Measurements of Myelin Water in Rat Spinal Cord In vivo

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Introduction

Changes in the amount of myelin water in spinal cord (SC) occur at the time of spinal cord injury and during the subsequent deterioration and recovery phases. Tracking the progression of myelin water fraction (MWF) can therefore be an important marker of SC pathology over time, and can be used to measure the success of potential SC therapies (e.g. drugs which aim to rebuild the myelin at the injury site [1]). In addition, measuring MWF may be important in tracking the progression of multiple sclerosis in the SC. MRI is a powerful tool in tracking myelin water because it allows serial *in vivo* measurements in the same subject over time. This preliminary work presents MR myelin water measurements in injured and control rat spinal cords.
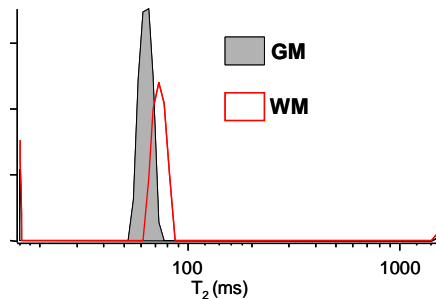
Methods

Implantable coils were developed to optimize NMR signal around the rat spinal cord, as described in [2]. A curved rectangular copper coil (15x8.5mm) is surgically implanted between T9 and T11 along the dorsal surface of the rat spinal column. The implantable coil is covered with polyolefin heatshrink tubing and a medical grade elastomer (Dow-Corning MDX4-4210) to provide electrical isolation and biocompatibility. The implanted coil is inductively coupled with a circular pickup coil (3.2 cm diameter) on the dorsal surface of the rat. A contusion injury is inflicted at T10 by performing a laminectomy and crushing the exposed SC. *In vivo* MRI experiments were performed on a 2.35T Bruker/SMIS animal scanner. Axial images were acquired using a multi-echo CPMG sequence [3] (128x128, TR/TE=2000/17ms, NA=4, 4 cm FOV, 1.5 mm slice thickness, 1 slice, 16 echoes). T2 distributions were calculated from the multi-echo data using non-negative least squares analysis [4]. Myelin water map in the control spinal cord was generated by integrating the short T2 peak in the T2 distribution in each pixel within the cord.

Results

An axial cross-section through the spinal cord of a control rat (Figure 1) represents the first echo of the CPMG sequence. The characteristic grey matter (GM) butterfly pattern surrounded by white matter (WM) can be easily recognized. The mean T2 distributions within ROI's encompassing GM and WM in the control cord (Figure 2) show a short-T2 myelin water component ($T_2 < 20$ ms), a large peak associated with intra- and extracellular water ($T2 \approx 50\text{-}90$ms), and a small CSF component at $T_2 > 1$sec. The myelin map of the control spinal cord shown in Figure 3 indicates that the MWF in the central GM is smaller than that of the surrounding WM. The mean MWF of GM and WM was measured from the T2 distribution as 13.2% and 25.1%, respectively. Figure 4 shows the T2 distributions calculated from an ROI positioned in the WM in the dorsal portion of the SC, acquired at 3 different time points following injury. Qualitative analysis suggests that there are significant changes in T2 distribution following injury. Both myelin and main intra-/extra-cellular water peaks shift towards longer T2 values immediately following injury, but within four days recover close to their normal values. Myelin water peak also displays a T2 distribution much broader than that in the control cord, which also recovers at the 4th day post-injury. This suggests severe disruption in myelin structure immediately following injury, which partly recovers within four days.
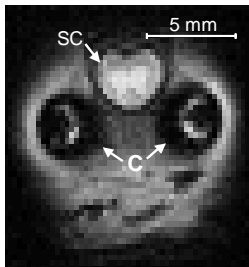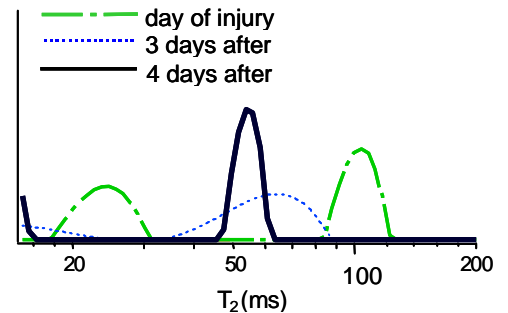

Figure 1: Axial image corresponding to first echo of CPMG scan (SC = spinal cord, C = wires of implantable coil).

Figure 2: T_2 distribution of GM and WM in a control rat spinal cord.
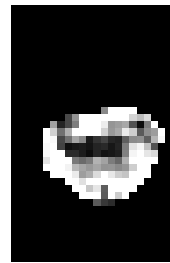
Figure 3: Myelin water map of a control rat spinal cord.

Figure 4: T2 distributions in an injured rat spinal cord.

Discussion

An MR-based method to measure MWF was developed for rats, since rats are one of the most common animal models for studying SC injury. SNR in the region of interest is greatly increased by the placement of an implantable coil very close to the spinal cord. Generation of T2 distributions may benefit from the relatively low B0 used in our study, since the T2 values may decrease at higher fields. The *in vivo* MWFs in the control rat SC are comparable to the results described in [5], where *in vivo* human SC measurements yielded MWF values of 17.0% and 23.2% in GM and WM, respectively. Partial volume effects may be responsible for the heterogeneity of myelin water in the control GM as indicated by the myelin map in Figure 3. Qualitative analysis of the T2 distributions in the injured rat SC suggests that myelin structure is severely disrupted by SC injury, but recovers by the 4th day following the injury. Further work is needed to improve quantitation of MWF of injured rat SC. ROIs from different experiments in a serial study can be registered, to improve consistency of MWF measurements over time. Increasing the spatial resolution and SNR is also important, considering the small size of the SC in rats. In addition, decreasing TE may improve quantitation of the full T2 distribution.

Conclusion

This pilot study indicates that *in vivo* MR measurements of MWF are feasible in rat SC, and can provide useful information about myelin structure during SC injury. This technique will be used in future work to characterize patterns of spinal cord injury, and can also be used to measure the success of rehabilitative therapies.

References [1] Ianotti C et al., Exp Neurol 2003; 183(2):379-93. [2] Bilgen M et al., Magn Reson Med 2001; 46(6):1250-3. [3] Foltz WD et al., Magn Reson Med 1997; 38(5):759-68. [4] Whittall KP et al., J Magn Reson 1989; 84:134-52. [5] Minty EP et al., ISMRM 2002; 940.