Multiple parameter extraction and skeletal muscle characterization from a standard multi spin-echo sequence

Noura Azzabou[1,2] and Pierre G. Carlier[1,2]
[1]NMR Laboratory, Institute of Myolgy, Paris, France, [2]NMR Laboratory, CEA, I²BM, MIRCen, IdM, Paris, France

Introduction: Skeletal muscle structural changes can be characterized non-invasively and quantitatively by NMR imaging [1]. In general, several sequences, such as T2w SE, fat-satT2w SE, STIR, GE or SE Dixon are necessary to evaluate 1/ T2 relaxation abnormalities, 2/ fat fraction and 3/ signal heterogeneity, that respectively reflect muscle oedema and inflammation, fatty degenerative changes and muscle tissue disorganisation, in particular fibrosis [2]. Running several imaging sequences is time consuming, which can be a problem in a clinical context. In this work, we show that, using a standard multi spin-echo (MSE) sequence and a multi-exponential model, one can derive the three most relevant parameters needed to characterize a diseased skeletal muscle: muscle water T2s, muscle fat percentage and muscle water T2 heterogeneity.

Materials and Methods: The examinations were performed on a 3T TIM Trio system (Siemens Healthcare). Ten subjects with a variety of neuromuscular diseases (limb girdle muscular dystrophies, congenital myopathies, Charcot-Marie-Tooth disease, inflammatory myopathies) were routinely scanned and their data compared to data obtained in x healthy volunteers. Data Acquisition: The core sequence was a standard multislice multi-echo sequence, with a FOV of 22x44cm², voxel size of 1.4mm², and 11 slices of 10 mm thickness. The sequence was run with TR 3000 ms, nominal flip angles 90 and 180°, and a train of 17 echoes with TEs ranging from 9.5ms to 161ms. In addition, the transmit field spatial distribution (B1) was evaluated using an optimized version of the actual flip angle imaging (AFI) method [3]. For the purpose of validation, muscle fatty infiltration was also quantified using a three-point proton-density-weighted Dixon sequence [4] (TR: 10ms, TE1:2.75 ms, TE2:3.95 ms, TE3: 5.15 ms, flip angle: 3°). Data Processing: Thigh muscles were identified and ROIs drawn manually. Three class of parameters were computed from the MSE sequence, muscle water T2 and fat fraction from the tri-exponential model introduced in [5], as well as the standard deviation of water T2 values. The B1 map served to discard pixels out of the [90%-120%] range of the prescribed flip angle. Dixon based fat fraction maps were compared with the fat fraction map extracted from the MSE sequence.

Results: The three parameters that were extracted from the MSE sequence are presented in figure 1. Muscle water T2 of healthy volunteers was 36.4±0.88 ms when restricting flip angle deviation into the range of [90%-120%] from the nominal flip angle. Based on this, T2 values that were greater than 38ms were considered as abnormal. Fifteen % of the analysed muscles were abnormal in the patient population sample. There was no correlation between T2s and Dixon based fat fraction (R^2=0.06).

Regarding T2 distribution heterogeneity across voxels belonging to same muscles, standard deviation of T2s was 1.98±0.34 ms in normal subjects. In patients, 80% of muscles were above 2.6ms, the upper normal range limit. This was confirmed by non parametric statistical tests (Mann-Whitney Utest) ($p<0.0001$). Besides, There was no correlation between Dixon fat fraction and T2 heterogeneity (R^2=0.19).

The third parameter that was extracted from the MSME sequence was the fat fraction map (noted FF), for each region of interest we computed the mean value of the fat fraction and we derived its relationship to the Dixon based fat fraction (noted F_{dx}). To this end, we took into consideration two elements. First, due to the magnetization transfer process, the water signal is underestimated in the MSME sequence in multi-slice mode. Hence if m is the water attenuation coefficient we have $F_0 = \frac{mFF}{1-FF(1-m)}$ (1), where F_0 is the actual fat fraction. We estimated the m-value by measuring the water signal ratio between a multi-slice and mono-slice acquisition for a healthy volunteer and it was equal to 0.56. Second, Dixon-based fat quantification underestimates the fat signal because it accounts only for the methylene component in the triglyceride molecule in body fat. Knowing the fat spectrum and using numerical simulations, we derived a linear relationship between the actual fat signal and that measured by Dixon (where p is the coefficient and is equal to 0.68). Thus we have: $F_0 = \frac{F_{dx}}{(1-p)F_{dx}+p}$ (2). Hence, using relations (1) and (2) we computed F_0 values. Both measurement techniques were in agreement as shown in figure 3.

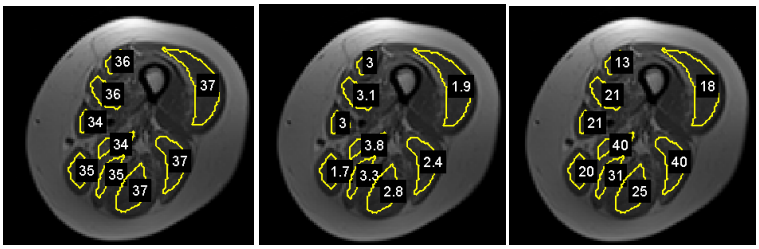

Figure 1: Parameters extracted from MSE sequence for each muscle of the thigh, from left to right. Muscle T2 values (ms) muscle T2 heterogeneity values (ms) and fat fraction (%).

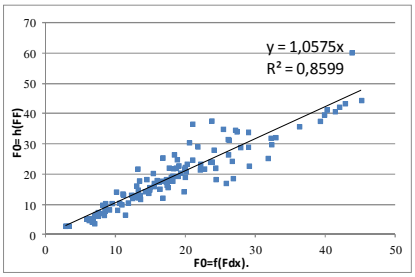

Figure 3: Relationship between fat fractions (F0) extracted from Dixon and from MSME.

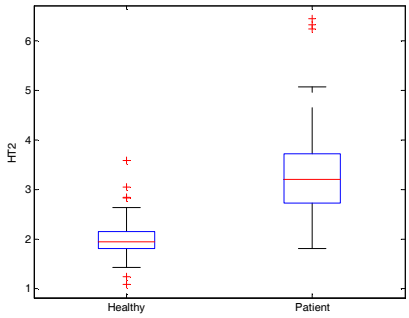

Figure 2: box plot of muscle T2 heterogeneities values ($p<0.00001$)

Conclusion: we showed here that using a MSE sequence only, one can extract several parameters: muscle water T2s, fat fraction and muscle T2 heterogeneity. The three classes were to a variable extent abnormal in the patient population sample analyzed. The poor correlation between these parameters suggests that they reflect different facets of muscle structural changes in diseases. The approach proposed here might be a simple, practical and time-saving alternative to skeletal muscle characterization by NMR imaging.

Bibliography: **[1]** Hollingsworth, KG. et al, Neuromuscul Disord, 2012 Suppl (2):S54-67, **[2]** Thibaud, JL. et al,Neuromuscul Disord,2007, 17(7): 575-584. **[3]** Yarnykh, YL. Magn Reson Med, 2007, 57(1):192–200. **[4]** Glover, GH. et al Magn Reson Med, 1991, 18(2):371-382. **[5]** Azzabou, N. et al, ISMRM, 2012.