**T₂ mapping and Single Voxel ¹H-MRS Detect Skeletal Muscle Involvement in Young Boys with Duchenne Muscular Dystrophy**

Sean C Forbes1, Glenn A. Walter1, William Rooney2, Dah-Jyuu Wang3, William Triplet1, Rebecca Willcocks1, James Pollaro3, Barry Byrne1, Richard Finkel4, Barry Russman5, Erik Finanger5, Gihan Tennekoon1, Lee Sweeney2, and Krista Vandenborne1

1University of Florida, Gainesville, Florida, United States, 2Oregon Health & Science University, Portland, Oregon, United States, 3Children’s Hospital of Philadelphia, Philadelphia, Pennsylvania, United States, 4Nemours Children’s Hospital, Florida, United States, 5Shriners Hospital for Children, Portland, Oregon, United States

**Target Audience:** This study will benefit those interested in using T₂ mapping or single voxel ¹H-MRS to evaluate disease involvement in skeletal muscles of muscular dystrophies or other neuromuscular diseases.

**Introduction:** Duchenne muscular dystrophy (DMD) is an X-linked recessive disorder that is due to a mutation in the dystrophin gene.¹ DMD has an incidence of 1 in 3600-6000 male births and is characterized by progressive muscle deterioration, loss of functional abilities, and reduced life expectancy.² Functional deficits in motor performance, such as reduced distance walked in the timed 6 minute walk test, are often not observed in DMD until after age 7, and therefore these functional measures may not be sensitive for detecting disease progression at a young age.³ In this study, we hypothesized that: 1) MRI-T₂ and ¹H₂O T₂ derived using ¹H-MRS will be sensitive to muscle involvement at a young age (5-7 years) consistent with increased inflammation and muscle damage in DMD compared to controls and 2) MRI-T₂ will increase with disease progression in DMD due to progressive lipid infiltration.

**Methods:** MR data were acquired from 111 boys with DMD (ages 5-14 years; mean 8.7 SD 2.3 years; 5-6.9 years, n=34; 7-8.9 years, n=34; 9-10.9 years, n=21; 11-14 years, n=22) and 26 healthy controls (age 9.6 SD 2.1 years; 5-6.9 years, n=5; 7-8.9 years, n=5; 9-10.9 years, n=10; 11-14 years, n=6) using 3T MR systems at three institutions (University of Florida, Oregon Health & Science University, and Children’s Hospital of Philadelphia). The MRI data were acquired to have even deletions (62%), duplications (13%), or point mutations (25%) in the dystrophin gene. T₂-weighted multi-slice spin echo (SE) axial images were acquired (0.75 mm ², 7 mm slices, 3.5 mm gap; 16 TE’s, 20-320 ms evenly spaced; TR 3 s) from the lower leg (Fig. 1) and thigh. Single voxel ¹H-MRS data were acquired (TE 108 ms; TR 3 s; NA64) for assessment of lipid fraction using stimulated-echo acquisition mode (STEAM) from the soleus (Sol; Fig.1) and vastus lateralis (VL). Finally, ¹H spectroscopic relaxometry was performed using STEAM in the Sol and VL (16 TE’s non-linearly spaced from 11-288 ms; TR 3 s; NA4). MRI and spectroscopic ¹H₂O T₂ values were derived using a single exponential function. Intramuscular lipid fraction was determined using area integration of the phase corrected spectra from the lipid (0.5-2.75 ppm) and ¹H₂O (4.3-5.10 ppm) regions of the spectrum.

**Results and Discussion:** MRI-T₂, ¹H₂O T₂, and lipid fraction were greater (p<0.05) in DMD compared to controls (Fig. 2). In the youngest age group, DMD were different (p<0.05) than controls for the Sol MRI-T₂ (effect size (ES) 4.0), ¹H₂O T₂ (ES 4.3) and lipid fraction (ES 2.7) and VL MRI-T₂ (ES 2.2) and ¹H₂O T₂ (ES 2.1). In the boys with DMD, MRI-T₂ and lipid fraction were greater (p<0.05) in the oldest age group (11-14 years) than the youngest age group (5-6.9 years), whereas ¹H₂O T₂ was reduced in the oldest age group compared to the youngest age group (Fig. 2). The reduced ¹H₂O T₂ in older boys with DMD may be due to increased fibrosis or reduced inflammation/damage.⁴ The VL presented with larger increases across age group in MRI-T₂ and lipid fraction than the Sol, suggesting that the VL muscle pathology progresses faster than the Sol. No differences were observed in these MR measures among gene mutation type.

**Conclusion:** MR measures of T₂ and lipid fraction revealed differences between DMD and Controls, including in the youngest age group (5-6.9 years). Furthermore, MRI-T₂ was greater in the older age group compared to the young age group, which was associated with higher lipid fractions. Overall, MR measures of T₂ and lipid fraction may be sensitive to disease involvement and potential therapeutic interventions in DMD, even in the younger boys.

**References:**


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**Figure 1.** Example lower leg axial SE image (TE 60 ms) with single voxel ¹H-MRS spectrum from the soleus of a boy with DMD.

**Figure 2.** ¹H₂O T₂ (ms), MRI-T₂ (ms), and lipid fraction [lipid/(lipid+water)] in the soleus (A) and vastus lateralis (B) of Control and DMD age groups. Bars represent mean (SEM). * indicates significantly different (p<0.05) than Controls and # indicates different (p<0.05) than 5-6.9 age group in DMD.

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**Graphs:**

- **A.** Soleus:
  - Control and DMD groups are represented.
  - Significant differences (p<0.05) are indicated.

- **B.** Vastus Lateralis:
  - Similar representation as A.