Water proton relaxation times exhibit muscle fibre orientation dependence, while water to creatine magnetization transfer rates do not

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Figure 1

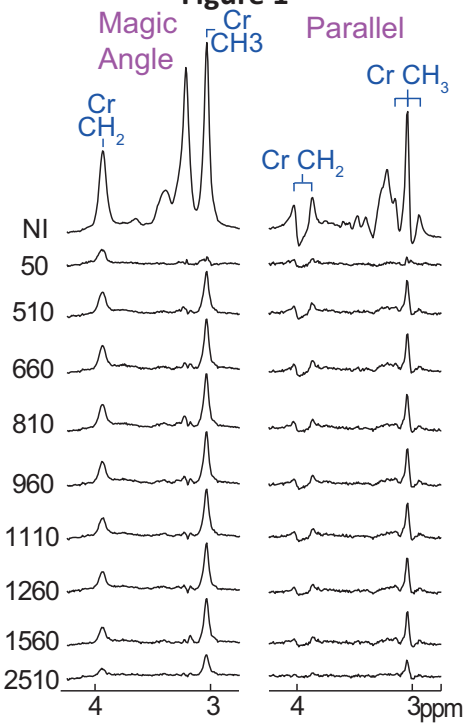
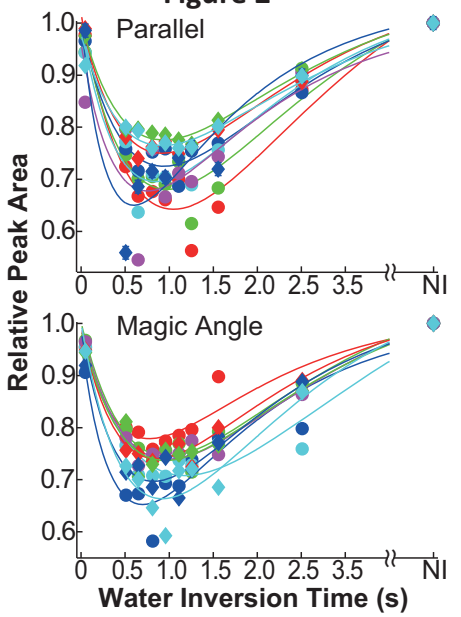


Figure 2



	Cr CH_3	Water
	MT Rate (s^{-1})	**T_2 (ms)**
MA	0.44 (0.39-0.57)	28.7 (28.2 – 29.9)
PA	0.51 (0.44-0.60)	27.6 (27.3 – 27.9)
p	*0.49*	*p=0.002*
	T_1 (ms)	**T_1 (ms)**
MA	1223 (894-1326)	1370 (1328-1393)
PA	1166 (979-1361)	1321 (1308-1326)
p	*1.0*	*p=0.018*

INTRODUCTION Investigations of magnetization transfer (MT) effects on creatine (Cr) suggest that the MT is mediated by water, most likely via cross-relaxation between water and a motionally restricted Cr, revealing information about how water and Cr interact *in vivo* [1,2]. It has recently been shown that Cr in the soleus and tibialis anterior (TA) muscles exhibit different rates of MT from water, however it was not possible to determine whether this effect was due to a biochemical difference, or reflects a dependence on fibre orientation [3]. In addition, while the orientation-dependence of water proton T_2 relaxation in excised rat skeletal muscle has been demonstrated [4], it has yet to be observed *in vivo*. In the present work, MT between water and Cr and water proton T_1 and T_2 were measured in the TA aligned both parallel and at the magic angle with respect to the external magnetic field, to investigate the potential effects of muscle fibre orientation on MR properties.

METHODS Nine healthy volunteers (3m, 6f, 21–48y, median 27y) were scanned on a Siemens VERIO 3T MR system (Erlangen, Germany) using a flexible phased-array coil after obtaining informed consent. Spectroscopy voxels were placed in the TA, with mean volume of 7.0mL. PRESS without water suppression (WS) was applied (TE/TR=26/4000ms, 32 shots) preceded by an adiabatic radiofrequency pulse to invert the upfield or downfield metabolites in alternating shots [3]. Water to metabolite MT was measured with an additional pulse to invert water with increasing mixing times (TI = 50, 510, 660, 810, 960, 1110, 1260, 1560, 2510 ms) prior to PRESS, and without water inversion (non-inverted "NI"). Single-shot STEAM spectra without WS were also obtained with TE = 12, 14, 17, 20, 24, 29, 34, 40, 48, 68, 96, 136, 192, 272 ms. Subjects were positioned lying on their side, with their right lower leg aligned at the magic angle (MA), and then the entire measurement was repeated with the right leg parallel (PA) to the external magnetic field. PRESS spectra were processed by frequency aligning shots, then eddy current correcting using the 2510 ms delay water spectrum (the NI case was self-corrected). Metabolite spectra with varying TI were aligned to the NI case, and then fit in the frequency domain using FiTAID [5], which models spectra from all TI times together. Water peak areas were fit to an inversion recovery curve to extract water T_1, while Cr peak areas were fit to a two-pool Bloch-McConnell model described previously [6] to extract metabolite T_1 and MT rates. Non-WS STEAM spectra were fit with a single water peak, and peak areas were fit to a monoexponential decay using least-squares minimization in MATLAB.

RESULTS Non-WS spectra from the TA averaged over all volunteers are shown in Fig. 1 for both the magic angle (MA) and parallel (PA) orientations. The difference between the NI case and each TI time is plotted below the NI spectra, where it is clear that Cr peak amplitudes exhibit MT from water. Cr CH_3 peak areas at each TI time for each volunteer are plotted in Fig 2. with the fit curve from the MT model (error bars indicate the Cramér–Rao minimum variance bounds but are usually smaller than the marker size). The table lists T_1 values and MT rates for the Cr CH_3 peak for both muscle orientations (median (25^{th} and 75^{th} percentiles)) with the Wilcoxon rank sum p values from the orientation-effect comparisons, as well as the T_1 and T_2 relaxation rates of water.

CONCLUSIONS The agreement of water-Cr MT rates between muscle orientations suggests that the previously reported difference between the soleus and TA muscles arises from a physiological distinction. While Cr in the soleus and TA have been reported to exhibit different T_1 relaxation rates [7], the T_1 trend cannot account for the different water-Cr MT rate since it acts in the opposite direction. Meanwhile, water proton relaxation exhibited a consistent effect with muscle fibre orientation: at the magic angle both the T_1 and T_2 values were longer than with the muscle parallel to the field. The lengthening of the relaxation rates when dipolar coupling has collapsed at the magic angle is in agreement with similar measures from tendon and cartilage [8].

REFERENCES [1] Kruiskamp et al. NMR Biomed 2001;14(1):1 [2] Kruiskamp & Nicolay. JMR 2001;149(1):8 [3] MacMillan et al MRM in press. [4] Kasturi S et al. Biophys J 1980;30(3):369 [5] Chong et al. MAGMA 2011;24(3):147 [6] MacMillan et al. MRM 2011;65:1239 [7] Kršśák et al MAGMA 2004;16(4):155 [8] Momot et al. NMR Biomed 2010;23(3):313

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