Simulation and Application of a Variable Resolution Echo-Planar Imaging Approach for Improved Quantification of Hyperpolarized ^{13}C Metabolism

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Highlights:
Utilizing the multi-resolution simulation framework, lactate and bicarbonate multi-resolution images have respective improved peak SNR of 3.3-fold and 6.2-fold in comparison to the peak SNR of high resolution images. AUC ratios and kinetic rate fits for multiresolution images accurately estimate the ground truth values for [1-^{13}C]pyruvate metabolites.

Abstract:
Hyperpolarized (HP) substrates have been used to non-invasively image metabolism in preclinical [1] and clinical research applications [2], but SNR is a limiting factor in imaging metabolic products like ^{13}C bicarbonate for [1-^{13}C]pyruvate or TCA metabolites for [2-^{13}C]pyruvate. These metabolic products can exhibit reduced signal due to slow transport, low conversion rates, and short T1 times. Unlike ionizing imaging modalities, SNR scales with voxel volume for MRI but downsampling or voxel averaging after acquisition only increases SNR by the square root of voxel volume [3]. Acquiring at a coarser resolution can increase SNR and improve quantification of hyperpolarized ^{13}C MRI studies. However, acquiring high resolution pyruvate data is important to minimize partial volume effects between vasculature and extravascular/extracellular compartments that confound quantification. To explore the optimal SNR and resolution for each metabolite, a simulation framework to perform multi-resolution acquisitions of [1-^{13}C]pyruvate was developed.

The simulation framework uses functions in the hyperpolarized-mri-toolbox from the LarsonLab GitHub (https://github.com/LarsonLab/hyperpolarized-mri-toolbox) to generate metabolite signals and simulate acquisition of a digital phantom. Conversion of pyruvate to lactate and bicarbonate (k_{PL} = 0.01 s^{-1}, k_{PB} = 0.007 s^{-1}) was mapped to a brain phantom with metabolite and vascular ROIs. This brain phantom was simulated with a metabolite-selective imaging approach [4], using a singleband spectral-spatial RF excitation pulse and a single-shot echoplanar readout for encoding. Noise levels and conversion rates were determined based on prior pre-clinical studies in healthy rat kidneys. The first experiment acquired data at 5 x 5 mm^2 constant in-plane resolution, the second experiment acquired data at 15 x 15 mm^2 constant in-plane resolution, and the third experiment acquired data at variable resolutions (5 x 5 mm^2 for pyruvate, 10 × 10 mm^2 for lactate, 15 × 15 mm^2 for bicarbonate). For analysis, peak SNR, area under the curve (AUC) ratios, and kinetic rates were estimated.

The benefits of the multi-resolution approach can be seen in the single timepoint of pyruvate to lactate and bicarbonate metabolism in Figure 1. Lactate and bicarbonate multi-resolution images have respective improved peak SNR of 3.3-fold and 6.2-fold in comparison to the constant high resolution peak SNR. With these SNR gains, kinetic rates calculated from multiresolution images accurately estimate the ground truth values for both lactate and bicarbonate. As seen in Figure 2,

the noisy multi-resolution kinetic rate map yielded the most accurate and precise results compared to other maps. The high resolution kinetic rates are overestimated due to non-zero mean noise in the low SNR images used for calculation. The vascular ROI in the center of each image, with high pyruvate signal and no other metabolite signals, contributes to partial volume effects and ringing artifacts in the low resolution map. The AUC ratios exhibited similar results, with overestimation for high resolution signals due to the non-zero mean noise in the magnitude images and a high noise floor that exceeded the bicarbonate signal level.

This simulation framework enables quantitative analysis of different resolution schemes for future HP [1-^{13}C]pyruvate studies, such that the acquisition for eventual clinical studies can maximize metabolite SNR and allow for accurate quantification.

