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Electrical Impedance Myography for Evaluating Paretic Muscle Changes After Stroke

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Abstract

Electrical impedance myography (EIM) was used to assess the paretic muscle intrinsic electrical properties post stroke. Twenty-seven subjects with chronic hemiparesis participated in this study. Muscle impedance was measured by applying high-frequency, low-intensity alternating current to biceps brachii muscles. Major EIM parameters, resistance (R), reactance (X), phase angle (θ), and electrical anisotropy ratios (AR) of the three parameters, were examined at 50 kHz. Statistical analysis demonstrated significant reduction of reactance, phase angle, AR of resistance, and AR of reactance in the paretic muscle compared with the contralateral side (Paretic X: $6.16 \pm 0.55 \Omega$, contralateral X: $7.62 \pm 0.46 \Omega$, and $p < 0.001$; Paretic θ : $10.97 \pm 0.84^\circ$, contralateral θ : $14.5 \pm 0.82^\circ$, and $p < 0.001$; Paretic AR of R: 0.969 ± 0.013 , contralateral AR of R: 1.008 ± 0.011 , and $p < 0.02$; and Paretic AR of X: 0.981 ± 0.066 , contralateral AR of X: 1.114 ± 0.041 , and $p < 0.02$). Correlation analysis, however, did not show any significant relationship between EIM parameters and clinical assessments. Findings of this paper indicated significant changes in the muscular intrinsic electrical properties after stroke, possibly related to structural modifications induced by loss of muscle fibers or fat infiltration as well as changes in the quality of cell membranes post stroke.

Keywords

Hemiparetic stroke; muscle; electrical impedance myography (EIM); anisotropy

I. Introduction

STROKE remains the leading cause of long-term disability worldwide. Following a stroke, more than 60% of survivors undergo incomplete recovery, 50% suffer from hemiparesis and 30% are unable to walk unassisted [1]-[3]. Given that more than \$30 billion is spent in healthcare and loss of productivity each year, stroke imposes a dramatic burden on patients' family, healthcare, and the economy [4].

The general goal of physical rehabilitation is to help patients restore various motor functions such as grasping, reaching or locomotion so they can resume daily activities and live more independently. To achieve that, rehabilitation intervention focuses on improving motor control and the quality of movement [4]. Smooth control of movement relies on fine adjustments of strength in individual muscles. For stroke survivors who have chronic weakness in the contralesional side, restoration of muscle strength is an essential step in rehabilitation. Muscle weakness possibly involves both neural and muscular factors. Characterizing changes of the intrinsic properties in muscles after stroke may improve current knowledge on the mechanisms of muscle weakness.

Muscle structural changes may occur after a cerebral lesion as a consequence of disrupted synaptic inputs to the motor neurons [1], [5]–[7]. The typical process includes muscle denervation followed by motor axonal sprouting and collateral reinnervation [8], [9]. Previous studies have applied electrophysiological, histological, and imaging techniques to examine different aspects of muscular changes in stroke. In the current study, a novel technique named electrical impedance myography (EIM) was applied to explore muscle intrinsic properties in the paretic muscles.

EIM evolves from bioelectrical impedance analysis (BIA), which has been used as a non-invasive bedside technique for nutrition assessment for decades [10]–[12]. The conventional BIA technique estimates whole body volume, mass, fat-free mass or other compartmentalized body compositions based on appropriate equations. In clinical studies, such measures require population-specific models and are often influenced by a number of factors including hydration, fat fraction, and geometrical boundary conditions [12], [13]. In contrast, EIM measures well-defined local body segments and outputs raw bio-impedance data [12], [14]. It involves minimal setting time and achieves high reproducibility [15], which may have great potential in the clinical evaluation and diagnosis of the conditions of muscles in stroke.

Unlike conventional electrophysiological techniques that involve neuronal and muscular depolarization, EIM applies weak alternating current to assess muscle resistive and capacitive properties [14], [16]. Muscle resistance (R) is defined as the inherent resistivity of skeletal muscle to current passing through extracellular and intracellular fluid. Muscle reactance (X) represents the delay in conduction caused by cell membranes, tissue interfaces

and nonionic substances [10], [13], [17], [18]. Both resistance and reactance are proportional to muscle length and inversely proportional to the cross sectional area of the muscle. Therefore, they are influenced by muscle mass, shape and tissue quality. To reduce the impact of muscle anatomy on impedance analysis, phase angle is used to describe the relation between resistance and reactance ($\theta = \arctan(X/R)$) [19], which evaluates membrane oscillation properties of the muscle. Another important feature of muscle is its anisotropy, illustrated as directional dependence of the muscle impedance. Muscle anisotropy represents the degree of columnar order in the arrangement of the fibers [20].

