MR Spectroscopy (MRS) in objective measurement of intramuscular fat as a non-invasive biomarker: Comparison study in boys with Duchenne muscular dystrophy (DMD) and healthy boys.

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Introduction: DMD is one of the most fatal neuromuscular disorders and is characterized by progressive fatty infiltration of the muscles. Objective measures of intramuscular fat are important for diagnosis of pathologic fatty infiltration and follow up of therapeutic response. Muscle biopsy has been utilized to assess degree of fatty infiltration of the muscles. However, muscle biopsy is limited due to its invasiveness. Therefore, noninvasive biomarkers of skeletal muscle disease that quantify fatty infiltration are critically required in clinical practice. Our prior work using T2 relaxation time mapping demonstrated disease distribution in DMD; the gluteus maximus muscle has most significant disease involvement in DMD. [Kim et al.].

Purpose: In this work, we aimed to validate MRS as an objective measure of intramuscular fat in the pelvic muscle and to determine whether MRS can segregate boys with DMD from healthy boys.

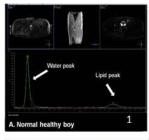
Material and Methods: In this IRB approved prospective study, we recruited 21 boys with DMD and 27 healthy age-matched boys (age ranged 5-15 years). Pelvic MR images including MRS were performed using a 3.0T MR scanner (Achieva, Philips Healthcare) with a 32-channel cardiac/torso coil. Age, height, weight, body mass index (BMI) and body surface area (BSA) were obtained from both groups. Grading of fatty infiltration of the gluteus maximus muscle was done on T1-weighted image (T1-WI) (Grade 0-4). Lipid to water ratio of the gluteus maximus muscle was obtained from MRS. For consistency; voxel size and positioning were maintained across all scanned subjects. No water suppression was applied. A volume shim was performed over the chosen voxel. Acquisition time for MRS was approximately 2-4 minutes. The lipid-to-water ratios from the two groups were compared. The analyses were conducted using SAS statistical software ver. 9.3 (SAS Institute, Cary, NC).

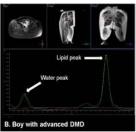
Results: 6 boys with DMD (6/21) and 27 healthy boys demonstrated minimal degree of fatty infiltration (grade 1) on T1-WI. Lipid to water ratios obtained from boys with DMD were significantly higher than those values from healthy boys (Figure 1 and 2). There was separation of two groups and this result was observed as the values from MRS were plotted as a function of age (Figure 3) and BMI (Figure 4).

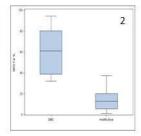
Conclusions: MRS enabled quantitative measurement of fatty infiltration of the skeletal muscle. This quantitative and non-invasive method enabled separation of boys with DMD from healthy boys, which gives MRS an advantage over T1-WI, which cannot differentiate boys with early disease state of DMD (grade 1 fatty infiltration on T1-WI) from healthy boys.

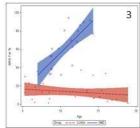
References:

Kim HK, Laor T, Horn PS, Racadio JM, Wong B, Dardzinski BJ. T2 mapping in Duchenne muscular dystrophy: distribution of disease activity and correlation with clinical assessments. Radiology. 2010;255(3):899-908.









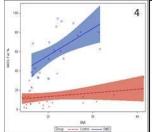


Fig 1: A representative MRS of (A) an 8 year-old healthy boy and (B) an 8 year-old boy with advanced DMD showing the difference in the lipid-to-water ratio in the gluteus maximus muscle.

Fig 2: Box plot shows the MRS values for DMD patients and healthy boys (p<.001). Significance was determined by linear models adjusting for age and BMI using least square means. The box represents the area between the first and third quartiles. The line in the middle of each box is the median, and the whiskers extending from each box are the maximum and minimum values.

Fig 3: MRS values as a function of age for the two groups of boys (mean +/- 95% CI).

Fig 4: MRS values as function of BMI for the two groups of boys (mean +/- 95% CI).