References:

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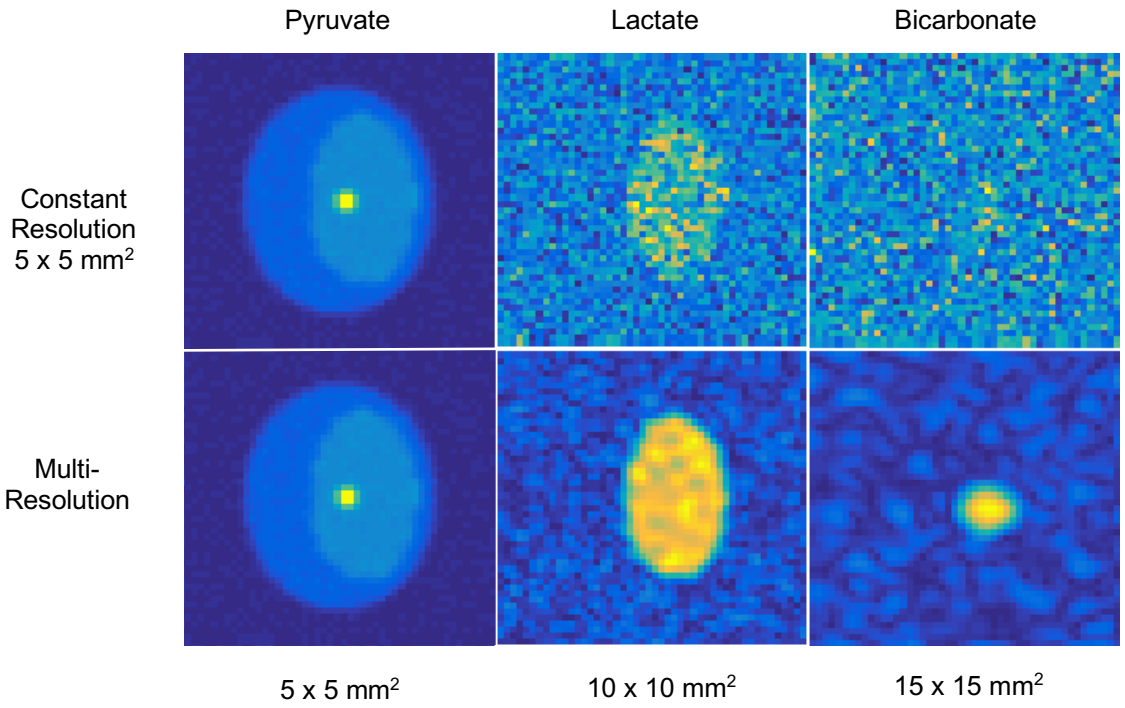

Figure 1. Simulated brain phantoms of hyperpolarized [1-C^{13}]pyruvate, lactate, and bicarbonate signals from 30 seconds after pyruvate bolus delivery. The multi-resolution images of lactate and bicarbonate have a respective SNR gain of 3.3-fold and 6.2-fold compared to the constant resolution images.

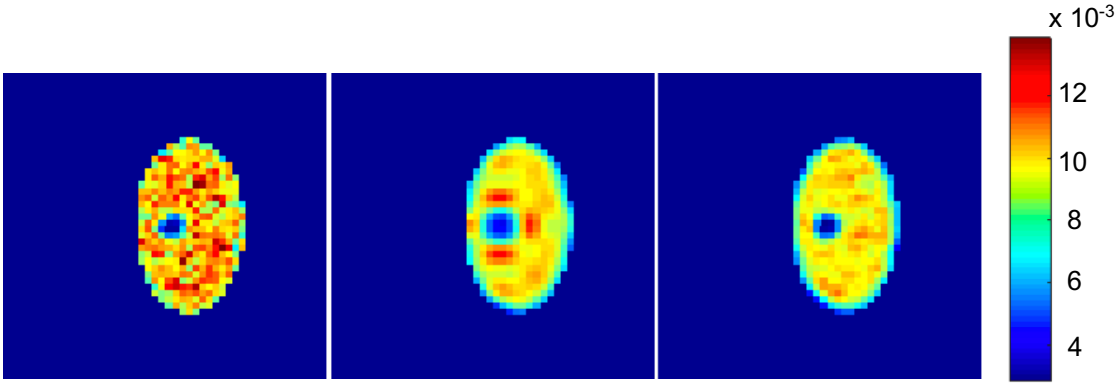

Figure 2. Kinetic rate maps for pyruvate to lactate using images with different resolution schemes (left to right: high, low, multi-resolution). The zero magnitude area in the center of the images is a vascular ROI with high pyruvate signal and no lactate signal, which contributes to partial volume and ringing effects in the low resolution maps. The noisy high resolution map overestimates the kinetic rate due to nonzero mean noise in the low SNR images used for calculation. Compared to the other maps, the multi-resolution map yields the most accurate and precise estimation of the true kinetic rates for each voxel.