Spectral-spatial EPI sequence with frequency correction for dynamic 3D imaging of pre-polarized 13C metabolites

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Introduction Metabolic imaging using 13C-labeled compounds pre-polarized using DNP-dissolution [1,2] requires some form of spectral encoding along with the acquisition of imaging data, which strongly influences the design of pulse sequences for this application. The most straightforward method for accomplishing this spectral and spatial encoding is by conventional chemical-shift imaging. The strategy is flexible in that no prior knowledge about the number and relative frequency separation of the spectral components are needed. However, the underlying pulse sequences are limited in terms of SNR efficiency [3]. Motivated by the need for 3D metabolic images at multiple timepoints, a rapid spectral-spatial echo-planar imaging (ss-epi) pulse sequence tailored for clinical application was developed.

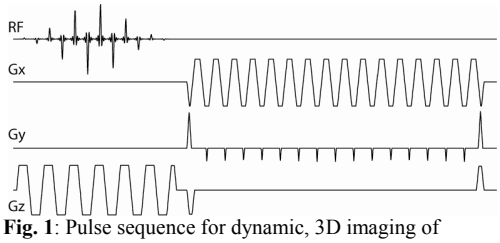

Fig. 1: Pulse sequence for dynamic, 3D imaging of pyruvate and its metabolic products. With 12 phase encodes in the through-slab direction, a 128 x 16 x 12 matrix (5 mm isotropic spatial resolution) is acquired in 600 ms.

Theory In pulse sequences employing spectrally-selective excitation, efficient, long-duration data readouts are required for adequate SNR efficiency. These long readouts are typically sensitive to the unavoidable frequency shifts that occur in practice due to tissue susceptibility differences as well as B0 eddy currents. However, the echo-planar readouts used below behave in a relatively benign fashion, with a spatial shift negligible in all but one imaging direction.

The feasibility of using this spatial shift as a method for measuring and correcting the frequency-induced spatial shifts [4] that occur *in vivo* was investigated. The idea is that by reversing the k-space trajectory for every other time point, the direction of the spatial shift for a given frequency is reversed. This is demonstrated in Fig. 2.

To correct for the resulting mis-registration, the spatial shift that maximally aligns the two shifted images must be found. However, this is non-trivial because the images to be aligned result from different timepoints, and will thus contain different (but similar) pyruvate and lactate distributions. To cope with this, we propose to use mutual information [5] to find the "best" alignment between images.

Methods and Results A spectral-spatial excitation pulse was designed with 18.2 ms pulse duration, giving a 120 Hz spectral passband width (FWHM). The RF pulse was implemented with a rapid 'flyback' echo-planar readout gradient shown in Fig 1. The image resolution and encoding matrix were tailored to the desired 3D coverage of the human prostate using an endorectral receiver coil [6,7]: 5 mm isotropic spatial resolution, field of view: 8 cm A/P, 8 cm R/L and 6 cm S/I. *In vivo* studies were performed using a GE MR750 3 T scanner (GE Healthcare, Waukesha, WI) and a micro-strip dual-tuned 1H-13C rat coil (Magvale, San Francisco, CA). All animal experiments followed a protocol approved by the local institutional animal research committee. A HyperSense DNP polarizer (Oxford Instruments, Abingdon, UK) was used to polarize neat (99% purity) [1-13C] pyruvic acid for 1 hour following previously described methods [1]. Tail-vein injections of 2.0mL/80mM of pre-polarized [1-13C] pyruvate were performed in RNU nude rats (n=3) implanted with U87 tumors in the flank. The injections were 10 seconds, with data acquisition started at the beginning of the injection. Time resolved 3D images of pyruvate, lactate and a urea reference were acquired with 5 s temporal resolution over a 1 minute duration in each study. For each rat, a second injection was performed with the center frequency purposely mis-set by +35 Hz to test the correction for erroneous shifts in the images.

