MRI-index: an automatic tool for early quantitative evaluation of fat infiltration at muscle MRI in neuromuscular diseases

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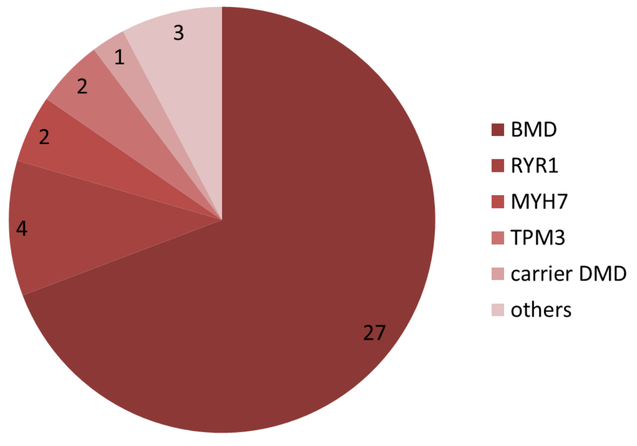
Introduction: Quantitative skeletal muscle MRI (mMRI) has been widely studied as a reliable outcome measure in patients with Neuromuscular Disorders (NMD). In previous studies, we have developed a MRI-Index, a measure extrapolated with an automatic algorithm implemented for the segmentation of skeletal muscle (SM), intermuscular adipose tissue (IAT) and subcutaneous adipose tissue (SAT) compartments from T1-w MRI images of the thigh.

A *fuzzy c-mean* algorithm was used to perform a classification of different tissues: SM, adipose tissue (AT) and bone. IAT and SAT segmentation was performed by an active contour model able to evolve and converge toward the muscle fascia. An example of the obtained masks is shown in **Figures 1A** and **1B**. Normative values for each slice of thigh images acquired in 30 healthy subjects, were extrapolated: the MRI-index range resulted between 4.1% and 18.9% (mean 10.7; SD ±3.7).

Methods: 46 patients (age range 6-69) with variable disease severity were enrolled (**Graphic 1**).

Among the 27 BMD patients, 6 cases were excluded from the study both for artifacts in images or for high degree of muscle involvement that resulted in difficult segmentation process.

Genotype and phenotype correlations were subsequently made.



Graphic 1

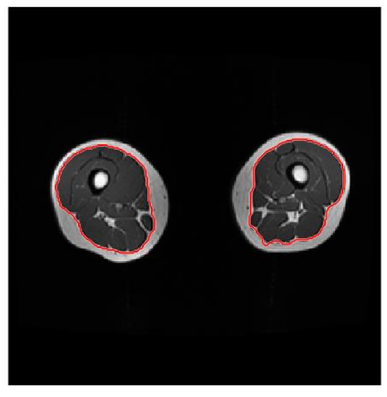


Figure 1A

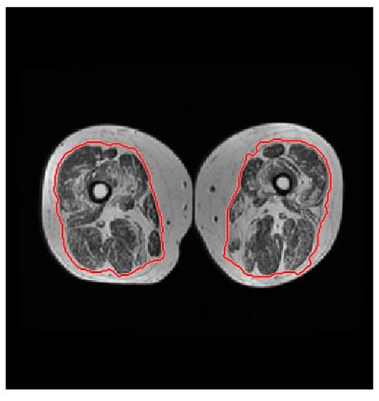


Figure 1B

Results: Analyzing patients with MRI-Index higher than the maximum cut-off obtained in healthy patients (>18.9%), we observed that all of them harboured mutations in genes encoding structural muscular proteins (12 BMD and 2 *MYH7* patients) regardless of their age.

Among patients with a lower quantitative of IAT (<18.9%), we identified those with a milder phenotype or with asymptomatic hyperCKemia, particularly due to mutations in *RYR1*; 9 BMD patients were also included in this group.

Analyzing BMD patients only, we observed that disease severity correlates with the degree of fat percentage in muscle (high MRI-Index): only 4 (19%) patients showed an MRI-Index >18.9% before the age of 30 years; 8 patients (38%) showed an MRI-Index >18.9% after age 30 (**Figure 2** and **Table 1**). BMD patients (19%) who presented deletions involving exons 45-47 showed lower MRI-Index (<18.9%), even if age >30 years.

