Free-breathing cardiac and respiratory-gated imaging of hyperpolarized pyruvate and bicarbonate in the heart

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Introduction: Non-localized ^{13}C MR spectroscopy studies on ex vivo and in vivo hearts following perfusion of pre-polarized [1-^{13}C]pyruvate have shown that metabolic changes in substrate usage occur following induction of ischemia [1-3]. The development of rapid pulse sequences for hyperpolarized ^{13}C imaging allows investigation of spatially varying metabolic changes occurring in vivo [4]. Previous ^{13}C cardiac imaging studies have required the use of a breathhold to remove respiratory motion. In this abstract, we incorporate respiratory gating into a previously described multi-slice imaging pulse sequence to obtain time-resolved images of [1-^{13}C] pyruvate, [1-^{13}C] lactate, and ^{13}C bicarbonate *in vivo*.

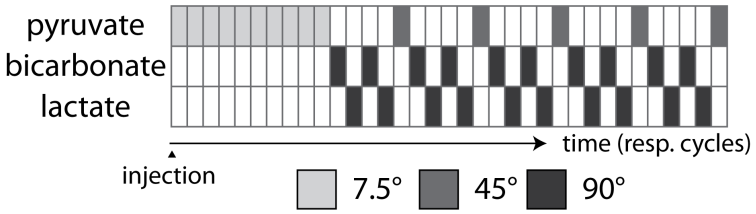

Fig. 1. Ordering scheme used for imaging of metabolism in vivo. Ten frames, intended to capture the first pass of pyruvate through the heart are acquired, followed by an interleaved set of 25 frames corresponding to bicarbonate, lactate, and pyruvate. Each frame corresponds to a single respiratory cycle. 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. The flip angle is chosen to avoid saturation of signal in future frames and to maximize the SNR of each acquired image.

Methods: Animals: All animal experiments were approved by the local animal care committee. ^{1}H and HP ^{13}C MR imaging was performed on normal female pigs (n=4, mean 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].
Hardware, pulse sequences: Studies were performed on a MR 750 3T GE scanner (GE Healthcare, Waukesha, WI) with a custom-built ^{13}C T/R surface coil placed on the chest wall. A cardiac-gated multi-slice ^{13}C imaging pulse sequence [4] was modified to include respiratory gating. Short axis images were acquired at end-expiration (TR = 2.5s, 24 breaths/min) in diastole (2 slices (mid+apical), single-shot 16384x1, T_{read} = 64 ms, SlThk = 10 mm, Spc 10 mm, FOV 48cm, in-plane res. 9x9 mm^2). The ordering scheme is shown in Fig. 1. 15 ml of 83 mM HP [1-^{13}C] 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 bicarbonate and lactate frames were reconstructed with a sliding window average of 3 frames to increase SNR. Maximum anterior bicarbonate to maximum LV pyruvate ratios (BPR) were calculated.

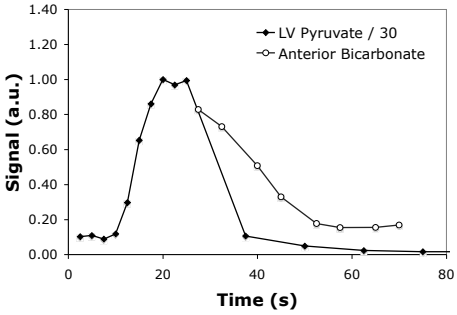

Fig. 3. Time-resolved data showing LV pyruvate and bicarbonate in the anterior myocardium.

