

Quantification of Lower Extremity Muscle Fat Infiltration in Pediatric Patients with Spina Bifida using Water-Fat MRI

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Target Audience – This work is relevant to investigators surveying applications of chemical-shift water-fat MRI and those interested in studies of muscle diseases and the quantification of fatty infiltration in muscles.

Purpose – Spina bifida is one of the most common permanently disabling conditions in children in the United States. Myelomeningocele is the most common form of spina bifida, referring to a birth defect in which the backbone and the spinal canal fail to close before birth. This results in permanent spinal cord and nerve damage and varying degrees of muscle paralysis or weakness. Consequent loss of muscle function can be progressive, with ambulatory ability declining during the teenage years and into adulthood. Similar to Duchenne muscular dystrophy patients, the loss of muscle function in patients with spina bifida can also be accompanied by fatty infiltration. The current standard for clinical measurement of lower extremity muscle function is manual muscle testing (MMT)^{1,2}, which provides only a semi-quantitative assessment that can be subjective and dependent on the evaluator performing the tests. MMT is also limited in its ability to predict future function. In this pilot work, we hypothesize that fat-signal fraction measures from chemical-shift water-fat MRI will (a) correlate with physical strength and function scores in children with spina bifida, and (b) also provide a more quantitative and objective assessment of muscle health and integrity. A secondary goal was to assess inter-rater reproducibility of measurements of muscle fat-signal fraction.

Methods – Five pediatric patients with spina bifida (3F, 2M, age: 13.4±1.0 years, all Hispanic) were studied. Physical examination and MMT were performed by an experienced physical therapist. MMT scores for muscle strength range from 0 (no palpable contraction), 1 (trace contraction, no joint movement), 2 (poor, completes range of motion-ROM-with gravity eliminated), 3 (fair, completes ROM against gravity without resistance), 4 (good, completes ROM against gravity with moderate resistance), to 5 (normal, completes ROM against gravity with maximal resistance). The scores also have +/- modifiers (e.g., 4-plus, 4-minus). Table 1 lists the muscle groups for which strengths were measured. MRI exams were performed on a Philips whole-body 3T system (Achieva R3.2). A research mDIXON water-fat sequence was utilized³. Setup for the 3D SPGR sequence was: supine, feet first, axial acquisition, TR=10ms, first TE=1.48ms, ΔTE= 1.2ms, 6 echoes, bipolar readouts, 1mm isotropic voxels, flip angle=3°, bandwidth=1.3 kHz/pixel, and SENSE (A/P) × 2. Scan time was ~2 minutes for 125-170 contiguous slices. mDIXON was performed individually for the right lower leg, the left lower leg, the right thigh, and the left thigh. A 16-channel torso array was used. The reconstruction employed a seven-peak spectral model of fat and a single T₂* parameter to generate fat-signal fraction maps. Two evaluators independently measured fat-signal fractions. Region-of-interests were drawn in the muscles listed in Table 1 and average fat-signal fractions were tabulated. Intraclass correlation coefficients (ICC) were computed with Stata statistics software to assess inter-evaluator agreement.

MMT	MUSCLES	
Plantar flexor strength	Soleus	Sol
	Gastrocnemius medial	GC Med
	Gastrocnemius lateral	GC Lat
Dorsi flexor strength	Tibialis Anterior	TA
Knee extensor strength	Quadriceps	
	Rectus Femoris	Rectus
	Vastus Lateralis	Vas Lat
	Vastus Medialis	Vas Med
	Vastus Intermedius	Vas Int
Knee flexor strength (lateral)	Hamstrings	
	Semitiandinosus	S_tend
	Semimembranosus	S_mem
Knee flexor strength (medial)	Hamstrings	
	Biceps femoris	Biceps
Adductor strength	Adductors	Add

Table 1: List of manual muscle tests and associated muscles.

