Fat corrected ^{23}Na MRI quantification of skeletal muscle tissue of Duchenne muscular dystrophy patients

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Target audience: Clinicians and researchers involved in seeking new biomarkers for neuromuscular disorders characterization

Purpose

^{23}Na MRI has been previously proposed to examine several myopathies including Duchenne muscular dystrophy (DMD) [1]. DMD is a hereditary neuromuscular disease caused by a mutation in the dystrophin gene associated with inflammation, ionic homeostasis dysregulation, and exhaustion of regenerative capacities which leads ultimately to replacement of muscle by fatty and fibrotic tissue. Higher total sodium concentrations (TSC) and intracellular weighted sodium (ICW) signal have been measured by ^{23}Na MRI [2]. However, partial volume effects may lead to decreased TSC and ICW, in particular in patients with high fat fraction, since fat tissue has lower sodium concentrations than muscle tissue [3]. So far, no study took into account the presence of fat during the ^{23}Na signal quantification. In this study, we quantified ^{23}Na MRI parameters in DMD patients and took fat fractions into account.

Methods

MRI of the right calf was performed in five healthy women (age 24.1±1.6 years), nine DMD patients (age 9.9±3.2 years) and ten age-matched controls (age 10.0±2.4 years) on a 3T whole-body MR system (Magnetom Skyra, Siemens). A single-tuned (^{23}Na) volume knee coil (Stark Contrast) and NaCl references tubes were used for ^{23}Na MRI. Total tissue sodium concentration (TSC) was estimated from a density-adapted 3D-radial UTE (DA-3DPR) sequence acquired with the following parameters [4]: TE/TR 0.3/50ms, FA 80°, resolution 3x3x15mm^3, 8264 projections, Tacqu 6min53sec. Slight T_1 weighting was accepted to reduce acuisition time (in particular for the young DMD patients). An inversion-recovery (IR) sequence was used to reduce ^{23}Na-signal originating from unrestricted environments to achieve an intracellular weighted sodium signal (ICW) [5]: TE/TR 0.3/124ms, TI 34ms, FA 90°, resolution 4x4x20mm^3, 4760 projections, Tacqu 9min50sec. ^{1}H 3D FLASH images (TR 308ms, TE 4.77ms, FA 90°, 24 slices with a 1 x 1mm^2 resolution, 2NEX, total Tacqu 2min) were used to draw ROIs on the gastrocnemius medialis (Gas.m.), soleus (Sol), tibialis posterior (TP), tibialis anterior (TA) muscles, and the subcutanous fat. The sodium signals were calibrated using the signal intensities of the background noise and two reference phantoms (20mM and 40mM NaCl in 4% agarose). For the DMD and age-matched controls, a 15-channel quadrature knee coil (Siemens) was used to measure the fat fraction (FF) of the muscles with a 3D 3-pt DIXON method: TR 10ms, TEs 2.75/3.95/5.15ms, FA 3°, 64 slices with a 1.3x1.3mm^2 resolution, total Tacqu 3min12sec. The FF and the mean ^{23}Na concentrations of the healthy adult population were used to correct for TSC and ICW values of the children. Additionally, for water T2 determination a multi-slice-multi-echo (MSME) sequence was acquired with the following parameters: TR 3000ms, 32 echoes with TEs from 9.5ms to 304, 5 slices with a 1.4x1.4mm^2 resolution, Tacqu 3min41sec. Water T2 values were calculated based on a tri-exponential model [6].

Results

In the examined adults, the TSC and ICW maps show ^{23}Na signal arising from the subcutaneous fat tissue (Fig. 1). The subcutaneous fat exhibited a TSC of 8±1mM and a ICW of 6±1a.u.. The mean values were used to correct the ^{23}Na values for the DMD study.

In DMD patients, fatty muscle degeneration varied between muscle groups and FFs were elevated compared to controls (Fig. 2 and Table 1, significant differences in FF for all muscles compared to ctrl $p<0.05$). For DMD patients fat correlated negatively with TSC (R=-0.32) and ICW (R=-0.46) before the fat correction. This correlation vanished after taking the fat correction into account (TSC: R=0.08 and ICW: R=0.08). DMD patients showed an increased TSC and ICW in all muscles compared to age-matched controls (see table 1, significant differences in TSC and ICW for all muscles $p<0.005$). Mean water T2 were elevated in DMD patients compared to controls (38.6±3.9ms vs 35.1±1.2ms, p=0.006). Moreover, the ^{23}Na indices were frequently abnormal in DMD even when water T2 or FF remained in the normal range (data not shown).

