Candidate skeletal muscle outcome measures for therapy trials: dependence of MRI measures upon age, gender and weight
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Purpose: Quantitative skeletal muscle MRI offers strong candidate outcome measures for imminent therapy trials in neuromuscular diseases such as inclusion body myositis or limb girdle muscular dystrophy. Muscle fat content, which reflects chronic pathology, can be measured using the 3-point Dixon fat/water separation method [1,2], and more acute muscle water changes can be examined with T2-relaxometry [1] or magnetisation transfer (MT) imaging [3]. The dependence of these measures upon age, gender or body habitus is a key factor in assessing their suitability as outcome measures. We aimed to investigate these dependencies in the thigh and calf-level muscles of healthy volunteers.

Methods: With ethical approval and consent 47 healthy volunteers, 23 male, ages (mean ± s.d.; range) 44.4 ± 17.0y; 21.5-81.0y, weight; 44-115kg. Thigh- and calf-level lower limb imaging was performed at 3 Tesla (Siemens TIM Trio) feet-first supine with surface matrix coils and field of view (FOV) 400x200mm (thighs) and 400x188mm (calves). The 9-point Dixon technique (2D GRE, TR/TE1/TE2/TE3=100/3.45/4.60/5.75ms, flip angle α =10°, NEX=4, 512x256 matrix 10x10mm slice, 10mm gap) was used to generate water (W) and fat (F) images according to [4] and fat-fraction (F.F.) maps calculated as F.F. = 100% x F/(F+W). Pseudo-T2 maps were (M)MR parameters as outcome measures in neuromuscular diseases.

Results: Multivariate regression analysis of demographic parameters and mean quantitative MRI parameters in thigh and calf of healthy volunteers is summarised in the table. Mean muscle F.F. correlated with age in both thigh and calf. In the thigh but not calf F.F. correlated with weight.

Discussion: This is the first study to investigate the influence of demographic parameters on lower-limb muscle Dixon F.F. measures and thigh-muscle T2 and MTR. T2-age and MR-age correlations in the calf are consistent with previous findings [7,8]. As might be expected, muscle fat fraction increases with age, but the magnitude is small. The FF values for a 20 vs. 80 year old were approximately 1% vs. 2%; changes due to healthy ageing are therefore negligible compared with expected disease effects, an important factor in longitudinal patient studies. It is also notable that the weight influence all three measures in the thigh but not calf, suggesting differential weight gain responses. The negative correlation between MTR and age (Figure 2) was strongest suggesting a marked change in the free-water/macromolecule-bound proton pool exchange conditions with age.

Conclusions: These data describe the influence of key demographic factors on quantitative MR indices in skeletal muscle. That the magnitudes of the variations were small compared with expected pathological changes, strengthens the potential utility of quantitative MR parameters as outcome measures in neuromuscular diseases.