

Improved dynamic 3D spiral CSI with interleaved spectral band excitation for metabolic imaging of hyperpolarized [2-¹³C]pyruvate

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Introduction

There has been growing interest in using [2-¹³C]pyruvate (Pyr) as a substrate for hyperpolarized metabolic MRI/MRS because it allows following the label further down the metabolic pathway as the label is retained in the conversion of Pyr to acetyl coenzyme A¹⁻⁴. However, the large spectral dispersion of the resonances (~160 ppm, i.e. over 5000 Hz at 3T, between the C2 resonances of Pyr and alanine (Ala)) poses additional technical challenges. Park et al.³ applied non-selective excitation in combination with 3D spiral chemical shift imaging (spCSI) and spectral undersampling to image some of the resonances, Pyr, lactate (Lac), and [5-¹³C]glutamate (Glu), without spectral overlap. Josan et al.⁴ used spectrally selective excitation of limited frequency bands containing a subset of metabolites, interleaving different bands to acquire dynamic 3D spCSI data in rat heart. While this approach gives the flexibility of trading off temporal resolution vs. spectral content, acquiring a full set of metabolites, i.e. signals from C2-Pyr (208 ppm), C2-Lac doublet (71 ppm), C2-Ala doublet (52 ppm), and the spectral band containing Glu, citrate and [1-¹³C]acetylcarnitine (Alcar) (170-185 ppm), would require the interleaved acquisition of 4 bands corresponding to an acquisition time of over 11 s.

The aim of this work was to reduce the number of required bands and, hence, to increase temporal resolution by using an improved RF pulse design for different bands. The sequence also exploits the fact that Pyr-hydrate (PyrH, 96 ppm) is metabolically not active and in a pH-dependent equilibrium with Pyr, i.e., it provides information about distribution and kinetics of the injected substrate.

Methods

Two different spectrally selective RF pulse designs were used for exciting the two spectral bands. The RF pulse for Glu-Alcar band was the same as in ref.4, with 4-ms duration, 190 Hz passband. A wider passband RF pulse was designed for the second band containing Lac, Ala and PyrH: 1-ms long, passband=660 Hz with 1% ripple, FWHM = 2300 Hz. The spectral profiles are shown in Fig. 1. For both RF pulses, the resonance of [2-¹³C]Pyr frequency was placed in a null to avoid its excitation. For the Lac band, the transmit frequency was centered between Lac and Ala, which led to 70% passband magnitude at PyrH frequency. A slightly smaller flip angle at PyrH is useful to conserve Pyr magnetization and also aimed to achieve similar signal levels for the 3 metabolites.

Experiments were performed on a GE 3T MR scanner with a high-performance insert gradient coil (500 mT/m, 1865 mT/m/ms) using a custom-built ¹³C transmit/receive surface coil (dia=28 mm) placed over the liver or the heart. An 80-mM solution of [2-¹³C]Pyr, hyperpolarized using HyperSense (Oxford Instruments, UK), was injected i.v. into 3 male Wistar rats. Dichloroacetate (DCA) infusion (150 mg/kg) was administered i.v. prior to Pyr injection to stimulate PDH activity.

Dynamic 3D ¹³C data were acquired with FOV=80×80×60 mm³, 5×5×5 mm³ nominal resolution, 12 z-phase-encoding steps, 2 x-y spiral interleaves, spectral width=512 Hz, 58-64 echoes, T_{acq}=3-3.2s, 10° flip angle. A spectral width of 512 Hz was chosen to avoid overlap between Lac and the aliased Ala and PyrH peaks in the Lac band, given the spectral undersampling of these peaks. Imaging started at the same time as Pyr injection. The RF waveform was alternated for successive time-points between the one for the Glu-Alcar band and that for the Lac band. 10 time-points were acquired for each spectral band.

