Cervical Spinal Cord Injury in the Rat: Longitudinal MRI Comparison of Two Injury Severity Levels

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Introduction: Injury to the cervical spinal cord represents the majority (42%) of human spinal cord injury SCI [1], and typically results in tetraparesis and/or tetraparalysis, respiratory disturbances, and autonomic dysfunction. Cervical SCI animal models have been developed to study the time evolution of cervical trauma and treatment options. The objective of this study was to evaluate MRI as a potential alternative for serial sacrifice and histology in longitudinal studies of two injury levels in unilateral rat cervical SCI.

Methods: Thirteen rats were imaged prior to unilateral cervical SCI [2], and at 24 hours ,1, 2, and 3 weeks post injury (6.25g-cm injury, n=7 and 25 g-cm injury , n=6) using a 4.7T/40cm MRI (Bruker) with a home-built 3cm diameter Helmholtz transmit-receive coil. Axial and sagittal T1 weighted images (Gradient Echo: TR/TE/Flip angle=500/4.9ms/90^{O}, 5 averages, Scan time=10:40min) were acquired pre- and post- contrast (Omniscan, GE, administered in the jugular vein). Proton density-weighted images (PD Spin Echo: TR/TE=2000/15ms, 2 averages, Scan time=17:07min) were acquired with the same 175x175µm in-plane resolution and 1mm slice thickness with 0.1mm gap. In addition, 3D sagittal and axial T2 (Spin Echo, TR/TE/RARE factor= 1629ms/60ms/16, 2 averages, Scan time= 27:48min) were acquired with 182x175x625µm resolution. Rats were sacrificed at 3 weeks post SCI and additional isotropic resolution (195x195x195µm) T2, 3D MRI data were acquired on the fixed whole bodies (in situ) and isolated cords embedded in agar. Subsequently, spinal cords were sectioned and stained with Luxol fast blue for myelin and counterstained with cresyl echt violet for Nissl substance. Whole cord, right and left hemicord, hypo- and hyper-intense lesion areas were manually traced on axial MRI and histopathological images and used to calculate cord and lesion areas, lengths and volumes.

Results: Representative pre and post-injury images at the epicenter of the injury are shown in Figure 1. These images and quantitative data (not shown) demonstrate variable swelling of the cord depending on injury severity, with a significant difference in cord volume between the two groups at 24 hours and 1 week after SCI. Post contrast T1-images show clear enhancement up to 1 week post injury for severely injured group, indicative of disruption of the blood-spinal cord barrier [3]. With time, a hypo-intense region evolves likely representing blood decay products (Figure 2.A). A diffuse signal increase perhaps representing cytotoxic edema is also seen on early post injury T2 images. This appears as a more focused rim around the hypo-intense region at 2 weeks post injury (Figures 1 and 2.B). The correspondence between MR images of in situ and excised cord and histology at injury epicenter is shown in Figure 3. It appears that the cavity seen on histology is comprised of the hypo- and hyper-intense areas seen on MR images. Differences in terms of cord shrinkage (seen in MR images) and sparing of white-gray matter and demylination (seen in microscopy images) for the two injured groups are also depicted in Figure3.

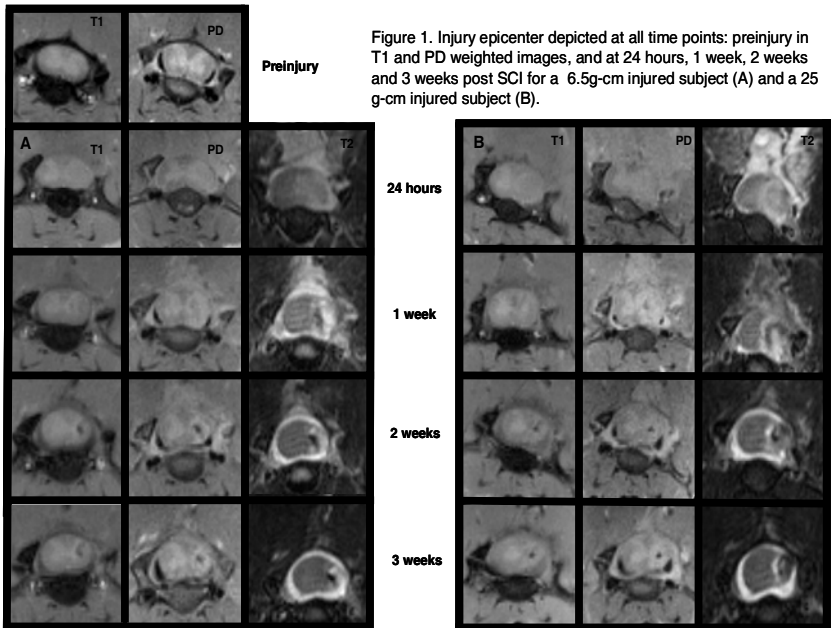

Figure 1. Injury epicenter depicted at all time points: preinjury in T1 and PD weighted images, and at 24 hours, 1 week, 2 weeks and 3 weeks post SCI for a 6.5g-cm injured subject (A) and a 25 g-cm injured subject (B).

Discussion: In this study we demonstrate that MRI has sufficient accuracy to quantify post injury cord abnormalities including swelling, evolution of edema, blood decay products and finally cavity formation. Two injury severity levels were clearly differentiated, and the evolution of pathology could be monitored. These outcomes suggest that in vivo longitudinal MRI can be used to monitor therapies and treatments aimed at slowing down and/or reversing pathology of spinal cord tissue after cervical SCI.

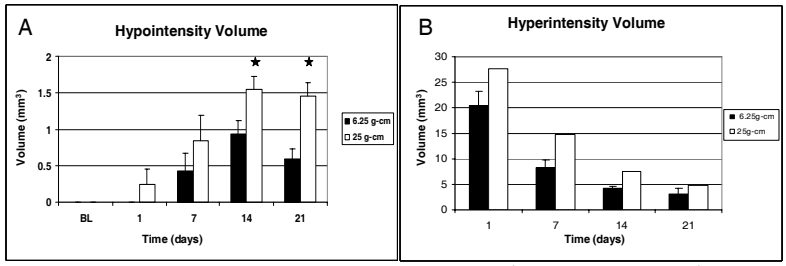

Figure 2. Hypointensity Volume (A) and Hyperintensity Volume (B) determined from in vivo MRI data. * significantly different ($p<0.04$) than the 6.5g-cm injured group (A).

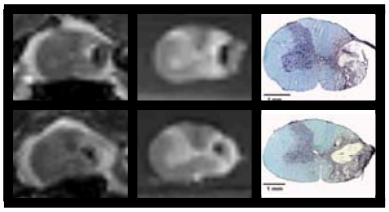

Figure 3. Lesion epicenter shown while imaged post-mortem in situ (left), isolated and embedded in agar (middle), and using microscopy (right) for one animal that received a 6.25g-cm SCI (top) and one animal that received a 25g-cm SCI (bottom).

References:

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[3] M. Bilgen et al. **Magn Reson Med**. 45:614-622, 2001.