Single Shot, Chemical Shift Specific Imaging Methods for Hyperpolarized Carbon-13 Studies at 14T

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Introduction: MRSI methods using, hyperpolarized, ^{13}C labeled biomarkers can provide novel *in-vivo* metabolic information for biomedical research. During hyperpolarized ^{13}C experiments, the magnetization is irreversibly lost due to RF saturation, metabolism and T_1 relaxation. Therefore the general approach when designing pulse sequences for such studies is to sample the magnetization quickly and to utilize the available magnetization very efficiently (1-2). At 14T, the large chemical shift dispersion imposes further challenges for hyperpolarization studies – 1) The RF pulses must be capable of covering a large bandwidth, 2) Chemical shift artifacts and errors in the slice and readout gradients are linearly increased as compared to lower fields, and 3) Sequences using EPSI readout schemes require large gradients to be switched rapidly to satisfy the minimum spectral width and resolution requirements. In this project, we have developed and applied specialized pulse sequences incorporating frequency specific excitation methods to overcome the problems related to wide chemical shift spread at high fields. Also, in order to utilize the magnetization efficiently, we have applied single shot, EPI and spiral readout acquisition schemes. The single shot methods, with acquisition times on the order of 50-200msec, can provide high temporal resolution for time course studies.

Methods: The experiments were carried out using a 14T, Varian 600WB micro-imaging spectrometer equipped with 55mm, 100G/cm gradients (Varian Inc.). A 10mm broadband (H-X) probe was used for signal detection. Pulse sequences incorporating EPI and spiral acquisition schemes were developed and tested using phantoms containing, a) [1-^{13}C] labeled urea and pyruvate, and b) hyperpolarized [1-^{13}C]-pyruvate. For the latter [1-^{13}C]-pyruvate was hyperpolarized using the Hypersense® (Oxford Instruments) for 1 hour and dissolved at a concentration of 10mM, as previously described (3).
The pulse sequence consisted of a spectral-spatial pulse, followed by two 180 degree refocusing pulses and either an EPI or spiral acquisition.

$$\mathbf{[Spectral\text{-}spatial]}_f - t1 - [\,180_f - t2 - 180_f\,] - t3 - \mathbf{[EPI/SPIRAL\ Readout]}$$

All of the RF pulses were designed to selectively excite the resonance of interest by placing the transmitter at the chemical shift frequency, *f*. The two 180° pulses refocused the transverse magnetization while preserving the longitudinal magnetization. The EPI and spiral acquisition schemes provided frequency specific images in a single shot. The sequence was repeated at different frequencies to sample multiple resonances by changing the transmitter frequency. For time course studies, the sequence can be repeated using variable flip excitation pulses so that each excitation generates a constant magnetization component in the transverse plane. The 180° refocusing pulses help to minimize the signal loss due to T_2* effects. By adjusting *t2*, the spinecho was set to form at the center of the EPI train and at the beginning of the spiral readout. Optionally, the 180° pulses can be omitted to generate gradient echo images thus reducing the overall scan time.

Results:
Figure 1. Gradient echo image of a phantom consisting of a 10mm NMR tube with 8M [1-^{13}C]-urea and an inner 5mm tube containing 4M [1-^{13}C]-pyruvate (and pyruvate hydrate). Both solutions were doped with a Gd relaxation agent. (TR/TE 200/4msec; Flip angle 20°.)
Figure 2. Single shot, frequency specific, images corresponding to [1-^{13}C] labeled (left) urea and (right) pyruvate taken from the phantom shown in Figure 1. EPI images are shown on top and the equivalent spiral images are shown at the bottom. Parameters: Data 64x64; FOV 32mm; THK 4mm; image resolution 0.5mm; Spectral-spatial pulse bandwidth 400Hz; 180 degree pulse bandwidth 550Hz; flip angle 90°; TE 138msec (EPI), 44msec (spiral); Scan time 205msec (EPI), 138msec (spiral).

Figure 1

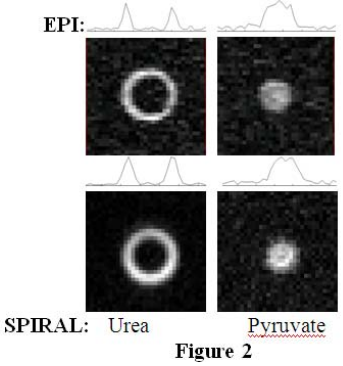

Figure 2

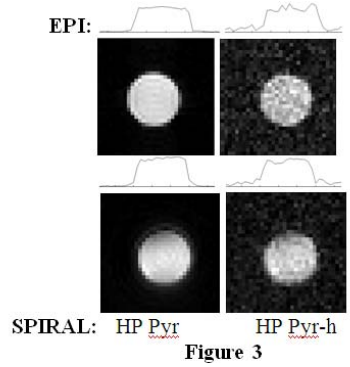

Figure 3

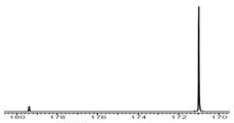

Figure 4

Figure 3: (Top) EPI and (bottom) spiral images corresponding to (left) pyruvate and (right) pyruvate-hydrate from a hyperpolarized [1-^{13}C]-Pyruvate sample were acquired sequentially. The pyruvate to pyruvate-hydrate signal ratios in the 1D spectrum was 17.5 and the values measured from the EPI and spiral images were 17.75 and 17.13 respectively. The same parameters were used as in Figure 1 except for a 5° flip angle.
Figure 4: ^{13}C spectrum from a 10mm NMR tube containing hyperpolarized [1-^{13}C]-Pyruvate sample.

Discussion: We have demonstrated single shot, chemical shift specific, images using EPI and spiral acquisition techniques at 14T. These methods address problems encountered with hyperpolarized ^{13}C MRSI methods at high fields related to the wide spectral dispersion. The RF pulses used in these sequences excite only the resonance of interest, thereby, avoiding one of the major limitations of dealing with large chemical shift dispersion. These single shot imaging methods can also be used to acquire time course measurements with temporal resolution of approximately 50-200msec. Special spectral-spatial pulses were designed in this study to excite only a single resonance of interest at a time for multiple ^{13}C resonances spread over wide spectral range. Thus, the pulse sequences described here are well suited for obtaining chemical shift specific images from hyperpolarized ^{13}C studies at high field strengths.

References: 1. Cunningham CH *et. al.* JMR 2008;193:139-146. 2. Yen Y-F *et. al.* MRM 2009; 62:1-10. 3. Ardenkjaer-Larsen et al. PNAS 100(18):10158-63.

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