Time-Resolved Metabolic Imaging in the Rat after Injection of Hyperpolarized ^{13}C-1-Pyruvate at 3 Tesla

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Introduction

The recent development of in vivo MRS of hyperpolarized ^{13}C-labeled substrates (1) provides a unique opportunity to non-invasively study metabolic products and reaction rates. Although high temporal resolution data from non-localized or slice-selective spectra have been previously demonstrated (2,3), only one study of time-resolved chemical shift imaging (CSI) has been reported (4). This work reports on the development of rapid time-resolved ^{13}C spiral CSI for the assessment of localized metabolic parameters.

Methods

All measurements were performed on a GE 3 T MR scanner equipped with self-shielded gradients (40 mT/m, 150 mT/m/ms). A custom-built dual-tuned (^{1}H/^{13}C) quadrature rat coil (∅ = 80 mm) was used for both RF excitation and signal reception. Healthy male Wistar rats (350-450 g body weight) were anesthetized with 1-3% isoflurane in oxygen (~1.5 l/min). The rats were injected in a tail vein with 1 ml of a 100-mM solution of ^{13}C-1-pyruvate that was hyperpolarized via DNP (15-20% liquid state polarization).

The implemented spiral CSI sequence (5) consists of a slice(z)-selective excitation and a spiral readout gradient for combined spatial(xy)-spectral(f) encoding. The spiral waveforms were designed for a FOV of 80×80 mm^2 with nominal 5×5-mm^2 in-plane resolution. With 3 spatial interleaves, the spectral width was 276.2 Hz and 32 echoes were acquired after each excitation using a TR of 125 ms. Five sequential CSI measurements were performed with a 10-s sampling interval starting 8 s after injection of hyperpolarized pyruvate. The excitation flip angles for the complete set of 15 excitations were progressively increased with $\theta_i = \mathrm{atan}\left(1/\sqrt{15-i}\right)$ (6), hence, exciting the same amount of transverse magnetization when neglecting longitudinal relaxation and metabolic turnover between the excitations.

Apodization of the spiral CSI (spCSI) data comprised Gaussian line broadening and zero-padding up to 128 points in k_f, and multiplication with a generalized Hamming window and zero-padding up to 64×64 pixels in k_x and k_y. After FFT along k_f, a frequency-dependent linear phase-correction was applied along the readout in order to remove the chemical shift (CS) artifact. As this can not simultaneously be done for spectral components that have been spectrally aliased a different number of times, multiple reconstructions were performed in which only components with resonance frequencies within a certain bandwidth are reconstructed "in-focus" while components outside of that band are severely blurred ("spectral tomosynthesis"). After gridding the data, a 2D-FFT was performed. Metabolic maps for pyruvate (Pyr), lactate (Lac), and alanine (Ala) were calculated by integrating the signal around each peak in absorption mode.

Results and Discussion

The pulse sequence was tested on a syringe filled with hyperpolarized pyruvate. A logarithmic plot of the signal intensity from a voxel at the center of the phantom for the 5 time points is shown in Fig. 1. A linear fit results in a T_1 of (77 ± 1) s. A time series of metabolic maps for Lac acquired from a 15-mm axial slice through the kidneys of a rat are shown in Fig. 2a. The signal from a reference phantom containing a 1.77-M solution of non-polarized ^{13}C-1-lactate increases because of the progressively increasing flip angle and recovery of magnetization due longitudinal relaxation. The average time course of Pyr, Lac, and Ala from two ROIs in the kidneys is shown in Fig. 2b. Data acquired from a slice through the liver are shown in Fig. 2c and 2d. Both Lac and Ala show a delayed peak with respect to Pyr compared to the data from the kidneys.

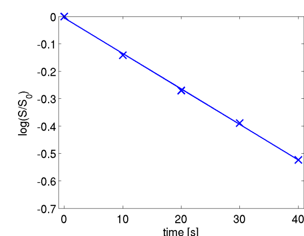

Fig. 1: Signal intensity from the center voxel of phantom filled with hyperpolarized ^{13}C-1-pyruvate.

Conclusion

These data demonstrate the feasibility of in vivo time-resolved metabolic imaging of hyperpolarized ^{13}C-label metabolites. The spatially-resolved time course for each metabolite may be used to estimate tissue and organ specific reaction kinetics and rate constants. The short acquisition time per image (375 ms) permits sub-second temporal resolution. A straight forward extension of the method to multi-slice acquisition allows trade off of temporal resolution for volumetric coverage.

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References

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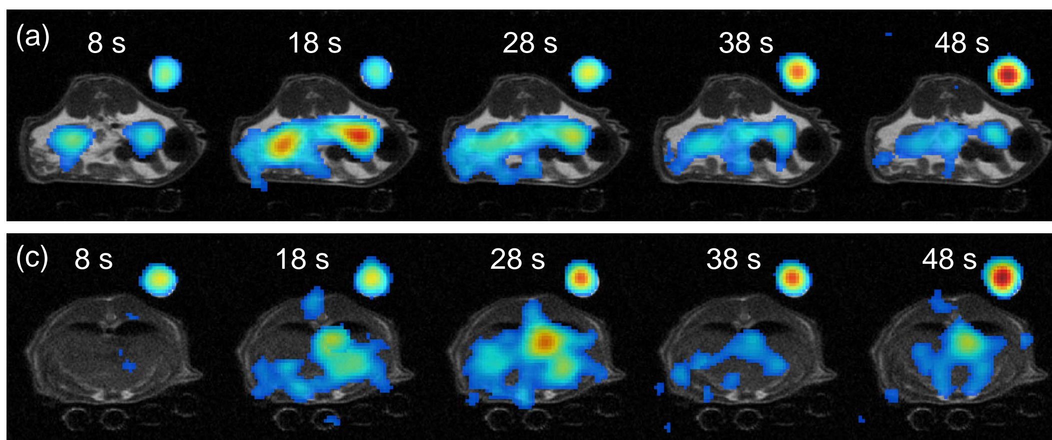

Fig. 2: (a) Metabolic maps of Lac after injection of hyperpolarized ^{13}C-1-pyruvate from a slice through the kidneys of a rat. The metabolic maps are overlaid onto the corresponding ^{1}H single-shot FSE image (2mm slice thickness). The time stamps are relative to the time of injection. (b) Averaged time course of Pyr (blue x), Lac (red □) and Ala (green o) from two ROIs in the kidneys. (c) Same as (a), but data acquired from a slice predominantly through the liver (different animal). (d) Same as (b), but from an ROI in the liver.