FUNCTIONAL ^{31}P MAGNETIC RESONANCE SPECTROSCOPIC IMAGING OF THE HUMAN CALF MUSCLE AT 7 T BY MEANS OF ECHO–PLANAR ACQUISITION TECHNIQUES

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INTRODUCTION: ^{31}P NMR spectroscopy (^{31}P MRS) allows noninvasive observation of the turnover of high–energy phosphates *in vivo*. Echo–planar spectroscopic imaging (EPSI)[1,2] enables acquisition of MR images with spectral information in each pixel in the shortest possible measurement time. Hence EPSI in high B_0 can help to reveal small metabolic changes on the timescale of a few seconds.
The purpose of this study was to demonstrate that echo–planar acquisition yields a valuable tool for performing *in vivo* functional spectroscopic studies with ^{31}P nuclei at 7 T with good spatial and temporal resolution.

METHODS: A modified ^{31}P EPSI sequence[3] with NOE preparation and reduction of aliasing artifacts was optimized to acquire localized ^{31}P NMR spectra with a temporal resolution of a few seconds. EPSI datasets were reconstructed and postprocessed with a home–built MATLAB routine. Spectral fitting of the reconstructed data was done using the AMARES[4] algorithm implemented in jMRUI. The calf muscles of eight healthy volunteers (2 female and 6 male subjects, age: 24–30 years) were measured with different exercise and sequence protocols. Non–isometric exercises were performed with help of a home–built non–magnetic mechanical foot pedal. All measurements were performed on a high–field scanner (MAGNETOM 7 T; Siemens Healthcare, Erlangen, Germany) with use of a ^{31}P/^{1}H double resonant volume coil (Rapid Biomedical, Rimpar, Germany). The data shown in Figs. 1 to 3 were obtained from a healthy 27–year–old male volunteer performing a mild exercise of dorsal and plantar flexion in two sessions separated by a 20–min recovery phase. In the first session, the exercise lasted 4.5 min where spectroscopic data were acquired. In the second session, exercise lasted 4 min and PCr–weighted ^{31}P images were obtained with the EPSI sequence.

RESULT: The localized ^{31}P NMR spectra obtained with the modified EPSI sequence allow reliable quantification of Phosphocreatine (PCr), Adenosine-5'-Triphosphate (ATP) and inorganic phosphate (P_i) (Fig. 1). With the onset of the exercise PCr signals decrease and P_i signals increase as expected. After the exercise, the recovery to the initial values is clearly visible. An analysis of different ROIs during the first session is shown in Fig. 2. While in the central compartment (ROI #2) no distinct metabolic changes are observable, significant changes in PCr and P_i signals and in intracellular pH value are observed for the anterior compartment (ROI #3) and the gastrocnemius muscle (ROI #1). In ROI #1, a splitting of the P_i resonance was observed (green line). In the second session, PCr–weighted ^{31}P images were obtained with EPSI, showing also significant changes in PCr intensity, but in higher spatial and temporal resolution (Fig. 3). These results correlate well with the spectroscopic data from the first session.

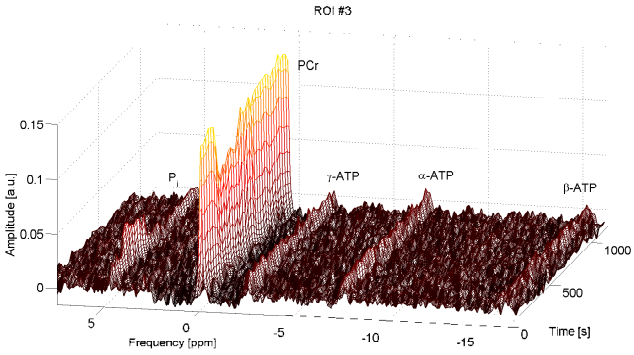

Fig. 1: Stack plot of localized *in vivo* ^{31}P NMR spectra obtained with EPSI at 30–s temporal resolution at B_0 = 7 T from the anterior compartment of the right lower leg (sum over ROI #3, Fig. 3a) of a healthy volunteer during the first exercise. While ATP signals show no significant changes during the complete series, distinct intensity changes of the PCr and P_i resonances are observed at the onset and the end of the exercise. Sequence parameters of 2D ^{31}P EPSI with measurement time of 30 s: *FOV = (165 mm)², slice thickness = 40 mm, matrix = 8×8×1, TR = 220 ms, Δf = 3000 Hz, 384 data points, nex = 14 weighted averages, NOE preparation 62 ms.* Data were Hamming–filtered in the spatial domain and interpolated onto a 32×32 grid. Time domain data were zero–filled to 1024 data points and an exponential filter with 40 Hz width was applied.