Figure 2. MRI-Index of BMD patients related to different age groups

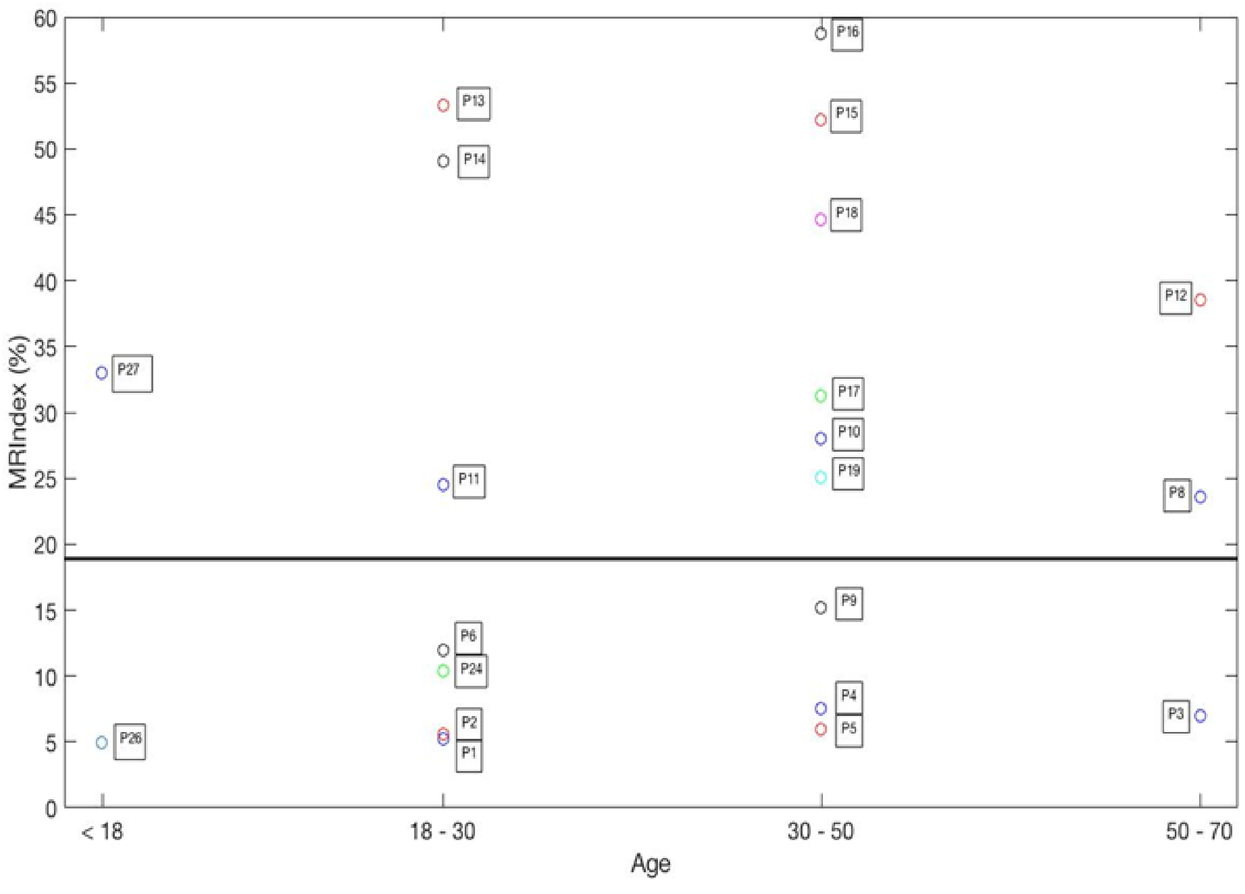


Table 1. Data on the 21 BMD patients

Patient	Age (yrs)	MRI-Index (%)	Mutation
P26	11	4,9 ± 1,5	Del. 48
P27	11	33,0 ± 4,3	Del. 51
P1	21	5,2 ± 0,9	Del. 45-51
P2	21	5,6 ± 0,9	Del. 45-51
P6	25	12,0 ± 1,1	Del. 45-48
P11	26	24,5 ± 4,9	Del. 45-48
P13	22	53,3 ± 5,3	Del. 45-48
P14	19	49,1 ± 2,5	Del. 45-51
P24	21	10,4 ± 2,2	Del. 14-15
P4	48	7,5 ± 0,8	Del. 45-47
P5	37	6,0 ± 1,1	Del. 45-47
P9	37	15,2 ± 4,5	Del. 45-47
P10	34	28,0 ± 6,4	Del. 45-48
P15	34	52,2 ± 2,5	Del. 45-51
P16	35	58,0 ± 5,1	Del. 48
P17	33	31,2 ± 4,5	Del. 48-56
P18	43	44,6 ± 3,0	Point mut. in Ex 13
P19	44	25,1 ±13,0	Del. 4
P3	61	7,0 ± 2,2	Del. 45-47
P8	62	23,6 ± 4,4	Del. 45-52
P12	70	38,5 ± 3,7	Del. 45-52

Conclusions: Our preliminary data suggest that MRI index is a useful tool in recognizing muscular involvement and quantifying the infiltration of fat on a muscular level in a totally automatic way and as an image analysis. Although our study sample is composed of patients of different ages and with different genotypes, this tool allowed us to stratify patients based on genotype and phenotype.

We also confirmed that younger BMD patients (<30 years) have rarely significant muscular impairment, since at a later age MRI-Index provided indications on clinical evolution. In our cohort at least, it seems that deletions involving exons 45-47 have a less severe muscle impairment.

To sum up, the MRI-Index can be a valid tool to detect muscle involvement and assist early genotype-phenotype correlations in NMD.