Time-resolved phosphorous magnetization transfer of the human calf muscle at 3T and 7T: a feasibility study

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Introduction:

Steady-state concentrations of energy metabolites (adenosine triphosphate [ATP], phosphocreatine [PCr] and inorganic phosphate [Pi]) measured by phosphorus magnetic resonance spectroscopy (^{31}P-MRS) do not reflect the function of cells, i.e., the synthesis of ATP. Only kinetic measurements by magnetization transfer (MT) or dynamic ^{31}P-MRS during exercise and recovery provide assessment of metabolism, in a range of pathologies [1]. The utilization of MT at field strengths ≤3 T is limited by the measurement time (~30-120 minutes) [2, 3], thus, to date, it is not possible to observe metabolic changes such as the early effects in clamp studies (<15min) [3]. Ultra-high-field MR systems, such as 7 T, offer advantages for ^{31}P-MRS in terms of spectral quality, which has been shown recently [4]. Thus the aim of this study was to compare the precision of MT experiments at 3 T and 7 T in the human muscle, and to analyse the potential time resolution of MT at 7 T.

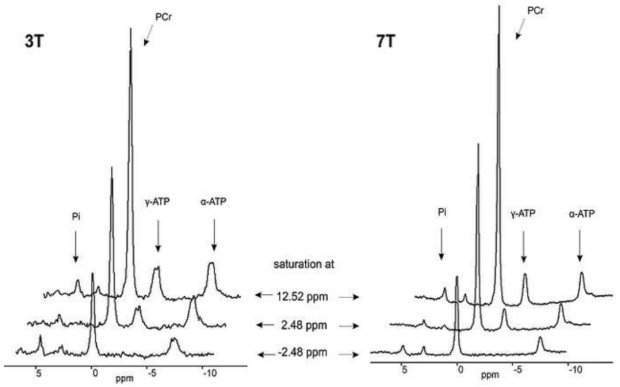

Fig. 1 Representative spectra of MT experiment obtained in the human calf muscle at 3 T (left) and 7 T (right). (bottom) Suppression of γ-ATP at -2.48 ppm; (center) suppression frequency mirrored relative to PCr at +2.48 ppm; (top) suppression frequency mirrored relative to Pi at +12.52 ppm. Spectra are displayed with a 3 Hz exponential filter.

Materials and Methods:

After the approval from the local ethics committee, six healthy, non-obese volunteers (two females; mean age, 25 years) were measured after overnight fast consecutively on two MR scanners of different field strengths, a 3T TIM TRIO and a 7T Magnetom (Siemens Healthcare, Erlangen, Germany). Subjects were examined in the supine position with the right gastrocnemius muscle positioned over similar surface coils (^{1}H/^{31}P, 10 cm in diameter, Rapid Biomedical, Rimpar, Germany). The exchange between γ-ATP and Pi (ATP synthesis), and between γ-ATP and PCr (creatine-kinase [CK] reaction), were investigated using an MT experiment [5] (Fig. 1). To investigate the possibility of time-resolved MT experiments the protocol was split into four equal parts, including acquisition of spectra w/o γ-ATP saturation (saturation pulse at -2.48 ppm, 2.48 ppm and 12.52 ppm, TR=15s, NA=8 for each saturation positon) and T_1 measurement during γ-ATP saturation (eight inversion times 100-8000 ms, TR=15 s, NA=2 each T_{IR}) at both field strengths. The measurement time of each saturation transfer experiment block was 10 min and 36 sec, the total measurement time of four experiment blocks was, therefore, ~45 min. The pseudo-first-order rate constant of the ATP synthesis (k_{ATP}) and the CK reaction (k_{CK}) were computed using equation $k_{for} = (1 - M_z/M_0)/T_1^{app}$ [6]. The corresponding forward metabolic fluxes (F_{ATP}, F_{CK}) were the product of k_{ATP} and k_{CK} times the concentration of Pi and PCr, respectively. A comparison of these exchange parameters, apparent T_1s, data quality (i.e., signal-to-noise ratio [SNR] and linewidths), quantification precision, and reproducibility was performed.

