Volumetric quantitation of metabolic kinetics of hyperpolarized [1-13C]pyruvate using multiband RF pulses

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Introduction

Although hyperpolarized 13C spectroscopic imaging has been used to visualize metabolic activities in various organs and pathologies, robust quantification of metabolic kinetics remains an important area of investigation [1]. Xu et al [2] demonstrated an efficient quantification approach employing an inflow-based single-slice dynamic spiral chemical shift imaging (CSI) acquisition such that metabolic kinetics, including saturation effects, can be quantified with a single bolus injection. The 13C labeling of lactate and alanine after a bolus injection of [1-13C]pyruvate were modeled using a Michaelis–Menten-like formulation, with the resulting estimated apparent maximal reaction velocity $V_{\text{max}}$ and apparent Michaelis constant $K_{\text{M}}$ being unbiased with respect to substrate dose, bolus shape and duration.

Given the heterogeneity of metabolic kinetics within an organ or pathology, it is desirable to have a volumetric quantification method that can measure the kinetics in 3D/multiple slices following a single pyruvate injection. The single-slice dynamic acquisition in [2] used a 90° flip angle for all metabolites, relying on inflow of Pyr to replenish the slice each TR. The extension to the volumetric case necessitates a low flip angle for Pyr to preserve its magnetization while exciting a 90° flip angle for the metabolic products, hence multiband RF pulses are used for the 3D dynamic acquisition. This work extends the single-slice quantification method in [2] to the volumetric case and applies it to measuring apparent maximal reaction velocity $V_{\text{max}}$ in rat kidney and liver.

Methods

All measurements were performed on a GE 3T MR scanner with a high-performance insert gradient coil (operating at 292 mT/m, 125-mM solution of [1-13C]-pyruvate. The samples were hyperpolarized via Dynamic Nuclear Polarization using HyperSense (Oxford Instruments Molecular Biotools, Oxford, UK), achieving approximately 20% liquid state polarization.

Two multiband spectral-spatial RF excitation pulses were designed as described in [3] – RF1 with a 5° flip angle for Pyr and stopbands at lactate (Lac) and alanine (Ala), and another pulse RF2 with a 90° flip angle for Lac and Ala and a stopband at Pyr. The stopband ripple was less than the passband ripple of the other pulse. Both RF pulses were designed for the same slab-select gradient waveform (EPI flyback design) with maximum gradient amplitude of 9.795 G/cm, duration=17.78ms for 4cm slab excitation. The RF2 pulse amplitude was scaled every TR and combined with RF1 in real-time on the scanner to achieve a variable flip angle scheme up to 90° for Lac and Ala while keeping a constant 5° flip angle on Pyr.

Dynamic 3D 13C data were acquired from a 6 cm slab including the kidney and liver. Imaging parameters were: FOV=80×80×60mm³, 5×5×5mm³ nominal resolution, 12 phase-encoding steps per volume, TR=6.27s, to allow 4.55 s reaction window time every TR for metabolic conversion. Dynamic 2D 13C CSI data from 1-cm thick slices through liver and kidney were also acquired from the same animals following separate injections. The 2D slice locations matched the corresponding slices in the 3D acquisition. The use of a single-shot spiral waveform (EPI flyback design) with maximum gradient amplitude of 9.795 G/cm, duration=17.78ms for 4cm slab excitation. The RF2 pulse amplitude was scaled every TR and combined with RF1 in real-time on the scanner to achieve a variable flip angle scheme up to 90° for Lac and Ala while keeping a constant 5° flip angle on Pyr.

The dynamic data were analyzed using the saturable kinetics model described in [2]. For modeling the 3D data, a new parameter was added to the model: pyruvate transit time (PTT), corresponding to the average duration a pyruvate spin is affected by RF excitation. PTT is used to estimate the effect of the RF sampling from prior excitations on inflowing Pyr spins magnetization.

Results and Discussion

Figure 1 shows the spectral-spatial profile of the multiband RF pulses. The 90° flip angle on Lac and Ala every TR obviates the effect of $T_1$ decay while the low flip angle on Pyr preserves longitudinal magnetization for later time points. The cumulative effect of 12 excitations of 5° each leads to an effective flip angle of approximately 17.2° on Pyr for the volume acquisition (estimated as $\cos^{-1}(\cos^3\alpha)$, ignoring any changes in Pyr magnetization during the time between excitations).

This work demonstrates the extension of the single-slice quantification using a Michaelis-Menten-like formulation to the volumetric case using multiband RF pulses, obtaining consistent results for the 2D and 3D acquisitions.


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Figure 1: Multiband RF pulse for 3D 13C CSI. Top=RF1 with 5° on Pyr (-180Hz). Center=RF2 with 90° on Lac (210Hz) and Ala (0Hz). Bottom=RF1 and RF2 combined. Scale for RF1 is [0 0.09], others is [0 1]. The peak B1 was 0.73G for the combined pulse.

Figure 2: Saturable kinetics measured from kidney (left) and liver (right) show consistent results between 2D and 3D.

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<th>Rat ID</th>
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