Fat infiltration in Duchenne muscular dystrophy: quantification on T1-weighted images for steroid-treated DMD boys and control subjects

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Introduction

Duchenne muscular dystrophy (DMD) is a genetic disorder affecting males characterised by progressive muscle weakness and wasting due to muscle fibre necrosis and replacement by fat and connective tissue. With appropriate medical management, including use of corticosteroids, spinal surgery, and treatment of respiratory and cardiac complications, the mean age of death in the North East of England is now around 28 years[1]. Previous studies have investigated the degree of fat infiltration in DMD muscle using visual assessment of T1-weighted images[2,3] or by quantitative measurement of T1[4] or T2[5] values for defined regions of interest (ROIs). Increasing fat content gives rise to increasing signal intensity on T1-weighted images. To date, there is no published MRI work on the degree and pattern of muscle involvement in boys treated with steroids, which is the current standard therapy. Furthermore, with several promising new therapies for DMD reaching the stage of clinical trials, there is an urgent need for the development of quantitative non-invasive measures of the degree and progression of muscle involvement for use in future clinical studies. This work evaluates the use of signal intensity of muscle ROIs on T1-weighted images for the quantitative investigation of fat infiltration in DMD.

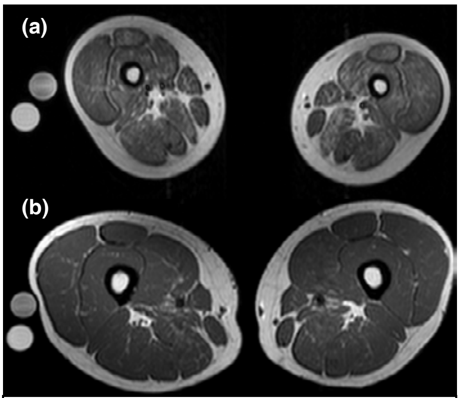

Fig 1 : T1w images of thigh muscles for (*a*) DMD subject and (*b*) control adult. Elevated signal intensity is found in most muscle groups.

Methods

Recruitment: 8 boys with DMD (age range 6.63 - 9.91 years, average 8.52 years) and 5 healthy male adult volunteers (29.58 – 34.99 years, average 33.22 years) were recruited. The boys' families were initially approached at their routine clinic visits and consent was taken after a home visit to further discuss the study. Adult control volunteers were recruited from research staff at the Institute of Human Genetics, International Centre for Life. One child was unable to complete the scanning protocol and was excluded from the analysis. A favourable opinion was obtained from the local Research Ethics Committee prior to commencement of the study.

MR protocol: All scans were performed on a 3T Philips Achieva scanner (Best, NL) using the in-built body r.f. coil for transmission and reception. Axial T1w images of the musculature from the ankles to the iliac crest were acquired using a turbo spin echo sequence (TSE factor 3, low-high profile order, TR/TE/NSA = 671/10/2, slice thickness/gap = 5 mm/10 mm, 256 x 192 matrix interpolated to 512 x 384, bandwidth/pixel = 438 Hz). The children were scanned using a field of view of 380mm and 3 stacks of 16 slices, the adults were imaged with an FOV of 410mm and 6 stacks of 16 slices. Images were analysed by using MRIcro[6] on a standard desktop PC to draw regions of interest outlining the tibialis anterior, medial and lateral gastrocnemii, biceps femoris (long and short heads), rectus femoris, gracilis, and gluteus maximus muscles bilaterally. A single slice at mid-calf level was used for delineation of the tibialis anterior and gastrocnemii. In the adults, a single slice at mid-thigh was used for assessment of all thigh muscles, but in the children it was usually necessary to consider 2 adjacent slices – one for the biceps femoris and the next slice proximally for the rectus femoris and gracilis. A single slice at mid-pelvis was used for assessment of the gluteus maximus. Conservative ROIs were drawn avoiding areas of chemical shift artefact and blood vessels at the margin of muscles. A phantom tube containing sunflower oil was positioned in the FOV as an intensity reference. The ROI signal intensities were expressed as a percentage of the phantom intensity in that slice. For each muscle the left and right percentage intensity averages were combined and a Mann-Whitney (SPSS v13) test was used to determine the significances of differences between the signal intensities of the adults and children.

