In Vivo Quantification of Soleus Muscle Changes from Fat Infiltration using Magnetic Resonance Imaging and Spectroscopy in Children with Duchenne Muscular Dystrophy

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Introduction
Duchenne muscular dystrophy (DMD) is a degenerative and devastating muscular disease caused from the lack of the muscle protein dystrophin. This inherited disease negatively affects the musculature of boys and results in weakness, impaired functional abilities, and a decreased life span. Boys with DMD demonstrate fatty infiltration within their muscles [1] and an alteration in skeletal muscle metabolites [2]. The purpose of this study was to quantify the fatty infiltration, metabolite changes, and maximal cross sectional area (max CSA) of the soleus muscle in boys with DMD using magnetic resonance imaging (MRI) and proton magnetic resonance spectroscopy ($^1$H-MRS).

Experimental
Measurements were obtained from the soleus muscle of six children with DMD aged 5-12 years (mean age 8.8 ± 2.8 years) and six age-matched, healthy control boys (mean age 8.5 ± 2.6 years). MRI and $^1$H-MRS measurements were performed on either a 1.5T (Signa, GE Medical Systems) or 3.0T (Achieva, Philips Medical Systems) whole-body scanner. The subjects were positioned in supine with their lower leg inside either a lower-extremity quadrature coil (1.5T) or an eight channel SENSE receive only extremity coil (3.0T). Gradient-Echo imaging was performed to obtain transaxial, fat suppressed T$_1$ weighted images of the lower leg from the knee to the ankle with the following parameters: mean acquisition matrix 231x231 pixels, mean field of view 108x106 cm, mean pulse repetition time of 17.6 ms, mean echo time of 2.3 ms, mean slice thickness of 6 mm, and a mean slice gap of 2.1 mm. Max CSA was determined for the soleus muscle for each subject using OsiriX software. For $^1$H-MRS measurements, a voxel (mean volume of 5,762 mm$^3$) was selected using transaxial T$_1$ weighted images and was placed inside of the soleus muscle with care to avoid visible vasculature, subcutaneous fat, and myofascial layers. The following acquisition parameters were used for MRS of the soleus: repetition time 3,000 ms, echo time of 108 ms, 64 scans, 2,084 data points, and a spectral width of 2,500 Hz. Concentrations of creatine, total lipid, and water were determined using jMRUI software. Two sample t-tests were used to assess differences between the two groups for max CSA, Creatine:Water, Lipid:Water, and Lipid:Creatine ratios.

Results and Discussion
Differences were noted between children with DMD and healthy control subjects for max CSA of the soleus (19.1 ± 7.2 cm$^2$ versus 10.9 ± 3.5 cm$^2$, p < 0.016) as well as for Lipid:Water (0.077 ± 0.068 versus 0.021 ± 0.011, p < 0.038) and Lipid:Creatine (154.4 ± 165.0 versus 30.9 ± 13.3, p < 0.049) ratios. No difference was noted for the Creatine:Water ratio between the two groups (DMD 0.0008 ± 0.0006 versus control 0.0006 ± 0.0002, p = 0.319).

Conclusions
Children with DMD demonstrate greater soleus max CSA than age matched control subjects; however, this greater CSA is not necessarily a reflection of a greater amount of contractile area (e.g. greater proportion of skeletal muscle). It appears that the muscle tissue becomes infiltrated with adipose tissue, and the results of this study demonstrate a novel way to quantify this fatty infiltration via MRI and $^1$H-MRS. Quantification of muscle composition in boys with DMD could be used to monitor disease progression and/or changes in muscle from interventions aimed at decreasing the deleterious effects of DMD on skeletal muscle.

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References