High resolution hyperpolarized metabolic imaging with three-dimensional spectral-spatial EPI at 7T

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Target: Researchers interested in cardiac metabolism and hyperpolarized ^{13}C metabolic imaging.

Purpose: Hyperpolarized metabolic imaging has the potential to revolutionise the management of diseases in which metabolism is dysregulated, such as heart disease.[1] Progress has been made on imaging hyperpolarized compounds, but most sequences are limited in spatial coverage or temporal resolution. Spectral-spatial excitation enables efficient multi-slice imaging of hyperpolarized metabolites,[2] but this approach is challenging at higher fields when gradient requirements become prevalent.[3] Multi-echo approaches have been proposed for high field multi-metabolite imaging in the rat, but these are single-slice and very susceptible to off-resonance effects. [3] We present here a 3D fly-back pulse approach that sidesteps G_{max} demands and can image hyperpolarized metabolites with a spatial resolution of 1x1x2 mm^3 (after zerofilling by two) and a temporal resolution of 1.8 s in the *in vivo* rat heart at 7T.

Methods. Pulse sequence. A fly-back spectral-spatial pulse was designed to provide slab excitation (45.5 mm thk; 250 Hz passband; 2 kHz stopband)[2] (Fig. 1) running at S_{max} rather than G_{max}. The pulse was placed inside a 3D EPI sequence with centric-ordered phase encoding in the slab direction (Fig 2). The EPI phase encode blip direction is alternated on alternate acquisitions. The sequence is ECG gated, and a custom hardware device timestamps when each scan occurs. Metabolite acquisition is interleaved. Matrix: 32x32x12, FOV 64x64x45.5 mm^3, acquired resolution 2x2x4 mm^3, TE 16.3 ms, TR = 1RR interval ($\approx$150 ms); TR/metabolite $\approx$ 1.8s, G_{max}=10 G/cm, S_{max}=87.5 G/cm/ms, FA 3º pyruvate (17º/3D image), 20º bicarbonate/lactate (61º/3D image); 3 navigators. Cine ^{1}H images were also acquired. *In vivo* study: Male Wistar rats (n=4, 475 g) were scanned using a volume Tx birdcage and 2-channel Rx surface array (Rapid Biomedical). Rats were scanned in three metabolic states: 1) fasted, 2) fed, 3) fed and administered the PDK inhibitor dichloroacetate (DCA). [1-^{13}C]pyruvate was polarized with a trityl radical in a prototype DNP hyperpolarizer. 2 mL of hyperpolarized [1-^{13}C]pyruvate was injected over 20 seconds via the tail vein. The scan was started prior to injection. Image reconstruction: Data were re-gridded and n/2 ghost correction of the EPI data was performed. Multi-coil data were recombined by the method of McKenzie.[4] Data were zero-filled by a factor of two, for a final image resolution of 1x1x2 mm^3. The alternating EPI blip direction was used to correct bulk frequency shifts.[5] Data were then overlaid on anatomical images, and maximum bicarbonate/pyruvate ratios computed on a manually segmented ROI in the myocardium and LV lumen respectively.

Results: Time-resolved volumes of pyruvate, bicarbonate and lactate can be obtained with unprecedented spatial and temporal resolution in the healthy rat heart (single slices shown in Fig. 3). The acquisition slab reports simultaneously on a volume including the heart and the liver. Reflecting the known biochemistry, a large difference in bicarbonate-to-pyruvate ratios across the three metabolic states was observed, confirming the sequences' sensitivity to metabolism.

Discussion: We demonstrate that three-dimensional spectral-spatial metabolic imaging brings many benefits over multi-slice approaches: the pulse is less taxing for hardware to reproduce, and exciting a large slab with every shot improves SNR. Three-dimensional approaches trade z resolution for time, and we are able to resolve metabolism *in vivo* with an interpolated resolution of 1x1x2 mm^3. We anticipate imaging peri-infarct metabolism and ischaemia at high resolution in future studies.

Conclusion: Three-dimensional spectral-spatial cardiac metabolic imaging can be performed at high spatial and temporal resolution in the rat heart at 7 T.