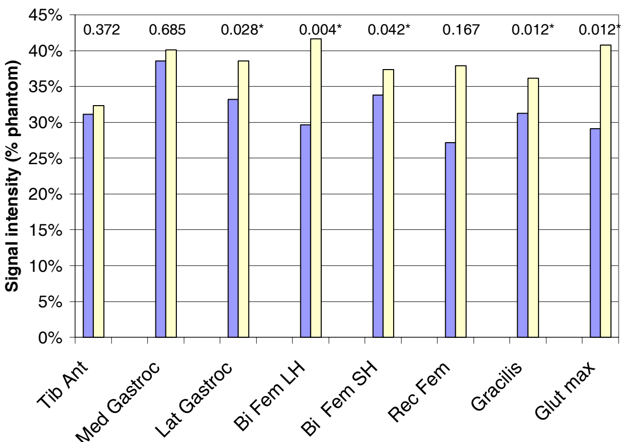

Fig 2 : Signal intensity as a % of phantom intensity for adult controls (blue) and DMD boys (yellow). The significance of the difference is given above.(* $p < 0.05$ with Mann-Whitney test)

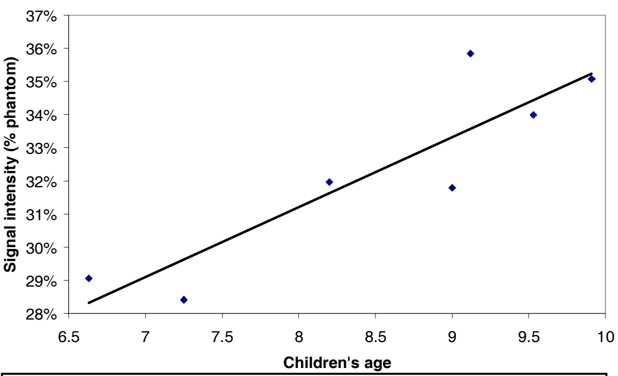

Fig 3 : Correlation between decimal age of DMD boys and signal intensity observed in tibialis anterior (rho = 0.82, p = 0.012)

Results

The degree of fat infiltration on visual assessment of the images varied between individual DMD boys, but for all muscles studied, the mean signal intensity, referenced to the phantom, was greater for the children than for the adults (figures 1 & 2). This did not reach statistical significance for all muscles. A significant difference was found for the lateral gastrocnemius, biceps femoris (both long and short heads), gracilis and gluteus maximus muscles. This is broadly in line with previous MRI observations in DMD that the gluteii are affected early, followed by the adductor and biceps femoris muscles of the thigh and that in the lower leg, the gastrocnemii are affected before other muscle groups. The degree of involvement of gracilis was surprising, however, in that this muscle has previously been described as being relatively spared until the later stages of the disease[2,4]. The difference in signal intensity for rectus femoris was not significant due to two children having percentage signal intensity values below that of the adults. There were correlations between the percentage signal intensity for tibialis anterior (Spearman-rho 0.82, p = 0.012, figure 3) and biceps femoris short head (rho = 0.68, p = 0.047) versus decimal age in the DMD group. In the adults, as expected, no such age-related correlations were found.

Conclusions

This work shows that it is possible to use a relatively simple analytical technique to quantify fat infiltration in dystrophic muscle. The small number of current participants and the degree of interindividual variation means that not all affected muscles necessarily show a significant difference from controls. Further participants will be recruited and future work will include assessment at multiple levels through the muscles and consideration of other muscle groups. The change in fat infiltration in individuals over two years will be investigated, in conjunction with the change in boys' muscle strength and functional test scores.

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