T_2 based analysis of fat infiltration in muscular dystrophy using quantitative, sub-voxel estimation of fat and water fractions

Jannette Nassar[1], Dvir Radunsky[1], Noam Omer[1], Yann Le Fur[2], David Bendahan[2] and Noam Ben-Eliezer[1,3]

[1]Department of Biomedical Engineering and Sagol School of Neuroscience, Tel Aviv University, Tel Aviv, Israel; [2]Aix Marseille University, CNRS, CRMBM, Marseille, France;

[3]Center for Advanced Imaging Innovation and Research, New York University, New York, NY, USA

1. Introduction

- T_2 relaxation time is a highly efficient biomarker of muscle health, being sensitive to both macro- and microstructural changes in muscle tissues, which can be caused by various muscle dystrophies, inflammatory processes, or neuromuscular disorders[1,2].
- These diseases result in an infiltration of subcutaneous fat and a corresponding loss of muscle volume, leading to a mixture of two tissue types, fat and muscle, and results in the appearance of two T_2 components in each imaged voxel.
- Quantification of these fat and water components holds great diagnostic and prognostic value by allowing an accurate assessment of the muscle status and the stage of the disease.
- Achieving a reliable quantification of single- T_2 values in clinical setting is a challenging task due to the bias of fast Multi Spin-Echo (**MSE**) protocols by stimulated and indirect echoes[3]. The Echo-Modulation-Curve (EMC) algorithm[4,5] can overcome these limitations and deliver accurate and reliable maps of the true tissue T_2 values, independent of the scanner and protocol-implementation[6].
- **In this work**, an extension of the EMC algorithm for two-component fitting is presented, simultaneously estimating sub-voxel water and fat fractions, along with the T_2 and Proton Density (PD) corresponding to each component.

2. Methods: EMC Algorithm

- **Data acquisition**: The calf muscle of a healthy volunteer and a patient with Dysferlinopathy was scanned on a whole-body 3T Siemens Prisma scanner using a standard MSE protocol.
- **Data postprocessing**: Bloch simulations of the MSE protocol were performed using identical scan parameters. Simulations were repeated for a range of T_2 [ms] and B_1^+ inhomogeneity values [%], producing a database (DB) of EMCs, each associated with a unique $[T_2, B_1^+]$ value pair ($\mathbf{DB_{water}}$). A similar DB was created for the fat signal by repeating this process at 3.5 ppm off-resonance ($\mathbf{DB_{fat}}$).
- **Generation of quantitative maps**: Water T_2, fat T_2, and water fraction (f_{water}) maps were generated on a pixel-by-pixel basis by matching the experimental MSE time-series to the simulated EMCs, calculated as the weighted sum of two decay curves:

$$\mathbf{EMC_{experimental}} = \mathbf{f_{water}} \cdot \mathbf{EMC_{water}} + (\mathbf{1} - \mathbf{f_{water}}) \cdot \mathbf{EMC_{fat}}$$

- Matching was done via l2-norm minimization of the difference between experimental and theoretical EMCs over the range of simulated $[T_2^W, T_2^F, B_1^+, f_W]$ values.

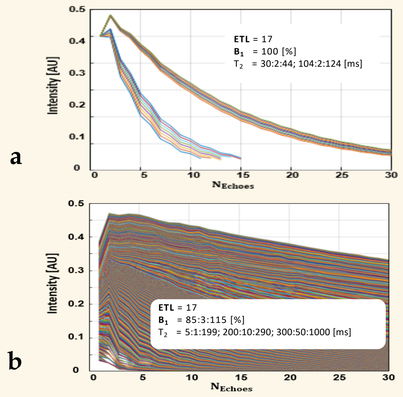

Figure 2: (**a**) Example of 20 simulated EMCs for a range of T_2 values and a single B_1 scale. (**b**) Actual EMC database, consisting of ~5000 simulated EMCs, each corresponding to a unique (T_2,B_1) value pair.