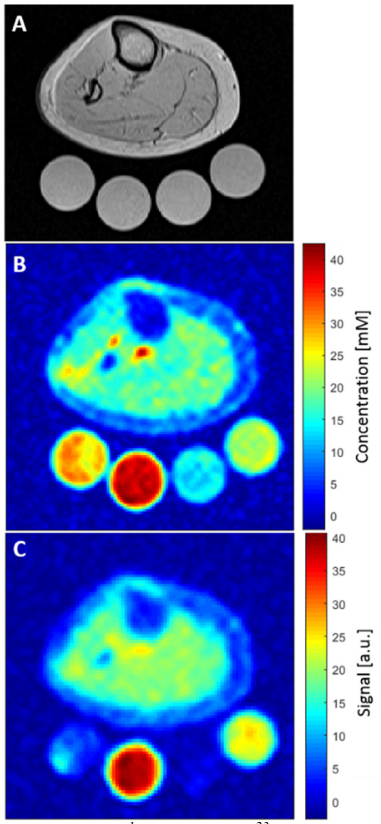

Figure 1 A) ^{1}H FLASH, B) ^{23}Na DA-3DPR, and C) ^{23}Na DA-3DPR IR image of the right leg in a healthy 22-year-old female subject.

Discussion & Conclusion

This study measured the Na^+ signal of the subcutaneous fat tissue by DA-3DPR ^{23}Na MRI sequences. In DMD patients, the FF has to be taken into account for the sodium quantification. The present T1w of the ^{23}Na images might impact sodium quantification, in particular whenever T1 of muscle tissue deviates from the phantom's T1 values. Another limitation is that ^{23}Na MRI signal of subcutanous fat tissue might deviate from the signal of fat tissue in muscle. Using the IR method (Fig. 1c), the signal of the free sodium (NaCl solution containing phantoms) is not completely suppressed mainly due to B_1 inhomogeneities. In addition, this study indicates that sodium anomalies are systematically present in patients with DMD compared to controls independent of fatty degenerative changes. Also muscles that were relatively spared, such as the TA and TP, showed increased TSC and ICW in all participating DMD patients.

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Table 1 : Fat-corrected ^{23}Na TSC and ^{23}Na ICW as well as the FF of DMD patients and age-matched controls in the gas.m., sol, TA, and TP muscles. Results presented as mean and std dev.

		^{23}Na TSC [mM]		^{23}Na ICW [a.u.]		FF [%]	
		mean	std	mean	std	mean	std
DMD	Gas.m.	25	± 3	26	± 5	0.117	± 0.092
	Sol	25	± 5	28	± 4	0.091	± 0.074
	TA	22	± 3	26	± 3	0.046	± 0.040
	TP	24	± 3	29	± 3	0.028	± 0.014
Ctrl	Gas.m.	18	± 3	19	± 2	0.025	± 0.011
	Sol	18	± 2	21	± 3	0.020	± 0.006
	TA	15	± 2	17	± 2	0.014	± 0.006
	TP	16	± 3	20	± 4	0.017	± 0.006

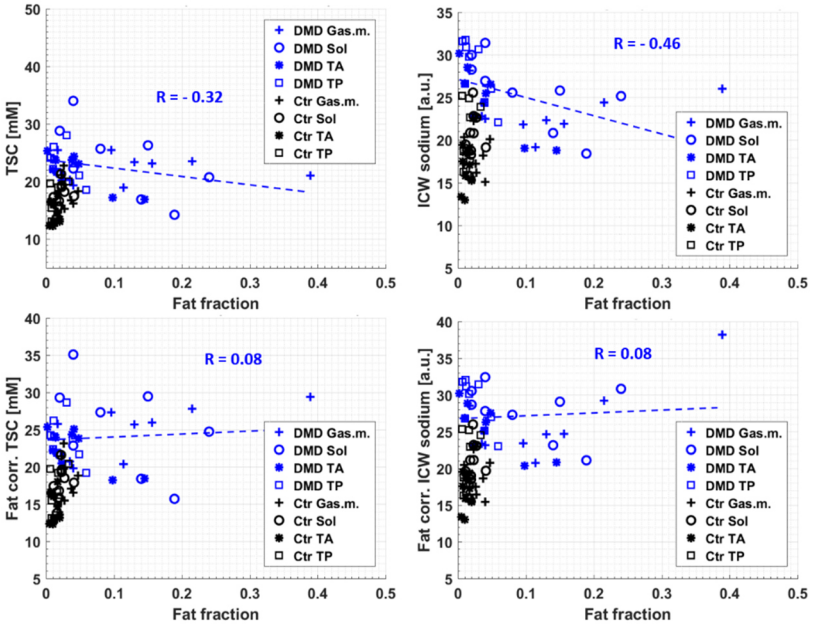

Figure 2 : Correlation of the FF and the ^{23}Na TSC and ICW before and after fat correction.

References: [1] Nagel AM, Weber MA, et al. MRI Skl Musc 2013: 115-133. [2] Weber MA, Nagel AM, et al. J Neurol 2012: 259(11): 2385-2392. [3] Umathum R, Rösler MB, Nagel AM. Radiol 2013: 269(2): 569-576. [4] Nagel AM, Laun FB, et al. MRM 2009: 62:1565-1573. [5] Nagel AM, Amarteifo E, et al. Invest Radiol 2011: 46(12):759-766. [6] Azzabou N, Loureiro de Sousa P, Caldas E, et al. J MRI 2015: 41(3): 645-653.