In Vivo Single-Scan 13C Spatiotemporally-Encoded Spectroscopic Imaging of Hyperpolarized Metabolites

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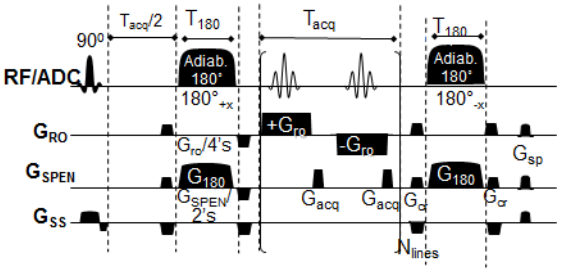
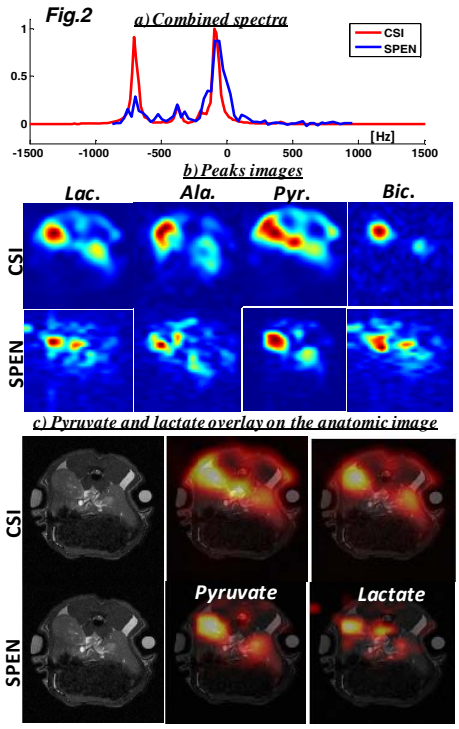
Introduction. Hyperpolarized [1-^{13}C]pyruvate dynamic metabolic imaging [1,2] is a growing field being developed to provide an essential tool especially in cancer diagnosis. Fast and effective scanning methods are required to allow the dynamic imaging, mainly the chemical shift imaging, that are demanded by the short time available before the hyperpolarized signal decays. Several fast-scan approaches have been implemented in the hyperpolarized ^{13}C arena, including CSI with spiral encoding, EPSI, and spectrally-selective pulses with EPI acquisitions [3-5]. Recent studies described the potential of single-shot alternatives based on spatiotemporal encoding (SPEN) principles [6,7] to derive chemical shift images within a sub-second period. SPEN encoding utilizes a chirp pulse and a gradient to impart a quadratic phase encoding, followed by an acquisition gradient yielding an object's spatial density directly in the time-domain. Also valuable, and by contrast to the EPSI, SPEN does not require oscillating the acquisition gradients to deliver chemical shift information: the signal contains the spatial as well as the shifts information at no extra costs. Sequences with slice-selective excitation and 180° chirp pulses were recently shown to yield single-shot chemical shift images [7], endowing SPEN with the potential to provide the kind of fast acquisitions required for dynamic metabolic imaging. The present work demonstrates the first in-vivo results using a SPEN sequence; showing [1-^{13}C]pyruvate and the metabolic derivatives in the kidneys after hyperpolarized [1-^{13}C]pyruvate injection to healthy rats at 4.7T.

Methods. Slice selective single shot sequence using spatiotemporal encoding in the phase encoding direction and k-space encoding in the readout direction was conducted to obtain chemical shift images of four peaks: the pyruvate, lactate, alanine and bicarbonate. Figure 1 displays the sequence scheme, when $T_{180}<T_{acq}$ (the chirp pulse and acquisition duration respectively), is required to collect chemical shift information. The SPEN scan parameters were: ~1300 Hz bandwidth, ~30 Hz spectral resolution, 90° excitation flip angle and total scan duration of 51 ms. The effective spatial resolution of SPEN was 3x3.75mm^2 with a slice thickness of 2 cm. These results were compared to CSI scans with spiral 2D phase encoding for the spatial dimensions. The CSI parameters were: ~4000 Hz bandwidth, ~15 Hz spectral resolution, 10° flip angle, total scan duration of 16 sec, spatial resolution of 3.75x3.75 mm^2 and 2cm thickness. Two male Sprague-Dawley rats (250-300 g) were anesthetized with isoflurane and prepared for administration of hyperpolarized [1-^{13}C]pyruvate. For improving these comparisons each experiment contained three injections followed by different scan acquisitions: first with SPEN, then with CSI, and then with SPEN again. MR was carried out on a 4.7 T horizontal bore magnet (Oxford Instruments, Oxford, UK) equipped with a Varian Direct Drive console (Varian, Palo Alto, USA), and the operating software was Vnmrj 3.2. A dual tuned ^{1}H/^{13}C linear volume transmit coil (Rapid Biomedical, Würzburg, Germany) was used for ^{13}C excitation, for data reception a 4-channel ^{13}C phased array (Rapid Biomedical, Würzburg, Germany) was used. Hyperpolarization was carried out with a HyperSense polarizer (Oxford Instruments Molecular Biotools, Oxford, UK). A volume of 20 µL [1-^{13}C]pyruvic acid (Sigma Aldrich, Munich, Germany) containing 15 mM trityl radical OX063 (Oxford Instruments, Oxford, UK) and 1.5 mmol/L Dotarem (Guerbet, Villepinte, France) was inserted into the polarizer. The solution was polarized for approximately 45 min using 100 mW microwaves at 94.108 GHz. The ^{13}C polarization was monitored by solid state NMR with an average 600 s build-up time. The hyperpolarized sample was dissolved in 4 mL of a dissolution medium (80 mmol/L TRIS, 100 mg/L EDTA, 50 mmol/L NaCl, 80 mmol/L NaOH) yielding 80 mmol/L [1-^{13}C]pyruvate at physiological pH. A volume of 1 mL was injected into the tail vein over 10 s. The transfer time between dissolution and injection was 10 s on average, and MRI/MRS data acquisition was initiated 20 s after start of injection.

Fig.1 - Multi-slice 2D spatial / 1D spectral SPEN Imaging





Results. Figure 2 compares one of the single-shot 2D spatial / 1D spectral SPEN sets collected versus a multi-scan CSI acquisition. Fig.2a compares the normalized combined spectra of CSI and SPEN. Figure 2b compares the peak images of CSI and SPEN: lactate, alanine, pyruvate and bicarbonate respectively. Figure 2c shows the pyruvate and lactate signals as an overlay on the anatomic image. The results show good correlation of the spectral and spatial information. The measured SNR of the pyruvate image was similar between the two experiments. Still the lactate image had lower signal in SPEN image than in the CSI.

Conclusions. The first set of in-vivo experiments using SPEN for chemical shift imaging of hyperpolarized injected [1-^{13}C]pyruvate was conducted. This approach allowed us to obtain, within 100 ms, 2D images for the 4 metabolic peaks arising in the experiment. These images had comparable quality to the CSI scan, despite the fact that the latter required 16 s and 256 excitation pulses. Although further steps should be done for parameters optimization to improve the spectral and spatial resolution as well as the sensitivity, the results show that SPEN sequence can be utilized as an alternative for fast dynamic imaging.

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