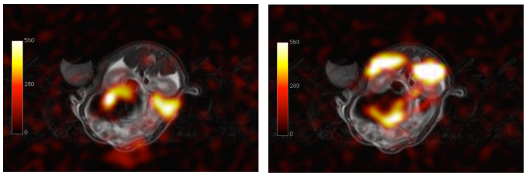

Fig. 2: Lactate (orange colour map) within the rat kidneys is seen in these two timepoints, 10 s and 15 s after the start of the injection, respectively. An erroneous shift in signal frequency causes misregistration of the 13C images relative to the anatomical scans. With blip-reversal, this shift switches in direction for each consecutive timepoint.

Representative images resulting from the pulse sequence are shown in Fig. 3. Note the excellent correspondence between 13C signal and anatomical detail in the T2-weighted images. The spatial shifts required to correct the lactate images at the level of the kidneys, computed by mutual-information registration, are listed in the Table. Even without an intentional frequency error, there are non-zero shifts due to inhomogeneous B0, and these are different for the different rats. Overall, the change in shift induced by the 35 Hz frequency offset was 5.5 +/- 0.3 mm. This agrees well with the expected 5.7 mm shift based on the 2.02 ms delay between k-space lines (giving 30.9 Hz per pixel). The 0.5 mm range in values corresponds to a frequency sensitivity of 3 Hz.

Frequency offset (Hz)	Lactate shift (mm)	Δ (mm)
0	2.6	
35	8.4	5.8
0	2.7	
35	8.0	5.3
0	4.4	
35	9.7	5.3

Conclusions A spectral-spatial echo-planar imaging sequence was designed for clinical metabolic imaging and was tested in animal models. A correction for spatial mis-registration due to frequency shifts based on blip-reversal was implemented and validated. Excellent image quality and apparent agreement with the underlying anatomy was observed. The frequency correction method was shown to have an accuracy of 3 Hz.

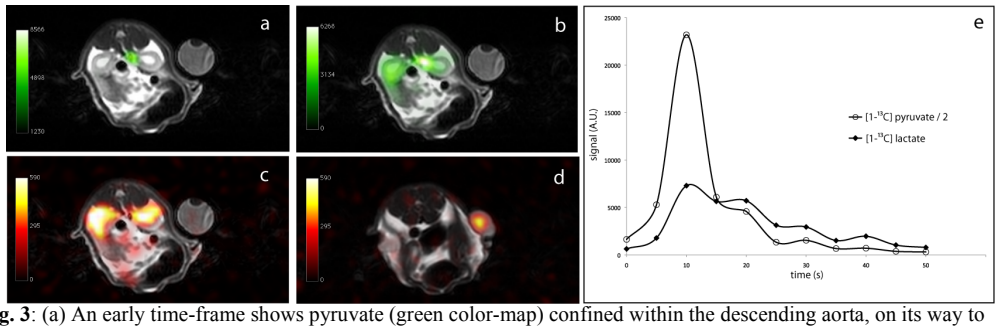

Fig. 3: (a) An early time-frame shows pyruvate (green color-map) confined within the descending aorta, on its way to downstream tissues. (b) The next time-frame (5 s later) shows [1-13C] pyruvate within the kidneys. (c) Lactate (orange color-map) within the kidneys can be observed at this time-frame 10 seconds after the start of the injection. (d) At this same time-point, [1-13C] lactate within the implanted tumour can be seen. (e) Plotting the signal vs. time for one voxel in the kidney shows the quality of the dynamic enhancement curves that can be obtained with this pulse sequence.

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] A. Macovski. *Magn Reson Med*, 36:494–497, 1996.

[4] D. Gallichan et al. *Magn Reson Med*, 64:382–390, Aug 2010.

[5] F. Maes et al. *IEEE Trans Med Imaging*, 16:187–198, Apr 1997.

[6] A. P. Chen et al. *Magn Reson Imaging*, 24:825–832, Sep 2006.

[7] SJ Nelson et al. ISMRM, p. 536, 2007.