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Age and gender associated differences in electrical impedance values of skeletal muscle

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Abstract

Electrical impedance measurements of skeletal muscle may be sensitive to age-associated declines in muscle health. In an effort to evaluate this concept further, we performed electrical impedance myography (EIM) using a handheld array on 38 individuals aged 19–50 years and 41 individuals aged 60–85 years. Individuals either had 7 upper extremity or 7 lower extremity muscles measured. The 50 kHz reactance, resistance and phase were used as the major outcome variables. Although the phase values were similar in both groups, both reactance and resistance values were lower in the lower extremities of the older individuals as compared to the younger ($-23 \pm 6\%$, $p = 0.001$ for reactance and $-27 \pm 7\%$, $p = 0.005$ for resistance), whereas changes in upper extremity values were not significantly different ($-9 \pm 5\%$, $p = 0.096$ for reactance and $+5 \pm 9\%$, $p = 0.55$ for resistance). When analyzing the genders separately, it became clear that this reduction in lower extremity values was most pronounced in men and less consistently present in women. These findings suggest that age- and gender-associated differences in muscle condition are detectable using EIM. The relationship of these easily obtained parameters to standard functional, imaging, and pathological markers of sarcopenia deserves further study.

Keywords

Aging; electrical impedance; sarcopenia; gender

1. Introduction

The term sarcopenia is defined as the age-related loss of muscle quantity and quality (Thompson, 2009; Narici and de Boer, 2010). It is a major health concern ultimately resulting in loss of mobility and independence. Approximately 25% of individuals >70 years of age have established sarcopenia (i.e., loss of muscle mass < 2 standard deviations below young reference means) and this proportion increases to 30–50% for individuals >80 years of age (Baumgartner *et al.*, 1998). The direct and indirect health costs associated with aging muscle loss are estimated to be over \$300 billion in the United States alone (Booth *et al.*, 2000). There is increasing recognition of the importance of preventing or reversing sarcopenia and maintaining muscle function. Indeed, much ongoing work seeks approaches to forestalling its onset, such as exercise and dietary/pharmacological interventions (Pillard *et al.*, 2011). However, present methods of identifying the presence of sarcopenia and assessing the effects of such interventions rely largely on strength measurements or

radiological imaging (Bijlsma *et al.*, 2012). Strength measurements require active participation and introduce subjective elements, such as patient motivation, that extend well beyond the properties of the muscle tissue itself. Imaging methods, such as CT and MRI, while sensitive to sarcopenic change (Pahor *et al.*, 2009), are costly and inconvenient thus rendering them an unfavorable choice to use in a clinical setting. A tool for the rapid, bedside evaluation of muscle condition and the presence of sarcopenia could be valuable both for individual patient care and clinical research.

Electrical impedance myography (EIM) is a localized tetrapolar bioimpedance-based technique that could serve in this role. EIM has been shown to be sensitive to disease-induced changes to muscle's normal composition and architecture, including myocyte atrophy, hypertrophy and loss, edema, reinnervation, and the deposition of endomysial connective tissue and fat (Rutkove, 2009). Specifically, EIM phase values obtained at 50 kHz show substantial alterations in a variety of neuromuscular disease states, including amyotrophic lateral sclerosis (ALS), myopathy, and disuse atrophy (Rutkove *et al.*, 2012; Tarulli *et al.*, 2005; Tarulli *et al.*, 2009). One study also suggested the 50 kHz EIM phase shows a consistent decline across individuals with increasing age (Aaron *et al.*, 2006). In further support of EIM's potential application to the evaluation of sarcopenia, standard whole-body bioimpedance analysis methods have shown large reductions in overall muscle mass with age (Janssen *et al.*, 2002).