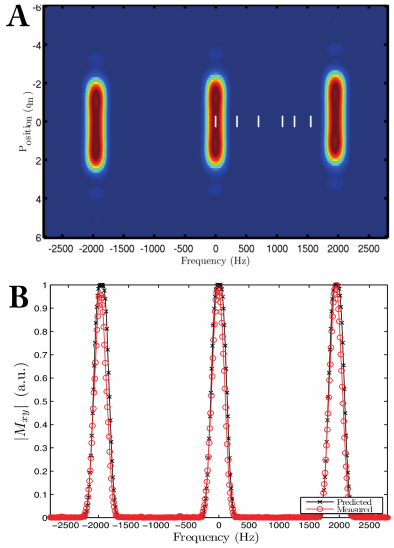

Fig.1. The fly-back pulse used operates at S_{max} rather than G_{max}. Its predicted spectral (x) and spatial (y) excitation profile (**A**; [1-^{13}C]Pyruvate and ^{13}C Urea resonances in white) is reproduced when measured (frequency profile **B**).

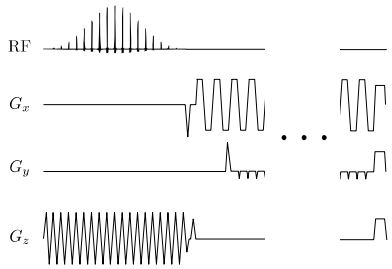

Fig.2. The 3D EPI sequence used in this study: spectral spatial excitation is followed by centric phase encoding in the z direction and an EPI readout with three navigators.

References: [1] Neubauer, S. (2007). The failing heart – an engine out of fuel. NEJM. [2] Lau, AZ. et al, (2010) Spectral-spatial excitation for rapid imaging of DNP compounds. NMR Biomed [3] Schmidt, R., et al, (2014) In vivo single-shot ^{13}C spectroscopic imaging of hyperpolarized metabolites by spatiotemporal encoding. [4] McKenzie, C., et al, (2002) Self-calibrating parallel imaging with automatic coil sensitivity extraction. MRM. [5] Cunningham, C, et al. (2014), Frequency correction method for improved spatial correlation of hyperpolarized ^{13}C metabolites and anatomy, NMR Biomed.

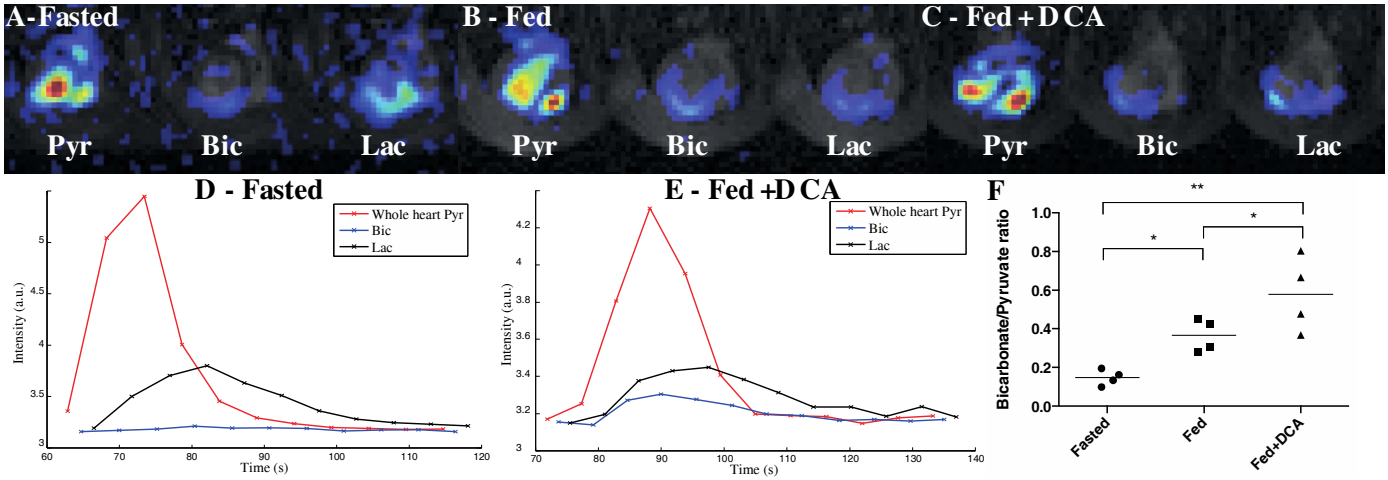

Fig.3: Single mid-ventricular slices from data obtained in fasted rats (A, D), fed rats (D), or fed rats given DCA (C, E). We are able to resolve metabolism across time (timecourses in D, E) and space (A-C show a single timepoint; metabolites are in the order pyruvate [Pyr], bicarbonate [Bic], lactate [Lac] for each). The observed PDH flux is significantly altered between all three groups (* $p < 0.05$, ** $p << 0.05$).