Results and Discussion

Figure 2 shows representative time-averaged ¹³C metabolic maps of [2-¹³C]Lac, Ala, PyrH and Alcar acquired after a single Pyr injection and superimposed onto ¹H SPGR images. The signal fall-off in A/P direction is due to the sensitivity profile of the surface coil. Lac, Ala and PyrH were acquired in one frequency band while Alcar is from the second frequency band. There was not sufficient SNR for a Glu image. The Lac and Ala signals are mostly from the liver while the Alcar signal is present mainly in the chest muscles.

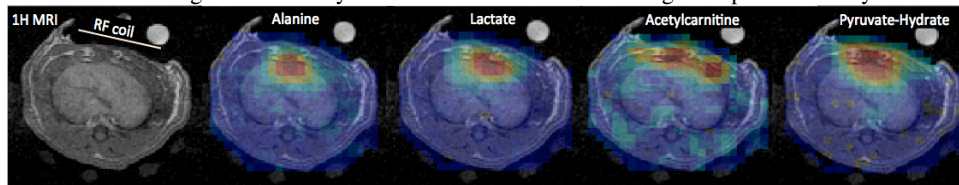


Figure2: Time-averaged ¹³C metabolic maps of a slice through the liver from a 3D dataset.

The spectra for the two bands are shown in Fig. 3 along with metabolite time-courses, from a liver ROI. In the Lac band spectra, the Ala doublet is aliased once and PyrH is aliased twice given the 512 Hz spectral width. Also shown in Fig. 3d is a spectrum of Glu band from a heart ROI in the same rat demonstrating higher signal levels due to the higher rate of metabolism.

Different flip angles can be used for the 2 frequency bands to optimize SNR. Given the short T1 of C2-Lac and C2-Ala, a high flip angle per time-point may be desirable to readout the magnetization every TR. As Pyr is not excited/imaged, PyrH signal can be used instead to estimate the bolus and this also preserves the Pyr magnetization for dynamic acquisitions.

Conclusion

This work presents an improved sequence for dynamic 3D CSI of hyperpolarized [2-¹³C]Pyr acquiring different spectral bands in an interleaved manner and demonstrates results from an in vivo application to rat liver. The improved design allows imaging of Lac, Ala and PyrH in one band, compared to three bands required in the earlier design, allowing measurement of all resonances with improved temporal resolution.

References: [1] Schroeder et al, Circ Cardiovasc Imaging 2012, p201 [4] Josan et al, MRM doi:10.1002/mrm.24871

[2] Chen et al, NMR Biomed 2011, p305 [3] Park et al, ISMRM 2013, p3938

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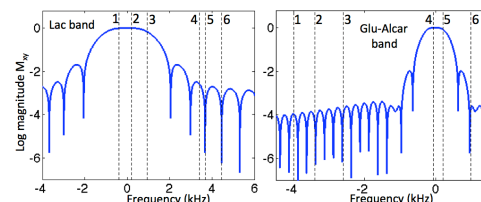


Figure1: Spectral profiles of RF pulses for the two interleaved bands. Lines 1, 2, 3 mark the C2 resonances of Ala, Lac and PyrH, excited by the pulse used for Lac band (left). Lines 4, 5 indicate Glu and Alcar, excited by the pulse used for Glu-Alcar band (right). Signal from ¹³C₂-Pyr (line 6) is suppressed in both designs.

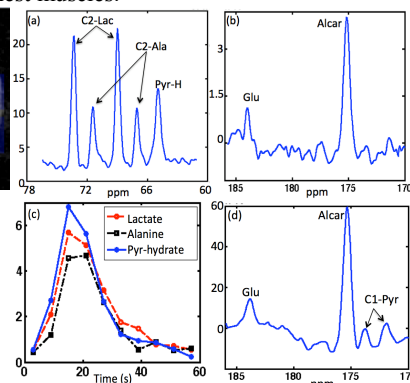


Figure3: Time-averaged spectrum for (a) Lac band, with Ala aliased 1x and PyrH aliased 2x, (b) Glu-Alcar band from liver ROI (c) Metabolite signal time-courses from liver. (d) Spectrum for Glu-Alcar band from heart ROI with higher SNR also showing natural abundance ¹³C₁-Pyr doublet.