We recently studied the application of EIM in the diagnosis of spinal nerve root compression (radiculopathy) (Spieker *et al.*, 2013). In that project, using a handheld electrode array, we evaluated individual muscles of bilateral upper or lower extremities in adults with radiculopathy, comparing the asymptomatic, non-radiculopathic side to the diseased side, as well as to values from healthy adults (Narayanaswami *et al.*, 2012). While analyzing the data, we noticed an age-dependent decline in 50 kHz EIM values. In this study we formalize that analysis, comparing EIM data from a group of younger adults to that of a group of older.

2. Materials and Methods

2.1 Subjects

Data was obtained from the limbs of normal healthy volunteers with no history of significant neuromuscular disease affecting either the upper or lower extremities as well as patients with a history of radiculopathy affecting the contralateral limb. Individuals were recruited by advertisement, word of mouth and directly through the neurology clinic and electromyography laboratory. After signing the informed consent form, all underwent a detailed neurological history and examination to confirm the absence of appendicular edema and any underlying neuromuscular disease affecting the limb to be studied. All subjects had either upper extremities or lower extremities evaluated, but not both.

Two groups of people were included in this analysis to maximize sample size: a younger group of individuals aged 19–50 years (38 adults) and a group of older individuals aged 60–85 years (41 adults). Table 1 provides a detailed breakdown of the patient demographics by age and sex.

2.2 EIM measurements

EIM measurements were obtained using the Imp SFB7 bioimpedance spectroscopy device (Impedimed, San Diego, CA), measuring at frequencies from 3 kHz -1 MHz. This device provides an output of resistance (R) and reactance (X) values, from which phase is calculated via the relationship $\text{phase} = \arctan(X/R)$. In this analysis, however, only the 50

kHz data was utilized. The choice of using only the 50 kHz data is based on the fact that values obtained at this single frequency are most physiologically important as sensitive indicators of muscle status. Indeed, in most of our earlier studies referenced above, only 50 kHz data, rather than multifrequency data, was studied. The sensitivity stems from the fact reactance and phase values of healthy muscle peak at approximately 50 kHz, and in disease states, declines in impedance values at this frequency are most readily observed. The measurements were made with a handheld electrode array (HEA) as previously described (Narayanaswami *et al.*, 2012). The HEA consisted of four stainless steel electrodes, the inner two serving as voltage-measuring electrodes and the outer two serving as current-emitting electrodes. Prior to applying the array, the skin overlying the various muscles studied was moistened with isotonic saline to ensure good electrical contact.

In the upper extremities, EIM testing was performed on deltoid, triceps, biceps, brachioradialis, wrist flexors, wrist extensors, and extensor indicis. In the lower extremities, EIM testing was performed on tensor fascia latae, vastus lateralis, vastus medialis, biceps femoris, medial gastrocnemius, tibialis anterior and extensor hallucis longus.

2.3 Subcutaneous fat thickness measurement

Since variations in subcutaneous fat may impact the measured impedance data, subcutaneous fat thickness was measured using a Terason 2000 ultrasound system (Teratech Corp, Burlington, MA). Measurements were made at the same location as the EIM measurements, using electronic calipers provided with the ultrasound software.

2.4 Data Analysis

The 50 kHz impedance values for each muscle were extracted from the multifrequency data and are the only data reported here. Since the data across individuals was parametric in form, comparisons between groups and subgroups were made by unpaired t-tests. Significance was assumed at $p < 0.05$, two-tailed. For the figures, the actual mean impedance values \pm standard error were plotted. For the tables, differences between younger and older groups are reported as mean percent difference \pm standard error in the older group as compared to the younger group \pm standard error (e.g., a $-10\% \pm 4\%$ value would indicate that the mean older group values were 10% lower than that of the younger group with a standard error of the mean of $\pm 4\%$).

