Reproducibility of the 1D-ISIS localized ST experiment for hepatic Pi-to-ATP reaction rate measurement at 7T

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Introduction: ^{31}P hepatic MRS provides a range of parameters relevant to liver disease, particularly in measuring phosphomonoester (PME) and phosphodiester (PDE) levels as well as intracellular and extracellular pH. In addition, ^{31}P-MRS can be combined with a saturation transfer (ST) technique for the Pi-to-ATP chemical exchange rate measurement[1]. Recently, it has been shown that the ultra-high field strength (e.g., 7T) can reduce the measurement time needed for 1D-ISIS localized ST examinations of the liver[2], thus enabling measurements of the Pi-to-ATP exchange rate in clinically feasible times. This can lead to wider use of this method in future clinical investigations of the liver metabolism. The aim of this study was therefore to test the reproducibility/reliability of the fast ST technique *in vivo* at 7T for localized non-invasive measurement of Pi-to-ATP reaction.

Materials&Methods: Six healthy male volunteers (a= 32.0±6.7y) were examined in early morning hours after overnight fasting on a 7T MR system (Siemens, Erlangen, Germany) using a double-tuned (^{31}P/^{1}H) surface coil (Rapid Biomedical, Rimpar, Germany), with a diameter of 10 cm. Subjects were investigated in the lateral position with the right lobe of the liver positioned over the coil. The 30-mm-wide ISIS slab was placed parallel to the coil through the liver, avoiding muscle tissue (see Fig. 1). The ST experiment consisted of the interleaved acquisition of 1D-ISIS liver spectra w/o selective saturation of the γ-ATP frequency. The apparent longitudinal relaxation time (T_1^{app}) of Pi was measured with an inversion recovery (IR) sequence with continuous irradiation of the γ-ATP resonance. The sequence parameters were set as follows: rectangular 500 μs excitation; adiabatic broadband GOIA inversion pulse; TE*=0.4 ms; TR=5 s; total acquisition time was ~24 min. The ST experiment was repeated twice within one session, including full repositioning, shimming, and data acquisition for the test-retest measurements of the liver metabolism. The *in vivo* reproducibility of the fast ^{31}P-MRS ST measurement at 7T, particularly the T_1^{app} and the forward rate constant (k), was evaluated as a mean coefficient of variation (CV). To assess the possible contamination from the muscle tissue, non-localized spectrum was acquired. The residual PCr signal was used to quantify the muscle-signal suppression of the 1D-ISIS ST sequence[3].

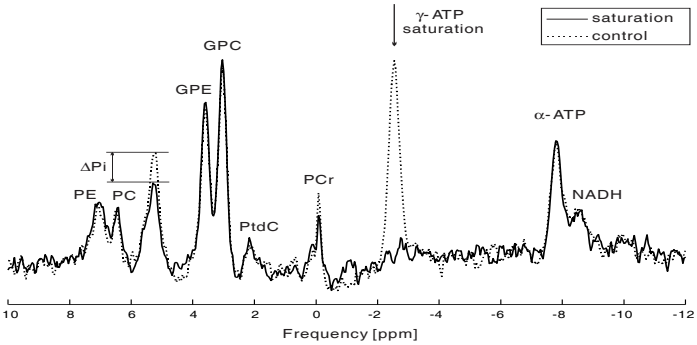

Fig 2. ^{31}P liver spectra showing the magnetization transfer effect on Pi (left). Arrows indicate the saturation frequency at γ-ATP in the saturation experiment (solid line) and the saturation effect on Pi compared to the control experiment (dotted line).

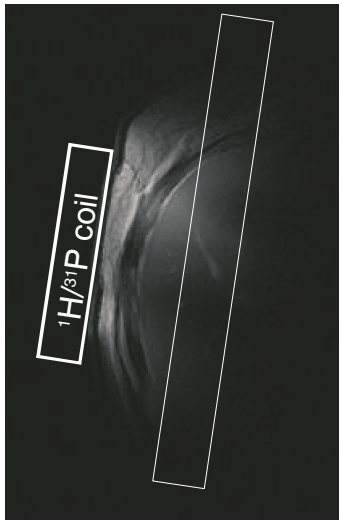

Fig. 1. Liver MR localizer image of the abdominal region with coil position and ISIS slab placement (~3 cm from the coil).

Results&Discussion: Representative spectra from the liver ST experiment of one volunteer are depicted in Fig. 2. Full saturation of the γ-ATP signal and minimal contamination from muscle phosphocreatine (PCr) was found in all measured data sets. The mean T_1^{app} and k values in healthy volunteers (n=6) were 0.67 ± 0.08 s and 0.32 ± 0.03 s^{-1}, respectively. This is in good agreement with previously reported hepatic k values[4,5]. Based on the non-localized acquisition and the residual PCr signal in some of the liver spectra, we calculated that the liver data contain up to 3% of the abdominal muscle signal, what can be considered negligible contamination. This is in agreement with a previous phantom study[2]. Table 1 denotes individual data from the localized ST reproducibility measurements. The mean test-retest k variability was only CV = 8.99%, what represents high reproducibility of the fast localized hepatic Pi-to-ATP reaction measurement at 7T.

Table 1. Individual data from the liver ST reproducibility measurements at 7T in healthy volunteers. Data in the table are given for each measurement in each volunteer (suffix 1 or 2) and as a mean ± standard deviation (CV). T_1^{app} is the apparent longitudinal relaxation of the Pi in the presence of γ-ATP-saturation, and k is the Pi-to-ATP exchange rate constant.

	$T_1^{app}{}_1$	$T_1^{app}{}_2$	T_1^{app} (s)	k_1	k_2	k (s^{-1})
Vol #1	0.69	0.73	0.71 ± 0.03 (4.8%)	0.32	0.31	0.32 ± 0.01 (2.4%)
Vol #2	0.84	0.60	0.72 ± 0.17 (23.9%)	0.27	0.31	0.29 ± 0.03 (10.4%)
Vol #3	0.69	0.59	0.64 ± 0.07 (11.1%)	0.34	0.30	0.32 ± 0.03 (7.9%)
Vol #4	0.49	0.51	0.50 ± 0.02 (3.6%)	0.39	0.34	0.37 ± 0.04 (9.8%)
Vol #5	0.91	0.79	0.85 ± 0.09 (10.0%)	0.29	0.34	0.32 ± 0.04 (12.9%)
Vol #6	0.65	0.54	0.59 ± 0.08 (13.4%)	0.31	0.27	0.29 ± 0.03 (10.7%)
mean	0.71	0.63	0.67 ± 0.08 (11.2%)	0.32	0.31	0.32 ± 0.03 (9.0%)

Conclusion: We report that the *in vivo* measurement of the liver Pi-to-ATP chemical reaction at rest under fasting conditions by the fast, 1D-ISIS localized ^{31}P-MRS ST technique at 7T, is highly reproducible.

References:

1. Brown TR, et al. Proc Natl Acad Sci USA, 1977; 74(12)
2. Valkovič L, et al. Proc Int Conf ESMRMB, 2012; 91
3. Keevil SF, el al. Phys Med Biol, 1990; 35(7)
4. Schmid AI, et al. NMR Biomed, 2008; 21(5)
5. Schmid AI, et al. Diabetes Care, 2011; 34(2)