	$T_1^{app}{}_{PCr}$ [s]		$T_1^{app}{}_{Pi}$ [s]	
	3T	**7T**	**3T**	**7T**
Vol. 1	1.7±0.1 (8.3%)	1.59±0.03 (2.1%)	2.5±0.5 (20.4%)	3.5±0.3 (7.8%)
Vol. 2	1.6±0.1 (6.7%)	1.42±0.03 (2.1%)	2.6±0.4 (16.7%)	3.6±0.5 (13.1%)
Vol. 3	1.7±0.1 (5.0%)	1.60±0.01 (0.8%)	2.8±0.5 (19.7%)	3.0±0.3 (10.6%)
Vol. 4	1.7±0.1 (5.3%)	1.52±0.01 (0.8%)	1.9±0.4 (22.1%)	3.2±0.4 (13.1%)
Vol. 5	1.6±0.1 (5.1%)	1.49±0.02 (1.3%)	2.3±0.6 (26.0%)	3.4±0.4 (10.5%)
Vol. 6	1.9±0.1 (7.0%)	1.64±0.04 (2.2%)	3.0±0.7 (22.5%)	4.0±0.3 (7.7%)
Average	**1.7±0.1 (6.3%)**	**1.54±0.02 (1.6%)**	**2.5±0.5 (21.1%)**	**3.5±0.4 (10.4%)**

Tab. 1 Mean intra-subjects values of T_1^{app} (±std (CV)) as calculated from four separate measurement blocks for each volunteer at 3 T and 7 T

Results and Discussion:

Overall, we found a significant improvement in spectral quality for 7 T compared to 3 T. The SNR at 7 T was 2.56 times higher, and the line-width was only 1.66 times greater compared to 3 T. Since the spectral range at 7 T is 2.3 times greater, this translates to an improvement in spectral resolution. This resulted in a higher inter-measurement block reproducibility for the results of T_1^{app} (3.9 times for PCr and 2 times for Pi, detailed in Tab. 1), k_{CK} (mean CV at 7 T was 2.7% vs. 9.1% at 3 T), k_{ATP} (mean CV at 7 T was 19.0% vs. 51.9% at 3 T), and metabolite fluxes (mean CV at 7 T was 2.7% and 18.8% vs. 9.2% and 53.4% at 3 T for F_{CK} and F_{ATP} respectively). Based on four measurement repetitions at both field strengths, we calculated that the intra-subject reproducibility at 7 T was 2.7 times better and 3.4 times better than at 3 T for the determination of k_{ATP} and k_{CK}, respectively (Fig. 2). Our results of calculated k_{ATP} and k_{CK} are in agreement with previous reports on MT experiments in skeletal muscle at 3 T [3, 7]. Previous MT studies on 7 T were focused on experiments in the brain [8], and thus, to our knowledge, no MT experiments of the skeletal muscle have been performed as yet at 7 T.

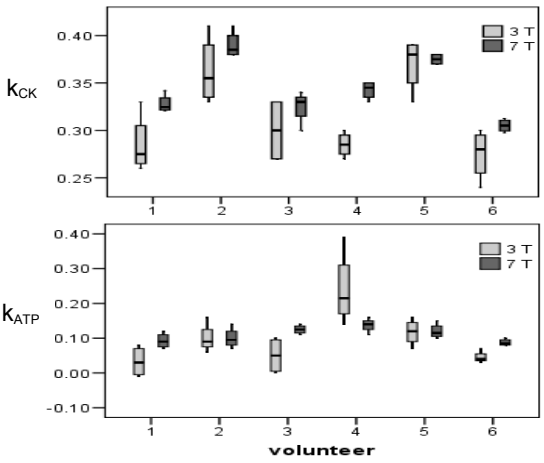

Fig. 2 Boxplots of k_{CK} and k_{ATP} values in 4 measurement blocks of MT for every volunteer show consistency between 3 T&7 T, but better reproducibility for 7 T

Conclusion:

We showed that the improved data quality at 7 T can be translated to a significant decrease of acquisition time (i.e., one-quarter of the measurement time at 3 T). This speed-up will enable time-resolved (~10 min temporal resolution) MT experiments to observe changes in muscle metabolism without a loss in precision. Another possibility would be to use this improvement in data quality at 7 T for the investigation of specific muscles with MT techniques. Fast and/or localised MT could be an attractive tool for future studies of human metabolism with ^{31}P-MRS

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