Quantification of the inflammatory process in muscles of patients with facioscapulohumeral muscular dystrophy.

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Purpose

Inflammation is known to play an important role in the pathophysiological mechanism of facioscapulohumeral muscular dystrophy (FSHD)[1]. It is thought that the inflammatory process precedes the fatty infiltration and fibrotic process[2, 3]. To protect the muscle against this fat infiltration and fibrosis some therapeutic interventions aim to reduce this muscle inflammation. Therefore, it is important to accurately quantify inflammation in the muscles. Inflammation is accompanied by oedema, which appears as hyperintense lesions on T2-weighted fat-suppressed MR imaging, such as in Turbo Inversion Recovery Magnitude (TIRM) images. Currently, only semi-quantitative scales to score the presence of oedema exist[2]. However, to evaluate potential treatment effects an objective quantitative biomarker is necessary.

The *aim of this study* was to develop a method that quantifies two parameters in TIRM images, reflecting severity of inflammation: volume of inflammation and intensity of inflammation, in patients with FSHD.

Methods

Patients and study design: Three patients with genetically proven FSHD type 1 were included (3 males, clinical severity score[4]: 3, 3.5 and 3.5). They underwent an MR scan at two time-points, baseline and follow-up (12 weeks).

MRI protocol: The patients were scanned using a 3T Siemens Trio and a ^{1}H volume coil that was placed around the upper leg of the patients. T1 weighted spin echo images (TR/TE 530/16 ms, slices thickness/gap 4/0.4 mm, slices 23, FOV 175x175 mm) and TIRM images (TR/TE 4000/41 ms, IT 220 ms, slices thickness/gap 4/0.4 mm, slices 23, FOV 175x175 mm) were acquired. For the TIRM images saturation bands were placed above the upper and below the lower slice to avoid blood inflow artefacts.

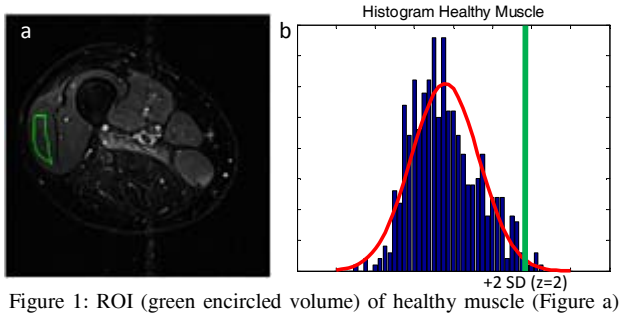

Figure 1: ROI (green encircled volume) of healthy muscle (Figure a) used to determine the threshold as + 2SD (z=2) (Figure b).

Data analysis: First, the TIRM images were visually assessed to determine which muscles were inflamed in both baseline and follow-up. These muscles were selected for further analysis. The mean value and standard deviation (SD) from healthy muscle within the same subject was obtained by drawing a region of interest (ROI) on the TIRM image. These values were used to compute a z-score for the TIRM hyperintense muscle quantifying the difference between signal intensity compared to normal. For each TIRM hyperintense muscle a region of interest (ROI) was drawn on every slice of the T1 weighted images using Matlab. We assumed that pixels with a z-score larger than 2, indicating a difference larger than 2 SD from normal (>99.7%), were inflamed (Figure 1). The number of pixels with a z-score > 2, times the pixel volume computed the volume of inflammation, expressed in cm^3 (Figure 2). For every TIRM hyperintense muscle the intensity of inflammation was expressed as the average z-score per volume of inflammation.

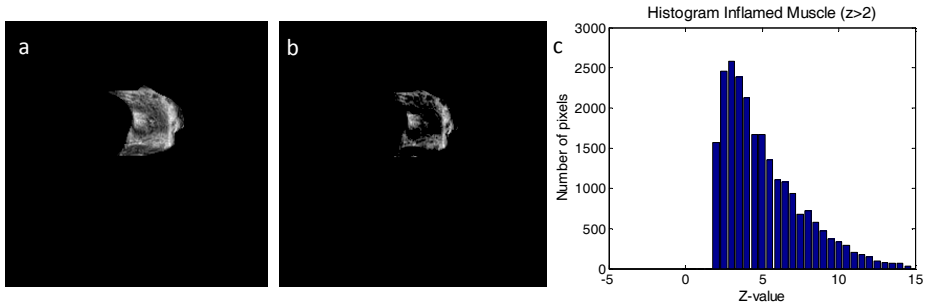

Figure 2: a) TIRM hyperintense muscle. b) Application of threshold z>2. c) Histogram of inflamed volume of the muscle.

	Baseline		Follow-up	
Muscle	**Volume (cm^3)**	**z-value**	**Volume (cm^3)**	**z-value**
1	51.5	4.9	29.3	5.2
2	13.1	3.9	22.8	4.7
3	20.7	4.7	35.6	5.8
4	67.5	5.1	30.7	4.1
5	67.8	4.3	46.5	4.8
6	57.8	5.6	43.7	5.1

Table 1: Volume and intensity of inflammation per muscle at baseline and follow-up. The muscles in of patient 1, 2 and 3 are in orange, purple and blue, respectively.

Results

During visual assessment 6 muscles were identified as inflamed during both baseline and follow-up. The volume and intensity of inflammation of these muscles are given in Table 1. In muscle 2 and 3 the volume and intensity of inflammation both increase. In muscle 4 and 6 the volume and intensity of inflammation both decrease. In muscle 1 and 5 the volume of inflammation decreases while the intensity increases.

Discussion

We developed a method that can quantify the process of inflammation in two components, intensity of inflammation and volume of inflammation. Together these express the severity of inflammation. We observed an increase in inflammation severity over time in muscle 2 and 3, while in muscle 4 and 6 the inflammation at baseline was more severe as compared to the follow-up. The decrease in inflammation severity at follow-up may indicate that the inflammatory process was followed and replaced by fatty infiltration. In muscle 1 and 5 the oedema centralized to a smaller volume. The nature of the inflammation as described by these two parameters needs to be characterised by targeted biopsy studies. The proposed method can be employed in future clinical trials to quantify these particular features of inflammation.

References

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