Quantitative MRI for muscle characterisation – initial comparison of young adults with cerebral palsy to normal subjects

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Introduction: Cerebral palsy is a condition that arises from an injury to the motor areas of the developing brain. A common secondary impairment is muscle deformity but imaging assessments of muscle in this group are uncommon [1]. It is possible to quantify the connective tissue infiltration through performing a muscle biopsy. However, this is a painful and invasive procedure and a non-invasive technique is therefore highly desirable. MRI has great potential for the non-invasive characterisation of muscle properties in CP utilising techniques such as Dixon-based imaging for fat-water quantification and diffusion MRI for probing muscle microstructure. The aim of this study was to compare quantitative MRI measurements from Dixon-based imaging and diffusion tensor imaging (DTI) in the calf muscles of young adults with CP and healthy volunteers.

Methods: Ten subjects were scanned, of which 5 had a diagnosis of CP (4 male, mean age 20.2 years, range 18-23) and 5 were normally developing (ND) volunteers (3 male, mean age 22.6 years, range 18-25). The walking ability of the subjects with CP was assessed using the Gillette Functional Assessment Questionnaire (GFAQ) (table 1). All MR data were acquired on a 3.0T Achieva system (Philips Medical Systems. Best, Netherlands) using an 8-channel receive phased array knee coil. One subject, however, was not suitable for the knee coil due to a 30° knee flexion contracture, and for this case a 32-channel cardiac coil was used instead. All subjects were scanned prone to avoid mechanical compression of the calf muscles which occurs when supine. *Imaging protocol:* T_1-weighted gradient echo images were acquired with TE/TR= 2.3/5.4 mm, flip angle=35°, 0.6 x 0.6 mm in plane voxel size, 4.0 mm slice thickness, 2 signal averages, 256 x 256 matrix size. Four point Dixon images were acquired with TE= 2.3 ms, 35° flip angle, 2 x 2 mm in-plane resolution, 3 mm slice thickness and a ΔTE of 1.0 ms from which the scanner software generated fat and water images. Spin echo-EPI DTI images were acquired of the calf muscles with b=0 and 700 s/mm^2, 16 directions, 4 mm slice thickness, TE/TR= 42/3653 mm, 1.8 x 1.8 mm in plane voxel size, from which apparent diffusion coefficient (ADC) and fractional anisotropy (FA) maps were calculated by the scanner. *Data Analysis:* Regions of interest (ROIs) were drawn on the T_1 weighted images around the three muscles: the medial gastrocnemius (MG), lateral gastrocnemius (LG) and the soleus (SOL) (an example slice is shown in figure 1) and these were combined for all images over the length of the muscle within the field of view to form a volume of interest (VOI), using Osirix [2]. Mean signal intensities were then measured for each VOI from the fat and water images to provide a percentage fat value, and from the ADC and FA maps. Fatty infiltration of the calf muscles was also assessed by a musculoskeletal radiologist using a qualitative scoring method [3]. Independent samples T-tests were performed using SPSS version 16.0 to investigate differences between the two subject groups with significance set for p≤0.05. Linear regression was used to investigate the relationship between GFAQ score and percentage fat, ADC, and FA values.

Subject	GFAQ scores
CP 1	8
CP 2	10
CP 3	9
CP 4	8
CP 5	7

Table 1: GFAQ scores of the subjects with CP

Results: Figures 2-4 show the mean (± 1 standard deviation) values for percentage fat, ADC, and FA for the CP and ND groups in the MG, LG and SOL muscles respectively, and for the muscle values combined. *Fat percentage:* A consistently higher average percentage fat content was observed for the CP group compared to the ND group, although no significant difference was found in percentage fat content between the groups for the individual muscles. However, when all three muscles are combined, the CP subjects exhibit a significantly higher percentage fat content compared to the ND subjects (p=0.019). Table 2 summarises the qualitative assessment of adipose tissue infiltration for each volunteer. *ADC:* The mean ADC value for the CP group was consistently lower than the ND group for all muscles investigated, although statistical significance was reached only for the lateral gastrocnemius (p=0.013) and when the values for all muscles were combined (p=0.009). Despite the lowest ADC value corresponding to the lowest functional ability, no significant linear relationship was observed for ADC value with GFAQ category. *FA:* There was no significant difference or apparent trend for FA between CP and ND subject groups for all muscles, individually and combined. However, a strong positive linear relationship was found between FA and GFAQ category for the medial gastrocnemius which may become significant with more subjects (R^2=0.7, p=0.077) and weak significant linear relationship was observed for the three muscles combined (R^2=0.298, p=0.035).

