spinal cord injury with a full control of the impact distance, speed, and force. Instead of using the conventional histological and behavioral evaluations, we characterized the injury severity in hyper acute phase using ADC measured using diffusion MRI. The sham-operated and contusion injured cords were examined acutely using *in vivo* diffusion measurements. The severity of injury assessed using ADC showed good agreement with the preset impact injury severity.

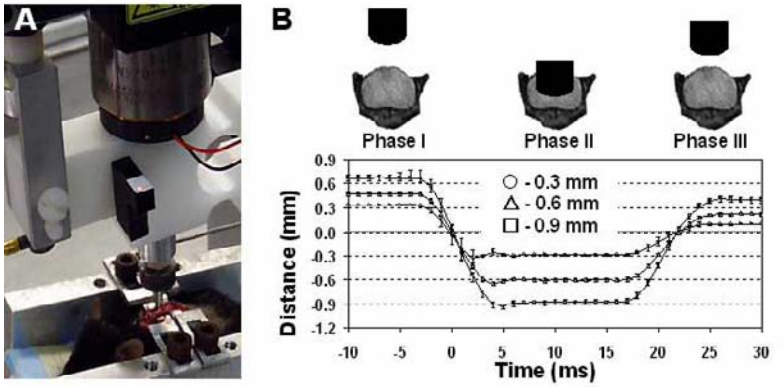

Fig. 1. Impactor (A) and impacting procedure (B). In panel B, measured displacements of impactor tip are shown as function of time - circle; 0.3 mm, triangle; 0.6mm, and rectangular; 0.9mm.

Methods

Twenty 10-week-old female C57BL/6 mice were randomly divided into control and three different contusion injury groups. The three injury groups were set by various impacting distances: 0.3 (mild), 0.6 (moderate), and 0.9 (severe) mm at vertebral segment T12. After impacting, standard postoperative procedures were performed. The control group underwent laminectomy without contusion. *In vivo* diffusion MRI data were acquired immediately after impacting. An inductively coupled surface coil (15 mm × 8 mm) was used as the receiver, covering thoracic levels T11 through T13, with a 9 cm i.d. Helmholtz coil as the RF transmitter. A spin-echo diffusion-weighted sequence was modified to acquire images under respiratory gating (5). All images were acquired with acquisition parameters of TR 1.2 sec (gated acquisition), TE 38 msec, Δ 20 msec, δ 7 msec, slice thickness 0.75 mm, field-of-view 1 × 1 cm^2, data matrix 128 × 128 (zero filled to 256 × 256), total data acquisition time ~ 2.5 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 .785 μm^2/ms. Image resolution was 78 × 78 × 750 μm^3.

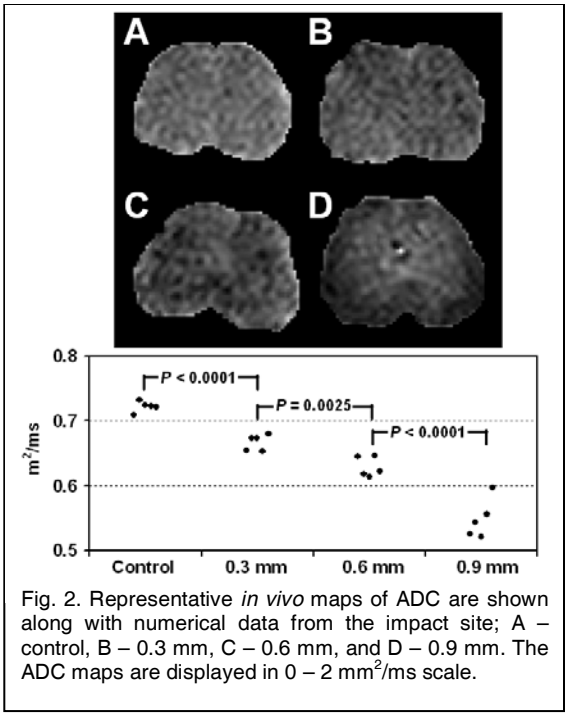

Fig. 2. Representative *in vivo* maps of ADC are shown along with numerical data from the impact site; A – control, B – 0.3 mm, C – 0.6 mm, and D – 0.9 mm. The ADC maps are displayed in 0 – 2 mm^2/ms scale.

Results and Discussion

The impact procedure is illustrated in Fig. 1 by detailed recordings of the impactor tip position as a function of time. Since impact (contusion) is conducted from dorsal to ventral direction, the negative sign of distance represents the downward direction (from dorsal to ventral). The measured displacement of impactor tip showed the accuracy of impacting procedures compared to preset (desired) impacting displacement and capability of impactor for multi degree injuries. In Fig. 2, the severity of contusion injury is qualitatively assessed using the ADC map. Quantification of the severity of the impact was performed on the entire cord (gray and white matter together). Differences in ADC values among groups are statistically significant. The most severe decrease in ADC is seen at 0.9 mm group. In conclusion, a new device for contusion spinal cord injury for rodents is demonstrated using mice. The injury severity produced may be characterized by MRI diffusion measurements in the injured cord non-invasively. It is straightforward to regulate the degree of injury by changing impact depth using this reported device. The application to mouse spinal cord injury showed good agreement between biomechanical parameters and diffusion parameters of injury severity.

References

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