Dynamic MRSI for Hyperpolarized [1-^{13}C]-Pyruvate with Multiband Pulses applied in the TRAMP Prostate Cancer Mouse Model

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Introduction: Metabolic imaging with hyperpolarized [1-^{13}C]-pyruvate [1] has been shown to detect and characterize tumors in the TRansgenic Adenocarcinoma of Mouse Prostate (TRAMP) mouse model for prostate cancer [2]. However the ^{13}C MRSI in the previous study was acquired in a single 14s acquisition, providing no temporal information. In this study, a new dynamic MRSI method was applied to the TRAMP model to investigate in vivo metabolic kinetics to better characterize [1-^{13}C] pyruvate metabolism in prostate cancer.

Methods: 2D dynamic ^{13}C MRSI was acquired using the pulse sequence described in [3], incorporating new multiband excitation pulses [4]. For these experiments, the pulses were designed to use a small flip angle (3.3º) for pyruvate (pyr), the injected substrate with the highest concentration, while applying a much larger flip angle (20º) to the metabolic products of lactate (lac) and alanine (ala), allowing smaller concentrations to be observed. This novel multiband approach preserved more pyruvate for later images in the series. The sequence also consists of a adiabatic double spin-echo and an EPSI readout gradient with TE = 160 ms, TR = 250 ms, and images acquired every 5 s. TRAMP mice were injected with hyperpolarized [1-^{13}C]-pyruvate polarized using DNP in an Oxford Instruments Hypersense and imaged with a dual-tuned mouse coil on a GE 3T scanner. The peak metabolite heights were used for all analysis, which included the first moment and the full-width half-maximum (FWHM) of the dynamic curves. We imaged nine mice and typical results are shown in Figs. 2 and 3.

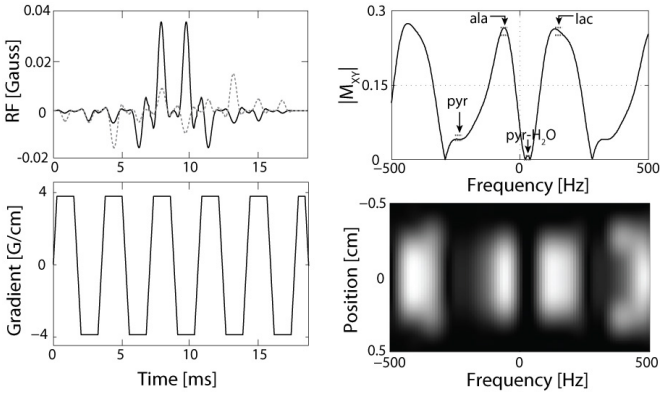
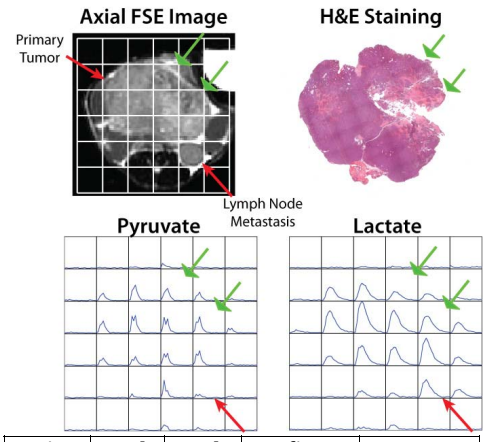


Figure 1: Multiband Excitation pulse for Dynamic MRSI

Results: In figure 2, the regions of highest lactate signal in the center and on the right side of this large tumor (green arrows) correspond to regions of highest H&E staining, indicating high cellular density. The lymph node metastasis also has significant lactate. The left anterior portion of the tumor (green arrows) has less lactate and a later pyruvate arrival, as well as lighter H&E staining. In Figure 3, the tumor is distinguished from other anatomy not only by the high lactate signal, but also by the later first moment and FWHM of the lactate curve. These dynamic characteristics are relatively consistent throughout the tumor and also similar to Fig. 2, even though the total lactate and pyruvate is variable. Alanine is observed in the liver, and the variations in pyruvate first moment is also shown.

Conclusion: This new dynamic imaging demonstrated the potential for characterizing prostate cancer based on varying dynamic metabolic parameters. These studies showed that prostate cancer can be discriminated from surrounding benign tissues based not only on high levels of hyperpolarized lactate at one time point but also differences in pyruvate uptake and metabolic kinetics. Additionally, dynamic data can be acquired at a high enough spatial resolution to assess tumor heterogeneity.

References:
[1] Golman K, et al. PNAS 2003; 100: 10435-10439. [2] Chen AP, et al. MRM 2007; 58:1099–1106. [3] Larson PEZ, et al. JMR 2008; 194:121-127. [4] Kerr AB, et al. 16th ISMRM 2008, p. 226.



Region	Total Pyr	Total Lac	Lac first moment (s)	Lac FWHM (s)
Densest Staining	9.00 ± 2.04	26.58 ± 6.77	36.49 ± 1.42	30.83 ± 2.04
Sparsest Staining	9.40 ± 1.42	16.39 ± 8.12	39.20 ± 0.25	32.50 ±3.54
LN Met	2.25	19.42	35.02	30.00

Figure 2: Dynamic metabolite curves and their characteristics in a large tumor showing some heterogeneity and a lymph node (LN) metastasis. No alanine was observed.

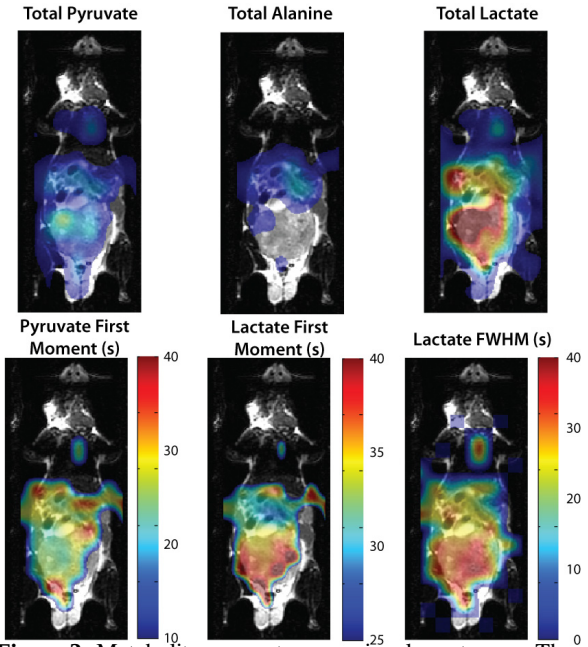


Figure 3: Metabolite parameter maps in a large tumor. The lactate FWHM and first moment characterize tumor tissue, with a mean ± standard deviation of 32.78 ± 2.64 s (lactate FWHM) and 36.75 ± 1.24 s (lactate first moment).

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