Validation of a practical approach to muscle T2 determination in fatty-infiltrated skeletal muscles

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Introduction: Skeletal muscle water T2 increases in a variety of pathological conditions, hypoxia, necrosis, dystrophy, inflammation, hydrostatic oedema, and also after exercises of moderate to high intensity. While non-specific, muscle water T2 changes are nevertheless important to monitor because they convey relevant information on disease activity or on muscle physiological status. In the field of neuromuscular disorders, muscle water T2 measurement is proposed as a marker of disease progression and also of response to treatment. However, in chronically affected muscles, fatty degenerative changes complicates the situation. Because of the long T2 of fat as compared to T2 of normal muscle tissue, monoexponential fits of non-fat-supressed echo trains will result in "muscle" T2 determination that reflect the degree of fat infiltration only [1,2]. Possible underlying alterations of muscle water T2 will be masked and the resulting T2 information will just be redundant with the fat fraction calculated from Dixon images. Selective water excitation or fat suppression are possible solutions, but only for small segments where sufficient Bo homogeneity can be achieved. In addition to the fat infiltration problem, B1 field inhomogeneities, increasingly challenging at higher field, render T2 determination hazardous in regions where the actual flip angles deviate from the prescribed ones. New approaches, that are not based on multiple echo trains such as T2-SSFP, are promising but still at an exploratory stage. Here, we propose and validate a practical solution for accurate muscle water T2 determination that is based on voxel selection using B1 mapping and on fatty components deconvolution and substraction in fat unsuppressed multiple echo series of lower limbs of patients.

Materials and Methods: All examinations were performed on a 3T whole-body Siemens Trio Tim scanner, with the body transmitter coil and two phased-array receiver coils covering the entire lower limb. Ten patients with a variety of neuromuscular diseases (limb girdle dystrophies, congenital myopathies, Charcot-Marie-Tooth disease, inflammatory myopathies) were selected and their thigh and leg data retrospectively analyzed.
Data acquisition and registration. For muscle T2 determination, a standard multislice multi spin echo (MSME) sequence was used with a TR of 3000ms, nominal flip angles of 90 and 180°, and a train of 17 echos with TEs ranging from 9.5 ms to 161 ms. Tri-dimensional maps of B1 transmit field were generated with a dual TR sequence and acquired two 3D volumes (TR1+TR2=100ms, TR2 =5TR1, TE=2.75 ms nominal flip angle :60°).
In addition, muscle fatty infiltration was quantified using a 3D 3 point Dixon sequence (TR:10ms, TE1:2.75 ms, TE2:3.95 ms, TE3: 5.15 ms, flip angle:3°). The B1 transmit and fat fraction maps were registered with the MSME volumes and ROIs were drawn on both thigh and leg muscles.
Voxel sorting. Bias induced by stimulated echos owing to absence of optimized crusher gradients on the vendor MSME sequence were minimized by eliminating voxels having experienced nutations too different from those prescribed. Preliminary measurements in normal subjects showed that retaining voxels with actual flip angles comprised between 90 and 120° was the best compromise between T2 exactitude and investigated muscle volume fraction.
Mono versus multi-exponential model of muscle T2. In standard non-chemically selective imaging, muscle signal must be considered as the combination of at least two components: fat and water. Different models were compared and the most robust -best fit with a minimum number of variables- was the following $S(TE) = A_f\left[c_l.\exp\left(-\frac{TE}{T2_{fl}}\right) + c_s.\exp\left(-\frac{TE}{T2_{fs}}\right)\right] + A_m\left[\exp\left(-\frac{TE}{T2_m}\right)\right]$ (1) with $T2_{fl}$ and $T2_{fs}$, respectively long and short T2s of the fat component, $T2_m$, the muscle water T2 and A_f,A_m, c_l and c_s, the coefficients that reflect the proportion of each component in the collected signal. Parameter estimation was performed in two steps. First, we segmented the subcutaneous fat and analyzed the signal decay of pure fat. Using a non-linear fitting approach, we calculated $T2_{fl}$, $T2_{fs}$, c_l and c_s. Using these fat parameters, we modeled the signal decay for each muscle ROI using equation (1) and we estimated $T2_m$, A_m and A_f.
Muscle water T2s obtained with the tri-exponential deconvolution were compared with muscle T2s obtained by mono-exponential fitting. In order to evaluate the sensitivity of the methods to fat infiltration, T2 values of voxels containing 0-20% fat signal fractions were confronted to T2 values obtained in voxels with 20-50% fat signal fraction.
We also computed, for both models, T2 values with all the pixels in the region of interest regardless of their fat infiltration ratio, and we classified the muscles into two groups based on the tri-exponential deconvolution results. We distinguished two groups: normal muscles with (T2 < 38ms) and abnormal muscle (T2>38ms). Finally, the impact of fat infiltration on T2 determination for each method was evaluated by plotting the relation between the measured muscle T2 and fat signal fraction calculated from the Dixon sequences.

