Assessment of thigh muscle in healthy controls and dermatomyositis patients with diffusion tensor imaging, intravoxel incoherent motion, and dynamical DTI

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Target Audience: Scientists and clinicians interested in skeletal muscle diffusion imaging.

Purpose: Dermatomyositis (DM) is an idiopathic inflammatory myopathy affecting skeletal muscle and skin, with the potential for other co-morbidities [1-3]. Standard serum markers, EMG and muscle biopsy are often insufficient to reliably differentiate its components (inflammation, activity, and damage), motivating the need for imaging biomarkers. Variants of diffusion-weighted imaging (DWI)—diffusion tensor imaging (DTI) and intravoxel incoherent motion (IVIM)—track water motion, and are sensitive to changes in muscle fiber size and integrity [4-6], and in blood flow [7-9]. A dynamic approach (single line multiple echo diffusion tensor acquisition technique, SL-MEDITATE) measures DTI at rest and immediately after exercise [10,11]. We evaluated proximal lower extremity musculature in DM patients and controls.

Methods: In this IRB-approved, HIPAA-compliant study, we have collected data in the proximal (thigh) muscles of 14 healthy volunteers (6M, 8F, ages 24-65, 38±13) and 15 DM patients (2M, 13F, ages 22-64, 48±16), using anatomical imaging (T1/T2-weighted), 2-point Dixon-based water/fat imaging, diffusion tensor imaging (DTI), and intravoxel incoherent motion (IVIM) protocols in a Siemens Skyra 3 T scanner with body matrix and spine array coils. DTI (MD, FA, eigenvalues) and IVIM (D_t, f_p, D_p) metrics were derived from each of 8 thigh muscle compartments in the quadriceps (rectus femoris (RF), vastus intermedius (VI), vastus medialis (VM), vastus lateralis (VL)) and hamstrings (biceps femoris (BF), semimembranosus (SM), semitendinosus (ST)), and adductor magnus (AD) bilaterally segmented on Dixon imaging. These regions of interest (ROIs) are used to measure water and fat fractions, and transferred and downsampled to the co-localized diffusion images. Diffusion images suffering large signal dropouts are excluded from analysis, an outlier rejection scheme achievable given 3 averages. DTI metrics are collected from the ROI averages of the parametric maps. IVIM-integrated signal decays within each ROI are fit with a segmented biexponential fit algorithm, to derive the IVIM metrics for each of three orthogonal directions. Single voxel dynamic DTI provides time series of radial and axial diffusion before and after a 3 minute unilateral leg lift exercise period, focusing on the anterior quadriceps (rectus femoris and vastus lateralis) (Fig. 2a). Relative exercise response and recovery rate were determined for radial and axial diffusion.

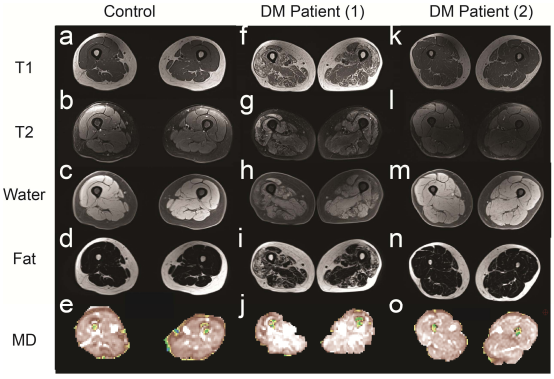

Figure 1: Example static bilateral thigh imaging in a ((a)-(e)) healthy volunteer and dermatomyositis patients with ((f)-(j)) and without ((k)-(o)) fat infiltration. Images show T1-weighted TSE, T2-weighted SPAIR fat suppressed TSE, 2-point Dixon water and fat images, and DTI mean diffusivity (MD).

