Spectrally Selective Imaging of Hyperpolarized ^{13}C Pyruvate with Multi-Echo, Multi-Phase Advance Balanced Steady State Free Precession

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Target audience: A multi-phase advance, multi-echo balanced steady-state free precession (bSSFP) technique is developed to allow spectrally selective imaging. In vivo imaging of hyperpolarized ^{13}C pyruvate shows its benefit as an alternative for fast, spectrally selective MRI.

Purpose: The proliferation of research involved with hyperpolarized ^{13}C metabolites has made use of their distinct spectral signatures[1]. The combination of spectral and spatial information provides further information in such studies, and has led to the development of techniques involving spectral-selective pulses[2], multi-echo acquisitions[3], and variants of bSSFP that employ a variable phase advance between successive RF excitation pulses to extract spectral information[4]. bSSFP offers high SNR but suffers from off-resonance banding artifacts[5]. Multi-echo variants of bSSFP generally require long TRs, resulting in increased off-resonance sensitivity. Multi-phase advance methods can achieve short TRs, but still have undesired sensitivity to off-resonance. We propose a technique that combines a variable phase advance with a short echo train to enable robust separation of metabolites with modest TR and reduced sensitivity to off-resonance.

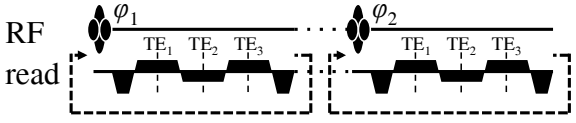

Figure 1 Illustration of multi-phase multi-echo sequence used to acquire phantom and in vivo data.

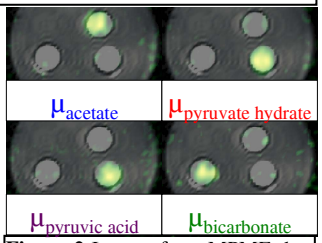

Figure 2 Images from MPME data (NEX=3) show specificity. Pyruvic acid tube has signal from metabolites at 2 distinct *f* values.

Methods: Figure 1 provides an illustration of the multi-phase advance, multi-echo (MPME) bSSFP sequence. In this case, three echoes are acquired per TR. The RF pulse amplitudes were modulated, over the phase encodes for a single image, with a Fermi function[6]. The phase advance value was constant during acquisition of each image, and incremented at the start of each new image. Frequency selective reconstruction of metabolites m=1,2…M was achieved by noting that the pixel-by-pixel image intensities $I_{\varphi\tau}$ acquired at phase advance φ and echo time τ are linear combinations of the metabolite signals μ_m described by the linear equations: $I_{\varphi\tau} = \sum_{m=1}^{M} e^{2\pi i f_m \tau} e^{-i(\varphi - 2\pi f_m \mathrm{TR})/2} \csc[(\varphi - 2\pi f_m \mathrm{TR})/2]\mu_m \equiv \sum_{m=1}^{M} S_{\varphi\tau;m}\mu_m$. A least-squares solution can be found using the Moore-Penrose pseudo-inverse: $\boldsymbol{\mu}=(\mathbf{S}^H\mathbf{S})^{-1}\mathbf{S}^H\mathbf{I}$. Typically, three echoes and two phase advance values are sufficient to resolve pyruvate and its metabolites. Off-resonance sensitivity is minimized by careful choice of TR and the phase advance values. In particular, for a given TR, each metabolite has a 'singular' phase advance where a bright band artifact occurs, resulting in severe off-resonance sensitivity. By appropriate choice of TR, one can arrange, for instance, that some singular points are clustered near 0º while others are clustered near 180º. Acquiring with a short TR and phase advance values near 90º and 270º minimizes the sensitivity to off-resonance. All data were acquired at 9.4T (Bruker Biospec, Billerica MA) after shimming. A ^{13}C saddle coil was used for phantom experiments and a 20mm surface coil was employed for in vivo data. MPME data were acquired with: 30/5º peak flip angle (phantom/in vivo); 1/1.25mm^2 in-plane resolution 48x256 matrix; and 4/5mm slice (see figure captions). The phantom was prepared with NMR tubes of acetate, pyruvic acid/pyruvate hydrate and bicarbonate, placed within agar. For in vivo experiments (using methods approved by our Insitutional Animal Care and Use Committee), 1-^{13}C pyruvate prepared in a commercial DNP hyperpolarizer (Hypersense, Oxford Instruments, Oxfordshire UK) was injected via tail vein into a nude mouse bearing an A498 cell line xenograft tumor as described previously[4]. Tumors were immersed in D_2O to reduce susceptibility effects at the tissue/air interface. A small (~100µl) bolus was injected first, and slice selective spectra were acquired to determine the metabolite frequencies. A second sample was prepared, and 250µl was injected prior to in vivo MPME bSSFP acquisition. TR was set to 3.683ms, and the center frequency was adjusted such that the critical phase advance of lactate was 52º, while the critical phase advances of pyruvate, alanine, and pyruvate hydrate were clustered approximately 180º away. Data were acquired continuously with RF phase advances of 131º and 334º, yielding spectrally selective images every 1.9s. Bicarbonate signal was known to be negligible from slice selective spectral data.