Results: In our view, adequacy of the proposed fat deconvolution algorithm can best be demonstrated if the calculated muscle water T2 becomes independent of the fat proportion in muscle ROI voxels . The voxels of each ROI were sorted according of their fat signal fraction, from 0 to 20% in one class, from 20 to 50% in the other class. The estimated T2m was identical in the two classes, both in muscles classified as normal and abnormal. In contrast, with the mono-exponential approach, the estimated T2m was not only abnormally high (>70ms), it was also heavily dependent on the degree of fat infiltration ($p<0.0001$). The T_{2m} values obtained for pixels with fat ratio ranging between [20%-50%] was 19% higher than those with fat fraction between [0%-20%] in "abnormal muscles" and 25% higher in normal muscles ($p<0.0001$). Also, the T_{2m} values calculated by the mono-exponential model were highly correlated with the fat signal fraction, with $r^2 = 0.9$ for normal muscles and $r^2=0.84$ for abnormal ones. The tri-exponential method, was insensitive to fat infiltration, with no correlation either in normal ($r^2=0.0006$) or in abnormal muscles ($r^2=0.07$). Finally, it is important to point out that for equivalent fat content, the muscles classified as "abnormal" with the tri-exponential method, also had higher T2 values than "normal" muscles using the mono-exponential method suggesting that the difference was real but masked by the fat infiltration.

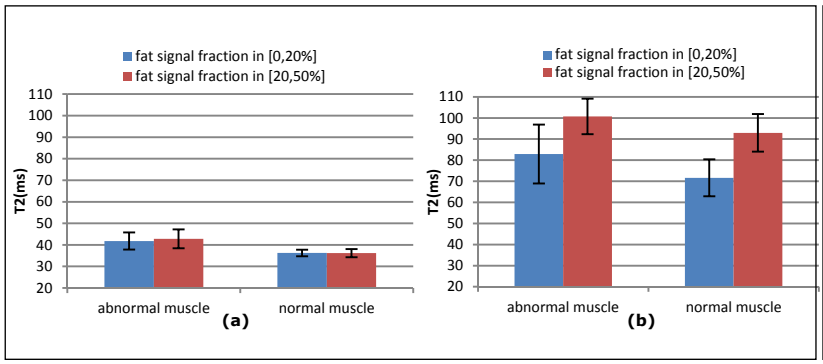

Figure1: Muscle T2 in voxels with different fat signal fraction calculated from **(a)** tri-exponential model **(b)** mono-exponential model.

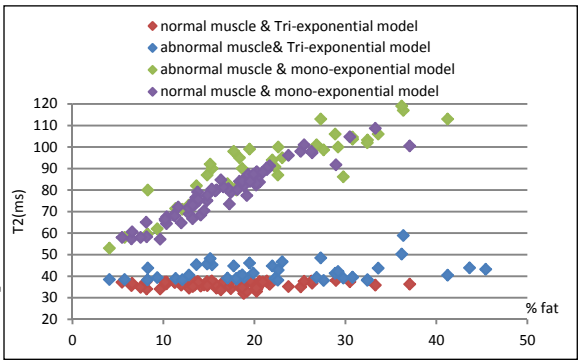

Figure2: T2 values variation with respect to fat signal fraction inside the muscle.

Conclusion: Standard MSME sequence associated with voxel sorting based on B1 mapping and signal deconvolution with a tri-exponential model is a simple, pragmatic approach to muscle water T2 determination in fatty infiltrated muscles. Robustness against the degree of fat infiltration was demonstrated.

Bibliography

[1] Garrood P et al, Journal of Magnetic Resonance Imaging, 2009 Nov; 30(5):1130-8. [2] Kim HK, et al. Radiology. 2010 Sep;256(3):1016