

Magnetization Transfer Effects from Water to Metabolites in Human Skeletal Muscle Observed by Non-Water-Suppressed MR Spectroscopy

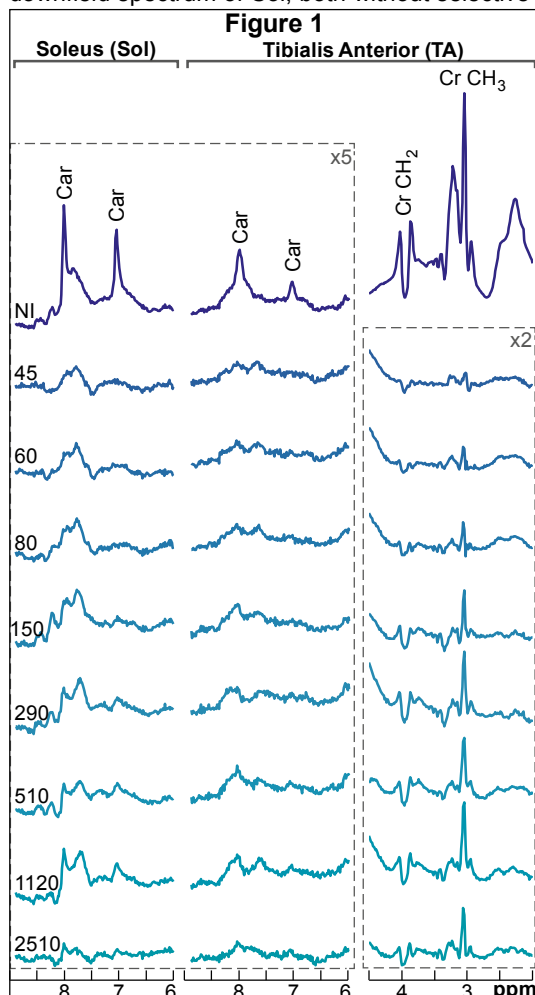
Erin Leigh MacMillan¹, Chris Boesch¹, and Roland Kreis¹

¹Depts Clinical Research and Radiology, University of Bern, Bern, Switzerland

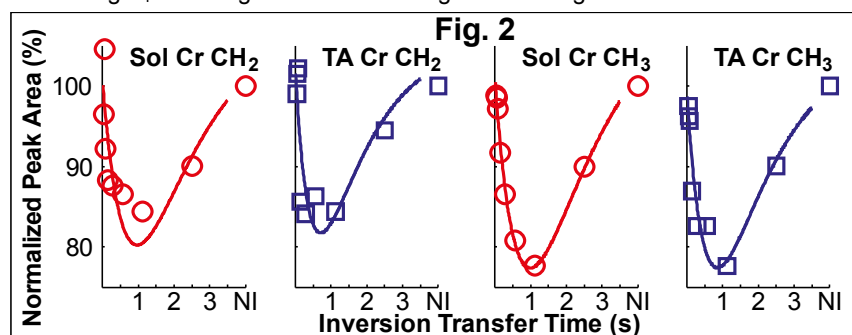
INTRODUCTION Proton MR spectroscopy (¹H MRS) without water suppression (WS) via the metabolite cycling (MC) technique has successfully been applied in the brain [1], spinal cord [2], and liver [3] to measure peaks from exchangeable protons and/or to improve spectral quality by using the water peak for frequency correction. In skeletal muscle, it has previously been shown using long TE ¹H MRS with WS that the Creatine (Cr) CH₃ peak exhibits general magnetization transfer (MT) with an immobilized Cr and/or macromolecular proton pool [4,5] but also with or via the water magnetization [6]. The MC technique offers a way to further investigate this MT effect in muscle at short TE and without the influence of WS, as well as to potentially observe and characterize previously unobserved downfield signals that may be affected or suppressed by WS. In the present study, non-water suppressed ¹H MR spectra were acquired from the soleus (Sol) and tibialis anterior (TA) muscles to further characterize MT and proton exchange in muscles with different fiber orientation and, hence, different residual dipolar coupling effects.

METHODS Twenty healthy volunteers were scanned on a Siemens TRIO 3T system using the standard extremity coil after obtaining informed consent. Spectroscopy voxels were placed in the Sol (n=10, mean volume 14.9mL) and TA (n=10, 12.3mL). PRESS with and without WS was applied (TE/TR=20/4000ms, 64 shots) preceded by an adiabatic radiofrequency (RF) pulse to invert the upfield or downfield metabolites in alternating shots [1]. MT was measured with an additional pulse to invert water with increasing mixing times (TI = 45, 60, 80, 150, 290, 510, 1130, 2510 ms) prior to PRESS. Individual shots were frequency aligned and eddy current corrected using the water signal obtained from the sum of all shots. Metabolite spectra with varying TI were aligned to the non-inversion (NI) spectrum. Average volunteer spectra were fit in the frequency domain using FIDAI [7], which models peak areas at all TI times together. Cr peak areas with varying TI were fit to a two-pool Bloch-McConnell model that included two phases of MT (saturation transfer in TR and inversion transfer TI) with the constraints that T₁ values were between 0.01 and 10s, and that steady-state reaction fluxes were equal.

RESULTS MR spectra of muscle obtained without WS showed altered peak intensities for Cr [8] and additional broad features in the downfield spectrum that have not been reported earlier *in vivo*. The top trace of Fig. 1 shows the non-WS muscle spectrum of TA averaged over 10 volunteers, upfield and downfield of water (excluding the lipid-dominated regions for clarity), and the averaged downfield spectrum of Sol, both without selective water pre-inversion. Lower traces show the differences between each TI time and the



NI case, where it is clear that negative magnetization from water is transferred to the upfield Cr CH₂ and CH₃ peaks, and to peaks between 6.5 and 8.5ppm in the downfield region that possibly arise from amide protons. The broad downfield peaks already appear in the difference spectra after the shortest exchange time of 45 ms, while substantial MT effects on the Cr and carnosine (Car) peaks appear at longer TI. Fig. 2 shows the MT effects on Cr CH₂ and CH₃ peak areas (similar in muscles with differing degrees of residual dipolar coupling) and the fit of the two-pool model. The resulting T₁ and magnetization exchange rates are given in the table below.



	Sol Cr CH ₂	TA Cr CH ₂	Sol Cr CH ₃	TA Cr CH ₃
T ₁ (s)	1.2	0.59	1.3	0.89
K (s ⁻¹)	0.33	0.53	0.38	0.46

CONCLUSIONS ¹H MRS without WS of human skeletal muscle features additional peaks in the downfield region in cases with and without appreciable residual dipolar coupling. These peaks are affected by fast MT from water, while both upfield Cr peak areas show slower transfer, with rates between 0.33 and 0.53s⁻¹. While the two-pool model adequately describes the measured data, it does not imply that there is a direct transfer of protons or magnetization from water to Cr; these transfer rates simply reflect the rate limiting step in the transfer of magnetization from water to Cr.

1. MacMillan EL, *et al.* MRM 2011;65:1239
2. Hock A, *et al.* 19th ISMRM 2011:406
3. MacMillan EL, *et al.* 19th ISMRM 2011:2996
4. Kruiskamp MJ, *et al.* JMR 2001;149:8
5. Renema WKJ, *et al.* MRM 2003;50:468
6. Kruiskamp MJ, *et al.* NMR Biomed 2001;14:1
7. Chong DGQ, *et al.* MAGMA 2011;24:147
8. Kreis R, *et al.* 6th ISMRM 1998:24