3. Results

3.1 Cumulative results

Figure 1 plots the actual impedance values \pm standard error. Table 2 shows that the overall percentage difference in mean reactance (combined upper and lower extremity data) was lower in the older as compared to younger groups ($-13 \pm 4\%$, $p = 0.009$); however, neither resistance nor phase showed a significant reduction. When evaluating the lower extremities alone, the reactance was lower ($-23 \pm 6\%$, $p = 0.001$) in older individuals as compared to the younger; resistance was also lower ($-27 \pm 7\%$, $p = 0.005$); interestingly, this was true not only on average, but also for almost every individual lower extremity muscle. In contrast, there was no significant difference in upper extremity values for any measure, although there was a trend for reactance to be lower in the older group ($-9 \pm 5\%$, $p = 0.096$), whereas resistance was non-significantly *higher* in the older group ($+5 \pm 9\%$, $p = 0.55$).

3.2 Results by gender

We next sought to determine if gender influenced these results. It is noteworthy that the average age of women in the study was slightly lower than that of men (50 vs. 56 years),

mostly due to a difference in younger group, where the average age was 28 years as compared to 39 years.

The gender-specific results are summarized in Figure 2 and Tables 3 and 4. Reactance values of combined upper and lower extremities showed small, near-significant differences between the younger and older groups for both men and women (-12 ± 6 , $p = 0.06$ for men and -12 ± 6 , $p = 0.07$ for women); resistance values were also near-significant for men but not for women; phase showed no difference for any of the measures. However, when we further separated the data into upper and lower extremities, and then evaluated muscles individually, the results were somewhat unexpected. In men (Table 3), no single muscle in the upper extremities was significantly different between the old and young group, whereas resistance and reactance values were consistently lower in the lower extremities of the older group (mean $-25 \pm 7\%$, $p = 0.007$ for reactance and $-21 \pm 8\%$, $p = 0.019$ for resistance). In women (Table 4), by contrast, a less consistent pattern was present. In the upper extremities, reactance was reduced on average (-17 ± 6 , $p = 0.03$), whereas resistance was reduced in the lower extremities (-21 ± 7 , $p = 0.02$); however, the difference across muscles was quite inconsistent.

3.3 Analysis of subcutaneous fat thickness

In order to help confirm that the subcutaneous fat thickness was not confounding our results, we also analyzed the average subcutaneous fat thickness separately in each of the subgroups of subjects (Table 5); these data confirmed that there were no significant differences in subcutaneous fat thickness and thus the influence of tissue on the results was likely very small.

4. Discussion

The goal of this study was to perform a preliminary analysis of EIM sensitivity to age-associated change in muscle, or sarcopenia. Our earlier work in this area had already suggested that such a relationship existed (Aaron *et al.*, 2006). However, the approach used during earlier studies involved inconvenient, adhesive electrodes placed on the distal extremities (Rutkove *et al.*, 2002), evaluated only the phase angle, and did not evaluate muscles individually nor make any effort to assess differences between the sexes or between upper and lower extremities.

Through our work in ALS and in other neuromuscular diseases, we have identified a major change in the impedance parameters with progressive disease severity (Ahad and Rutkove, 2009; Wang *et al.*, 2011). Changes in impedance values have also been reported in myotubes growing in cell culture (Rakhilin *et al.*, 2011). Older individuals have fewer muscle fibers and smaller muscle fiber cross-sectional areas than younger individuals, and thus, a difference in the impedance characteristics of the muscle might be anticipated (Lexell, 1995). Therefore, in aging muscle, impedance values might be expected to alter in a consistent fashion.

When comparing young and old individuals, the upper extremity muscles show smaller and for the most part non-significant differences in impedance values; in contrast, lower extremity muscles show more consistent differences, especially in men. This finding is consistent with work that shows that sarcopenia generally impacts the lower extremities to a greater extent than the upper (Janssen *et al.*, 2000). The unexpected result of this study, however, was the observed gender difference between upper and lower extremity alterations. In men the upper extremities showed no statistical difference for either reactance or resistance whereas nearly every muscle studied in the lower extremities showed large and highly significant differences for both measures. In women, in contrast, the picture was far

less consistent with several upper extremity muscles showing lower reactance values and several lower extremity muscles showing lower resistance values. As far as is known, physical activity generally remains similar in both men and women of older age, which renders an activity-based explanation unlikely. Thus, the reason for the gender differences in upper extremity values is also not easily identified.

