Spectroscopic Imaging of Cerebral Metabolism using Hyperpolarized [1-13C]Pyruvate and Multi-echo Single-shot RARE sequence

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Introduction: The use of exogenously prepared hyperpolarized (HP) metabolically active 13C-enriched substances has been demonstrated to have a great potential in studies of in vivo metabolism in MR diagnostics [1]. Efficient and rapid utilization of the available magnetization is of greatest importance in such studies since the in vivo decay time constant of the hyperpolarized signal is less than one minute. The bSSFP (TrueFISP, FIESTA,..) and RARE (FSE, TSE,..) sequences has been shown to be useful in the context of HP-media angiography [2] and kidney metabolism [3], respectively. Here we demonstrate the potential of a multi-echo single-shot RARE sequence for rapid spectroscopic imaging of cerebral metabolism using HP [1-^{13}C]Pyruvate.

Materials and Methods: A multi-echo RARE-sequence (FSEME) was implemented on a Varian 4.7 T pre-clinical MR-scanner (Varian Inc., USA) with an equidistant gradient-echo train surrounding the spin-echo. A 180° refocusing and a 90° flip-back pulse were added at the end of the sequence to enable re-usage of the transversal magnetization, remaining from one image acquisition in repeated acquisitions. All gradient moments were fully balanced from the 90° excitation pulse to the 90° flip-back pulse and phase encoding was centrically ordered. In vivo rat head 13C-scanning in the transversal plane was conducted with a volume transmit and a loop surface receive coil (Rapid Biomedical GmbH, Rimpar, Germany) on isoflourane anaesthetised healthy rats while monitoring body temperature and respiration. In vivo FSEME-images were acquired 10-15 s after the end of injecting hyperpolarized [1-^{13}C]Pyruvate (polarization ~25%). [1-^{13}C]Pyruvate was polarised in a HyperSense polariser (Oxford instruments) and dissolved in a buffer containing 80 mM TRIS,100 mg/L EDTA, 50 mM NaCl, 80 mM NaOH (pH ~ 7.5-8, temperature ~ 35^{o}C, isotonic). The FSEME scanning parameters were: FOV = 60x60 mm^2, matrix = 64x32, TR = 27.7 ms, slice thickness = 10 mm, no. of spectral encoding echoes = 17, spectral encoding echo spacing ΔTE = 1.04 ms, sampling time = 640 us, total scan time = 866 ms. The 17 spectral encoding echoes was selected taking into account: 1: Total scan time 2: The signal level, as assessed from separate measurements on thermally polarized Pyruvate and Acetate (= Lactate equivalent) phantoms (Fig. 1), and 3: Enough spectral resolution to perform spectral analysis and metabolite image reconstruction through direct Fourier transformation. A 3x3 kernel low-pass filter was applied to the metabolite maps to delineate gross structures.

Results and Discussion: Metabolite maps of transverse sections of the rat head from the FSEME-sequence are shown in Fig.2. Cerebral sub-structures, not visible using conventional CSI-scanning, can be depicted in the metabolite maps. In the lactate maps, the anterior region of the brain is divided into two separable symmetrical hyper-intense regions, with peak lactate signals in positions corresponding to the hippocampal regions, indicating a greater lactate dehydrogenase flux in these regions compared to surrounding cerebral tissue in the healthy rat brain. Hyper-intense pyruvate signals are located primarily in the surrounding vessels. The relative signal levels between metabolites are in concordance with corresponding CSI data (not shown). Signal decay through T2 relaxation (apparent T2 ~ 300 ms) and significant signal loss through an imperfect 180° refocusing pulse, from sub-optimal RF-coil performance, contributed to a 2nd time frame in vivo signal being only 20% of the 1st time frame signal, thus compromising multi time-frame imaging.

Conclusion: Identification of cerebral sub-structures in metabolite maps from hyperpolarized [1-13C]Pyruvate in the rat brain was for the first time demonstrated using the rapid FSEME spectroscopic imaging sequence.

References: [1] Golman, PNAS 103: 11270 (2006) [2] Svensson, MRM 50:256 (2003) [3] Leupold, MAGMA 22(4): 251 (2009) [4] Reader, MRM 54:636 (2005)

Acknowledgements: This work was partly sponsored by the Lundbeck foundation (grant R17-A175).

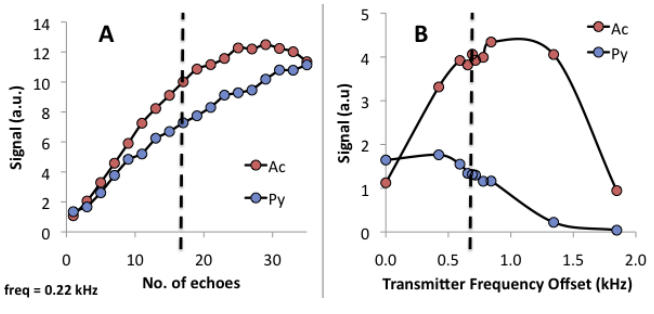

Fig.1: The FSEME-signal dependence on the no. of spectral encoding echoes (A) and transmitter frequency offset (B), measured on thermally polarized [1-13C] Acetate (Ac) and Pyruvate (Py) phantoms. Parameters used in vivo were as indicated (dashed line).

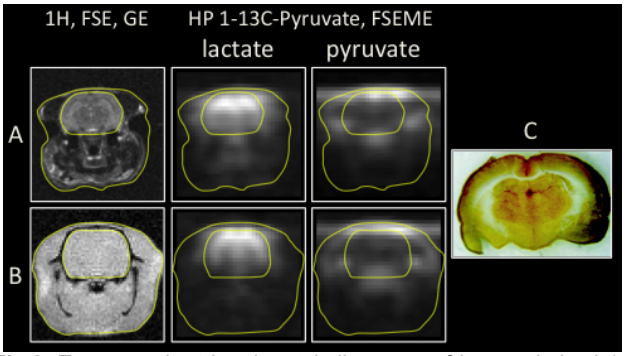

Fig.2: Transversal rat head metabolite maps of hyperpolarized 1-13C-Pyruvate acquired with the FSEME-sequence in two rats (A and B) with elevated lactate distribution in hippocampal regions. Anatomy comparison with transversal rat brain section (C).