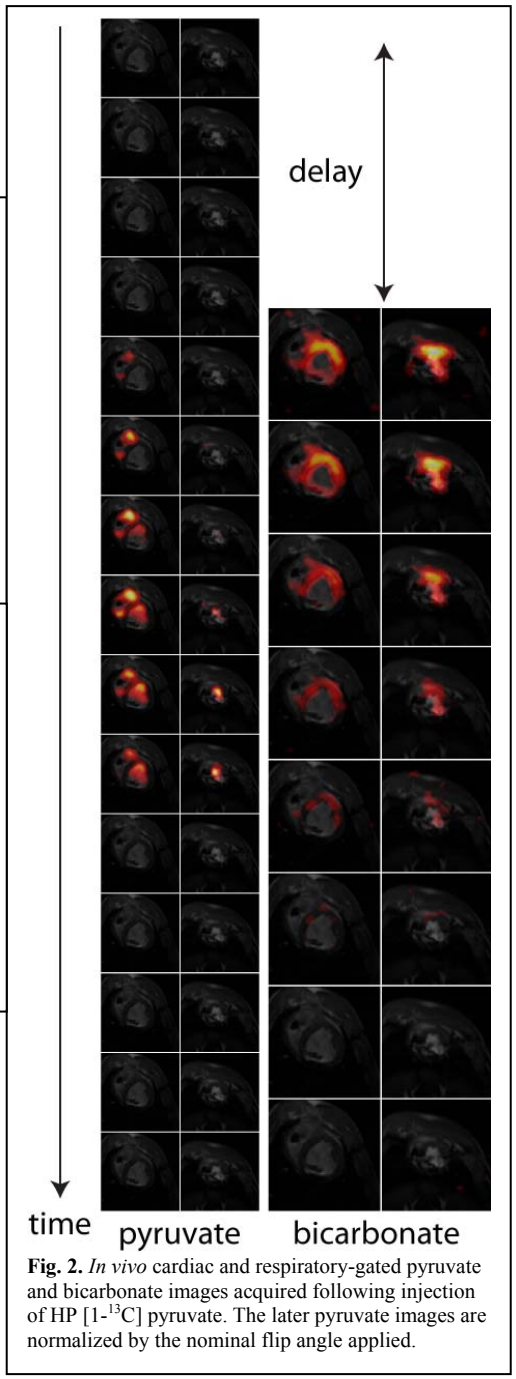

Fig. 2. *In vivo* cardiac and respiratory-gated pyruvate and bicarbonate images acquired following injection of HP [1-^{13}C] pyruvate. The later pyruvate images are normalized by the nominal flip angle applied.

Results and Discussion: *In vivo* ^{13}C data are shown in Fig. 2. The [1-^{13}C] pyruvate bolus appears in the heart consistent with an i.v. injection. The dynamic pyruvate images demonstrate the first pass of the contrast agent through the heart, and bicarbonate images acquired following the pyruvate bolus frames localize the metabolite to the myocardium. Lactate was below the detection threshold in these studies. Removing breath-holding may be more tolerable for certain patients, enhancing the clinical utility of this technique. Removal of the breathhold also increases the available imaging time, allowing imaging of both the first pass of pyruvate through the heart and the metabolic conversion of the substrate in the myocardium. This acquisition scheme spatially resolves pyruvate bolus signal in the different chambers of the heart. The time-resolved data was used to calculate **BPR = 0.017 ± 0.005** in 4 animals. Using the maximum chamber pyruvate value as normalization for myocardial bicarbonate accounts for differences in polarization, cardiac output, and slight delays in injection timing as contributing factors to the measured bicarbonate signal.

Conclusions: We have demonstrated the feasibility of acquiring temporally resolved images of pre-polarized [1-^{13}C] pyruvate, [1-^{13}C] lactate, and ^{13}C bicarbonate in a free-breathing mode using a multi-slice cardiac and respiratory-gated imaging sequence. The sequence is anticipated to improve quantitative measurements of hyperpolarized ^{13}C *in vivo*.

References: [1]Ardenkjaer-Larsen et al. PNAS USA 2003;100(18):10158–10163. [2]Merritt et al. MRM 2008;60(5):1029-36. [3]Golman et al. MRM 2008;59(5):1005-1013. [4] Lau et al. MRM 2010;64(5):1323-31. **Acknowledgements:** NSERC, CIHR, MCMM, GE Healthcare.