Another finding that deserves further study was the virtual *absence* of a difference in phase values for any single muscle examined. This is in obvious contrast to our earlier study in which the 50 kHz phase value was the only measure reported (Aaron *et al.*, 2006). The major difference between this study and that earlier study was that the current study utilized a handheld array and evaluated a number of upper and lower extremity muscles whereas in the previous study we evaluated only biceps and quadriceps using a very different electrode setup (with current-emitting electrodes placed on the palms of the hands for biceps measurement and the dorsum of the feet for quadriceps measurement). This difference in electrode set-up could potentially be responsible, since the earlier approach would be sensitive to overall muscle mass whereas our current approach, using a handheld array, is likely less sensitive since the current penetrates only the superficial aspects of the muscle (Jafarpoor *et al.*, 2013).

Importantly, in this analysis we only evaluated EIM data obtained at 50 kHz. However, impedance values can be analyzed over a much larger frequency range, and such analyses may offer additional useful information and potentially sensitivity to age-dependent changes (Esper *et al.*, 2006). However, due to the limitations of this retrospective analysis, and the current complexity of analysis already presented, such work is best left for future prospective studies specifically addressing this question.

This study has a number of clear limitations. Most importantly, the data analyzed here represent a retrospective analysis drawn from a larger data set from a study not focused on age effects but rather on the diagnosis of radiculopathy; moreover, we have integrated data from true healthy controls with that from unaffected limbs of radiculopathy subjects. Nonetheless, repeating this study with larger groups of truly healthy individuals would be ideal. Second, we arbitrarily chose our cut-off ages to attempt to maximize our group sizes, and a more precise analysis by decade with larger numbers would be useful. Third, having a larger number of older individuals would also be helpful such that trends within the older population could be identified. Finally, it is likely that subcutaneous fat thickness influences the results to some extent (Sung *et al.*, 2012). Fortunately, the absence of a significant difference in values between the younger and older adults makes any contribution from this factor relatively small.

In summary, we have observed significant gender-specific differences in the 50 kHz reactance and resistance values between younger and older individuals obtained using a handheld array configured with a commercial bioimpedance measuring system. These observations suggest that EIM deserves further study as a method for assessing sarcopenia. However, more work is needed to better understand the relationship between these differences in impedance values and the functional and structural alterations in muscle associated with aging.

Acknowledgments

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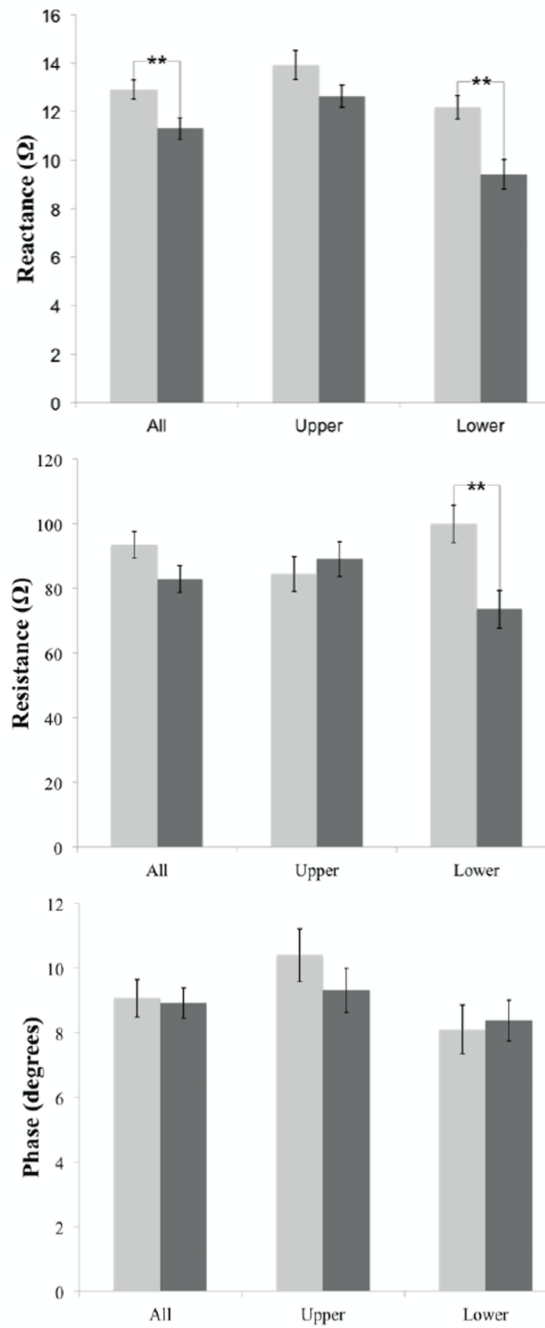


