

Interleaved Imaging and Frequency-Selective Spectroscopic Acquisition for *in vivo* Pyruvate Polarization Monitoring

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Target audience: Researchers interested in a quantitative treatment of hyperpolarized ¹³C metabolic images

Purpose: Real-time acquisition of *in vivo* ¹³C MR images is possible with dynamic nuclear polarization (DNP), which can provide a temporary signal enhancement of up to four orders of magnitude.¹ A quantitative analysis of these metabolic images requires signal intensity normalization to account for the gradual loss of signal enhancement. We have previously reported a calibration-based approach² to polarization monitoring using the asymmetry of the pyruvate C₂ doublet^{3,4}. This work aims to investigate the feasibility of interleaved imaging and selective spectroscopic acquisition, which is a step toward image intensity normalization to facilitate the extraction of quantitative information from hyperpolarized ¹³C images.

Methods:

A mixture of 27 μ L [1-¹³C] pyruvic acid, 3 μ L [1,2-¹³C₂] pyruvic acid (Isotec), 1 mM Prohance (Bracco), and 15 mM OX63 (Oxford) was polarized using a SpinLab DNP Polarizer (GE Healthcare). Animal experiments were performed in accordance with institutional animal care protocols. A 650 g male Sprague-Dawley rat was administered two 2 mL shots of 80 mM pre-polarized pyruvate over 12 s via the tail vein. Measurements were performed at 3 T using a GE MR750 scanner with a dual-tuned ¹H/¹³C rat coil (GE Healthcare). An 18.2 ms spectral-spatial (Sp-Sp) pulse, Figure 1a, with 120 Hz passband (FWHM) was used to selectively excite lactate C₁, pyruvate C₁, and urea in alternating order with nominal flip angles of 2.5°, 20°, and 15° respectively. A 3D flyback echo-planar trajectory (TE 11.6 ms, TR 56 ms) was used to obtain 64 \times 8 \times 6 cm³ volumetric data with 5 mm isotropic spatial resolution. After every 3 volumes imaged, spectroscopic acquisition (256 ms readout, 500 Hz spectral width) was performed over a 3 cm slice concentric with the imaging volume after nominal 10° excitation using an 18.2 ms Sp-Sp pulse with 284 Hz passband, Figure 1b.

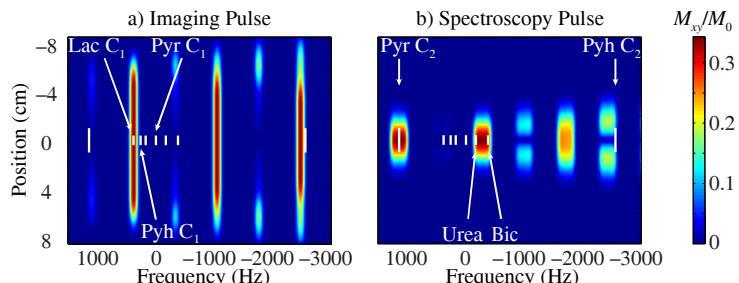


Figure 1: Spectral-spatial excitation profiles for a) selective imaging of pyruvate (Pyr) and lactate (Lac) and b) spectroscopic observation of pyruvate C₂. The digital filter for spectroscopic acquisition sufficiently suppresses any excited signal from bicarbonate (Bic) and urea. The pyruvate hydrate (Pyh) resonances lie just beyond the passbands.

