Repeatability of Diffusion Tensor Imaging and Water-Fat MRI in Lower Extremity Muscles in Children

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Target Audience – This work is relevant to investigators surveying applications of chemical-shift water-fat MRI and diffusion tensor imaging. It is also of relevant to researchers interested in studies of muscle diseases in the pediatric population.

Purpose – Clinical evaluation of pediatric muscle diseases such as Duchenne Muscular Dystrophy is hindered by the lack of objective noninvasive measures. The current practice does not involve imaging, but rather an assessment of muscle strength and flexibility through tests performed by a physician or physical therapist. Quantitative MRI such as chemical-shift water-fat methods and diffusion tensor imaging (DTI) are well-suited for characterizing muscles in pediatrics because of their objective, quantitative measurement, high spatial resolution, lack of ionization radiation, greater sensitivity to change, and ability to evaluate individual muscles. Water-fat MRI has been utilized in evaluating muscle fat infiltration [1]. Likewise, DTI has been shown to be a useful research tool to study skeletal muscle architecture and injury [2]. Although several studies have evaluated the feasibility of these techniques in the adult population, the repeatability of these quantitative biomarkers in the pediatric population have not been reported [3]. _In this pilot work, we hypothesize that apparent diffusion coefficient (ADC) and fractional anisotropy (FA) measures from DTI and likewise muscle fat-signal fraction (MFF) measures from chemical-shift water-fat MRI will demonstrate high test-retest and inter-rater reliability._

Methods – Imaging: The thigh and lower leg of seven healthy children (5F, 2M, age: 8.9±3.5 years, age range 5-15 years) were studied. The measured side (left, right) was selected randomly. After completion of the first exam, the subject was taken off the table and repositioned to obtain test-retest intra-rater measurements. MRI exams were performed on a Philips whole-body 3T system (Achieva R3.2). A research mDIXON water-fat sequence was utilized. Setup for the 3D SPGR sequence was: supine, feet first, axial acquisition, TR=10ms, first TE=1.48ms, ΔTE= 1.2ms, 6 full echoes, bipolar readout, 1mm isotropic voxels, flip angle=3°, bandwidth=1.3 kHz/pixel, FOV=120-160mm, and SENSE (A/P) × 2. Scan time was ~2 minutes for 125-170 contiguous slices. A 16-channel torso array was used. The reconstruction employed a seven-peak spectral model of fat and a single T_2* parameter to generate fat-signal fraction maps. A DTI scan utilizing a multi-slice spin-echo single-shot EPI sequence covering the same anatomical volume of the mDIXON scan was also performed. It involved: TR=2.479s, TE=43ms, partial Fourier=70%, adiabatic fat suppression using inversion recovery (SPAIR), 1.5mm in-plane resolution, 6mm slices, 15 diffusion directions + 1 baseline, b={0, 250, 500s/mm^2} and SENSE (A/P) × 2. Scan time was ~6 minutes for 28 slices. **Analysis:** Slice selection and region-of-interests were drawn independently by two board certified radiologists for each thigh and lower leg examination. For each dataset, ADC, FA, and MFF were individually calculated for the following muscles: thigh (rectus femoris, vastus medialis, lateralis, and intermedius, semimembranosus, semitendinosus, biceps femoris, and combined adductors); leg (anterior and posterior tibialis, peroneus longus, gastrocnemius, and soleus). The test-retest and inter-rater variability were assessed by calculating the Pearson correlation coefficient **(r)**, intra-class correlation **(ICC)**, coefficient of variation **(CV)**, and Bland-Altman analysis.

Results – Bland-Altman plots show the difference between test-retest and inter-rater measurements of ADC, FA, and MFF **(Figure 1).** In all cases, the mean difference was near 0, indicating that the measurements were free from systematic bias. **Table 1** summarizes the correlation coefficient, ICC, and CV statistics. The correlation coefficients and ICC were generally high, and CV was reasonably low, suggesting good reliability of the measurements. MFF measurements from mDIXON water-fat MRI exhibited the highest correlation coefficients and ICC, but also had the highest CV. Inter-rater agreement was consistently better than test-retest comparisons. A significant positive correlation between mean MFF of the measured lower extremity muscles and age was observed (r = 0.9197, p<0.001) **(Figure 2)**. There was no relationship between ADC and FA and age.