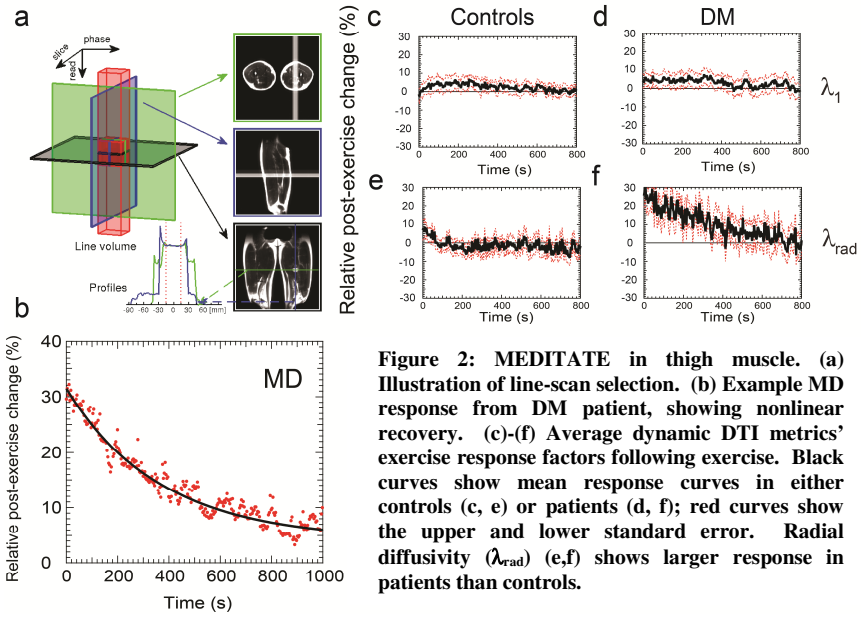

Figure 2: MEDITATE in thigh muscle. (a) Illustration of line-scan selection. (b) Example MD response from DM patient, showing nonlinear recovery. (c)-(f) Average dynamic DTI metrics' exercise response factors following exercise. Black curves show mean response curves in either controls (c, e) or patients (d, f); red curves show the upper and lower standard error. Radial diffusivity (λ_{rad}) (e,f) shows larger response in patients than controls.

Results: Bilateral thigh images from a healthy volunteer (F, 55y), a DM patient with fatty infiltration (M, 66y), and a DM patient without fatty infiltration (F, 63y) are shown in Figure 1. Fat fraction is significantly elevated in the first DM patient, but not the second. MD values are elevated across the leg in both DM patients compared with the control. The fat fraction from Dixon imaging was significantly greater in patients than controls at the whole group level as well as within the hamstring and quadriceps subgroups. The hamstring fat fraction was also significantly larger than quadriceps fat fraction in both subject groups. In quadriceps, patients showed significantly lower radial diffusion λ_{rad}, transverse tissue diffusivity $D_{t,xy}$, and transverse pseudodiffusivity $D_{p,xy}$ than controls. Hamstrings of patients showed larger values of these parameters than controls. Figure 2 shows the group mean and standard error of the post-exercise normalized response curves of the MEDITATE metrics. The recovery profile is often nonlinear (Fig. 2b). Each individual response was fitted to an exponential recovery: $R = R_0 \exp(-d \cdot t) + b$. DM patients' radial diffusion response is significantly larger than controls (Fig. 3). Radial / axial diffusion recovery rates are slower for patients than controls.

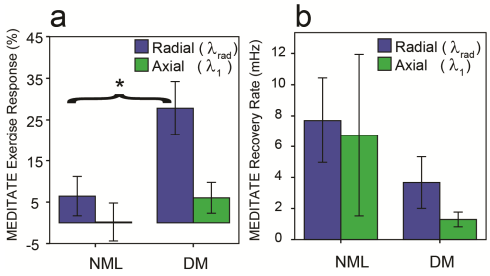

Figure 3: Group comparisons of MEDITATE exercise response metrics in controls and DM patients. (a) Patients show a significantly higher radial diffusion response than controls. (b) Recovery rates were slower for patients than controls.

Discussion: Static imaging results indicate several diagnostic biomarkers that can help to differentiate DM patients from controls with some regional variations possibly due to variable fatty infiltration. For the quadriceps muscle group, a larger relative increase in fat fraction dominates diffusion by adding restriction, while in the hamstrings muscles the combined inflammation and fiber degradation increased diffusivities. Dynamic measurements suggest DM patients show larger fiber hypertrophy and a slower return to equilibrium, possibly deriving from a more compromised myofiber supply, in which larger changes per fiber are required to compensate for the missing functional reserve. Inflammatory swelling may also contribute to patients' response. Ongoing work will investigate the prognostic potential of these markers in predicting response to immunosuppressive therapy.

References: 1. Arnson , IMAJ 2007; 2. Sato , Curr opin in rheumatol 2010;3. Mammen, Ann N Y Acad Sci 2010;4. Galban Eur J Appl Physiol 2004 5. Sigmund, JMRI 2013. 6. Li, Nmr Biomed 2014 7. Qi JMRI 2008; 8. Karampinos, JMRI 2010; 9. Morvan, MRI 1995 10. Baete, NMR Biomed 2013; 11. Baete, ISMRM 2014. p 825.