# Single voxel localization for dynamic hyperpolarized 13C MR spectroscopy

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**Introduction:** Dynamic (time resolved) hyperpolarized $^{13}$C MR spectroscopic data has been shown to be a valuable tool for real time investigation of cellular metabolism *in vitro* and *in vivo* (1-3). Dynamic $^{13}$C MRS data can provide valuable information related to delivery, uptake and metabolic conversion of the per-polarized substrate, and the data can potentially be used to derive enzymatic conversion rates and to determine an appropriate window for imaging experiments. For most of the dynamic hyperpolarized $^{13}$C MRS experiments, localization has been accomplished by RF excitation of large slabs through the subject. Thus the acquired data would include contributions from not only the tissue/organ of interest but also from surrounding tissue and vasculature. The PRESS technique has been widely used to achieve voxel localization for *in vivo* $^{1}$H MRS, but has not been successfully applied in hyperpolarized $^{13}$C MR to date. The hypothesis is that the transition bands of the spatially-selective refocusing pulses may saturate the pre-polarized substrate spins moving into the voxel. This limitation may be overcome by designing refocusing pulses that do not perturb the resonance of the hyperpolarized substrate, but do refocus the spins of the metabolic products. In this study, a PRESS pulse sequence incorporating spectral-spatial refocusing pulses that have a stop band ('notch') at the substrate resonance is tested *in vivo* using hyperpolarized [1-$^{13}$C]pyruvate.

**Methods:** RF Pulse Design: The spectral-spatial refocusing pulse and gradient waveform were designed in MATLAB. A single band digital filter with time-bandwith 9 and 0.1% ripples was computed by least squares. Then "root flipping" (4) was used to create a non-linear phase modulation, reducing peak B1 by 75%. This filter was modulated by the sum of two complex exponentials to create the two passbands. Then a time-bandwith 3 filter was created for the spatial profile, and the 2D SLR transform (5) was applied to compute the RF pulse. The pulse shapes and simulated spectral-spatial profile of the 'notch' refocusing pulse are shown in Fig. 1. Hardware and agent: All studies were performed using a 3T GE MR750 scanner (GE Healthcare) with a dual-tuned $^{1}$H/$^{13}$C birdcage rat coil and a SPINLab polarizer (GE). Neat [1-$^{13}$C] pyruvic acid (Isotec) doped with 15mM of OX63 radical (Oxford Instruments) and 1mM Gd chelate (Prohance®, Bracco) was polarized and then dissolved with a $H_2O$/EDTA solution and neutralized with a NaOH/TRIS buffer post dissolution. *In vivo* experiments: A (2cm)$^3$ single voxel centered on the rat brain (Sprague Dawley rat, Harlan Laboratories), was prescribed for $^{13}$C spectroscopic acquisition with a PRESS pulse sequence (Fig. 2, top). Two hyperpolarized MRS experiments were performed in the same animal following two separate infusions of 2cc/80mM [1-$^{13}$C]pyruvate solutions. One experiment was performed using the PRESS sequence with the default conventional refocusing pulse and the other one with the spectral-spatial refocusing pulse described above (20° nominal excitation tip angle, 2s TR, 64 transients for both experiments). The stop band of the spectral-spatial pulse was positioned at where [1-$^{13}$C]pyruvate resonance would be expected. Data acquisitions began at the start of the ~12s infusion of the substrate.

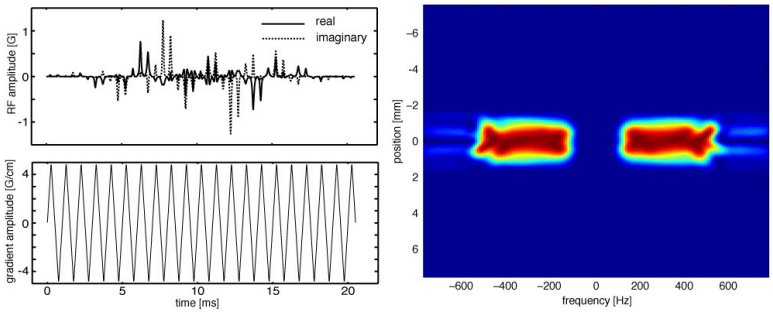


**Fig. 1** RF and gradient waveform (left) and spectral-spatial profile of the refocusing pulse designed to have a stop band for the resonance of the hyperpolarized $^{13}$C substrate.

**Results and Discussion:** Dynamic hyperpolarized $^{13}$C MRS data acquired from a voxel on the rat brain using the PRESS pulse sequence with the conventional refocusing pulse and with the 'notch' spectral-spatial refocusing pulse are shown in Fig. 2. Only signal from the [1-$^{13}$C]pyruvate substrate was observed in the data acquired using the conventional refocusing pulse, likely because the metabolite signals were below the detection limit, as much of the substrate polarization was saturated prior to entering the voxel. However, in the data acquired using the modified PRESS sequence with the spectral-spatial refocusing pulse, signal from the metabolite [1-$^{13}$C]lactate was observed. No substrate signal was clearly detected in this dataset since [1-$^{13}$C]pyruvate was not refocused by the spectral-spatial pulse in the modified PRESS sequence.

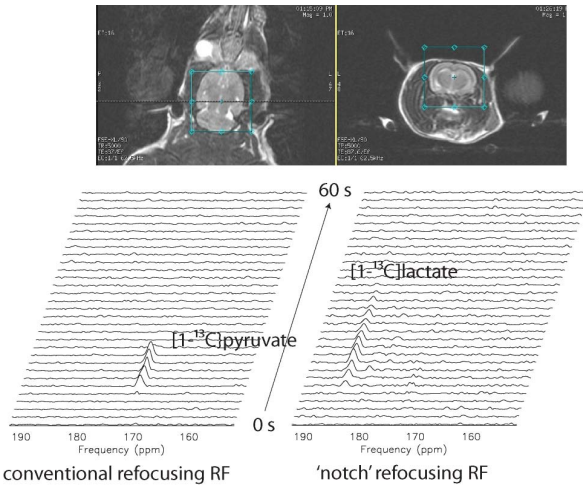


**Fig. 2** A (2 cm)$^3$ voxel centered on the rat brain was prescribed for the dynamic $^{13}$C MRS experiments (top). Data from this voxel using the PRESS sequence with the conventional refocusing pulse (left) and the spectral-spatial refocusing pulse (right).

**Conclusions:** A method for single voxel dynamic hyperpolarized $^{13}$C MRS acquisition was demonstrated using a PRESS sequence incorporating spectral-spatial refocusing pulses that do not perturb the pre-polarized substrate resonance. This technique enables acquisition of dynamic $^{13}$C MRS data from within the tissue / organ of interest.

**References:** 1. Nelson SJ et al. Sci Transl Med. 2013;5(198):198ra108. 2. Merritt ME et al. PNAS. 2007;104(50):19773-7. 3. Day SE et al. Nat Med. 200;13(11):1382-7. 4. Pickup S et al. Magn Reson Med 1995; 33:648–655. 5. Pauly JM et al. Magn Reson Med 1993; 29:776–782.