Pulse Sequence for Dynamic Volumetric Imaging of Hyperpolarized Metabolic Products

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INTRODUCTION: With the recent development of a method for retaining dynamic nuclear polarization (DNP) in solution [1, 2, 3], high SNR metabolic data have been demonstrated in vivo following injection of a hyperpolarized 13 C agent. In studies to date, this has been accomplished with spectroscopic techniques in which the full spectrum is acquired, including the injected com-pound and downstream metabolic products [4, 5, 6, 7, 8, 9]. When there is one particular resonance of interest, such as 13 C-lactate for metabolic imaging of cancer when hyperpolarized 13 C-1-pyruvate is used as the injected substrate, then a different strategy can be used. In this abstract, a spectral-spatial excitation pulse is designed to excite a single line of the carbon spectrum and an echo-planar readout trajectory is employed to give volumetric coverage every 3.5 seconds.

METHODS AND RESULTS: A spectral-spatial RF pulse was designed for exciting a single component of the spectrum resulting from injection of 13 C-1-pyruvate in vivo. The RF pulse (shown in Fig. 1) consisted of 21 sub-lobes, each with 600 μs duration, a spatial time-bandwith product of 10 and a spectral time-bandwith product of 3. The RF pulse gives a 180 Hz passband (full-width-at-half-max) and a 440 Hz stopband (60 dB attenutation). The RF pulse was implemented in the rapid, "flyback" echo-planar imaging pulse sequence shown in Fig. 2. The sequence is designed to resolve a volume of 32 x 32 x 16 voxels every 3.5 seconds, and can be run continuously to acquire time-resolved data. The maximum spatial resolution is 2.5 mm in-plane and 2 mm through slice. With eight phase-encode lines acquired per excitation, 64 excitations are required to resolve the volume. The dynamic nu-clear polarization (DNP) and dissolution method [1] was used to achieve ~15% polarization for 13 C-1-pyruvate in the solution state. The sample was rapidly dissolved to a concentration of 79 mM. The polarized sample was rapidly carried to a General Electric EXCITE 3 T (Waukeshaw, WI) clinical MRI system equipped with 40 mT/m, 150 mT/m/ms gradients and a broadband amplifier.

The production of lactate was studied in a Transgenic Adenocarcinoma of Mouse Prostate (TRAMP) mouse model. A custom-designed dual-tuned mouse birdcage coil (5 cm inner diameter and 8cm length) was used for RF transmission and reception. Intravenous access was established by a semi-permanent jugular vein catheter placed in a surgical operation one day before the MR exam. An injection of 0.3 mL of the hyperpolarized solution was made through the catheter at the same time as the start of of the scan. The injection was made over a period of 12 s. The pulse sequence was run continuously, with a 3-dimensional 13C data set acquired every 5 seconds and a total imaging time of 1 minute 20 seconds for sixteen data sets. The center frequency of the passband was set on the expected frequency of lactate, based on previous in vivo 13 C studies. The results of this experiment, shown in Fig. 3, suggest that significantly different dynamic curves are observed in tumour vs. non-cancerous tissue.

CONCLUSIONS: In conclusion we have developed an echo-planar pulse sequence for rapid imaging of hyperpolarized metabolic products. By using a spectral-spatial excitation, only the resonance of interest is excited, alleviating the need for a spectroscopic acquisition and enabling volumetric coverage in 3.5 s. This high frame rate was used to measure the different lactate dynamics in different tissues in a normal rat model and a mouse model of prostate cancer.

REFERENCES: [1] J. H. Ardenkjaer-Larson et al, Proc Natl Acad Sci U S A 100, 10158–10163 (2003), [2] K. Golman et al. Proc Natl Acad Sci USA 100, 10435–10439 (2003), [3] J. Wolber et al. Nucl Instr Meth Phys Res A 526, 173–181 (2004), [4] K. Golman et al. Proc Natl Acad Sci U S A 103, 11270–11275 (2006), [5] K. Golman et al. Cancer Res 66, 10855–10860 (2006), [6] K. Golman et al. Acad Radiol 13, 932–942 (2006). [7] S. Kohler et al. Magn Reson Med 58, 65–69 (2007), [8] A. P. Chen et al. Magn Reson Med In Press (2007). [9] C. H. Cunningham et al. J Magn Reson 187, 357–362 (2007).

