Quantitative assessment of the inter- and intra-muscle fat fraction variability in Duchenne muscular dystrophy patients

B. Wokke¹, J. van den Bergen¹, A. Aartsma-Rus², A. Webb³, J. Verschuuren¹, and H. Kan³
¹Neurology, Leiden University Medical Centre, Leiden, Netherlands, ²Human genetics, Leiden University Medical Centre, ³Radiology, Leiden University Medical Centre

Introduction: Duchenne muscular dystrophy (DMD) is an X-linked recessive disease characterized by progressive muscle weakness. In young patients the weakness predominates in the pelvic girdle and upper leg and eventually becomes more generalized leading to wheelchair dependence in patients’ early teens and death in their late twenties. Regular T1-weighted MR imaging of the muscles shows increased fatty infiltration with age, with some muscles being earlier and more severely affected at an earlier stages of the disease³. With the recent development of potential therapies for the disease²,³, interest in non-invasive methods for longitudinal follow up has increased. A promising method is the 3-point Dixon technique⁴ which can be used for quantitative evaluation of the fat fraction in the muscle.⁴ For this technique to be used in therapy evaluation, a quantitative and detailed overview of the natural history and variability of the disease is very important. In this study, we aimed to quantitatively assess the variation in fat fraction between and within muscles in DMD patients from 8–13 years of age.

Methods: Ten DMD patients (age 10.5 ± 2.5 years) and eight healthy age-matched controls were scanned on a 3T Philips Achieva Scanner (Best, NL). The scanning protocol consisted of a T1-weighted (twenty five 5 mm slices, 0.5mm gap, TR 600, TE 16) and a 3-point Dixon scan with multipeak reconstruction⁵ (twenty five 5 mm slices, 0.5mm gap, TR 400, TE 4.41, FA 8°) for both the upper- and the lower leg. Regions of interest (ROIs) were manually drawn on the co-registered T1 images in the muscles in the 12 central slices in the upper- and the 10 central slices in the lower leg using MIPAV.¹³ Fat fraction was obtained as SIfat/[(SIfat+cSIwate)], where the factor c corrects for the differences in proton density and T2 relaxation effects⁶. Seven muscles were analyzed in the lower leg (medial gastrocnemius, lateral gastrocnemius, soleus, anterior tibialis, extensor digitorum longus, peroneus and the posterior tibialis) and eleven muscles in the upper leg (rectus femoris, vastus lateralis, vastus intermedius, vastus medialis, biceps femoris short and long head, semitendinosus, semimembranosus, adductor magnus, gracilis and sartorius muscle). For each muscle, fat fractions were correlated with age and approximated with linear regression to obtain an overview of the rate of fatty infiltration per muscle. Additionally, the variation between the fat fraction in the two most proximal and two most distal slices were compared with a paired t-test.

Results: All controls and nine patients completed the protocol successfully, in one patient only the lower leg was scanned because the patient could not be positioned comfortably. In the upper leg all muscles in all patients were clearly affected (fig.1) with fat fractions ranging from 5.5% to 92.5%. Interestingly, the semitendinosus, gracilis and sartorius muscles were relatively spared in the younger patients. In the lower leg fat fractions ranged from 3.7% to 76.5% and were lowest in the posterior tibialis and highest in the peroneus muscle (fig.2). Linear regression of the data showed that the peroneus muscle increased with 14% per year (R²=0.87) while the posterior tibialis muscle only increased with 5.6% per year (R²=0.74). In addition to differences between muscles, variation in fatty infiltration within muscles was also present. In the medial and lateral gastrocnemius differences up to 3%, and in the anterior and posterior tibialis muscle differences up to 18% were observed between the most distal and most proximal slices. In the gastrocnemius the fat fraction was higher in the distal slices than in the proximal ones, however in the tibialis muscles the fat fraction was higher in the proximal than in the distal slices. In healthy controls there was a significant difference in the medial and lateral gastrocnemius muscle as well. However, this difference was in opposite direction with a higher fat fraction in the proximal slices.

Conclusion: In this study we carried out a detailed and quantitative overview of fatty infiltration in 18 different muscles in the legs of DMD patients. In agreement with previous qualitative methods¹⁰, a large variation is present in the amount of fatty infiltration between the various muscles in DMD patients, especially in the early stages of the disease. Our quantitative analysis shows differences in the rate of fatty infiltration between different muscles. We approximated the increase in fatty infiltration with linear regression due to the relatively low number subjects in our study, however the increase is likely to be sigmoidal. We also observed differences in the fat fraction between the distal and proximal regions of the same muscles which, to our knowledge, has not been reported before. If the amount of fatty infiltration is used as a method for quantitative therapy follow-up in DMD patients, it is not feasible to analyze all muscles. Our study suggests that analyzing only the most affected, such as the peroneus muscle and the least affected muscle, the posterior tibialis, might provide sufficient information to evaluate the disease process. Nevertheless the variation between the distal and proximal slices, as observed in several muscles, underlines the importance of analyzing multiple slices.

References