Ultra-Fast In Vivo Metabolic Imaging in the Rat after Injection of Hyperpolarized ^{13}C-1-Pyruvate at 3 Tesla

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Introduction

The development of hyperpolarized MRI agents presents unprecedented opportunities for metabolic imaging and new technical challenges. In particular, with signal-to-noise ratio (SNR) enhancements on the order of the 100,000-fold, dynamic nuclear polarization (DNP) (1) of metabolically active substrates (e.g., ^{13}C-labeled pyruvate or acetate) permits in vivo imaging of not only the injected agent, but also downstream metabolic products (2-4). The aim of this work was to apply undersampled ^{13}C spiral CSI (spCSI) (5) to achieve sub-second metabolic imaging of the rat in vivo after injection of hyperpolarized ^{13}C-1-pyruvate.

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 sequence 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. The spectral width (SW) was 109.7 Hz in single-shot mode (single-shot spCSI) and could be increased to 276.2 Hz when performing 3 spatial interleaves (3-shot spCSI, TR = 125 ms). The excitation flip angles for the three interleaves were 35º, 45º, and 90º, hence, exciting the same amount of transverse magnetization for each acquisition when neglecting longitudinal relaxation and metabolic turnover between the excitations. The spCSI experiments were compared to conventional phase-encoded pulse-acquire CSI (FIDCSI) with the same spatial parameters (TR = 80 ms, T_{acq} = 17 s). CSI started 18 s after the bolus injection of hyperpolarized pyruvate.

Apodization of the 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

Metabolic images of Pyr (aliased 1x), Lac, and Ala (aliased 1x) acquired with 3-shot spCSI in 375 ms from a 10-mm axial slice through the kidneys of a rat are shown in Fig. 1a. The metabolic images are overlaid onto the ^{1}H single-shot FSE image (2-mm thickness, also in Fig. 2d) from the same slice which depicts the rat anatomy and the position of a 1.77-M ^{13}C-1-lactate reference phantom. For comparison, Fig. 1b shows metabolic images acquired with FIDCSI. Differences in intensity and distribution between Fig. 1a and 1b are mainly due to the different total acquisition times of the two methods (375 ms vs. 17 s). The 3-shot spCSI spectra from the same voxel in the left kidney (Fig. 1c), with the reconstruction bandwidth focused on Lac (solid-blue line) and Pyr and Ala (dashed-red), illustrate the high SNR despite the sub-second acquisition time.

Single-shot spCSI data acquired in 155 ms from a different animal are shown in Fig. 2a. The comparison with FIDCSI data (Fig. 2b) demonstrates similar quality for the metabolic image of Pyr. But due to spectral overlap between Lac and Ala (aliased 2x), artifacts are present in the single-shot spCSI images for the two metabolites.

Conclusion

The presented data demonstrate the feasibility of sub-second hyperpolarized ^{13}C metabolic imaging in vivo using spCSI. In the case of imaging hyperpolarized samples and neglecting in-flow effects, there is no SNR penalty for the proposed technique compared to phase-encoded CSI as the longitudinal magnetization does not recover. This method can be applied to time-resolved measurements of the spatial distributions of the metabolites. The artifacts in the single-shot experiment can potentially be reduced by using prior knowledge of resonance frequencies, scalar coupling constants, and transverse relaxation times, and estimating the amplitudes with a minimum least-squares solution (6).

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References

[1] Ardenkjaer-Larsen JH et al. Proc Natl Acad Sci U S A 2003;100:10158-10163. [2] Golman K, Petersson JS. Acad Radiol 2006;13:932-942. [3] Golman K et al. Proc Natl Acad Sci U S A 2006;103:11270-11275. [4] Kohler SJ et al. Magn Reson Med 2007;58:65-69. [5] Mayer D et al. Magn Reson Med 2006;56:932-937. [6] Levin YS et al. Magn Reson Med 2007;58:245-252.

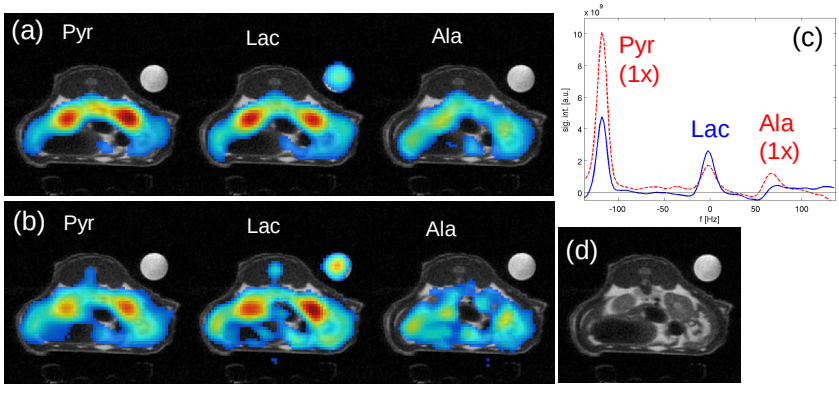

Fig. 1: (a) Metabolic maps of Pyr, Lac, and Ala reconstructed from the 3-shot spCSI data overlaid onto the corresponding ^{1}H single-shot FSE image (also shown in (d)). The metabolic images have the same intensity scale, but the Pyr image was scaled down by a factor 3. (b) Same as (a) but data acquired with FIDCSI. (c) 3-shot spCSI spectra from a voxel in the left kidney with the reconstruction bandwidth focused on Lac (solid-blue line) and Pyr and Ala (dashed-red).

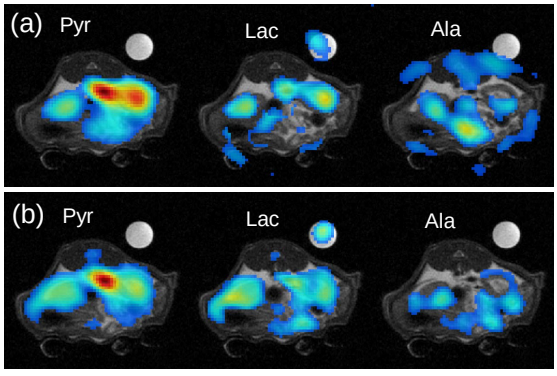

Fig. 1: (a) Metabolic maps of Pyr, Lac, and Ala reconstructed from the single-shot spCSI data overlaid onto the corresponding ^{1}H single-shot FSE image. The metabolic images have the same intensity scale, but the Pyr image was scaled down by a factor 3. (b) Same as (a) but data acquired with FIDCSI.