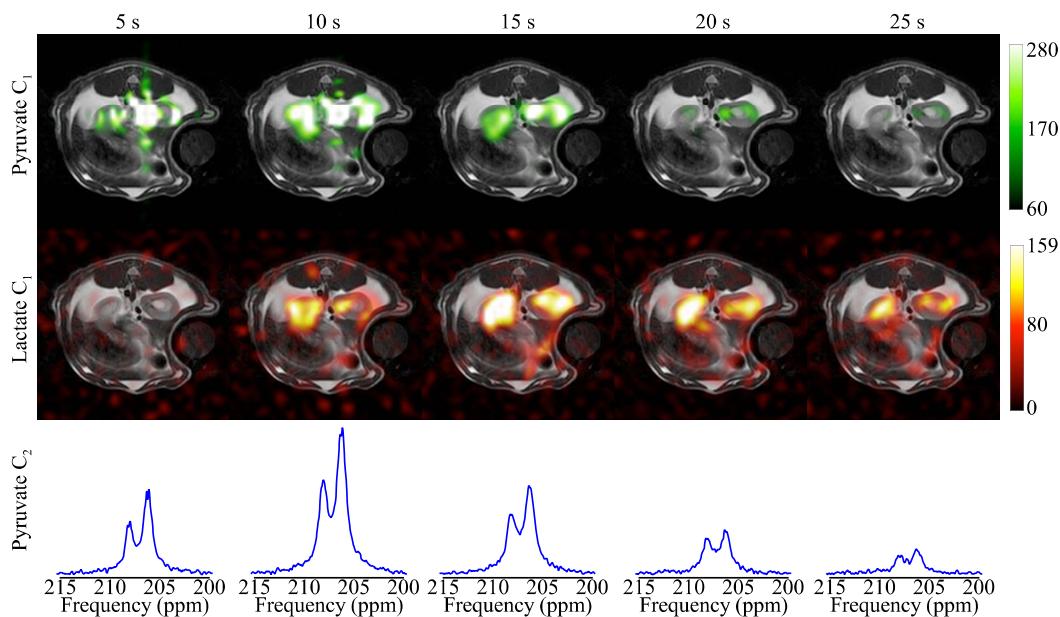


Figure 2: Images of pyruvate C₁ (top) and lactate C₁ (middle) are shown with corresponding pyruvate C₂ spectra (bottom) for a representative axial slice through the rat kidneys in the first repetition (Shot #1). The pyruvate C₂ spectra are shown on the same scale in magnitude mode. The maximum observed ¹³C SNR were 265 for pyruvate and 25 for lactate.

Discussion:

The evolution of pyruvate C₂ asymmetry within the spectrally selective excitation scheme used in this study is similar to the behaviour previously observed in the rat kidneys using non-spectrally selective excitation,² for which a slope of -0.0092 s^{-1} was measured. The effects of dipolar cross-relaxation⁶ on the evolution of C₂ asymmetry are likely more apparent under the selective excitation regime explored in this work. The acquisition of calibration data in solution and in blood is underway. Co-polarization of [1-¹³C] pyruvic acid with 10% [1,2-¹³C₂] pyruvic acid afforded good signal intensity for spectroscopic observation of pyruvate C₂ without appreciable effect on pyruvate C₁ image quality.

Conclusion: In this work, we have demonstrated the feasibility of interleaved imaging and selective spectroscopic acquisition. Co-polarization of [1-¹³C] pyruvic acid and [1,2-¹³C₂] pyruvic acid yielded good spectroscopic SNR without compromising image quality. This investigation is a promising step toward hyperpolarized signal intensity normalization for quantitative *in vivo* metabolic image analysis by polarization estimation using the pyruvate C₂ asymmetry.

Acknowledgements: Funding support from the Ontario Institute for Cancer Research (OICR) and the Natural Sciences and Engineering Research Council of Canada.

References: [1] J.H. Ardenkjær-Larsen *et al.* *Proc. Natl. Acad. Sci. USA* 100: 10158-10163 (2003). [2] J.Y.C. Lau *et al.* *NMR Biomed.* 26(10): 1233-1241 (2013). [3] R.E. Hurd *et al.* 50th ENC, p438. [4] A.P. Chen *et al.* *Proc. Intl. Soc. Mag. Reson. Med.* 18: 3261 (2010). [5] W. Dominguez-Viqueira *et al.* *Proc. Intl. Soc. Mag. Reson. Med.* 20: 4294 (2012). [6] M.E. Merritt *et al.* *J. Mag. Reson.* 189: 280-285 (2007).

Results:

A representative axial slice through the rat kidneys is shown in Figure 2 with overlaid ¹³C images of pyruvate C₁ and lactate C₁ and corresponding spectra of the pyruvate C₂ doublet. A correction for spatial mis-registration⁵ due to frequency shifts based on blip-reversal was applied. The magnitude spectra were fit with a sum of two Lorentzian functions to find the upfield and downfield integrals. The *in vivo* C₂ asymmetries are summarized as a function of time in Figure 3. A rate of change in asymmetry of -0.0096 s^{-1} was determined with linear regression.

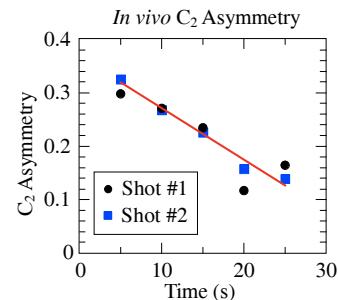


Figure 3: Summary of measured *in vivo* C₂ asymmetry in the rat kidneys for two repetitions. Linear regression (red) gives a slope of -0.0096 s^{-1} ($R^2 = 0.98$).