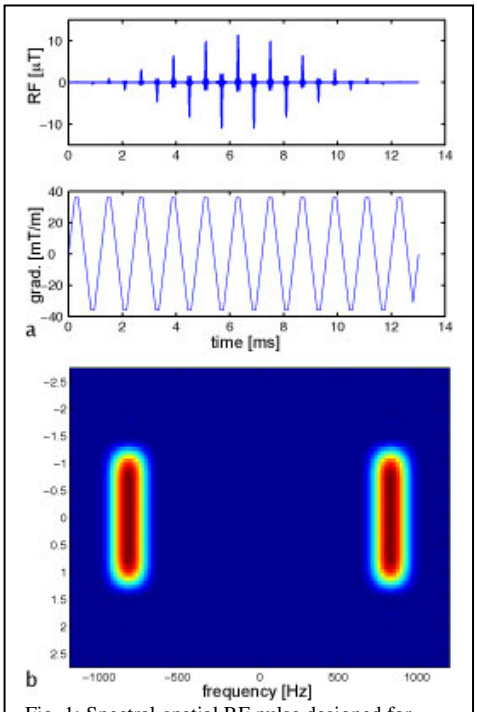


Fig. 1: Spectral-spatial RF pulse designed for imaging single components of the 13C spectrum. (a) The RF pulse and gradient waveform. (b) The spectral-spatial profile shows the large spectral stopband and the sharp spatial selectivity of the pulse. (c) The spectral profile, through the middle of the spatial profile, shows the quality of the stopband, with >= 60 dB attenuation.

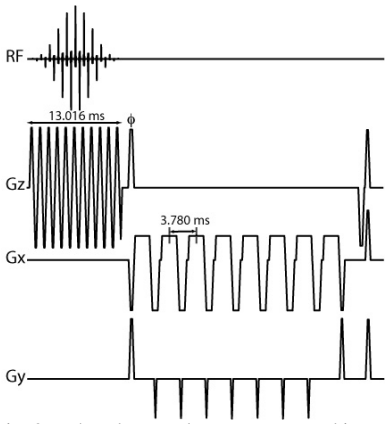
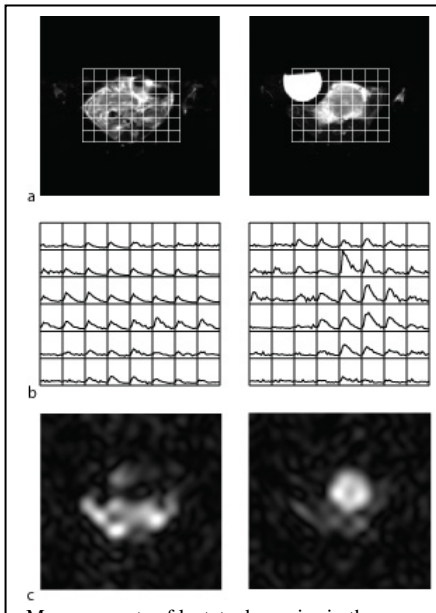


Fig. 2: Echo-planar pulse sequence used in experiments. The sequence consists of a 13.016 ms spectral-spatial RF exciation pulse followed by a gradient lobe to phase-encode the through-slice direction (labeled ϕ). The four lobes of the echo-planar readout gradient on Gx are separated by 3.780ms, with blips on Gy in-between.



Measurements of lactate dynamics in the TRAMP mouse model. (a) The voxel (3 x 3 x 4 mm) locations for the 13 C data are shown overlaid on an axial proton image through two slices, through the abdomen of the mouse (left) and through the tumour (right). (b) The time-course of the 13 C lactate produced in each voxel (each grid element shows the lactate signal as a function of time). (c) The lactate image taken at the 5th timepoint.