Evaluation of skeletal muscle DTI in Duchenne Muscular Dystrophy

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Purpose: To evaluate the effects of SNR, T2 relaxation time and fat percentage on skeletal muscle DTI in patients with Duchenne Muscular Dystrophy (DMD) in assessing muscle fiber organization compared to healthy controls.

Introduction: Recently, diffusion tensor imaging (DTI) measurements have become popular for assessing skeletal muscle fiber architecture in healthy and diseased/damaged conditions. (1-4) However, from simulation based measurements it is known that the reliability of estimating DTI parameters in muscle tissue is highly affected by SNR and the percentage of fat in a particular voxel. (5-7) As fat infiltration, and associated changes in mean T2 (fat+ water), are part of the pathophysiological process in the muscles of patients with DMD, they could therefore directly affect the quality and reliability of DTI measurements in this population, and obscure the actual pathophysiological effect on the measured DTI-parameters. (8)

Methods: Multi-contrast MR images of the right lower leg were acquired in 21 DMD patients (5-16 years) and 12 age-matched healthy controls (5-14 years) using a 3T MR scanner (Ingenia, Philips Healthcare, Best, the Netherlands) with a 32-element receive coil. The MR examination contained DTI measurements (TR/TE 2990/49ms; number of signal averages 6; b-value 0,450 s/mm^2; voxel size 2x2x6mm; no gap; 12 slices; SPAIR fat suppression on the aliphatic fat and selective suppression of the olefinic fat), SE-EPI acquisition for SNR assessment (TR/TE 3020/49ms; NSA 6; b-value 0s/mm^2; 10 dynamics), T1w images for anatomical reference (TR/TE 630/30ms; voxel size 1.5x1.5x6mm; no gap) 3-point DIXON images to determine muscle fat fraction (TR/TE/ΔTE 210/4.41/0.76ms; FA 8°; voxel size 1x1x10mm; gap 5mm;) and multi spin echo images to assess the water T2 relaxation time (9)(17 echoes; TR/TE/ΔTE 3000/8/8ms; voxel size 1.4x1.8x10mm; gap 20mm;)(Fig. 1).

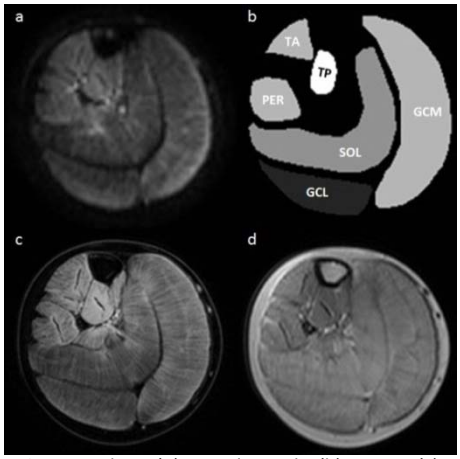

Fig 1. *Axial DTI (a), muscle masks (b), DIXON (c) and T2 image (d) in a DMD patient obtained for the individual lower leg muscles. Gastrocnemius Lateralis (GCL), Gastrocnemius Medialis (GCM), Soleus (SOL), Tibial Anterior (TA), Peroneus (PER) and Tibial Posterior (TP) muscles .*

Data Analysis: A dedicated toolbox (1) was used to calculate mean diffusivity (MD) and fractional anisotropy (FA) from the DTI data. All outcome parameters (FA, MD, %fat, DTI_SNR, water T2) were determined in the same region of interest (ROI) drawn for 6 individual lower leg muscles and presented as a mean value over multiple slices. The effect of water T2, % fat and SNR on the DTI-parameters was evaluated with a Spearman correlation. Subsequently, to ensure image quality, DTI measurements with a SNR<15 and muscles with fat infiltration> 25% were excluded from statistical analysis between groups. (7) Finally, differences in DTI parameters and mean water T2 between healthy controls and DMD patients were assessed with a general linear model, where water T2 was taken as a covariate for the analysis of the DTI-parameters. The significance level was set at $p<0.05$.

Results: Values of FA correlated positively with %fat (R=0.23), correlated negatively with SNR (R=-0.44) and showed no correlation with mean water T2 (fig. 2). The correlation between SNR and FA disappeared with a SNR above 25. MD did not correlate with mean water T2, %fat or SNR suggesting that the estimation of FA is more highly affected by confounders. A total of 42% (83/198) of the ROIs were excluded for the between-group analysis. Group comparisons showed increases in MD in the GCL, GCM and TA muscles in DMD patients compared to healthy controls ($p<0.05$). No differences in FA were observed between groups (fig. 2). All individual muscles showed a significant increased mean water T2 in DMD patients compared to controls.

Discussion and Conclusion: Our results show that the proposed quality criteria from simulation-based work (5-7) combined with an optimized and clinically feasible DTI-sequence are suitable to reliably determine MD in DMD patients and young healthy controls. However, the correlation between FA and SNR confirms that for an accurate estimation of FA in skeletal muscles higher quality levels are required (SNR>25). The positive correlation between %fat and FA in these relatively high SNR ranges is in contrast to simulation based work, in which an decrease in FA was observed with increasing fat% due to partial volume effects. (5) The absence of a correlation between the DTI measures and mean water T2 is in line with literature and confirms that minor increases in water T2 in relatively high SNR ranges have a negligible effect on the DTI parameter estimation. (6) Therefore, both the increase in MD as well as the positive correlation between FA and %fat could potentially be ascribed to pathophysiological processes. Overall, multi-parametric MRI is essential to distinguish between confounding effects and pathophysiological processes in skeletal muscle DTI.

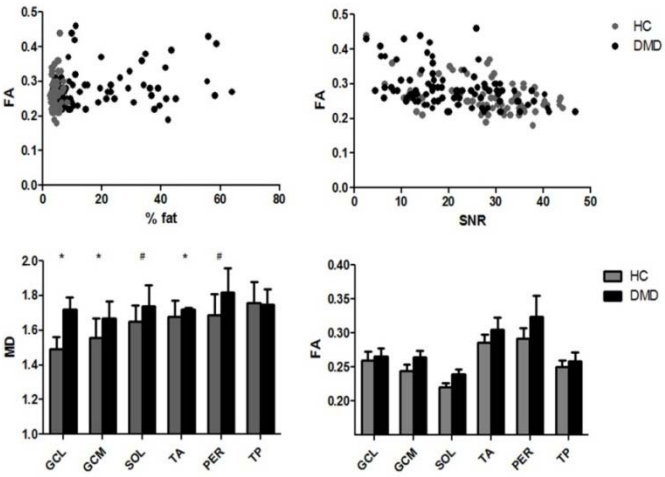

Fig 2. *Overview of the results. In the top graphs the correlation between both DTI measures (MD and FA) and SNR, DMD patients are presented in black and healthy controls in grey. Each dot presents a muscle. In the bottom graphs the mean and stdv of the MD and FA presented for the individual lower leg muscles in healthy controls and DMD patients. Significant differences between groups (p>0.05) are marked with an asterisk(*)and trends (p>0.1) are visualized with a hashtag (#).*

References: [1] Froeling et al. *MRM 2010* [2] Zaraiskaya et al. *JMRI 2006* [3] Bryant et al. *NMR in Biomed 2014* [4] Scheel et al. *NMR in Biomed 2012* [5] Damon et al. MRM 2008 [6] Froeling et al. *NMR in Biomed 2013* [7] Williams et al. *JMRI 2013* [8] Ponrartana et al. *Pediatr Radiol 2014* [9] Azzabou et al. *JMRI 2014*