Potential for polarization measurement of pre-polarized [1-13C] pyruvate in vivo using Jcc spectral pattern

Introduction: The ability to accurately measure or predict the polarization of hyperpolarized 13C metabolic imaging substrates at the time of the MR experiment is necessary for quantitative kinetics data or metabolite concentrations. Measuring the asymmetry of one of the nuclei in a coupled spin system may allow the estimation of the polarization while preserving the magnetization of the other nucleus needed for a subsequent imaging or spectroscopy experiment (1-2). Hyperpolarized [1-13C] pyruvate in solution has been utilized to demonstrate non-invasively assess real time metabolism in animal models (3-4). In this study, we demonstrate the potential of using asymmetry of the pyruvate C2 resonance (from 1% natural abundance of [1,2-13C2] pyruvate) to estimate the polarization of the [1-13C] pyruvate in vivo.

Methods: Hyperpolarized substrate and hardware: ~30 mg of [1-13C] pyruvic acid (99%, Isotec, Miamisburg, OH) with 15 mM OX63 trityl radical (Oxford Instruments, Abingdon, UK) and 1mM of Gd-DOTA was polarized for each experiment using a Hypersense DNP polarizer (Oxford Instruments). NaOH/Tris/EDTA solution was used to dissolve the sample for a nominal pyruvate concentration of 80 mM with a pH of 7.4. All experiments were performed using a GE MR750 3T Scanner (GE Healthcare, Waukesha WI) equipped with the multinuclear spectroscopy package. A custom-built dual-tuned 13C/H volume coil was used in all experiments. All data were processed using SAGE software (GE Healthcare). In vivo experiments: A double spin-echo pulse sequence was used in all experiments (n=6) with a 100ms readout window centered on the second spin-echo (TE/TR=140ms/3s, 64 transients) (5). A spectrally selective excitation pulse applied on the C2 pyruvate resonance (90° nominal flip angle, 200 Hz bandwidth, 10° flip angle, 8x8x16 matrix, 0.5cc spatial resolution) over a 14s period.

Results and Discussion: Representative in vitro MRS data of [1-13C] pyruvate with spectrally selective excitation or the C2 pyruvate resonance followed by non-selective excitation are shown in Fig. 1. Asymmetry (due to polarization and AB character) of the C2 doublet from the 1% natural abundance [1,2-13C2] pyruvate is clearly observed in the large tip angle selective excitation spectrum. Very little of the [1-13C] pyruvate magnetization appeared to have been consumed by the selective excitation. The small C2 doublet observed in the first spectrum (anti-phase in real mode) is likely the result of coherence transfer from the selectively excited C2 resonance. The disagreement between the two methods of polarization measurement was 22% and 20% (of the polarization measured by using C1 pyruvate signal) for the 15s and 65s low field transfer times, respectively. Although different decay constants for the C2 peaks were observed at 3T and 14.1T previously (6), long transfer time at low field didn’t seem to contribute additional errors for predicting polarization using C2 asymmetry. Further more, the T1s of the C1 carbon in [1-13C] pyruvate and [1,2-13C2] pyruvate are similar (60s and 56s respectively, at 3T (6)), thus the error contributed by the T1 difference during low field transfer is likely to be insignificant. The errors observed in these experiments may be due to the limited spectral resolution used, thus decreasing the accuracy of the C2 asymmetry estimates. Figure 2 shows an in vivo spectrum from C2 selective excitation and CSI data from the same bolus of [1-13C] pyruvate injected into a normal rat. The C2 asymmetry in this spectrum yielded a polarization of 5.1%. In this study, the feasibility of measuring polarization of [1-13C] pyruvate in vivo using Jcc spectral pattern is demonstrated. More accurate measurement of the C2 asymmetry and correction for the differential decays of the C2 peaks at the imaging field may be necessary in future studies.

References: