

Multi-parametric Classification of Inflammatory Myopathies at 3.0 T

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Target audience: Musculoskeletal radiologists and imaging scientists interested in quantitative MRI methods for skeletal muscle.

Purpose: The idiopathic inflammatory myopathies (IIM), including polymyositis (PM), dermatomyositis (DM), and inclusion body myositis (IBM), are chronic disorders whose pathological features may include muscle inflammation, fibrosis, fat infiltration/replacement, and atrophy. IIM patients experience weakness, pain, fatigue, and difficulties in daily activities. Common laboratory tests often show elevated serum concentrations of creatine kinase (CK), lactate dehydrogenase (LDH), and aldolase. However, poor correlations have been established between the variations in clinical presentation of these diseases and these laboratory findings. MRI and MRS have been employed to identify inflammation, fat infiltration and metabolic abnormalities^{1,2}. The purposes of this work are 1) to develop a multi-parametric MRI protocol to provide an improved understanding of the pathological processes associated with IIM at a microscopic level and 2) to characterize muscle damage more objectively and quantitatively. The protocol includes quantitative T₁ and T₂, quantitative magnetization transfer (qMT), fat/water imaging, and diffusion tensor imaging (DTI).

Methods: Subjects: Seven physician-diagnosed IIM patients (5 PM, 2 DM, age = 58 ± 6 yrs, BMI = 27 ± 10 kg/m²) were imaged with a group of healthy subjects of similar age and gender-matched. Data acquisition: Data were collected on a 3.0 T Philips Achieva MR scanner, with a two-channel body coil for excitation and a six-channel cardiac coil for signal reception. Images were acquired in the center of one thigh, with the subject lying supine. T₁-weighted (T1w) images were acquired for anatomical reference. Dixon fat/water imaging was performed using a six-echo gradient echo sequence³ with TE₁/ΔTE = 1.34/1.53 ms. T₁ was measured using an inversion-recovery sequence, with a 1-ms block pulse for inversion and a single-shot 3D FLASH readout. T₂ was measured with a multiple spin-echo sequence with composite refocusing pulses⁴, ΔTE = 14 ms, TR = 4 s, and 22 echoes. The T₁ and T₂ measurements were repeated with fat-signal suppression (FS). QMT MRI used a MT-weighted spoiled gradient echo sequence, with frequency offsets of 1, 2, 5, 10, 20, 50, 100 kHz, nominal saturation flip angles of 360° and 820°, TR = 50 ms, and MT pulse width of 20 ms. B₁ maps were acquired using an actual flip angle method⁵. B₀ maps were acquired using a dual-echo gradient echo sequence. Water-only excitation was performed by using a 121 binomial excitation pulse for T1 and qMT sequences. DTI data were acquired with b-value = 450 s·mm⁻² in 15 directions and one b = 0 image. All images had FOV of 256 × 256 mm², slice thickness = 7 mm, and matrix size = 128 × 128. High-resolution

Data analysis: The data were fitted to corresponding quantitative models^{6,7}. To determine the parameters in each muscle, regions of interest (ROIs) were drawn along the muscle boundaries and applied to each parameter map with minor adjustment for motion if necessary. Quantitative indices studied in this work include fat/water fractions, T₁, T₁(FS), T₂, T₂(FS), PSR, FA, ADC, and λ₃. Lab tests: CPK and LDH levels were evaluated with a blood sample collected from each subject. The maximum voluntary contraction (MVC) forces of thigh muscle groups were measured with a hand-held force device. The 30-foot walk time was recorded as a test of gross motor function.

Results: Fig. 1 shows example T1w images and quantitative parameter maps in example control (top row) and PM (bottom row) subjects. In this PM patient, fat infiltration was observed in the vastus lateralis (VL) muscle, and inflammation was also identified with increased T₁, T₂ and ADC values, decreased PSR and FA values, and multi-exponential analysis of the multi-echo data⁸. Fig. 2 shows the individual subject data for all muscles in the control and patient groups. The quadriceps muscles were more likely to be fat-infiltrated than other muscle groups. Table 1 summarizes the mean quantitative MRI indices of all muscles studied. For eight muscles, between control and patient groups, significant differences were observed for the fat/water fractions, T₁, T₁(FS), T₂, and T₂(FS) values (p < 0.05); but no significant differences were observed in PSR, FA, ADC, and λ₃ (p > 0.05). Most patients had elevated CPK and LDH values, lower MVC values, and longer walking times (p < 0.05).

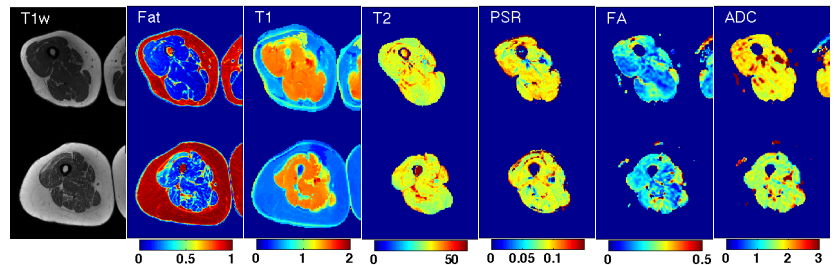


Fig. 1. T1w, fat fraction, T₁, T₂, PSR, FA, and ADC maps of a control subject (top) and a PM patient (bottom). Units: T₁, s; T₂, ms; ADC, ×10⁻³ mm²/s.

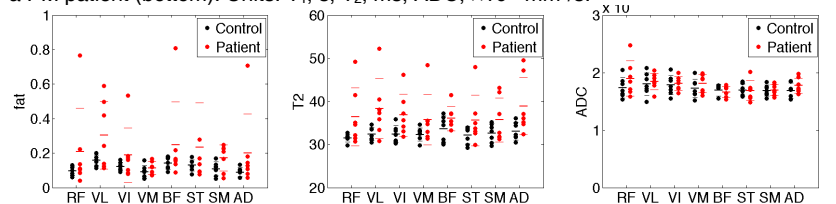


Fig 2. Comparison of fat fraction, T₂, and ADC between controls (black points) and patients (red points). Horizontal lines indicate the mean and inter-quartile range.

Discussion & conclusion: Among the patients, a large variation was observed in the levels of fat infiltration, inflammation, and atrophy. In spite of this, significant differences were observed between the patient and control groups in many of the MRI and muscle function parameters. The quantitative methods described above provide a more specifically and quantitatively measure of muscle pathology than conventional MRI, and may thus provide a correspondingly more comprehensive understanding of neuromuscular pathologies, and may eventually provide clinicians with quantitative tools for the evaluation and therapeutic management of patients.

Table 1. Mean (standard deviation) of quantitative MRI indices in the control and patient groups. *p < 0.05, control vs. patients.

	Fat	T ₁ (s)	T ₁ (FS) (s)	T ₂ (ms)	T ₂ (FS) (ms)	PSR	FA	ADC	λ ₃
Control	0.117 (0.038)	1.46 (0.04)	1.48 (0.04)	32.5 (1.9)	31.7 (2.1)	0.088 (0.007)	0.188 (0.040)	0.0017 (0.0001)	0.0014 (0.0001)
Patient	0.209* (0.192)	1.36* (0.22)	1.54* (0.10)	36.6* (5.5)	34.1* (3.8)	0.081 (0.029)	0.201 (0.046)	0.0018 (0.0002)	0.0015 (0.0001)

References: [1] Park JH et al, *Radiology*, 177:473 (1990); [2] Qi J et al, *JMRI*, 27:212 (2008); [3] Berglund J et al, *Magn Reson Med*, 67:1684 (2012); [4] Poon CS et al, *J Magn Reson Imaging*, 2:541 (1992); [5] Yarnykh VL, *Magn Reson Med*, 57:192 (2007); [6] Ramani A et al, *Magn Reson Imaging*, 20:721 (2002); [7] Berglund et al, *Magn Reson Med*, 67:1684 (2012); [8] Fan RH, et al, *NMR in Biomedicine*, 21:566 (2008).