Quantification of Fat Infiltration in Thigh and Calf Muscles in Oculopharyngeal Muscular Dystrophy: Comparison of Three MRI Methods

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Introduction. Oculopharyngeal muscular dystrophy (OPMD) is an autosomal-dominant muscle disorder of adult onset, which appears in individuals with a mutation on the nuclear poly(A) binding protein (PABN1) gene [1]. OPMD is characterized by bilateral, progressive muscle weakness, muscle fiber necrosis and muscle infiltration by fatty tissue. The development of non-invasive measures of the degree and progression of muscle involvement is essential for clinical trials. In this study, three quantitative measures of muscular fat infiltration are compared. The measures are evaluated with regard to applicability for longitudinal studies of the pattern and involvement of fat infiltration in OPMD patients.

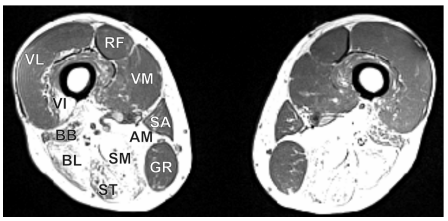

Fig. 1: Exemplary T_1-weighted images of thigh muscles of an OPMD patient. Abbreviations: AM: adductor magnus, BB: biceps femoris caput breve, BL: biceps femoris caput longum, GR: gracilis, RF: rectus femoris, SA: sartorius, SM: semimembranosus, ST: semitendinosus, VI: vastus intermedius, VL: vastus lateralis, VM: vastus medialis.

Methods. 8 patients with OPMD (age range 41 - 76 years, mean 61.5 ± 10.7 years, 6 female, 2 male) were recruited. Written informed consent was obtained from all patients and the measurements were approved by the local ethics committee. All experiments were performed on a 1.5 T scanner with a 16-element matrix coil. For imaging, a 384×384 matrix was used yielding 1 mm in plane resolution with 3 mm slice thickness. Two axial slice groups were chosen at predefined distances from the knee joint, one in the thigh and one in the calf. A T_1-weighted turbo spin echo (TSE) sequence (30 slices, TR = 457 ms, TE = 7.5 ms, bandwidth = 343 Hz/pixel) was used for anatomical reference (Fig. 1). Two gradient echo sequences with different TE for in-phase and out-of-phase imaging were acquired (3D, 30 slices, TR = 20 ms, TE_1 = 2.38, TE_2 = 4.76 ms, flip angle = 25°). T_2 quantification was based on a multi-contrast TSE sequence (3 slices, TR = 1330 ms, TE = 10 ms, 20 ms,..., 320 ms). Finally, the TR and flip angle of an FID steady-state free precession (SSFP) sequence were optimized to yield maximal fat-muscle contrast (3D, 52 slices, TR = 6.92 ms, TE = 3.46 ms, flip angle = 50°, bandwidth = 343 Hz/pixel). The protocol was completed within 20:44 min including thigh and calf.
Regions of interest (ROI) were drawn in thigh (Fig. 1) and calf muscles avoiding areas of chemical shift artifact. Water and fat images and hence the relative fat fraction were calculated based on the in-phase and out-of-phase images according to the 2-point Dixon method [2]. T_2 relaxation times were calculated from an pixel-by-pixel monoexponential fit of the echo points from 20 ms to 320 ms. The SSFP fat fraction was estimated from a histogram analysis of signal intensity.

Results. Figure 2 shows the results from linear regression analyses between measures in 22 (11 left and 11 right) thigh muscles for 8 patients. A very high linear correlation is observed between fat infiltration according to the 2-point Dixon method and quantitative T_2 values (R^2 = 0.95, Fig. 2a). Fat infiltration according to SSFP histogram analysis exhibit a lower linear correlation with T_2 values (R^2 = 0.88, Fig. 2b). Mean fat fractions over left/right side and all muscles for every patient (Fig. 3a) clearly illustrate that patients 2, 4 and 5 are most affected by fat infiltration, independent of the quantification method. For all patients, mean fat fractions (2-point Dixon) over left/right side for every thigh muscle are plotted in Fig. 3b. The data suggest that fat infiltration is highest in adductor magnus (AM), semimembranosus (SM), biceps femoris caput longum (BL) and semitendinosus (ST) muscles. Fat infiltration in the calf muscles will be analyzed likewise.

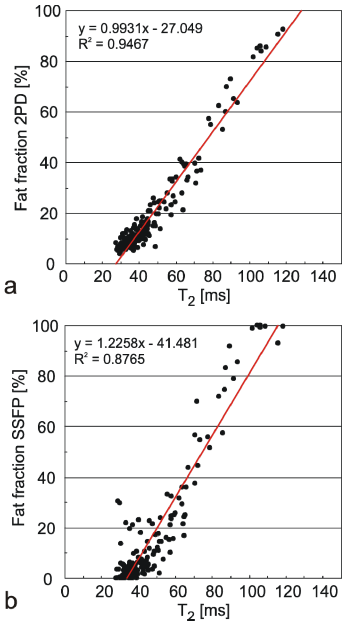

Fig. 2: Linear regression with Pearson's correlation coefficient of fat fractions according to the 2-point Dixon (2PD) method (a) and fat fractions according to SSFP histogram analysis (b) with T_2 relaxation times in 22 thigh muscles for 8 OPMD patients.

Discussion & Conclusion. This work demonstrates that non-invasive quantification of fat infiltration in OPMD patients can be performed with either T_2 values or the 2-point Dixon method and may serve as a baseline to study the pattern and involvement of fat infiltration longitudinally. SSFP-based quantification benefits from halved acquisition times and higher SNR as compared to the other methods. However, accuracy of quantification based on pure signal intensity maps, as shown here, is limited by field inhomogeneities. On the other hand, traditional T_2 measurements are limited by the fact that only a few slices can be imaged within a reasonable time frame. Therefore, Dixon or fast T_2 mapping techniques, which cover 3D volumes, may be favorable for longitudinal studies.

References. [1] Brais B et al., Nat Genet **18**:164-167 (1998); [2] Dixon WT, Radiology **153**(1):189-194 (1984)

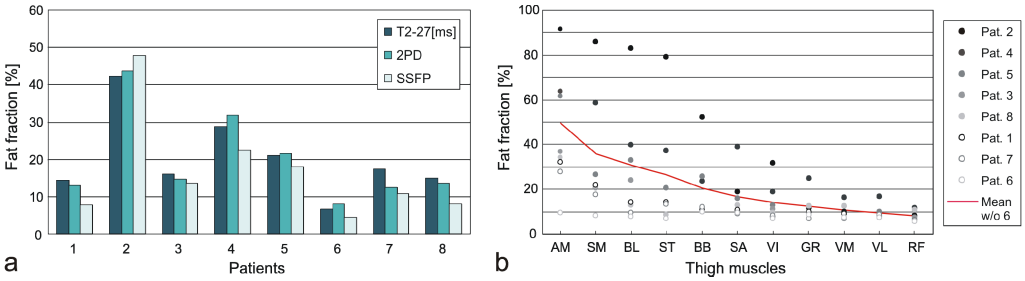

Fig. 3: (a) Mean fat fractions over left/right side and all muscles for 8 OPMD patients using T_2[ms]-27ms according to the linear regression (Fig. 2a), 2-point Dixon (2PD) and SSFP. (b) Mean fat fractions over left/right side for every thigh muscle of all patients using 2-point Dixon. Darkest filled circles represent most affected patients, open circles represent least affected patients. The least affected patient (Pat. 6) was excluded from the mean fat fraction (red line).