Combination of a fat volume fraction quantification method with a dedicated automatic segmentation algorithm for simultaneous measurement of infiltrated fatty tissue fraction and muscle relaxation times.

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Introduction: Due to its sensitivity to oedema, inflammation and fatty infiltration occurring in diseased muscle MRI is emerging as a suitable quantitative method that could provide reliable surrogate markers of disease severity and progression (1). In contrast to muscle biopsy, which provides anatomo-pathological information from a limited amount of superficial tissue, MRI offers a repeatable, non-invasive, whole-organ approach that should provide useful indices of muscle disease processes. Regarding the fatty infiltration commonly reported in diseased muscle, several approaches have been developed to distinguish intramuscular (IMAT) and subcutaneous adipose tissue (SCAT) (2,3). However, given that most of the analysis procedures were performed on T_1-weighted images, the corresponding results were not satisfactory. Dixon techniques providing information about the individual contribution of fat and water in each voxel have also been used but T_1 and T_2* relaxation times and complexity of fat spectrum may introduce quantitative biases (4). Advanced methods combining low flip angle and multiple gradient echoes acquisition with T_2* measurements and taking into account these confounding factors have been developed for quantitative purposes of steatosis (5). Nevertheless, these methods did not solve the dominant component ambiguity, which is a required condition for any quantitative application for skeletal muscle. Recently, complex based methods using T_2*-IDEAL fat/water separation algorithm have been introduced in order to resolve this ambiguity (6). The aim of this study was to evaluate a method combining a magnitude-based fat volume fraction (FVF) quantification method with a dedicated automatic segmentation algorithm in order to (i) distinguish IMAT and SCAT components, (ii) to measure muscle T_1 and T_2* relaxation times and to quantify the infiltrated fatty tissue fraction (IFTF).

Subjects and Methods: ***Subjects***: 9 healthy subjects (9 men; 35 ± 7.1 year-old; 74 ± 7.3 Kg) and 7 myopathic patients (3 women, 4 men; 50.1 ± 18.2 year-old; 70.4 ± 11.0 Kg) were included after their written informed consent was obtained. The protocol was approved by the Timone Hospital Ethics Committee. ***MR acquisition*****:** MR acquisitions were performed at 1.5 T (*Magnetom Avanto, Siemens Medical Solutions, Erlangen, Germany).* A FLASH 3D sequence was repeated three times with 5, 10 and 15° flip angles. Acquisition parameters were: 4 first Out-of-Phase (OP) echoes and 4 first In-Phase (IP) echoes; TR/TE = 22/n × 2.38 ms with n ranging from 1 to 8, 128 × 256 matrix; 180 × 360 mm^2 FOV; 454 Hz.pixel^{-1} bandwidth; 2 averages and 32 slices of 4 mm thickness in the axial plane. ***Images processing***: A quantification algorithm correcting for relaxation time effects using a disjointed estimation of T_1 and T_2^* relaxation times of fat and water, accounting for the NMR spectrum of fat and resolving the dominant component ambiguity led to seven parametric maps: a FVF map, a relaxation times (T_1 and T_2*) and proton density maps of fat and water respectively. Then, these maps were processed using an automatic segmentation algorithm in order distinguish SCAT, bone marrow fatty tissue, IMAT and muscular tissue. Using these segmentation masks on water relaxation time maps, histogram of relaxation-time values were computed on the segmented muscular tissue. On that basis, the infiltrated fatty tissue fraction (IFTF), *i.e.* the number of pixels included in the infiltrated pathologic fatty tissue class normalized by the number of pixel included in both infiltrated fat and muscular tissue classes, was quantified.

Results: In the control group, mean water relaxation times of muscular tissue were 1107 ± 67 ms and 29.2 ± 0.4 ms for T_1 and T_2*-values respectively. Mean IFTF was 4.8 ± 2.3 %. In the patient group, mean IFTF was significantly increased: 21.6 ± 9.3 %; $p<0.001$ with a large subjects variation, *i.e*. 43.2 %. Relaxation times were longer in the patients group: 1164 ± 98 ms and 31.4 ± 1.1 ms for water T_1 and T_2*-values respectively. Interestingly, in patients with high IFTF (> 18%), water relaxation times of muscular tissue were significantly longer as compared to the corresponding valued in the control group (1217 ± 58 ms; $p<0{,}05$ for T_1-values and 31.9 ± 0.7 ms; $p<0.01$ for T_2*-values).

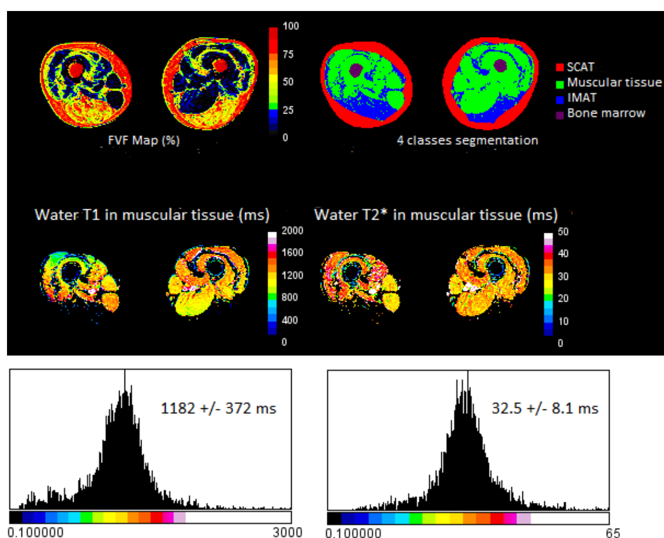

Fig.1 FVF maps computed from a 43 years-old man with myopathy and corresponding 4-classes segmentation. This mask was used to extract pixels included in the muscular tissue class from the water relaxation time maps (T_1 and T_2*). Histograms were computed and mean water relaxation times of muscular tissue were calculated.

Discussion: The method we described in the present study allowed the quantification of FVF in muscle taking into account confounding factors related to relaxation processes and fat spectral complexity. FVF quantification was possible on a 0 to 100 % range given that we solved the dominant component ambiguity problem, a mandatory step for the segmentation of pathologic fatty infiltration. Thanks to the four-classes segmentation, bone marrow, SCAT and IMAT were separated and justified the introduction of the IFTF parameter. The IFTF-values varied significantly between the patient and the control group and a large between subjects variation was quantified. On that basis, this index could be a relevant biomarker allowing to assess the severity of muscle diseases. Moreover, thanks to the disjointed estimation of water and lipids relaxation times, water relaxation times could be a good quantitative index of inflammation or oedema. Indeed, T_1 and T_2*-values were significantly longer in patients with high IFTF as compared to the control group. A limitation of this method was that T_1 estimation procedure was sensitive to the non-uniformity of the transmitted B_1 field as well as to the non-linearity of the radiofrequency transmission chain which may particularly affect the small flip angles. Further work will be devoted to the implementation of a flip-angle-mapping technique to improve T_1 measurement accuracy and to whole 3D volume segmentation.

References

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