Spectrally Interleaved Multi-Echo Sequence for Measurement of Hyperpolarized [1-13C]pyruvate Metabolism

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Purpose: Hyperpolarized ^{13}C metabolic imaging using dynamic nuclear polarization (DNP) [1] has been widely used to assess metabolic kinetics between substrates and downstream products [2, 3]. However, the short observable time-window (~ 90 s) and unrecoverable hyperpolarized magnetization require the optimized utilization of the decaying signal. Despite the recent developments of several MR pulse sequences [4-7] that improve efficiency, there remains a need for higher SNR for 3D imaging, dynamics, and currently non-detectable metabolites due to low SNR. Recently, Yen et al. [8] demonstrated *in vivo* T_2 measurement of hyperpolarized substrates using a spectral-spatial RF excitation followed by a non-CPMG echo train [9, 10] with an improved SNR. In this work, we exploit the long T_2 of ^{13}C-labeled metabolites by developing a spectrally interleaved multi-echo sequence using spectral-spatial RF pulses to increase SNR. We demonstrate the feasibility of this technique *in vitro* and *in vivo* by imaging two spectral peaks in one acquisition.

Method: Spectral-spatial selective RF pulses, which excite off-resonance peaks without slice displacement artifacts [6], with 90° and 180° flip-angles were designed to have two pass-bands at ± 250-350 Hz of FWHM as shown in Fig.1 with 10 mm and 12 mm slice-selective gradients, respectively (27 sub-lobes, pulse width = 43.680 ms for 90° with a rewinder and 42.120 ms for 180°). The RF pulses were designed to excite individual metabolites based on the chosen center frequency. After 90° excitation, targeting one metabolite (e.g., lactate (Lac) as shown in Fig.1A), a series of 180° spectral-spatial RF refocusing pulses (Fig.2) on the metabolite were applied with echo spacing of 87.736 ms. EPI readouts (FOV = 8 x 8 cm^2, 2.5 x 2.5 mm^2 in-plane nominal resolution, readout time = 41.360 ms) were used to acquire locally generated signals after each refocusing pulse. The same scheme, with a new center frequency, was then applied to the next metabolite, e.g., pyruvate (Pyr). All studies were performed with 3-T GE clinical MR scanner and a custom-built $^{1}H/^{13}C$ dual-tuned quadrature birdcage RF coil (Ø = 50 mm). Syringes containing 1-M [1-^{13}C]glycine and gadolinium-doped 8-M ^{13}C-urea, whose resonance frequencies are 290 Hz apart at 3T, were used for phantom studies (30 echoes, TR = 1.5 s, T_{acq} = 3 s). The sequence was further applied to a single time-point measurement of hyperpolarized ^{13}C metabolites in a rat brain *in vivo* (10 echoes, TR = 0.9 s, T_{acq} = 2.7 s). For the *in vivo* study, a male Wistar rat (220 g) was anesthetized with 1-3% isoflurane in oxygen (~1.5 L/min), and were injected through the tail vein with 2.5 mL of 80-mM solution of hyperpolarized [1-^{13}C]Pyr (~25% liquid-state polarization), followed by a scan with 25 s of delay between the injection and start of scan.

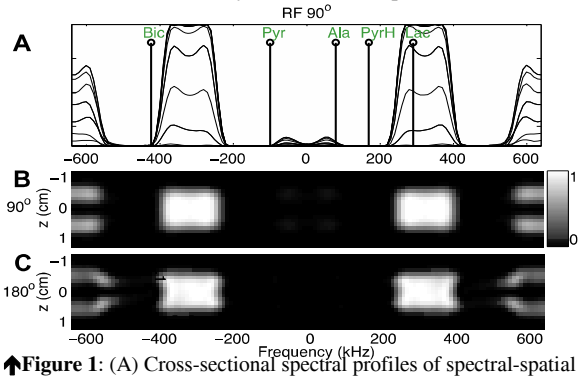


Figure 1: (A) Cross-sectional spectral profiles of spectral-spatial selective 90° RF pulse. Spectral location (Hz) of metabolites are overlaid on top as an example of [1-^{13}C]Lac excitation. Spectral-spatial profiles of the (B) 90° and (C) 180° RF pulses.

