Localized Dynamics of Hyperpolarized ^{13}C Pyruvate in Prostate Cancer Patients

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Introduction: Time-resolved MR spectroscopic imaging (MRSI) following injection of hyperpolarized [1-^{13}C]-pyruvate can provide valuable and detailed metabolic information, including perfusion, uptake and kinetics, and has been shown in a murine prostate tumor model to improve characterization of cancerous tissues [1-2]. As part of the first hyperpolarized [1-^{13}C]-pyruvate clinical trial, we developed and applied a specialized dynamic ^{13}C 2D MRSI sequence in four prostate cancer patients.

Methods: The two key features of the pulse sequence used were: (1) a multiband spectral-spatial excitation pulse for minimal [1-^{13}C]-pyruvate saturation and (2) and a free-induction decay (FID) echo-planar spectroscopic imaging (EPSI) readout for accelerated spectral-spatial sampling.

The multiband RF pulse was designed similarly to those in [3]. However, this pulse used minimal spectral specifications of a 10-degree flip angle for [1-^{13}C]-pyruvate and a 20-degree flip angle for [1-^{13}C]-lactate, with all other resonance designated as "don't-care" regions, which allowed for a relatively short (4.3 ms, vs ~20 ms for previous designs) multiband spectral-spatial pulse. The pulse had a 1 cm minimum slice thickness for a 4 G/cm maximum gradient strength. One study was acquired with a conventional constant flip pulse.

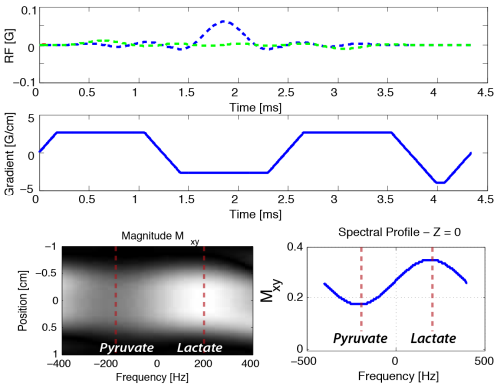

Figure 1: 4.3 ms Multiband Spectral-Spatial Pulse

The acquisition scheme consisted of phase encoding in one spatial dimension (x) and EPSI in one spatial dimension (y) and the spectral dimension (f), for a 2D MRSI acquisition. The EPSI used symmetric sampling of both gradient polarities, as well as ramp sampling (via gridding) to improve the SNR. The positive and negative lobes were separately reconstructed and first-order phase corrected based on their delays, and then combined with an automatic zero-order phase correction.

Imaging was performed on a GE 3T system using an FID sequence with TE = 3ms, TR = 125ms, 10 Hz spectral resolution, 581 Hz spectra bandwidth, 8 (PE) x 18 (EPSI) matrix, 10x10 mm resolution, 1.2 – 4.0 cm slice thickness, and 5 s per image. The sequence started 5 sec after completing the injection (including catheter flushing) of 250 mM hyperpolarized [1-^{13}C]-pyruvate (dose = 0.43 mL/kg). A "clamshell" volume C-13 transmit and endo-rectal (ER) receive RF coils were used.

Results:

	Voxel size	Pyr Peak SNR	Pyr Peak Time	Pyr Duration	Lac Peak SNR	Lac Peak Time	Lac Duration
Patient 1*	3.5 cc	62.4	20-25 s	75 s	7.0	30-45 s	45 s
Patient 2	4 cc	39.7	20-25 s	75 s	6.0	30-35 s	35 s
Patient 3	2 cc	339.5	10-15 s	75 s	16.7	25-30 s	70 s
Patient 4	1.2 cc	31.0	15 s	55 s	8.6	25 s	45 s

Table 1: Summary of dynamic characteristics within the prostate in our studies. The duration was calculated as the time for which SNR > 4. *Patient 1 was studied with a constant flip angle of 10-degrees for both pyr and lac.

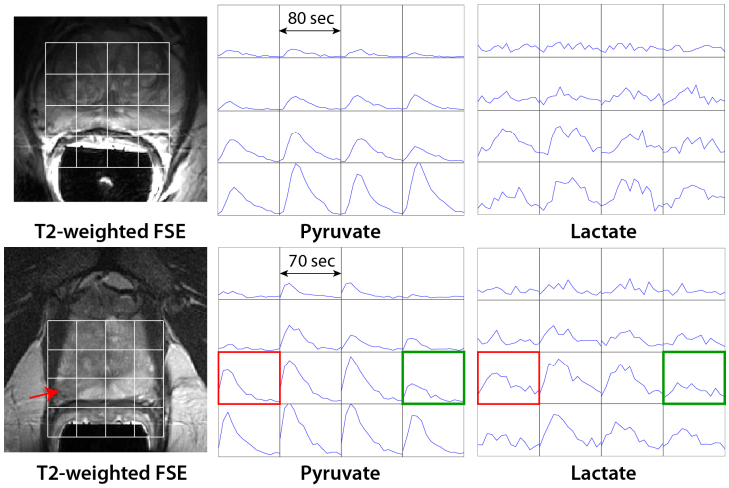

Figure 2 (top): Dynamic MRSI with conventional excitation and 10x10x35 mm resolution (*Patient 1*).

Figure 3 (bottom): Dynamic MRSI with multiband excitation and 10x10x12 mm resolution (*Patient 4*). The red indicates a biopsy-proven tumor, which has higher lactate and pyruvate than the contralateral prostate tissue (green). In this patient, voxels containing primarily rectal wall had higher SNR, likely because they were closer to the ER receive coil. Compared to the tumor region, they had lower lac:pyr. The tumor also had an earlier lactate arrival and longer lactate duration, consistent with previous studies in a prostate tumor mouse model [1].

Conclusions: We have demonstrated the feasibility of acquiring dynamic hyperpolarized [1-^{13}C]-pyruvate MRSI in prostate cancer patients. These first studies have shown adequate SNR to observe pyruvate and the metabolic product lactate for more than 60 seconds.

References: [1] Larson et al. MRM, 63:582-591, 2010. [2] Lupo et al. MRI 28; 153–62, 2010. [3] Larson, et al. JMR, 194:121-127, 2008. [4] Yen et al, MRM 62: 1–10, 2009. *Support from NIH P41EB013598 and R00 EB012064*