In Vivo Visualization of Spinal Cord Injury in Experimental Mouse Model: A Feasibility Study on A Clinical 3.0 Tesla MR System

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Introduction:

There is an increased trend to employ mouse spinal cord injury (SCI) models in preclinical experimental studies. One of the advantages is the availability of transgenic and gene knockout mice that can provide researchers a unique opportunity to investigate the impact of specific genes in the pathophysiology of SCI. Previous magnetic resonance imaging (MRI) of mouse SCI were mainly carried out on high field 9.4 Tesla(T) animal imaging systems which were equipped with specially designed implantable or surface coils [(1, 2)]. The accessibility to this MR system limited further application of MRI in mouse SCI. In current study, we aim to perform translational high resolution MRI to visualize the characterization of mouse SCI on a clinical 3.0 T MR system.

Materials and Methods:

Four adult female C56BL/6 mice (body weight of 22 ± 3g) were anesthetized with ketamine (137 mg/kg) and xylazine (10 mg/kg; i.p.), then received spinal cord contusion injuries at the T9 vertebral level[3]. Animals were imaged at 2 hrs, 24 hrs, 72 hrs, 7 days and 28 days post-injury (dpi) on a clinical 3T MR system (Achieva, Philips Medical System), which was equipped with a 3 cm small animal solenoid coil. Two conventional high resolution sequences were employed: 3D sagittal T2 Turbo Spin Echo(TSE): TR/TE= 724/100 msecs, scan matrix 304x304, reconstruction matrix 512x512, field of view (FOV) 60 mm, acquisition time 11 minutes 7 seconds, voxel resolution 120x120x300 μm^3; 2D axial T2 weighted TSE: TR/TE= 6286/77 msecs, matrix 256x256, reconstruction matrix 512x512, FOV 40 mm, slice thickness/gap 0.5/0mm, acquisition time 6 minutes 29 seconds, in-plane resolution 80μm. To eliminate the effect of respiration and vascular pulsation, a 15 mm wide saturation band was applied in 2D axial sequence. After 28 dpi MRI, animals were intracardially perfused with 0.1 M PBS followed by 4% Paraformaldehyde. An eriochrome cyanine (EC) staining protocol was used to differentiate spared myelin at injury site.

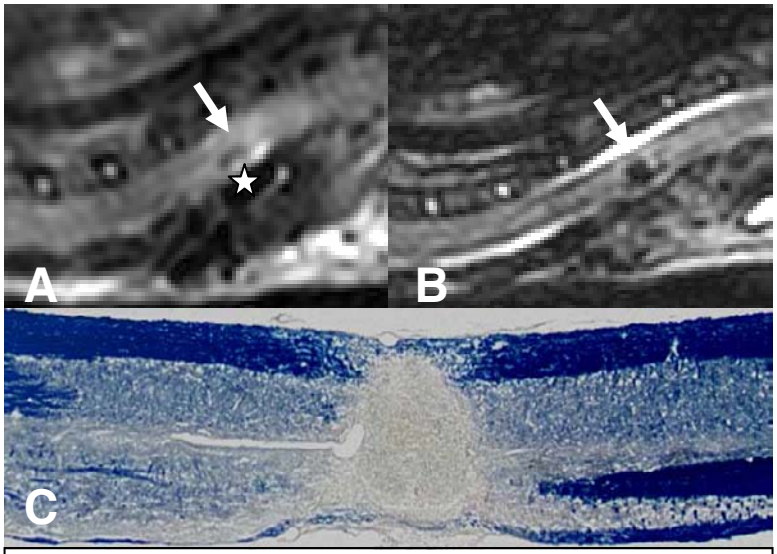

Figure 1. 3D T2-weighted sagittal high resolution MRI of SCI (focal) in one mouse. The injury site displayed as low signal lesion (arrow) with surrounding edema and hemorrhage (star) at 2 hrs post-injury (A), and low signal scar tissue at 28 dpi (B). Corresponding sagittal spinal cord EC staining (C) revealed the presence of the scar tissue and disruption of the white/gray matter interface, as well as stenosis of central canal.

Results:

High resolution 3.0 T MRI enabled us to visualize the evolution of a mouse spinal contusion lesion over an extended post-injury interval. Specifically, 3D sagittal MRI provided wide-ranging high resolution profiles of thoracic spinal cord (Figure 1); 2D axial MRI displayed details of the gray/white interface at the injury site (Figure 2). In addition, both sequences clearly revealed edema and hemorrhage at acute stage (2 hrs post-injury) and scar tissue formation at chronic stage (28 dpi). Histopathologic analysis confirmed the MRI results illustrating chronic myelin degeneration and disruption at injury site.

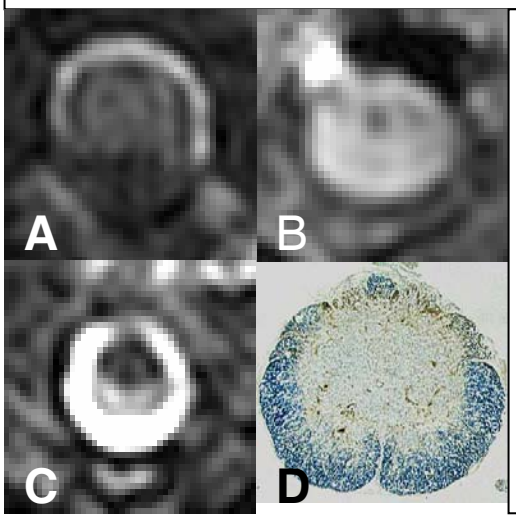

Figure 2. 2D T2 weighted axial high resolution MRI of the same animal in Figure 1. MRI at the normal T7 level (A), 2 hrs post-injury (B) and 28 dpi (C) at the T9 level. An EC stained section from a different animal showing the scar tissue formation after 28 dpi (D).

Conclusion:

Clinical 3.0T MRI is a valuable translational imaging tool in identification and characterization of pathophysiology progression in mouse SCI. With employment of clinical MR sequences, it has great potential in providing further detailed information in investigation of mouse SCI.

Ref:

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3. Jakeman LB, Guan Z, et al. Traumatic spinal cord injury produced by controlled contusion in mouse. J Neurotrauma 17:299–319