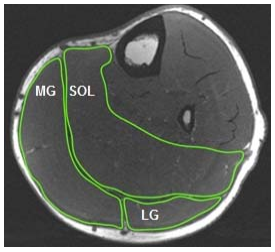

Figure 1: Example T_1-weighted axial slice showing the ROIs drawn for the MG, LG and SOL.

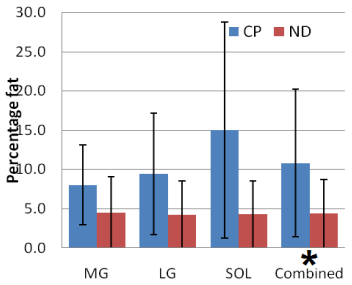

Figure 2: CP group (blue) and ND group (red) average percentage fat. * denotes significant difference p<0.05.

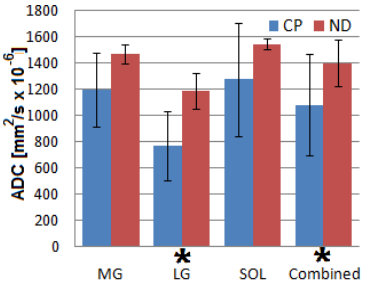

Figure 3: CP group (blue) and ND group (red) average ADC. * denotes significant difference p<0.05.

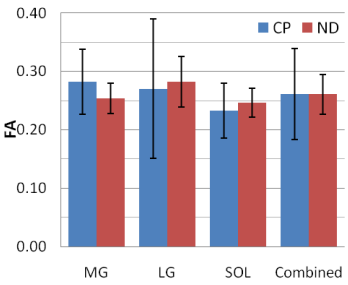

Figure 4: CP group (blue) and ND group (red) average FA.

Discussion: The increased percentage of intramuscular fat in subjects with CP quantified by the Dixon method is consistent with our qualitative assessment performed here, and to measurements of inter-muscular fat in younger subjects with CP made by Johnson *et al.* [4]. The reduced ADC values in CP subjects indicate increased restriction of diffusion, consistent with connective tissue infiltration. However, the connective tissue content does not appear to have a significant effect on the directionality of the diffusion, as assessed by FA, until the individual's function has been severely compromised (GFAQ category 7). These results findings suggest that the cross-sectional area fraction of connective tissue is increased in subjects with CP, a finding consistent with the results of biopsy studies of the quadriceps [5] and forearm flexors in this group [6], maintaining the high FA values, but may become increasingly isotropic with decreasing functional ability. This would explain the insignificant findings of FA value due to the relatively high functionality of the CP group subjects.

Improved differentiation between CP and ND groups when the three muscles investigated are considered as a group, suggests that a larger subject group will enable a statistically significant differences in ADC and percentage fat to be observed for individual muscles, although the large variability of the indices with functional ability in the CP subject group suggests an equal spread of functional abilities within the CP subjects would be desirable to investigate these observations in more detail. Furthermore, comparison of the MRI results with muscle biopsy studies is required. Overall, these results demonstrate the potential of MRI techniques for non-invasive muscle characterisation in CP subjects by quantitative measurements of fatty and connective tissue infiltration.

Subject	Grade
CP 1	mild 1
CP 2	mild 1
CP 3	moderate 3
CP 4	mild 1
CP 5	moderate 3
ND 1	normal 0
ND 2	normal 0
ND 3	normal 0
ND 4	normal 0
ND 5	mild 1

Table 2: Qualitative quality scores of axial T_1-weighted images

References: [1] Shortland 2009 Dev Med Child Neurol, 51 Suppl 4, 59-63 [2] Rosset *et al.* 2004 J Digit Imaging, 1, 205-16 [3] Kim *et al.* 2010 Radiology 255, 899-908 [4] Johnson *et al.* 2009 J Pediatr, 154 715-20. [5] Booth *et al.* 2001 Dev Med Child Neurol, 43 314-20 [6] Friden & Lieber 2003 Muscle Nerve 27 157-64