Figure 1. Summary of data; light gray, younger; dark gray, older. Impedance values \pm standard error of the mean; ** $p < 0.01$

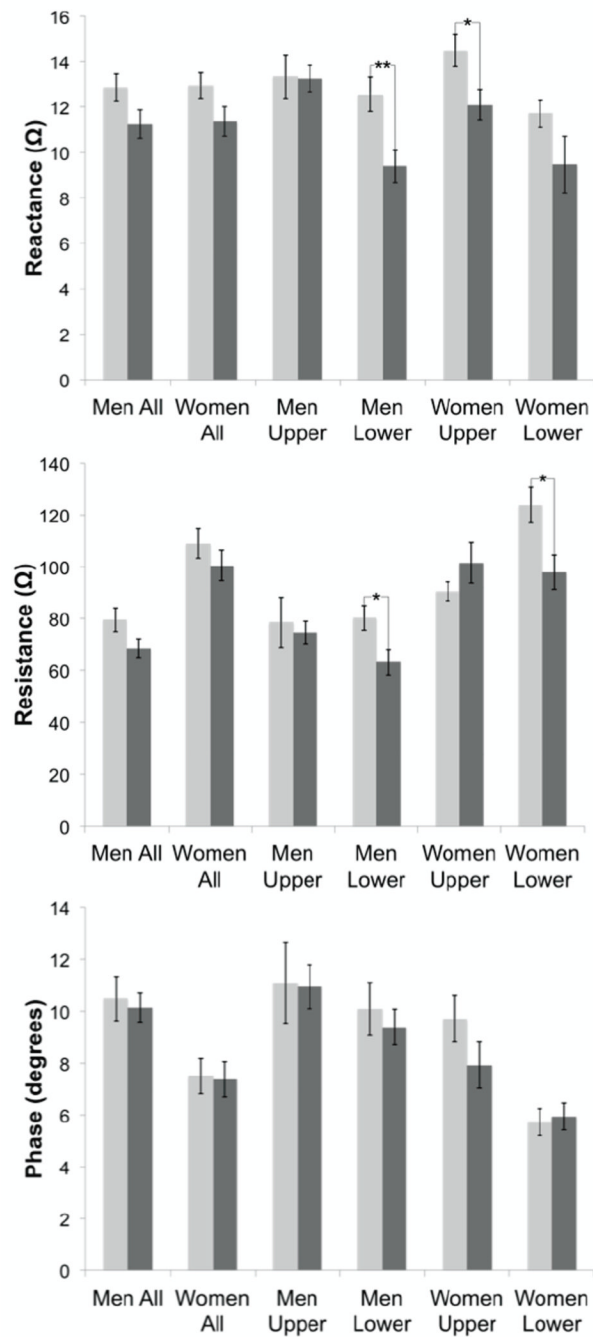


Figure 2. Summary of data broken down by gender; light gray, younger; dark gray, older. Impedance values \pm standard error of the mean; *p < 0.05, **p < 0.01