Previous EIM studies have demonstrated promising applications of impedance measurement in evaluation of muscle conditions in neuromuscular diseases including amyotrophic lateral sclerosis (ALS), muscular dystrophy, and spinal muscular atrophy (SMA) [14], [16], [20]–[24]. For example, abnormal impedance variables in terms of phase angle and resistance are observed in the affected muscles. In addition, there exist strong correlations between impedance measures and conventional measures of ALS severity [14], [25], [26]. In particular, the phase angle of the impedance has been used as a sensitive biomarker for tracking ALS progress [21].

The present study is the first application of the EIM technique in stroke. Impedance variables were measured bilaterally from the biceps brachii muscle and compared between the paretic and contralateral sides. By examining muscle impedance, EIM can help characterize muscular alterations in stroke, such as muscle fiber arrangement and membrane integrity, etc. This will provide new insights towards understanding the mechanisms of muscle weakness and other associated functional loss secondary to neural impairment.

II. Methods

A. Subject

A total of 27 subjects surviving from a hemispheric stroke (12 Female, 15 Male, aged 37–79 years) participated in the study. All participants had no history of any other neurological disorders. The time since stroke varied from 1 to 26 years (5.62 ± 5.36 years, mean $\pm$ std). Subjects gave written consent approved by the Committee for the Protection of Human Subjects (CPHS) at University of Texas Health Science Center prior to the experiment. Clinical assessments, including the Modified Ashworth Scale (MAS), Manual Muscle Testing (MMT) and the Fugl-Meyer Upper Limb Assessment, were performed to evaluate participants' spasticity and functional recovery (Table I).

B. Experiment

Subjects were informed not to exercise on the day before the experiment. They were instructed to remain relaxed and seated upright with the shoulder slightly abducted and neutrally rotated throughout the experiment. Impedance measurement was performed on the biceps brachii muscle using the EIM1103 system (Skulpt Inc, Boston, USA). Saline was applied to moisten the skin before each test. Subsequently, a handheld electrode array (P/N number: 20–00045) was placed on the muscle bulk with gentle pressure to ensure proper contact between the electrodes and the skin. The test involved low intensity stimulation (<

1mA) of alternating current across a wide range of high frequencies from 1 kHz to 10 MHz in discrete steps. Each muscle was measured multiple times and only three consistent trials were saved.

The handheld array has an arrangement of three pairs of current electrodes and two pairs of voltage electrodes. In particular, two pairs of current electrodes and one pair of voltage electrodes are arranged parallel to the muscle direction whereas the remaining pairs of current and voltage electrodes are perpendicular to the muscle fibers. The inter-electrode distance between each pair of voltage electrodes is 14 mm. The system outputs three configurations of impedance variables from three pairs of current electrodes respectively. Impedance of Configuration 1 was collected from the current electrode pair that has the largest inter-electrode distance of 68 mm. Impedance Configuration 2 and 3 were obtained from the other two pairs of current electrodes with an inter-electrode distance of 43 mm. Configurations 1 and 2 are parallel to the muscle and Configuration 3 is perpendicular to the muscle.

C. DataAnalysis

All data saved in the EIM system were exported to MATLAB®(MathWorks, Natick, MA) for offline analysis. Impedance variables included resistance (R), reactance (X), and phase angle ($\theta = \arctan(X/R)$) from three configurations across multiple frequencies. It is previously suggested that electrodes with a wider electrode distance can provide more reliable and representative data [27]. Thus, impedance analysis in this study mainly focused on variables from Configuration 1 except for calculations of the anisotropy ratios.

Impedance analysis included multi-frequency analysis as well as the conventional analysis at 50 kHz. In some trials, a small number of negative impedance values were observed at low frequencies and the number of negative values varied from trial to trial. The negative impedance indicates lag between the capacitor voltage and current, which may cause poor reproducibility in data processing [12], [28]. Therefore, only positive reactance values were used in the analysis. For each subject, a single frequency range was selected for all trials to guarantee positive values in the paretic and contralateral trials. The lower limit of the ranges was determined as the largest frequency of all trials of the subject which produced the first positive reactance after negative ones. The upper limit of frequency range was set as 3.55 MHz for all subjects. The frequency ranges may vary in different subjects for the multi-frequency analysis. Example plots of resistance, reactance and phase angle in selected frequency ranges are presented in Figure 1 and 2 from two representative subjects.