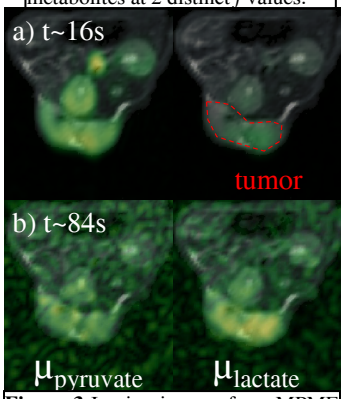

Figure 3 In vivo images from MPME data (1.25mm^2 in-plane, 5mm slice) at time, t, after first signal in vasculature.

Results and Discussion: Figure 2 shows the results from reconstruction of the phantom data. The relevant metabolite(s) are observed based on the expected value of *f*, and was confirmed by EPSI. From the reconstructed in vivo metabolite images, the expected dynamic features are observed: a strong pyruvate signal within the vasculature and tumor following injection (Figs. 3a, 4a), followed by a persistent lactate signal in the tumor at later time points (Figs. 3b, 4b). The peak lactate SNR with 1.25mm^2 resolution on 5mm slice (Fig. 3) was 41.4. With 1mm^2 resolution on a 4mm slice, it was 33.6.

Conclusions: A MPME bSSFP sequence can provide fast, high resolution hyperpolarized metabolic imaging with good SNR.

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References: [1] MRM 66(2011) 505-19; [2] JMR 194(2008) 121-7; [3] MAGMA 22(2009) 251-6; [4] Proc. ISMRM (2013) 3942; [5] MRI 31(2013) 163-70; [6] MRM 68(2012) 1894

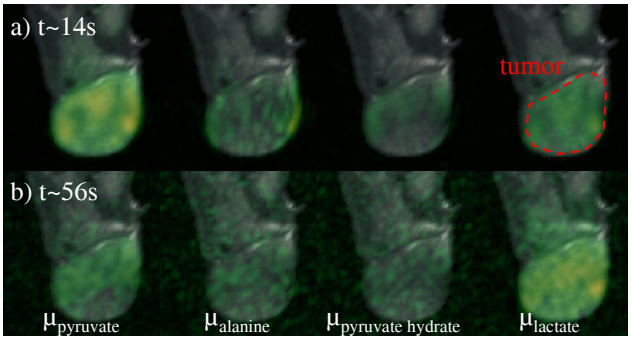

Figure 4 In vivo images from MPME data provide (1mm^2 in-plane, 4mm slice) spatial, spectral and dynamic (every 1.9s) information.