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INTRODUCTION

Spinal cord injuries (SCI) produce direct mechanical disruption and subsequent severe degeneration of axons; these processes cause the associated neurologic deficits. Histological studies of fixed tissue in animal models of SCI have described axonal loss and demyelination. Research at the U. Penn site brings novel magnetic resonance methodology to bear with the objective of obtaining quantitative information on axonal degeneration and myelin loss following SCI in a mouse model by pursuing the following specific aims per the work statement:

1. *We will perform q-space MR imaging (QSI) and simulations of QSI to quantify axonal architecture in healthy and injured mouse spinal cords.*
2. *We will quantify myelin content with three quantitative MRI techniques in healthy and injured mouse spinal cords and compare the results with histology.*

Specific Aim 1:

Normal and injured mice have been prepared for QSI analysis. A small pilot set of spinal cord specimens was used to refine the imaging approaches (normal & injured). Technical details have been worked out regarding injury placement, tissue collection and marking to enable reliable identification of the lesion site and rostral/caudal orientation of the tissue specimens. We have generated healthy (n=4) and injured spinal cord tissue (2-day, 3-week and 3-month sacrifice, n=4 per time point).

Upgrading the Bruker NMR/MRI system has delayed QSI experiments. Hardware modifications were needed to connect our previous custom gradient coil to the new system. The gradient coil also had to be optimized and recalibrated for the new system. As the old QSI pulse sequence program does not run on the new system, a new QSI pulse sequence program is currently under development.

Once the new pulse sequence program has been tested, QSI experiments will be performed and followed by histologic analysis and QSI simulations.

There has been significant progress toward translation of the QSI methodology to the clinic. Toward this goal a pulse sequence was designed and implemented for generating a series of images as a function of q (the spatial wave vector) at 1.5T on a clinical imager. Using this pulse sequence on fixed pig spinal cords, we have collected preliminary data to investigate the feasibility of using our previously published QSI methods on a clinical scanner.

Specific Aim 2:

Significant progress has been made towards 3D ultra-short echo-time (UTE) MRI of myelin. First, we succeeded in isolating bovine myelin and demonstrated that the spectroscopic and imaging characteristics of the hydrated myelin were identical to those obtained in situ in rat spinal cord. In the course of these experiments the MR signal of myelin was studied extensively with proton, carbon and phosphorus NMR spectroscopy. The results of this pilot study indicate that UTE MRI may have potential for directly imaging myelin. We

demonstrated the feasibility of a 3D dual-echo subtraction UTE sequence with adiabatic inversion long-T_2 suppression to directly image myelin in a freshly excised rat spinal cord (Figure 1). Lastly, we demonstrated a quantitative relationship between image-derived signal intensities and actual myelin concentration.

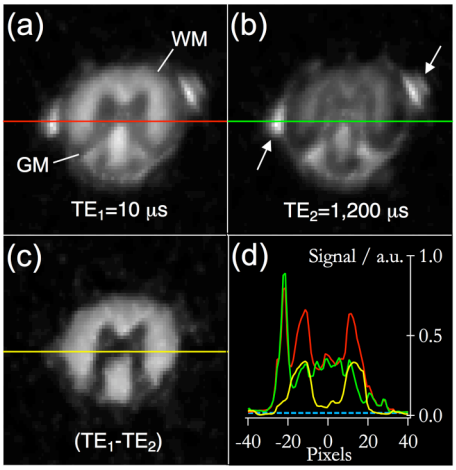

Figure 1. Sample 3D UTE images from rat thoracic spinal cords averaged over five central slices. Images obtained for a) TE=10 ms, b) TE=1,200 ms, and c) magnitude difference (maximum intensity range decreased by a factor of two to highlight myelin signal). D) Intensity profiles across the three images (delineated as red, green and yellow lines in panels a, b and c, respectively) to show relative white matter (WM), grey matter (GM) and background intensity. The dashed blue line represents the average noise level. WM and GM are indicated in panel a, and arrows highlight residual surface water in panel b.

Similar to Specific Aim 1, progress toward detecting myelin with IHMT and MR relaxometry has been hampered by the disruption in imaging capabilities caused by the upgrade of the Bruker Instruments micro-imaging system. However, as of the time of this report (10-15-11) software and hardware upgrades are complete and work should resume in November 2011.

KEY RESEARCH ACCOMPLISHMENTS

- Demonstrated feasibility of direct imaging of neural myelin as a new metric for the evaluation of SCI.
- Magnetic resonance characterization and feasibility demonstration of MR imaging of myelin *in situ* has been presented at the International Society for Magnetic Resonance in Medicine (ISMRM) Annual Meeting in Montreal, Canada (May 2011) and American Society for Neuroradiology Annual Meeting in Seattle (June 2011). See citations below.
- Submitted a manuscript on myelin MRI for publication to the Proceedings of the National Academy of Science.
- Generated the model injury mouse spinal cords.
- Tested the system upgrade of the Bruker Instruments micro-imaging system and interfaced custom-built gradients for high-resolution q-space imaging.
- Demonstrated the feasibility of translation of the q-space imaging technique in porcine model of the spinal cord on a 1.5T clinical imager and an abstract is being submitted for presentation at the ISMRM Annual Meeting in Melbourne, Australia in 2012.

OUTCOMES

The new myelin imaging technique has shown potential for quantitative assessment of myelin content in the CNS of the rat spinal cord.

CONCLUSION

While the project is slightly delayed, the progress made during the first year of the project gives the investigators confidence that the project will be completed in a timely fashion.

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