Fig. 1: Bland-Altman plots of test-retest (top row) and inter-rater (bottom row) measurements of mean **(A)** ADC, **(B)** FA, and **(C)** MFF. Each symbol represents a different subject and each data point represents the mean value from a different muscle measurement.

	FA		ADC		MFF	
	Test-retest	Inter-rater	Test-retest	Inter-rater	Test-retest	Inter-rater
r	0.7421	0.8709	0.7591	0.8885	0.8844	0.9576
ICC	0.7307	0.9268	0.7547	0.9385	0.8811	0.9781
CV%	6.78%	4.91%	4.43%	3.23%	15.3%	9.52%

Table 1: Test-retest- and inter-rater variability statistics.

Discussion/Conclusion – We have evaluated the repeatability of DTI and water-fat MRI measurements in lower extremity skeletal muscles in a pilot pediatric cohort. To our knowledge, such assessment has not been previously reported in the literature. The results suggest that ADC, FA, and MFF measurements are repeatable quantitatively and can potentially serve as objective biomarkers of disease progression in the clinical assessment of conditions such as Duchenne Muscular Dystrophy, in conjunction with current practices using scores from physical tests. Scan positioning and acquisition seem to be a larger source of variability than having different individuals perform the analysis. Interestingly, a significant association between increases in MFF and age was seen only with MFF measures, which may indicate normal fat infiltration during the aging process. While all three metrics (ADC, FA, and MFF) appear robust and reliable, additional studies are needed to determine whether DTI or water-fat imaging is more sensitive to disease progression and physiological change.

[1] Gaeta, et al. _Radiology_ 2011; 259:487-494. [2] Zaraiskaya, et al. _JMRI_ 2006; 24:402-408. [3] Heemskert A, et al. _NMR Biomed_ 2010; 23:294-303.
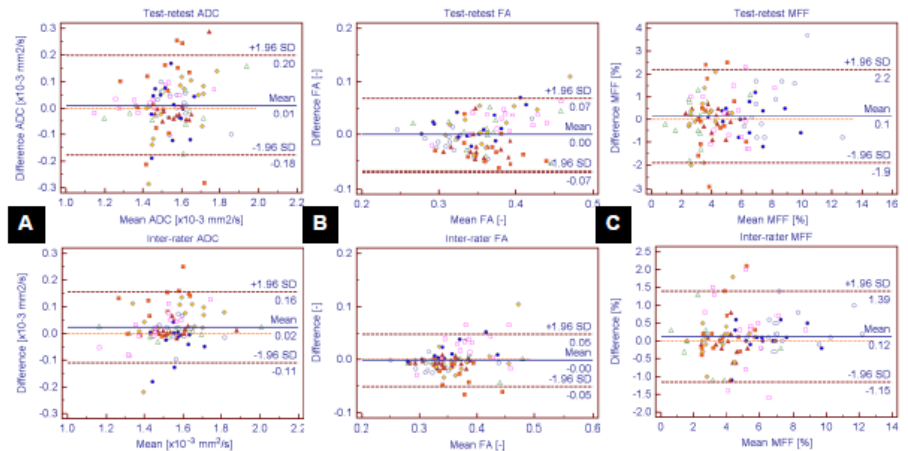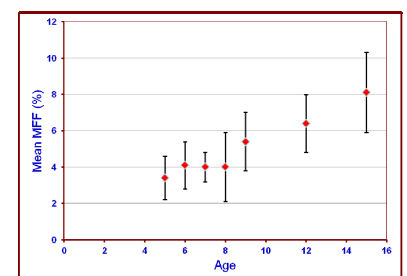
Fig. 2: Mean MFF of all muscles within the thigh and leg vs. subject age.