Longitudinal dynamic contrast-enhanced (DCE-) MRI of spinal cord injury in mouse

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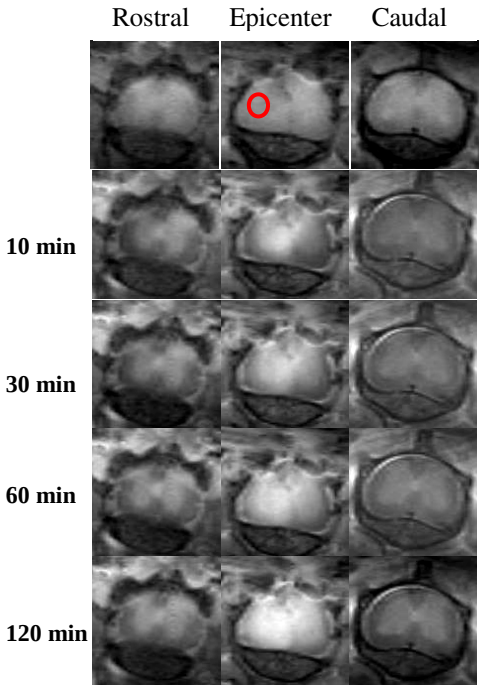
Introduction

Under normal physiological conditions, the blood-spinal cord barrier (BSCB) exhibits a selective permeability to the constituents of blood plasma to protect the cord. Traumatic insult to the SC disrupts the structural integrity of its vascular bed and BSCB. The evidence suggests that the disruption of BSCB leads to secondary injuries which result in permanent neurological deficits. But little is known about the relationship between the spatial extent of the compromised BSCB and the functional outcome. Recent trend indicates that mouse models are gaining popularity in spinal cord injury (SCI) research. However, mouse exhibits different inflammation response to SCI than those seen in rat. Applications of MRI modalities to investigate vascular changes in injured mouse SCI are very limited [1]. Our goal is to demonstrate vascular plasticity in injured mouse SC as monitored by the spatial and temporal changes in BSCB permeability using longitudinal dynamic contrast-enhanced MRI (DCE-MRI) and establish the relationship between the uptake of the contrast agent Gd-DTPA and fibrotic tissue deposition in injured mouse SC.

Materials and Methods

All MRI scans were performed on a 9.4 T INOVA Varian system (Varian Inc., Palo Alto, CA) with 31 cm horizontal bore magnet. The spinal cords of C57Bl/6 mice (n=5) were injured by contusion at the thoracic level [1]. A catheter (PE-10 tube) was inserted permanently in the jugular vein for the intravenous delivery of the contrast agent Gd-DTPA (Magnevist). The animals were scanned using anatomical and DCE-MRI protocols using an inductively coupled surface coil on postinjury days 0, 3, 7 and 14 while under isoflurane anesthesia (1.5 %) delivered through a nose mask. Following anatomical and T1-weighted pre-contrast scans, Gd-DTPA (0.2 mmol/kg) was delivered IV bolus (<2 min) and post-contrast images were acquired repetitively up to 120 minutes. The DCE-MRI parameters were TR/TE = 1000 ms/10 ms, field of view= 10mm X 10 mm, acquisition matrix=128x128, slice thickness = 1 mm, averaging=4 and number of slices= 12 contiguous axial views. The data were analyzed using the scanner software.

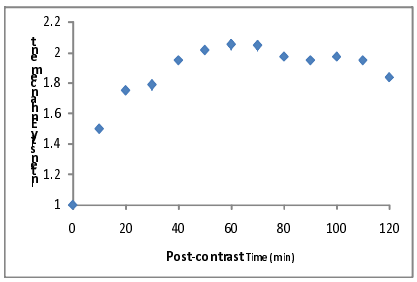
Figure 1. Pre- (top row) and post-contrast (remaining rows) axial DCE images of an injured SC on day 0.



Results and Discussion

Figure 1 shows pre- and post-contrast images acquired on postinjury day 0 at different time points following the delivery of Gd-DTPA. The excellent contrast between GM and WM in sections caudal and rostral to the site of injury can be appreciated. At the epicenter, the gray matter and white matter contrast is compromised, making it difficult to distinguish the structural features on the T1-weighted image. The contrast enhanced rapidly within the first hour of the Gd-DTPA delivery and decayed at later times (Fig. 2). This behavior was similar to those reported from the injured cords in rats [3]. Currently, we are analyzing our data from different postinjury days and computing enhanced area (EA) and volume (EV) parameters. Preliminary results so far indicate that both EA in each slice and EV increase with time early on following the delivery. In the following days, both quantities show gradually decrease, indicating BSCB recovery. Histological preparations of injured cord segments are underway. Angiogenesis was reported in injured rat SC [3]. It remains to be seen if our data detect such events in injured mouse cord and if it would influence the neurofunctional recovery.

Figure 2. Intensity enhancement within a selected ROI (red circle in Fig. 1).



Conclusions

This study demonstrates the feasibility of performing DCE-MRI of SCI in mouse. Vascular changes inferred by DCE-MRI may explain why the inflammation response to SCI in mouse is different than that of rat. Such measurements allow developing pharmacokinetic models to quantify the BSCB permeability, which may serve as a surrogate bioimaging marker for assessing the functional status of injured SC in experimental studies with mouse.

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References

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