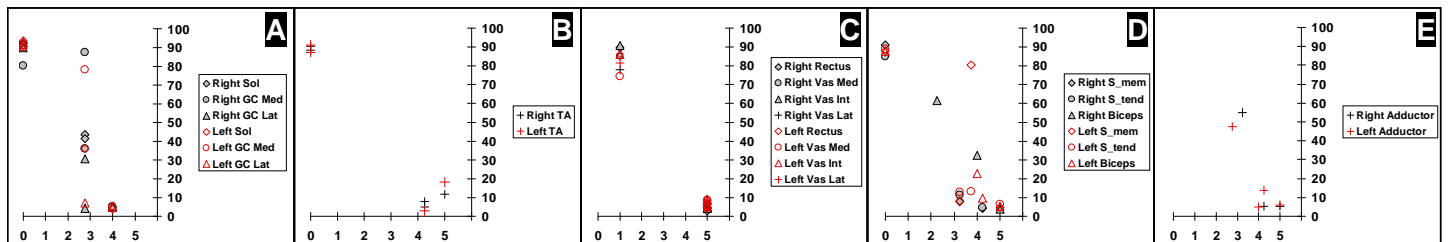


Fig. 1: Plots of MMT scores (x-axis, 0-5) against MRI fat-signal fraction measurements (y-axis, 0-100%). Plots are separated by muscle groups and by color for right (black) and left (red) legs. Plus-minus MMT scores are offset along the x-axis by 0.25 (e.g. 3-minus is plotted as 2.75; 4-plus is plotted as 4.25).

Results – Fig. 1 presents five similar plots. MMT scores are plotted on the x-axis; fat-signal fraction measurements are plotted on the y-axis. There is a negative correlation trend in all muscle groups of weaker muscles having increased fatty infiltrations. The lowest MMT scores (0-1) are consistently associated with the highest fat-signal fractions, and the highest MMT scores (4-5) are consistently associated with the lowest fat-signal fractions. The calf muscles (Fig. 1A) and hamstrings (Fig. 1D) show a large range of fat-signal fraction measurements corresponding to intermediate MMT assessments of 2 and 3. This suggests that MRI may be able to quantify muscle characteristics that cannot be detected based on standard clinical examinations. Fig. 2 illustrates representative grayscale fat and color-scaled fat-signal fraction images from three patients. The varying progression of fatty infiltration is evident, in particular with the subject in Fig. 2C (M, 13.7y, all MMT scores are 0) exhibiting complete infiltration of fat in all muscles. Interestingly, the subject in Fig. 2B (F, 14.9y) has preferential infiltration of fat in the soleus and medial gastrocnemius muscles, while the lateral gastrocnemius muscle is unaffected. This is in contrast to the subject in Fig. 2A (F, 12.7y) where all three muscles are noticeably affected. However, both subjects have the same MMT score of 3-minus (2.75 in Fig.1) for the soleus and gastrocnemius muscles. ICC for all measured muscles was extremely high (>0.98). The average difference in muscle fat-signal fraction between the two evaluators ranged from -2.8% (S_tend) to 2.9% (Sol).

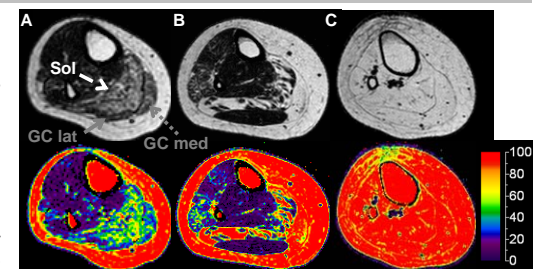


Fig. 2: Representative fat and fat-signal fraction images of the right lower leg in three patients.

Discussion & Conclusion – To our knowledge, this is the first study to report a relationship between muscle function and the manifestation of fatty infiltration in lower extremity muscles in pediatric patients with spina bifida. While it may be intuitive that strong muscles have low fat-signal fractions and weak muscles have high fat-signal fractions, the present data also showed interestingly a wide range of fat-signal fractions for muscle groups with intermediate MMT strength scores. In addition, one subject (Fig. 2B) exhibited striking differences in fat-signal fractions in different muscles that share similar functions. These preliminary findings suggest that MRI potentially has a greater diagnostic ability and a better capability to detect sub-clinical changes in muscles that are not discerned in standard physical and MMT assessment. Water-fat MRI may therefore have the potential to provide a more sensitive, quantitative and objective assessment of muscle health and integrity and may be a more useful tool in predicting changes in lower extremity muscle function in the spina bifida population. Additional research is needed to confirm and build on these preliminary findings.

[1] Kendall FP, et al. Muscles: Testing and Function, 2nd ed., Baltimore: Williams & Wilkins, 1971; p3-15. [2] Stuber WA & Metcalf WK. Physical Therapy. 1988; 68:977-982. [3] Eggers H, Brendel B, Duijndam A, Heriqault G. Magn Reson Med. 2011; 65:96-107.