Real-time Cardiac Metabolism in a Pig Model of Cardiac Disease Using Hyperpolarized ^{13}C MR

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Introduction: Hyperpolarization of spins via DNP has been explored as a method to non-invasively study real-time metabolic processes in vivo using ^{13}C labeled substrates [1]. Hyperpolarized ^{13}C has recently been used to image cardiac metabolism non-invasively *in vivo* in rat [2] and pig [3]. In this abstract, we investigate the use of hyperpolarized ^{13}C MR to study real-time cardiac metabolism in a pig model of cardiac disease.

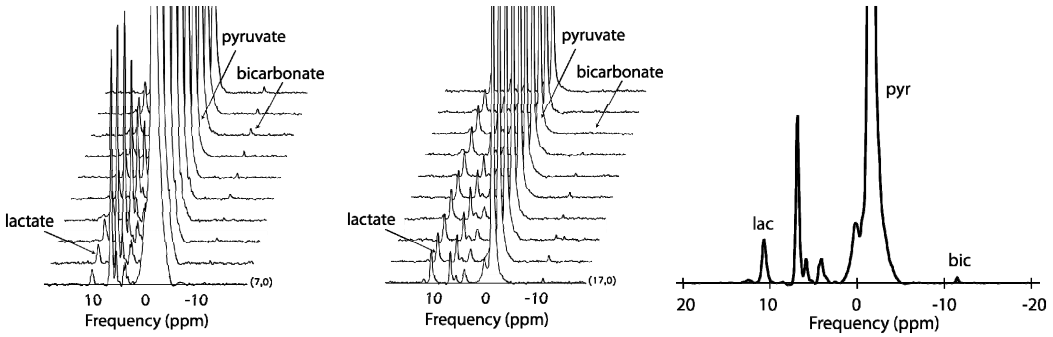

Fig. 1: ^{13}C spectra in the pig myocardium. The real channel is displayed. Each frame corresponds to 2 R-R intervals at a HR of 95 bpm. (**left**) Metabolic spectra acquired 10 to 22 seconds after injection. (**middle**) Metabolic spectra acquired 23 to 35 seconds after injection. (**right**) In vivo ^{13}C spectrum produced by summing the 8th to 17th frames after start of injection show peaks from administered pyruvate as well as downstream metabolites lactate and bicarbonate.

Methods: Animals: All animal experiments were approved by the local animal care committee. ^{1}H MR imaging and hyperpolarized ^{13}C MRS was performed on a normal female pig (19.5 kg) and a female pig (25 kg) with a 2 week-old myocardial infarct on the anterior wall. 140 mg [1-^{13}C]-pyruvate (Sigma) was hyperpolarized using a HyperSense polarizer (Oxford Instruments), producing a 250 mM solution. Delivery consisted of 5 mL injected into the right ear vein over 5 s, followed by a 5 mL saline flush.

Hardware, pulse sequences: Studies were performed on a 3T GE Signa EXCITE scanner (GE Healthcare, Waukesha, WI) with a custom-built ^{13}C transmit/receive surface coil placed on the chest wall. Anatomical imaging was performed using a separately, proton-tuned 5 inch surface coil. Proton axial MR images were acquired using a cardiac-gated Fiesta (SSFP) cine pulse sequence (TE/TR = 1.2ms/3.6ms, FA 45°, FOV 240mm, Slice thickness 8 mm).

Non-localized ^{13}C dynamic spectra were acquired during diastole using a cardiac-gated pulse-acquire spectroscopic sequence (Trig. interval = 2 R-R intervals, trig. delay 200 ms, HR 95 bpm, FA 10°, 128 frames, BW 5000 Hz, 2048 pts.). A cardiac-gated CSI pulse sequence [4] with an interleaved echo-planar flyback readout trajectory (FOV 96 mm, Thk 1cm, FA 20°, BW 892 Hz, 66 pts) was used to acquire a 16x16 (zero-filled to 32x32) 2D CSI of the heart. Respiratory motion was removed by breath-holding 20 s after the start of injection. The sequence was started 25 s after injection.

