Tracking Disease Progression in Duchenne Muscular Dystrophy: Longitudinal Changes in Quantitative MR Measures


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Synopsis:

This study investigates the utility of quantitative MR measures to track disease progression in DMD. 3T Data were acquired from 125 DMD and 28 control boys. 

Introduction:

Duchenne muscular dystrophy (DMD) is an X-linked recessive disease caused by a dystrophin gene mutation that occurs with an incidence of approximately 1 in 5000 male births. The disease is characterized by sarcolemmal fragility, myofiber degeneration, inflammation, increased synthesis and deposition of extracellular matrix proteins and ultimately replacement of contractile tissue with fatty infiltrate and connective tissue. There currently is no cure for DMD but promising therapies have been identified and there is a pressing need for improved biomarkers sensitive for disease progression. Quantitative MRI/MRS have excellent sensitivity for detection of muscle pathology associated with DMD and strongly correlate with clinical assessments.

Methods:

Data were acquired from 125 DMD boys (baseline ages 5-13 y, mean 8.6 y (±2.2 y; SD); 95 on corticosteroids) and 28 healthy controls (ages 5-15 y, mean 9.8 (±2.4 y) using 3T MRI instruments located at three institutions. Fat fraction (FF) was determined from spin-echo MRI, and the utility of these biomarkers to track disease progression in boys with DMD.

Results and Discussion:

Measurements were successfully collected on 125 DMD and 28 control boys using MRS and qT2 MRI of upper and lower leg muscle. Highly significant differences between controls and DMD boys were found for both FF (P<10^-6; effect size (ES) > 2.2) and qT2 (P<10^-6; (ES) > 2.3 for VL, BFLH, Sol, and Per). Paired analysis revealed significant increases in FF (see Fig 1A) and qT2 (Fig. 1C, 1D) for most DMD muscle groups between baseline and 12 month, and between 12 and 24 month follow-ups. Upper leg muscles (VL, BFLH) typically showed greater involvement as measured by absolute differences in FF or qT2 compared to controls. Regression analysis revealed a strong quadratic association between qT2 values determined by MRI and FF determined by MRS (R=0.875; P<10^-6; Fig. 2) suggesting that increased qT2 is largely determined by increased muscle fat content in DMD. In summary, both FF and qT2 provide excellent sensitivity for tracking DMD disease progression and both are likely surrogates for the same underlying pathologic substrate: fat infiltration. qT2 values also provide outstanding spatial resolution and total tissue coverage that greatly facilitates characterizing heterogeneity of DMD disease progression in differing muscles.

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Figure 2