Evaluating the Feasibility of Monitoring In Vivo Spinal Cord Metabolism Using Hyperpolarized Carbon-13 MR Spectroscopic Imaging

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Introduction: Spinal cord injury (SCI) is a devastating neurological disorder affecting approximately 12,000 individuals in the United States each year[1]. Secondary injury, which occurs hours to months following initial primary traumatic insult, contributes to metabolic stress and progressive tissue damage, and serves as prime targets for therapeutic intervention. Current non-invasive methods to monitor these processes are significantly limited. Proton (^{1}H) magnetic resonance spectroscopic imaging (MRSI) of spine suffers from low signal to noise, physiologic motion, and magnetic field inhomogeneity related to the bony spine[2]. A recent first-in-human study using hyperpolarized ^{13}C MRSI showed the safety and feasibility of this technology for evaluating real-time metabolism in humans[3]. The purpose of this study was to explore the feasibility of using hyperpolarized ^{13}C MRSI with [1-^{13}C]pyruvate for evaluating *in vivo* metabolism of spinal cord in rodents as a first step in preparing for an *in vivo* study of traumatic injury. To our knowledge this is the first study that has demonstrated the acquisition of hyperpolarized ^{13}C imaging from the spinal cord.

Methods: Healthy male Sprague-Dawley rats were included in this study. All experiments were performed using a GE clinical 3T scanner with a custom-designed ^{1}H/^{13}C coil. The cervical lordosis was straightened with a padding under the dorsal neck to minimize a partial volume with non-spinal tissue (Figure 1A). 35µL of [1-^{13}C]pyruvate (with 1.5 mM gadolinium) were pre-polarized using a HyperSense® DNP polarizer (Oxford Instruments, Abingdon, UK). Compressed sensing ^{13}C 3D MRSI data were acquired using a double spin echo sequence (TE/TR=140/215 ms) with centric k-space encoding, a variable flip angle scheme and flyback echo-planar readout on the z-axis at 20 s from the start of the injection of approximately 2.5 mL hyperpolarized [1-^{13}C]pyruvate through the tail vein[4]. The final dissolved solution had a concentration of 100 mM pyruvate and pH of 7.5. T2-weighted fast spin echo (FSE) images (TE/TR=60/4000 ms) were acquired in an axial plane.

Results: Figure 1 shows an example of cervical spine data. The sagittal scout image in Figure 1A shows a 5.4 mm slice around the cervical spinal cord at C4 vertebral level, where the representative ^{13}C spectra in Figure 1C were acquired from. The axial T2-weighted image in Figure 1B shows ^{13}C MRSI grid over the spine. The corresponding ^{13}C spectra in Figure 1C exhibited pyruvate peaks with excellent SNR and relatively small lactate peaks in the normal cord (highlighted voxels) and surrounding tissues. The SNR of pyruvate (Pyr) and lactate (Lac) in the spine was 63.0 ± 4.9 and 7.8 ± 1.4 (mean ± SD), respectively (Table 1). The ratio of lactate to pyruvate (Lac/Pyr) in the spine was 0.12 ± 0.01 (mean ± SD), which is smaller than the respective value from supratentorial normal brain tissue[5] (*p<0.01*, Wilcoxon rank-sum test) (Table 1). High spatial resolution of ^{13}C spectra (2x2 mm in-plane voxel size) enabled the voxel segmentation of the cord into hemicords, which will make possible the comparison of hemicontusion lesion with a contral-lateral hemi-cord. Figure 1D represents a T2-weighted MRI of cervical hemicontusion lesion, which will be studied with the method presented in this abstract in near future.

Table 1. Summary of ^{13}C metabolite quantification

	Pyr SNR	Lac SNR	Lac/Pyr
Normal spine (n=3)	63.0 ± 4.9	7.8 ± 1.4	0.12 ± 0.01[a]
Supratentorial normal brain (n=10)			0.29 ± 0.17 [a,b]

All values are reported as mean ± SD.
[a] *p<0.01*, Wicoxon rank-sum test. [b] Values from a previous study[5]

Conclusions: We have demonstrated the feasibility of using hyperpolarized ^{13}C metabolic imaging for assessing *in vivo* metabolism in the cervical spine of uninjured rats. The results from this study suggest that this technique may provide a unique non-invasive imaging tool that is able to monitor biochemical processes underlying spinal cord injury.

References: [1]Looby & Flanders, *Radiol Clin N Am.* 2009. [2]Stroman et al., *Neuroimage.* 2013. [3]Nelson et al., *Sci Transl Med.* 2013. [4]Park et al., *Cancer Res.* 2014. [5]Park et al., *Magn Reson Med.* 2012.

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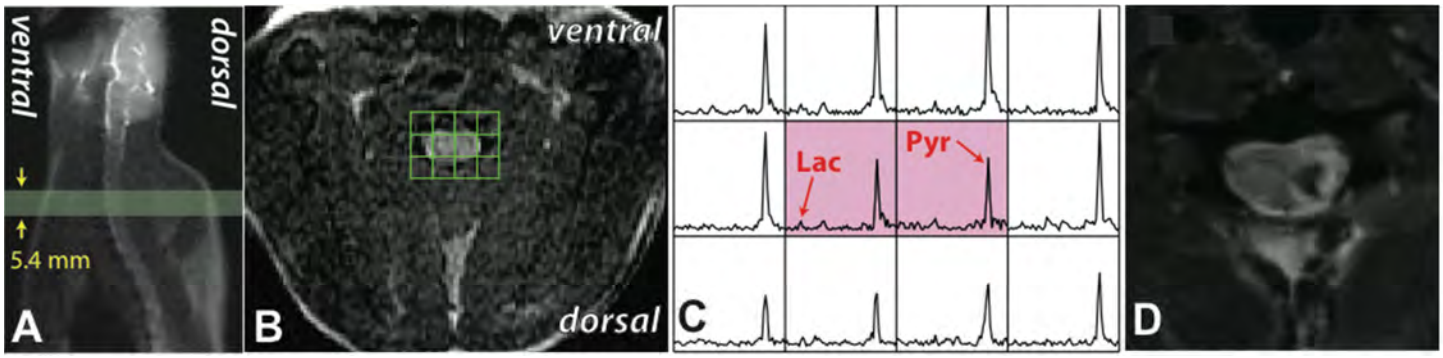

Figure 1. An example of hyperpolarized ^{13}C MRSI data from the cervical spine of an uninjured rat: A) a sagittal scout image showing a 5.4 mm spectroscopic slice, B) the corresponding axial T2 FSE image with ^{13}C spectral grid over the spine, C) the corresponding ^{13}C spectra with high spatial resolution (2x2mm in-plane voxel size), which show high pyruvate (Pyr) and relatively small lactate (Lac) signal in the spine (highlighted voxels), D) previously obtained T2-weighted MRI of cervical hemicontusion