Analysis: The acquired data was analyzed using SAGE (GE Healthcare, Waukesha, WI) and MATLAB (The Mathworks, Inc., Natick, MA). The acquired FIDs were spectrally apodized with a 5 Hz line broadening Gaussian function. The dynamic spectra were phase corrected by adjusting both zero-and first-order frequency-dependent phase components. Pyruvate, lactate, and bicarbonate were quantified by integrating over the respective peaks.

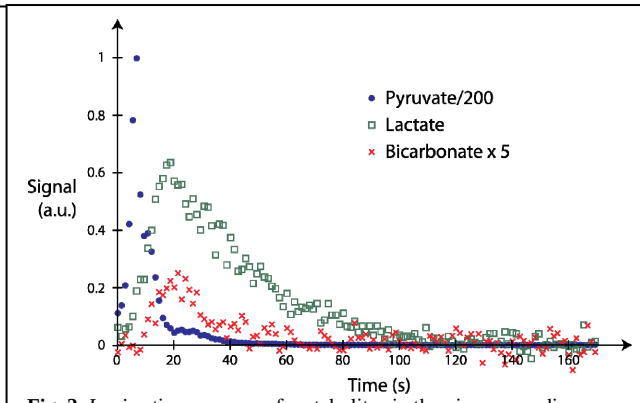

Fig. 2. *In vivo* time courses of metabolites in the pig myocardium.

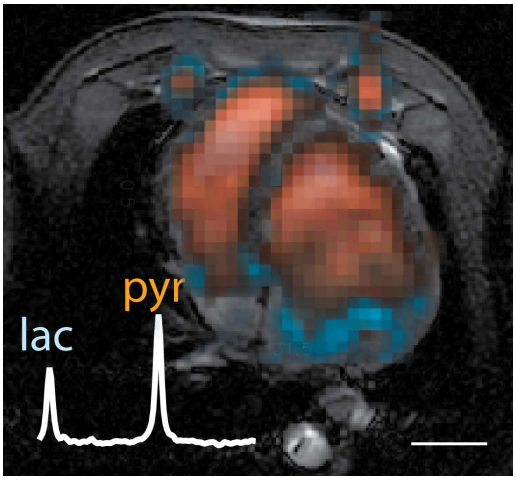

Fig. 3. Colour CSI spectra overlaid on a 2D axial SSFP image of the heart. Red indicates pyruvate, and blue indicates lactate. The scale bar indicates 2 cm. The inset magnitude spectrum is a sum over all voxels.

Results and Discussion: Dynamic spectra are shown in Figs. 1 and 2. The surface coil provided spatial localization to the anterior wall of the myocardium. Pyruvate, lactate, and bicarbonate peaks were identified. The peak between pyruvate hydrate and pyruvate is presumed to be a contaminant in the ^{13}C pyruvate sample. The pyruvate and lactate peaks were integrated to produce the time courses in Fig. 2. An exponential fit to the tail of the lactate and pyruvate time courses yielded apparent T_1s of 10 s and 30 s, respectively. A sharp decrease in the pyruvate signal subsequent to the peak at t = 10 s is likely due to the blood-pool component washing through the sensitive region of the coil. A representative anatomical image and ^{13}C CSI overlay is shown in Fig. 3. Although the acquisition was mistimed, resulting in very little substrate in the muscle, the pyruvate signal appears to be correctly spatially localized to the blood in the chambers. This demonstrates the feasibility of echo-planar spectroscopic encoding in the heart. The lactate signal is proposed to be contaminated by an aliasing artifact due to a combination of flow in the chambers and the interleaved echo-planar flyback readout used. This may not be an issue in the muscle.

Conclusions: This study demonstrated the feasibility of using hyperpolarized ^{13}C imaging to investigate real-time metabolism occurring in a pig heart. A ^{13}C transmit-receive surface coil was used to produce cardiac-gated dynamic ^{13}C spectra localized to the anterior wall of the myocardium. Pyruvate, lactate, and bicarbonate resonances were observed. Spatially registered CSIs were obtained displaying pyruvate predominantly in the blood in the chambers.

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]Cunningham et al. JMR 2007;187(2):357-362.