Table 1

Demographics and limb distribution

	Upper Extremity						Total Number
	Younger			Older			
	Number	Mean Age	Range	Number	Mean Age	Range	
Men	8	39	29-50	11	68	62-83	19
Women	8	32	21-44	13	74	62-85	21
Upper Extremity Totals	16	38	21-50	24	71	62-85	40
	Lower Extremity						Total Number
	Younger			Older			
	Number	Mean Age	Range	Number	Mean Age	Range	
Men	12	40	24-49	12	70	60-83	24
Women	10	25	19-38	5	70	63-78	15
Lower Extremity Totals	22	33	19-49	17	70	60-83	39
(Upper + Lower) Totals	38			41			79

Table 2

Percent differences between younger and older adults (mean ± standard error)

	Younger		Older		Reactance (X)		Resistance (R)		Phase (P)	
	Number	Number	% Diff	p value	% Diff	p value	% Diff	p value	% Diff	p value
Mean Total Body	38	41	-13 ± 4	0.01	-12 ± 6	0.09	-2 ± 8	0.84		
Mean Upper Extremity	16	24	-9 ± 5	0.10	5 ± 9	0.55	-11 ± 10	0.32		
Deltoid	16	24	-7 ± 8	0.44	-0 ± 8	0.97	-6 ± 14	0.70		
Biceps brachii	16	24	-8 ± 6	0.20	10 ± 12	0.41	-14 ±	0.39		
Brachioradialis	16	24	-5 ± 6	0.46	7 ± 11	0.48	-7 ± 11	0.59		
Triceps brachii	16	24	-20 ± 5	0.01	-3 ± 13	0.83	-15 ±	0.24		
Forearm	16	24	-7 ± 6	0.28	-5 ± 8	0.58	-1 ± 10	0.95		
Forearm flexors	16	24	-18 ± 5	2E-03	11 ± 12	0.35	-22 ± 9	0.05		
Extensor indicis	16	24	-12 ± 6	0.06	-0 ± 6	0.95	-9 ± 8	0.25		
Mean Lower Extremity	22	17	-23 ± 6	1E-03	-27 ± 7	0.01	3 ± 12	0.79		
Tensor fascia	22	17	-33 ± 5	8E-06	-20 ± 8	0.03	-16 ± 9	0.12		
Biceps femoris	22	17	-16 ± 8	0.05	-35 ± 6	5E-04	18 ± 19	0.32		
Vastus lateralis	22	17	-15 ± 8	0.10	-32 ± 9	0.01	24 ± 22	0.24		
Vastus medialis	22	17	-21 ± 7	0.01	-22 ± 8	0.03	0 ± 13	0.97		
Tibialis anterior	22	17	-20 ± 7	0.01	-32 ± 7	3E-03	13 ± 14	0.30		
Medial gastroc.	22	17	-24 ± 7	2E-03	-29 ± 9	0.02	-5 ± 14	0.76		
Extensor	22	17	-30 ± 9	4E-03	-34 ± 6	2E-04	-2 ± 12	0.88		

Significant differences shown in **bold**.

Table 3

Percent differences between younger and older men (mean ± standard error)