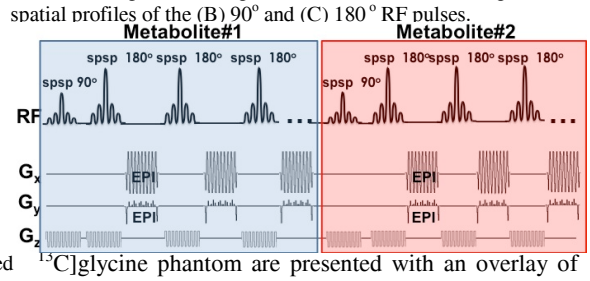
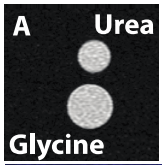
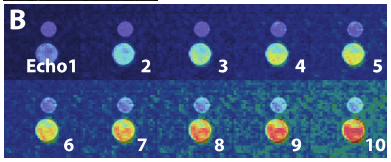


Figure 2: Schematic diagram of spectrally interleaved multi-echo sequence with spectral-spatial 90° and 180° RF pulses and EPI





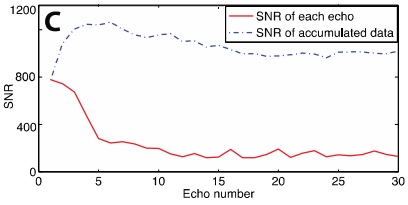


Figure 3: (A) Syringe phantoms. (B) Accumulated echo images of glycine phantom, and (C) its SNR change as compared to SNR of individual echoes.

Result: Accumulated echo images of a [1-^{13}C]glycine phantom are presented with an overlay of ^{1}H MRI (Figs. 3A-B). Combining the echoes, the [1-^{13}C]glycine sample showed a 58 % of SNR gain as compared to a more modest 13 % gain for the shorter T_2 urea (Fig.3C). Fig.4 shows *in vivo* [1-^{13}C]Lac maps reconstructed from the individual and accumulated echoes acquired from a rat brain. The decay of metabolite signals was slow enough to increase the brain SNR in Lac by 2-fold and vasculature SNR in Pyr by 1.2-fold by combining echoes.

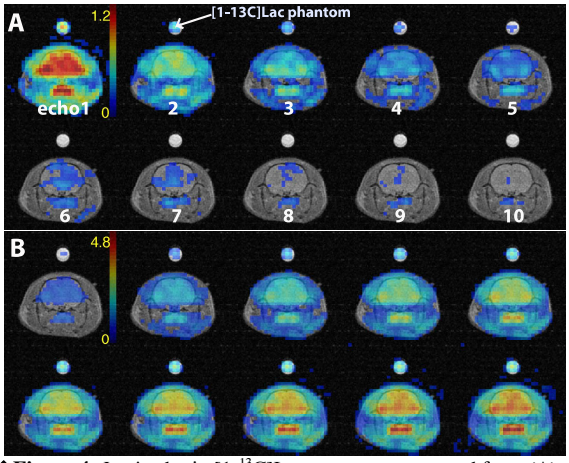


Figure 4: *In vivo* brain [1-^{13}C]Lac maps reconstructed from (A) individual and (B) accumulated echoes.

Discussion: We have demonstrated that, by exploiting the relatively long T_2 of ^{13}C-labeled metabolites, the SNR of *in vivo* metabolite maps can be substantially increased using the proposed spectrally interleaved multi-echo sequence. Because spins are excited and refocused within the slice the sequence is less sensitive to flow as compared to [8]. The sequence can be further applied for dynamic acquisition, additional metabolites, and other substrates, such as [2-^{13}C]Pyr and products.

References: [1] Ardenkjær-Larsen, JH et al, *PNAS* 2003;100(18):10158, [2] Golman, K et al, *Cancer Res* 2006; 66:10855, [3] Brindle K, *Nat Rev Cancer* 2008;8:94, [4] Mayer D et al, *MRM* 2006 Aug;56:932, [5] Wiesinger, F et al, *MRM* 2012 Jul;68(1):8, [6] Lau AZ et al, *MRM* 2010 Jun;64:1323, [7] Larson, PE et al, *IEEE Trans Med Imaging* 2012;31(2):265, [8] Yen, Y-F et al, *ISMRM*, 2012;4295, [9] Le Roux, P et al, *JMR* 2002;155-279, [10] Le Roux, P et al, *ESMRMB* 2009;114.

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