Quantitative muscle MR imaging versus quantitative ultrasound in facioscapulohumeral muscular dystrophy

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Target audience: persons interested in neuromuscular disorders, MRI ultrasound comparison, Facioscapulohumeral muscular dystrophy

Purpose: With the emergence of new muscular therapies, non-invasive biomarkers are needed to assess neuromuscular disorders. Imaging techniques like MRI and ultrasound (US) are non invasive and can be repeatedly performed without causing any discomfort for the patient. MRI and US have been compared for purposes such as cancer detection and when measuring specific muscle thickness, but not yet in their ability to describe specific muscle pathology. Facioscapulohumeral dystrophy (FSHD) is one of the most common muscular dystrophies with a progressive development. Currently no treatment is available for these patients but recent discoveries[1] on the genetic background are expected to generate new therapies. Recently, we established several MR detectable quantitative biomarkers for FSHD, with muscular fat fraction as the most valuable one, and used these to characterize a large cohort of FSHD patients[2]. Quantitative US (QMUS) has already proven its value in the diagnosis and prediction of childhood neuromuscular disorders including Duchenne muscular dystrophy[3]. The *aim of this study* was to compare quantitative MRI (QMRI) with QMUS in their ability to characterize specific muscle pathology.
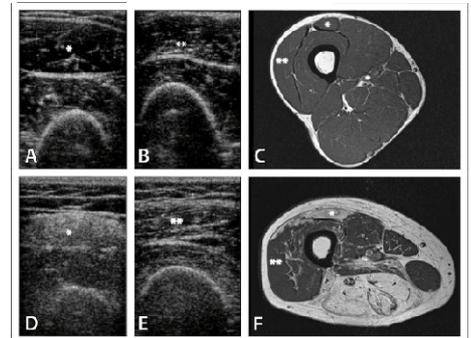

Figure 1: Ultra sound (A,B,D,E) and T2 weigthed MRI images (C,F) of the thigh of two FSHD patient. Top panels (A-C): normal echo intensity and MRI. Bottom panels (D-F) abnormal echo intensity of the RF (*), corresponding with complete fatty infiltration, clearly seen by the high intensity signal from the MRI image, and less abnormal VL(**).

Methods: *Recruitment:* Five male FSHD patients of varying ages (34 – 61 years) and disease severity were included. One obese patient was included (BMI: 33.6). The vastus lateralis (VL) and rectus femoris (RF) muscles were subject of this study.

MRI protocol: MRI exams were performed on a Siemens Trio 3T MR system, with a homebuilt proton birdcage coil placed around the upper leg of the patient. A fish-oil capsule was placed at 2/3 of the distance from the anterior superior iliac spine to the superior lateral aspect of the patella to enable slice matching between the MR and US exams.

T1-weighted images were acquired with a spin-echo sequence (TR/TE: 530 ms/16 ms, 23 slices, slice thickness/gap: 4 mm/0.4 mm, FOV 175 mm x 175 mm). Multi spin echo MR images were recorded of the same location (TR: 3 sec, TE: 16 echo times 7.7 ms - 123.2 ms, 4-8 slices; limited by SAR, slice thickness/gap 6 mm/9 mm, FOV 175 mm x 175 mm). Fat content was derived from multi spin echo images by fitting the signal intensity to a bi-exponential function with fixed T2 relaxation times for muscle (40 ms) and fat (143 ms)[4], this was done with a custom-made IDL program calculating muscle and fat fractions. Muscle fraction = 1- fat fraction. Every slice was analyzed separately (Fmus slice).

US protocol: Muscle ultrasound was performed using a Philips IU22 ultrasound scanner and a 8-4 MHz broadband linear transducer. QMUS measurements were performed of the VL and RF. All scans were made in the transverse plane. For each muscle three consecutive measurements were made to minimize variation in echo intensity during analysis.

The captured images were analyzed for echo intensity by means of computer-assisted gray scale histogram analysis and were converted to z-scores (number of standard deviations from the mean score for sex, age and weight using previously established reference values[5]); these z-scores were used for further analysis.

Results: An example of normal and abnormal muscle echo intensities are shown in figure 1. One muscle was excluded as from muscle fraction analyses as it showed signs of inflammation on more extensive MR examination (outside the scope of this abstract). One-tailed Spearmans correlation analysis showed a good correlation between QMUS determined z-score and between QMRI determined Fmus average ($p = 0.007$, $R = -0.80$). The correlation of the z-score with Fmus slice and T1 SI showed similar results ($p = 0.003$, $R = -0.65$ and $p = 0.01$, $R = 0.72$, respectively). Fisher r-to-z transformation showed no statistical difference, meaning that none of the QMRI parameters correlates significantly better with QMUS (and vice versa) than the others. The relationships Fmus and T1 SI with QMUS z-score could be very well fitted with a Boltzmann sigmoidal function (Fmus slice $R^2=0.996$, Fmus average: $R^2=0.942$, T1 SI $R^2=0.991$), figure 2.

The steepest slope was found for the relation between EI z-score and T1 signal intensity, while the EI z-score plotted against the Fmus average had the shallowest curve, indicating a slightly more gradual transition from normal to abnormal values.

One muscle had significant variation of fatty infiltration over the length of the muscle. This leads to a deviation of value from the curve fitted for Fmus average and z-score. The obese presented with severe clinical limitations but without any muscle abnormalities on either MRI or US. Apparently the poor clinical status of this patient was to due to his obesitas, diabetes and poor cardiovascular condition.
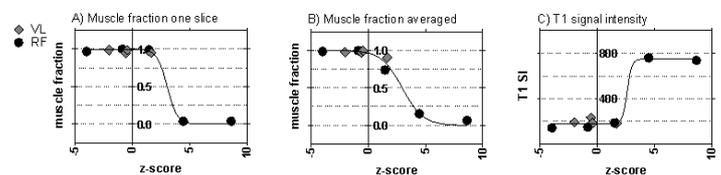

Figure 2: Correlation of QMUS with QMRI: A) z-score with muscle fraction of matched slice, B) z-score with average muscle fraction of the entire measured area, and C) z-score with signal intensity of ROI on T1 weighted MR image All relations are well- described with a Boltzmann Sigmoid function.

Discussion: QMRI and QMUS are highly correlated in their description of muscle pathology. Where muscle fraction and T1 SI have a limited range over which the entire spectrum of fatty infiltration is covered, QMUS z-scores seem to have a larger dynamic range. Increasing z-scores beyond the limit of Fmus might indicate a further architectural reorganization of the diseased muscle tissue beyond the replacement of myofibrils witih fat and fibrosis. Whether this holds clinical relevant information needs further investigation. QMUS is a fast, cheap technique that can be performed at bedside, while MRI is (relatively) time consuming, expensive and needs to be performed at the MR system. However MR has the advantages that it is able to image in multiple directions, multiple slices and deeper muscle layers. Further more in one MR exam diverse measurements can be performed focusing on different aspects of muscle pathology, like T1and T2 weighted, STIR/TIRM and DIXON imaging.

Conclusion: QMRI and QMUS are highly correlated and the relationship follows a sigmoid function. In muscular dystrophies, which a heterogeneous affliction over the length of the muscles (like in FSHD) analyses of multiple transversal or sagittal/coronal slices is necessary, making MRI a more suited technique. Both imaging techniques can be used as biomarkers and can discriminate between muscle pathology due to the neuromuscular disorder and loss of force and clinical severity due to other health issues like metabolic syndrome.

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