Optimal Variable Flip Angle Schemes For Multi-Band Dynamic Acquisition Of Hyperpolarized 13C MRSI

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Target Audience: Scientists and Engineers interested in RF pulse design, Hyperpolarized carbon-13, and metabolic imaging

Purpose: Hyperpolarized [1-^{13}C]pyruvate kinetics are particularly informative about cancer biology: pyruvate-lactate conversion can be used to discern cancerous from healthy tissues and to monitor cancer progression[1]. Conventionally, a single flip angle is applied to all metabolites; however, the amount of nonrenewable polarization rapidly diminishes over the duration of the scan. We developed a novel variable flip angle approach with multi-band RF excitation pulses to account for the metabolic conversion, RF excitation and T_1 relaxation, so that a constant signal level can be maintained by distributing the signal evenly throughout a dynamic acquisition.

Methods: Previous variable-flip angle approaches have progressively increased in the course of scan to account for T_1 relaxation and RF losses[2,3], but do not account for metabolic conversion. The optimization of the pyruvate and lactate flip angles taking account of the conversion from pyruvate to lactate (K_{PL}) and can be accomplished based on a two-site exchange model. In our 'pyruvate-only' approach to account for metabolic conversion, the flip angles are optimized based on effective relaxation rates of $\frac{1}{T1} - K_{PL}$ (pyr) and $\frac{1}{T1} + K_{PL}$ (lac) as in Eq. [1], which results in a constant pyruvate signal over time and a relatively flat lactate signal. The lactate flip angle can also be optimized for a constant signal over time by an empirical approach that assumes a constant signal level (S_{test}) over the duration of the scan and then corresponding flip angles are calculated to achieve this signal (Eq. [2]). This is named as the 'pyruvate-lactate' approach, where both have a simulated constant signal over time (Fig. 1).

$$\theta_n = \cos^{-1}\sqrt{\frac{E_1^2 - E_1^{2(n_{max}-n+1)}}{1-E_1^{2(n_{max}-n+1)}}},\ E_1 = \exp\left(-TR\left(\frac{1}{T1} \pm K_{PL}\right)\right)\ [1];\ \theta_L(n) = sin^{-1}\left(\frac{S_{test}}{M_L(n-1)}\right)\ [2]$$

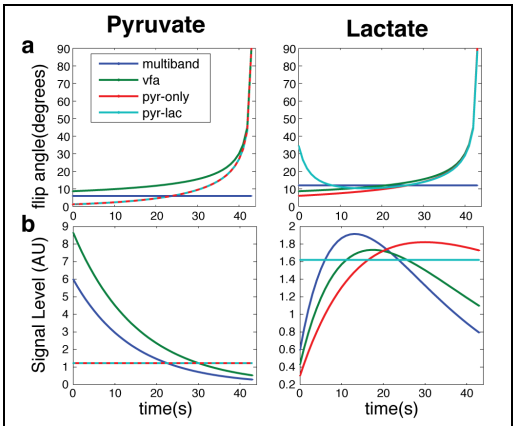

Figure 1: Simulations of multi-band, constant flip angle, variable flip angle (vfa)[2], as well as the new 'pyruvate-only' and 'pyruvate-lactate' approaches. Both new approaches theoretically provide increased metabolite signal in the latter half of the dynamic acquisition.

The flip angles for simulations and in vivo validation experiments were optimized using TR=1s, total time = 44s, K_{PL} = 0.025s^{-1}, T_1= 25s, and the initial magnetization levels = [1 (pyr), 0.05 (lac)]. A library of spectral-spatial RF excitation pulses was created using the Spectral-Spatial RF Pulse Design package for Matlab[4,5]. Experiments were performed on a clinical 3T MR scanner. Normal rat experiments used a 2.6mL injection over 12s of 100mM [1-^{13}C] pyruvate. Data acquisition of dynamic ^{13}C-spectra began 13s after the start of injection and were acquired with TE=50ms and adiabatic double spin-echo. Transgenic prostate tumor (TRAMP) mouse model experiments used a 350 µL injection over 12 s of 80 mM [1-^{13}C]pyruvate and 80 mM ^{13}C-urea and 3D dynamic MRSI was acquired using a compressed-sensing EPSI sequence[6].

Results:

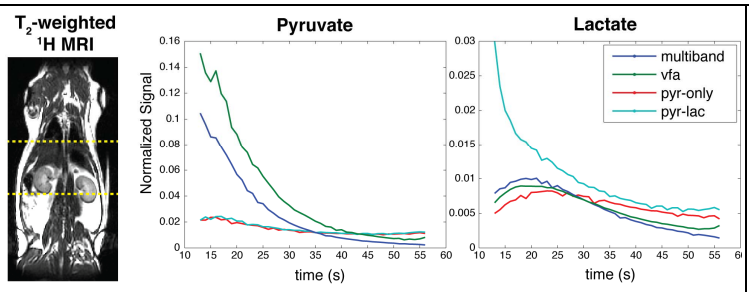

Figure 2: Experimental verification in normal rat study. Both the new flip angle schemes resulted in increased signal for all metabolites at later time points. Differences from the expected signal (Fig. 1) are likely due to differences in the actual T_1, K_{PL}, and initial magnetization from what was assumed by the RF pulse design.

Discussion and Conclusion: We have presented a novel variable flip angle, multi-band approach, where the signal of pyruvate and lactate can be maintained at a relatively constant level, ultimately leading to a more signal and more efficient use of the hyperpolarized magnetization. These flip angle optimization principles can be applied to other metabolically active compounds or pathways for improved signal in dynamic acquisitions.

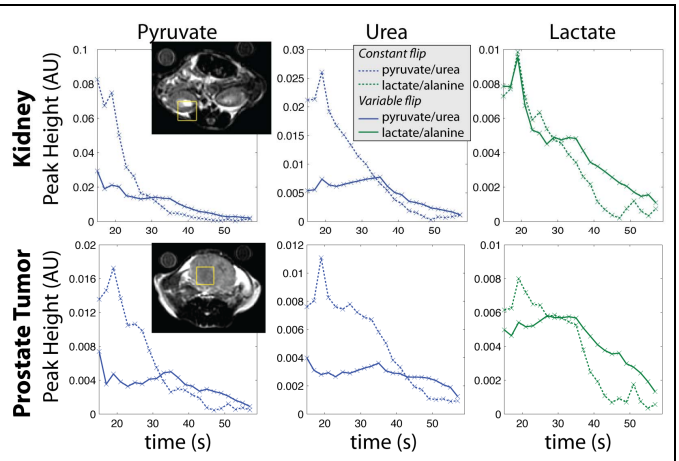

Figure 3: 3D dynamic MRSI in a TRAMP model, using flip angle schemes optimized based on K_{PL} = 0.025 1/s, T_1 = ∞, 44 s total acquisition time, and compared to previously used constant in time multi-band flip angle[6]. The metabolites all show increased signal at later time points in this dynamic acquisition, which accentuates the large, persistent lactate in the prostate tumor region.

References: [1]Kurhanewicz et al. *Neoplasia*. 13 (2011), 81-97. [2]Zhao et al. *JMR B*. 113 (1996), 179-183. [3]Nagashima, K. *JMR*. 190 (2008), 183-188. [4]Kerr et al. *Proc 16th ISMRM*. (2008), p. 226. [5]Larson et al. *JMR*. 194 (2008), 121-127. [6]Larson et al. *MRM*. 65 (2011), 610-619.