

Dynamic imaging of hyperpolarized [2-¹³C] pyruvate and [5-¹³C] glutamate in the heart

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Introduction: Non-localized ¹³C MR spectroscopy studies on ex vivo and in vivo hearts following injection of pre-polarized pyruvate have shown that metabolic changes in substrate usage occur following induction of ischemia [1-3]. Recently, the use of pre-polarized [2-¹³C] pyruvate has been used to probe Krebs cycle metabolism [4]. Spectroscopic imaging of the C2 pyruvate spectrum is challenging due to the large spectral bandwidth required. The development of rapid pulse sequences for hyperpolarized ¹³C imaging allows investigation of spatially varying metabolic changes occurring in vivo [5]. In this abstract, we investigate the feasibility of using spectral-spatial excitation with a respiratory and cardiac-gated multi-slice imaging pulse sequence to obtain cardiac images of [2-¹³C] pyruvate and [5-¹³C] glutamate *in vivo*.

Methods: Animals: All animal experiments were approved by the local animal care committee. ¹H and HP ¹³C MR imaging was performed on a normal female pig (n=1, wt. 25 kg). The pigs were fasted the night prior to the scan and were given a 1L electrolyte-sugar solution (25g glucose) (Life Brand) to drink 2 hours prior to the scan to raise plasma [glucose].

Spectral-spatial RF pulse design: A dualband spectral-spatial RF pulse [6] was designed to selectively excite the [2-¹³C] pyruvate spectrum (Fig. 1).

Hardware, pulse sequences: Studies were performed on a MR 750 3T GE scanner (GE Healthcare, Waukesha, WI) with a custom-built ¹³C T/R surface coil placed on the chest wall. A respiratory and cardiac-gated multi-slice ¹³C imaging pulse sequence was used to acquire short axis images at end-expiration (TR = 2.5s, 24 breaths/min) in diastole (2 slices (mid+apical), single-shot 16384x1, T_{read} = 64 ms, S/Thk = 15 mm, Spc 10 mm, FOV 48cm, in-plane res. 30x30 mm²). The ordering scheme is shown in Fig. 2. 15 ml of 165 mM HP [2-¹³C] pyruvate was injected intravenously over 15 s. The sequence was started at the beginning of the injection.

Analysis: The data was reconstructed as previously described. The pyruvate and glutamate frames were reconstructed with sliding window averages of 5 frames (~12 s) and 10 frames (~25 s), respectively, to increase SNR.

Results and Discussion: *In vivo* ¹³C data are shown in Fig. 3. The [2-¹³C] pyruvate bolus appears in the heart similar to images acquired during a [1-¹³C] pyruvate injection. The pyruvate images show the contrast agent arriving in the chamber consistent with an i.v. injection. The images acquired during the glutamate frames show localization of glutamate via Krebs cycle metabolism to the anterior myocardium, consistent with a surface coil acquisition. The SNR in the C2 pyruvate images is lower than in C1 pyruvate images acquired from separate studies with the same acquisition and half the dose. This is presumably due to differences in T₁ between C1 and C2 pyruvate, mis-setting of the transmit frequency for the spectral-spatial pulse leading to partial excitation of the resonance (~75 Hz, estimated by reconstruction algorithm), and inter-subject variability in cardiac output.

Conclusions: This study demonstrated the feasibility of imaging Krebs cycle metabolism with pre-polarized [2-¹³C] pyruvate and [5-¹³C] glutamate using a multi-slice cardiac and respiratory-gated imaging sequence.

References: [1] Ardenkjaer-Larsen et al. PNAS USA 2003;100(18):10158-10163. [2] Schroeder et al. PNAS USA 2008;105(33):12051-12056. [3] Golman et al. MRM 2008;59(5):1005-1013. [4] Schroeder et al. FASEB J 2009;23(8):2529-2538. [5] Lau et al. MRM 2010;64(5):1323-31. [6] Cunningham et al. JMR 2008;193(1):139-46.

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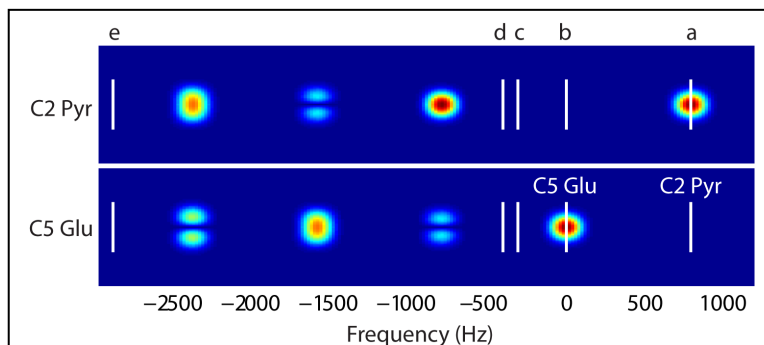


Fig. 1. A dualband spectral-spatial RF pulse was designed to selectively excite resonances in the C2 pyruvate spectrum. The displayed spectral-spatial profiles show the spectral placement of the pulse for (top) C5 glutamate and (bottom) C2 pyruvate. The list of chemical shifts at 3T, relative to C5 glutamate, are (a) 800 Hz for C2 pyruvate, (b) 0 Hz for C5 glutamate, (c) -310 Hz for C2 acetylcarnitine, (d) -410 Hz for C1 pyruvate, (e) -2900 Hz for C2 pyruvate hydrate, and (f) -3600 Hz for C2 lactate. These values were used to design a pulse with 1600 Hz stopband, 200 Hz FWHM passband, pulse length 13.5ms, and 15 mm minimum slice thickness.

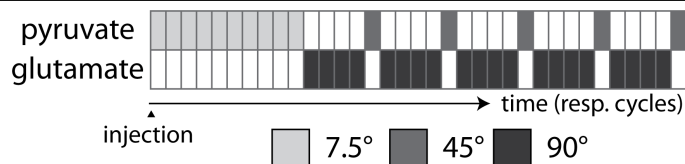


Fig. 2. Ordering scheme used for imaging of C2 pyruvate and C5 glutamate in vivo. Ten frames, intended to capture the first pass of pyruvate through the heart are acquired, followed by an interleaved set of 25 frames corresponding to glutamate and pyruvate. Each frame corresponds to a single respiratory cycle. The shaded boxes show the excited metabolite and nominal flip angle in each frame. Two slices are acquired per frame. The spectral-spatial pulse is used to excite only the appropriate resonance in each frame.

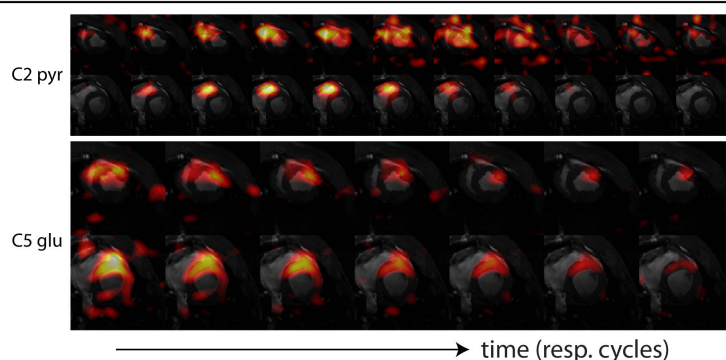


Fig. 3. *In vivo* cardiac and respiratory-gated [2-¹³C] pyruvate and [5-¹³C] glutamate images acquired following i.v. injection of HP [2-¹³C] pyruvate.