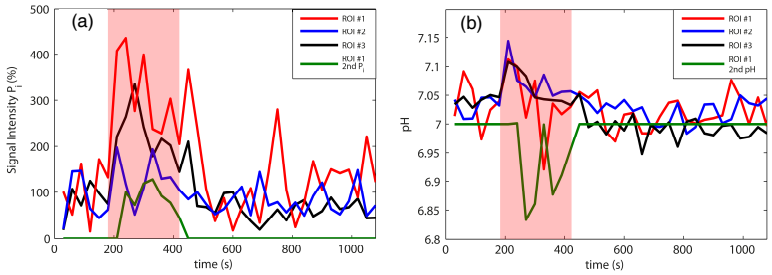

Fig. 2: Normalized ^{31}P signal intensity changes observed with EPSI with 30–s temporal resolution at B_0 = 7 T from different regions of the right lower leg of a healthy volunteer during the first exercise. The displayed data show the response of P_i (a) and intracellular pH (b) in the different ROIs (see black contours in Fig. 3a) as a function of time. Evaluated data are sum spectra over the complete ROI. ROI #1 (*parts of gastrocnemius muscle)* showed a splitting of the P_i resonance indicating a second pH compartment (green lines). Red areas indicate start and end of the exercise. See Fig. 1 for sequence parameters.

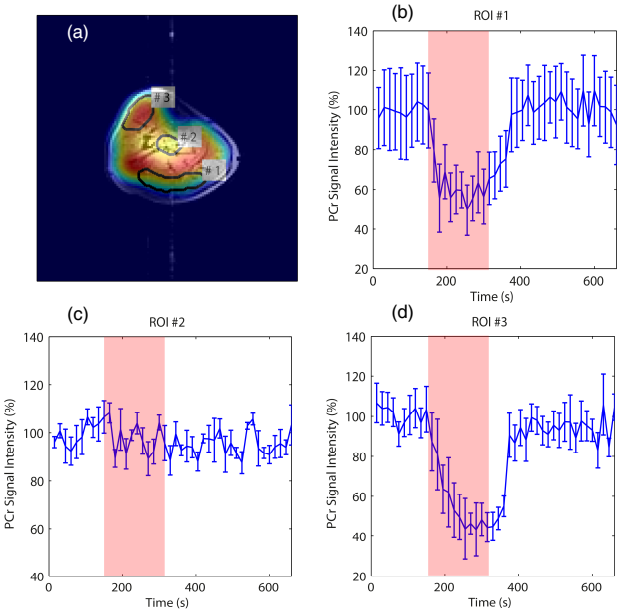

Fig. 3: Normalized PCr signal intensity changes of the right lower leg of a healthy volunteer obtained during the second exercise using ^{31}P EPSI as an imaging method with 15–s temporal resolution. (a) Overlay of an interpolated PCr–weighted ^{31}P image and a T_1–weighted morphological ^{1}H image of the right lower leg. Black contours indicate the evaluated ROIs: *#1 = parts of gastrocnemius muscle* (b), *#2 = central compartment* (c), *#3 = anterior compartment* (d). Values represent *mean ± standard deviation* of PCr signal intensity inside the ROI. Red areas indicate start and end of the exercise. Sequence parameters 2D ^{31}P EPSI with measurement time of 15 s: *FOV = (272 mm)², slice thickness = 40 mm, matrix = 16×16×1, TR = 230 ms, Δf = 1200 Hz, 128 data points, nex = 8 weighted averages, NOE preparation 91 ms.* Data were Hamming–filtered in the spatial domain and interpolated onto a 128×128 grid. Sequence parameters of ^{1}H TSE: *FOV = (272 mm)², in–plane resolution 128 px, 10 slices, slice thickness = 5 mm, TR/TE/α = 700ms/10ms/130°.*

DISCUSSION and CONCLUSION: The data demonstrate that ^{31}P EPSI techniques are capable to perform *in vivo* functional spectroscopic studies of human energy metabolism at 7 T with good spatial and temporal resolution. Limitations of spectral localization via point–spread function and of spatial resolution are mainly determined by the stability of the gradient system and must be optimized for each protocol. With the use of a non–magnetic ergometer comparable physiological studies can be performed with the technique presented here.

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