Multi-Parameter quantitation of coincident fat and water skeletal muscle pathology

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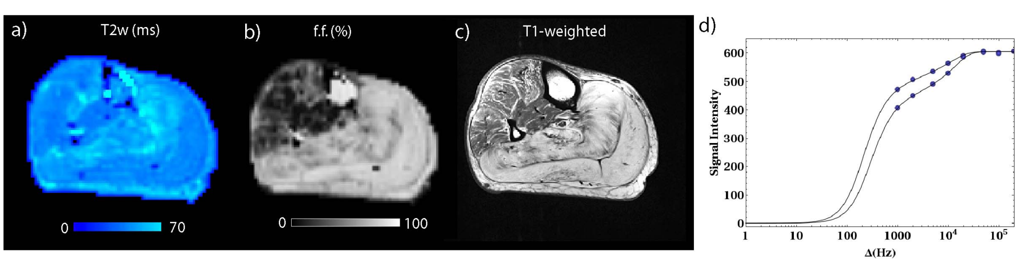
Introduction Quantitative MRI in skeletal muscle may provide important markers of disease progression for imminent clinical trials. Edema and chronic fatty degeneration are the two most common pathological manifestations in skeletal muscle tissue and may occur together or separately. Identifying and quantifying these changes early in the disease process is important to identify the most pertinent muscles in which to track treatment response and patients for whom treatment is most likely to be beneficial. We have investigated two complementary approaches to quantitative muscle imaging: (i) IDEAL-CPMG [1] allows quantification of muscle fat-fraction (f.f.) with simultaneous measurement of the T2 relaxation time of muscle-water without the confounding influence of the fat component; and (ii) quantitative magnetization transfer (qMT) modeling, providing physical insight into the 'free' and 'bound' proton populations, for which the presence of fat complicates measurement interpretation. In this work we examined patients with the inflammatory muscle disease inclusion body myositis (IBM) using both methods and muscles exhibiting a range of fat-infiltration/edematous pathological combinations to characterize findings across the spectrum of muscle injury in this representative disease.

Methods The right lower-limbs (mid-calf level) of 3 IBM patients were imaged at 3T (Siemens TIM Trio) with surface-array coils in body-coil transmit mode. All images had an in-plane field of view 18x18cm. IDEAL-CPMG data were acquired with 12 equally spaced spin-echoes with TEs from 10 to 120ms (TR=5s, 64x64matrix) and processed offline in MatLab generating f.f. and water-component only T2 (T2w) maps. QMT data were acquired with 14 variable-offset MT pulses (3D-FLASH, TR/TE/f.a.=50/3/6°, 16x10mm slabs, 12ms Gaussian MT pulse, variable offset Δ=1kHz-100kHz, repeated with 350° & 500° amplitudes) [2]. T1 maps were obtained with the DESPOT-1 method [3] (3D-FLASH, TR/TE/f.a.=25/3/(5°,15°,25°), 128x128matrix, 16x10mm slabs). Corresponding B1 transmit maps were acquired with the actual flip-angle method (TR1/TR2/TE/f.a.=50/150/3/60°, 64x64matrix) [4,5] for correction of the qMT flip angles. Images were registered to the same space and sampled to 128x128 in-plane resolution. On the central slice, 4 representative muscles were chosen based on their T2w and f.f. values, selected from the 3 patients with heterogeneous pathology (Type 1: normal, 2: f.f. elevated, T2w normal, 3: f.f. normal, T2w elevated and 4: both elevated). Small regions of interest (ROI) were drawn to determine the mean and standard deviation of the parameters in these muscles. QMT data were fitted to a 2-pool model [6,2] offline with Mathematica to derive 4 free-parameters including the T2 of the bound pool ($T2_b$), the compound parameters $f/(R_a(1-f))$, $1/(R_aT2_a)$ and RM_{0a}[2], as well as the bound pool fraction f and MT-ratio (MTR) in percentage units (p.u.).

Results The figure shows maps of calf-level T2w (a) and f.f. (b) from a representative patient, a T1-weighted anatomical image (c) and an example fit to the qMT data (d). The table gives muscle ROI values for the 4 representative muscle types for T1, IDEAL-CPMG and qMT measurements.



Discussion The T1 and qMT values of the Type 1 'normal appearing' muscle were consistent with previous measurements in healthy muscle [2]. T1 values decreased as expected in the presence of fat (Type 2 & 4) and increased in the presence of isolated edema (Type 3). Most of the variability in the qMT fits was reflected in the parameters $1/(R_aT2_a)$ and RM_{0a}, with accompanying changes in the bound-pool fraction f, which appeared to increase in the presence of fat. Type 3 muscle, where T2w is elevated without accompanying fat infiltration, will be the most important target for further studies to unequivocally determine if T2w changes are genuinely associated with changes in the fitted bound pool fraction f. Such early edematous changes preceding fat infiltration may be reversible on treatment, and an MRI marker specific to this pathological feature would therefore be of great practical importance. Future work will further elucidate the interactions between muscle fat and water component measurements, and their separation in combined IDEAL-CPMG and MT examinations.

Pathology Type	T1 (ms)	f.f. (%)	T2w (ms)	$T2_b$(μs)	f/(Ra(1-f)) (s)	1/(RaT2a)	RM_{0a} (s^{-1})	f (%)	MTR (p.u.)
1: f.f.→, T2w→	1568±81	6.0±1.1	30.8±0.5	5.7±0.3	0.15±0.01	46.8±5.7	16.7±5.6	8.5±0.7	36.7±3.1
2: f.f.↑, T2w→	1161±156	25.4±7.4	33.5±1.4	6.7±0.4	0.14±0.01	27.5±4.7	6.7±1.8	10.5±1.7	25.7±4.0
3: f.f.→, T2w↑	1887±188	5.9±0.1	44.4±1.7	6.8±1.2	0.11±0.004	36.5±2.3	11.8±1.6	5.4±0.6	32.1±2.1
4: f.f.↑, T2w↑	632±104	67.8±7.3	55.8±2.3	6.0±1.1	0.09±0.04	7.5±3.2	1.5±1.1	13.3±6.8	7.1±0.7

References [1] Janiczek et al., MRM, **66**, p1293 (2011), [2] Sinclair et al., MRM **64**, p1739 (2010), [3] Deoni et al., MRM, **49**, p515 (2003), [4] Lutti et al., MRM, **64**, p229 (2010), [5] Yarnykh et al., MRM, **57**, p192 (2007), [6] Ramani et al., MRI, **20**, p721(2002)