	Younger	Older	Reactance (X)	Resistance (R)	Phase (P)	
	Number	Number	% Diff	% Diff	% Diff	
	r	r	p value	p value	p values	
Mean Total	20	23	-13 ± 6	-14 ± 7	-3 ± 10	0.73
Mean Upper Extremity	8	11	-1 ± 8	-5 ± 13	-1 ± 16	0.94
Deltoid	8	11	6 ± 16	-5 ± 13	4 ± 26	0.88
Biceps brachii	8	11	-1 ± 9	-4 ± 16	-7 ± 21	0.77
Brachioradialis	8	11	6 ± 9	2 ± 13	2 ± 17	0.90
Triceps brachii	8	11	-11 ± 9	-18 ± 58	-1 ± 21	0.95
Forearm	8	11	2 ± 8	1 ± 12	2 ± 14	0.89
Forearm flexors	8	11	-14 ± 8	-7 ± 15	-12 ± 47	0.47
Extensor indicis	8	11	-9 ± 9	0 ± 7	-8 ± 9	0.38
Mean Lower Extremity	12	12	-25 ± 7	-21 ± 8	-7 ± 12	0.58
Tensor fascia	12	12	-36 ± 6	-20 ± 6	-22 ± 10	0.10
Biceps femoris	12	12	-17 ± 13	-30 ± 8	7 ± 20	0.73
Vastus lateralis	12	12	-17 ± 17	-32 ± 6	17 ± 21	0.38
Vastus medialis	12	12	-20 ± 9	-21 ± 7	-2 ± 14	0.89
Tibialis anterior	12	12	-26 ± 8	-28 ± 8	0 ± 12	0.98
Medial gastroc.	12	12	-27 ± 8	-21 ± 10	-14 ± 40	0.40
Extensor	12	12	-36 ± 6	-30 ± 6	-15 ± 26	0.26

Significant differences shown in **bold**.

Table 4

Percent differences between younger and older women (mean ± standard error)

	Younger r	Older r	Reactance (X) %	Resistance (R) %	Phase (P) %	
	Number	Number	% Diff	% Diff	% Diff	
	r	r	p value	p value	p value	
Mean Total Body	18	18	-12 ± 6	-8 ± 7	-2 ± 12	0.89
Mean Upper Extremity	8	13	-17 ± 6	12 ± 10	-18 ± 11	0.12
Deltoid	8	13	-16 ± 7	3 ± 9	-13 ± 13	0.34
Biceps brachii	8	13	-15 ± 8	17 ± 12	-19 ± 17	0.30
Brachioradialis	8	13	-13 ± 8	10 ± 14	-13 ± 15	0.41
Triceps brachii	8	13	-26 ± 6	7 ± 11	-25 ± 9	0.02
Forearm extensors	8	13	-14 ± 8	-11 ± 10	-2 ± 15	0.92
Forearm flexors	8	13	-22 ± 6	23 ± 15	-30 ± 11	0.02
Extensor indicis	8	13	-15 ± 9	-2 ± 8	-10 ± 12	0.47
Mean Lower Extremity	10	5	-19 ± 11	-21 ± 7	4 ± 12	0.76
Tensor fasciae latae	10	5	-26 ± 11	-9 ± 13	-17 ± 7	0.06
Biceps femoris	10	5	-18 ± 13	-30 ± 8	13 ± 18	0.47
Vastus lateralis	10	5	-17 ± 14	-19 ± 7	-5 ± 15	0.77
Vastus medialis	10	5	-26 ± 11	-11 ± 8	-15 ± 13	0.28
Tibialis anterior	10	5	-12 ± 11	-27 ± 8	21.6 ± 15	0.15
Medial gastroc.	10	5	-20 ± 12	-26 ± 8	-3 ± 18	0.89
Extensor hallucis	10	5	-16 ± 17	-33 ± 6	20 ± 19	0.30

Significant differences shown in **bold**.

Table 5Subcutaneous fat thickness (in cm) as measured by ultrasound (mean \pm standard error)

Mean Upper Extremity	Younger (Number)	Older (Number)	Upper Younger (cm)	Upper Older (cm)	P-value
Male	8	11	0.43 \pm 0.06	0.46 \pm 0.03	0.61
Female	8	13	0.45 \pm 0.06	0.60 \pm 0.08	0.13
All	16	24	0.44 \pm 0.04	0.54 \pm 0.05	0.11
Mean Lower Extremity	Younger (Number)	Older (Number)	Lower Younger (cm)	Lower Older (cm)	P-value
Male	12	12	0.56 \pm 0.07	0.61 \pm 0.07	0.62
Female	10	5	1.10 \pm 0.13	0.90 \pm 0.12	0.49
All	22	17	0.78 \pm 0.09	0.70 \pm 0.07	0.48