Signal differences between the fat and water EMCs

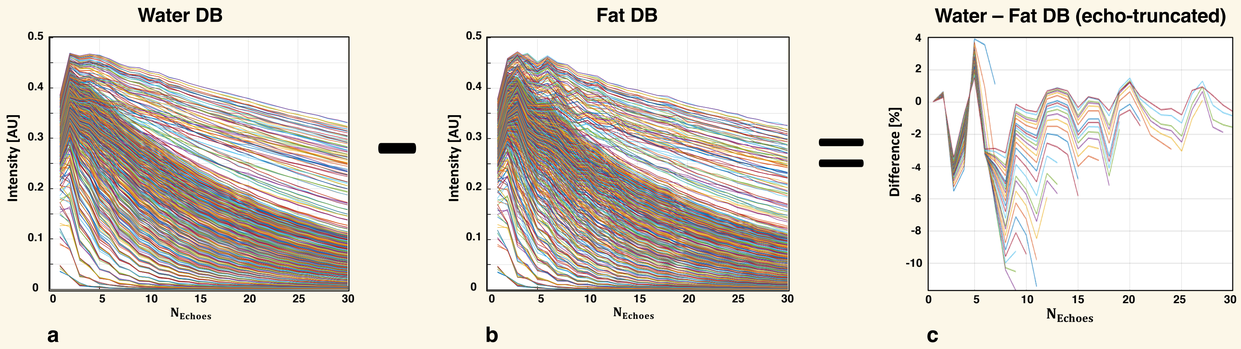

Fig. 1 shows the signal differences between the fat and water EMCs. (**a**) and (**b**) show a sparse water and fat DB, respectively. Each EMC in the presented DBs corresponds to a specific $[T_2, B_1^+]$ pair. (**c**) shows the normalized difference between the DBs; EMCs with a signal intensity below a certain threshold (10%) were truncated.

3. Results

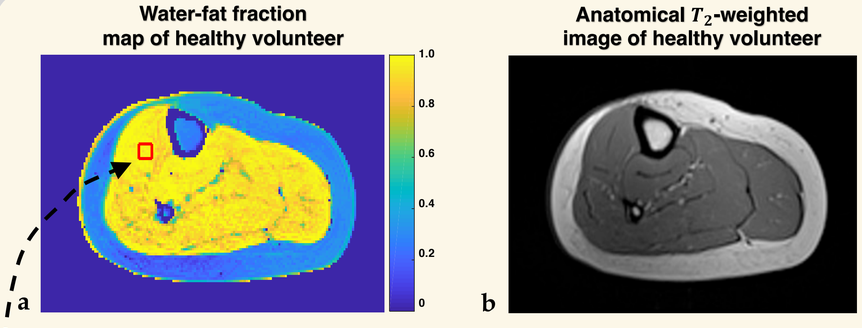

Figure 2. Axial slice of a calf muscle from a healthy volunteer (**a**) Water-Fat fraction map; ROI in red with mean water fraction = 0.97 ± 0.02, mean water T_2 = 28.37 ± 1.17 ms, mean fat T_2 = 135.47 ± 31.29 ms. (**b**) Anatomical T_2 -weighted image. Values match those reported in literature[7].

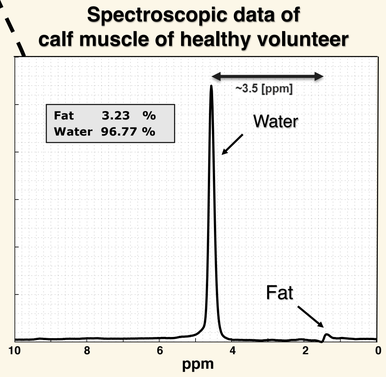

Figure 3. Spectroscopic data from a calf muscle of the same healthy volunteer. SVS of a muscle voxel produced 96.77% water and 3.23% fat, calculated based on [8].

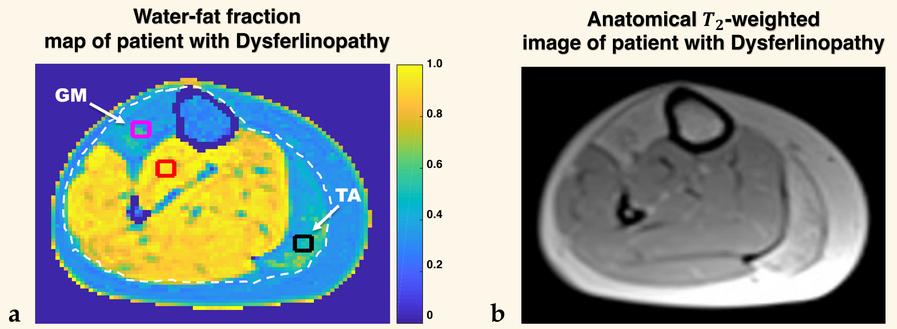

Figure 4. Axial slice of a calf muscle from a patient with Dysferlinopathy (**a**) Water-Fat fraction map; healthy (**red**) muscle ROI with mean water fraction = 0.92 ± 0.04; diseased medial gastrocnemius muscle region (**magenta**) with mean water fraction = 0.42 ± 0.09; diseased tibialis anterior muscle region (**black**) with mean water fraction = 0.48 ± 0.06. (**b**) Anatomical T_2 – weighted image.

- The fat-infiltrated muscle regions are indicated with arrows: The Medial Gastrocnemius muscle (GM) and the Tibialis Anterior muscle (TA).

4. Conclusions

- The ability to quantify sub-voxel tissue components is highly valuable for clinical applications.
- The extended EMC algorithm allows to quantify the relative fraction (i.e., proton density) of two decaying components, while at the same time probe changes in their corresponding T_2 values. This can improve the diagnosis and prognosis of pathologies in muscle and various other organs.
- The framework allows to separately track changes in the water and in the fat components.
- An appealing feature of this approach is that it employs a standard MSE protocol scheme, making it readily available on any clinical or animal scanner.
- EMC based quantitative maps are invariant across vendors, scanners and scan settings.

5. References

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