As illustrated in the figures, the resistance values decreased with increment of frequency (upper left plots of Figure 1 and 2). Regression analysis was applied to explore any linear relationship between muscle resistance and the logarithm of the stimulating frequency. Examples of the linear estimation of resistance and log-frequency relationship are presented in the bottom left plot of Figures 1 and 2. For confirmed significant linear relationship, comparisons of the slope of resistance-log (frequency) were made between the paretic and contralateral muscles.

Impedance variables, R , X and θ , obtained from Configuration 1 at 50 kHz were averaged. The frequency of 50 kHz has been widely used as a standard for single-frequency analysis in BIA and EIM [12]-[14], [20]. To examine the effects of handedness on impedance, the percent differences between the two sides were calculated as suggested in [29]. The robustness and variance of the impedance data were quantified using the coefficient of variation (CV), defined as the amount of variations divided by the mean, for all impedance variables.

Anisotropy ratios (AR) of each variable (X , R , and θ) were calculated using the impedance obtained from Configuration 2 and 3:

$$AR_V = \frac{V_{Con3}}{V_{Con2}}$$

where V_{con2} and V_{Con3} represent impedance variables of X , R , and θ at 50 kHz in Configuration 2 and 3, respectively. AR ratios were averaged over three trials for each muscle.

D. Statistical Analysis

All data was screened for outliers and normality of distribution. No significant deviations were found. Paired t-test was applied to compare the differences of impedance variables between paretic and contralateral muscles, which included resistance, reactance, phase angle, anisotropy ratios of $R/X/\theta$ at 50 kHz, and slope of resistance-log (frequency). Pearson correlation analysis was used to assess any linear correlation between EIM variables and clinical assessments in terms of the Fugl-Meyer scores and duration of the stroke. Due to the ordinal nature of the MAS and MMT, Spearman ρ coefficients were calculated to examine whether MAS score or MMT was associated with EIM variable changes. Statistical significance was defined as $p < 0.05$. Results are reported in a mean $\pm$ standard error format.

III. Results

All subjects underwent the Modified Ashworth Scale assessment on the elbow flexors. Functional evaluation using the Fugl-Meyer assessment and MMT were performed on 18 out of the 27 subjects.

A. Impedance Patterns

Different patterns of impedance parameters were observed in two representative subjects (Figure 1 and 2). Impedance variables are displayed in semi-log plots with a logarithmic scale of frequency in the x-axis and impedance in the y-axis. In Figure 1, subject S1 showed larger resistance and similar reactance values in the paretic muscle compared with the contralateral muscle in the frequency range from 5.6 kHz to 3.55 MHz (values averaged over 3 trials at 50 kHz: paretic R : 37.48 Ohm, contralateral R : 29.68 Ohm; paretic X : 8.4 Ohm, contralateral X : 8.81 Ohm). The second subject (S2) showed similar resistance in the paretic and contralateral muscles, but smaller reactance values in the paretic muscle (Figure 2) in the frequency range from 16 kHz to 3.55 MHz (paretic R : 19.16 Ohm, contralateral R : 18.96

Ohm; paretic X: 5.04 Ohm, contralateral X: 8.12 Ohm). Both subjects showed smaller phase angles in the paretic muscles than in the contralateral side (S1: paretic θ : 12.74°, contralateral θ : 16.76°; S2: paretic θ : 14.88°, contralateral θ : 23.28°). In total, there are seven subjects demonstrating the same pattern as in Figure 1 and twelve subjects demonstrating the same pattern as in Figure 2.

B. Multi-Frequency Analysis

Examination of the relationship between the resistance and the logarithm of the frequency was performed in the paretic and contralateral sides for all subjects. Examples of the regression analysis from the two subjects are presented in the bottom left plots of Figure 1 and 2 respectively.

Significant negative linear relationships between the resistance and log-frequency was found in all other subjects (paretic: $r^2 = 0.89$, $p < 0.0001$; contralateral: $r^2 = 0.85$, $p < 0.0001$). Then the slope of resistance was averaged and compared between the paretic and contralateral sides across all subjects. Statistical analysis, however, did not confirm any significant differences of the slope between the paretic and the contralateral sides (paretic slope: -8.79 ± 0.55 Ohm/Hz, contralateral: -9.15 ± 0.39 Ohm/Hz, $p = 0.21$, Figure 3b).

C. Conventional Analysis at 50 kHz

Impedance variables of R, X and θ were compared between the paretic and contralateral muscles at 50 kHz. The reactance and phase angle were substantially lower in the paretic muscle and no significant difference in resistance between the paretic and contralateral sides was found (paretic: 32.06 ± 1.96 Ohm, contralateral R: 30.36 ± 1.57 Ohm, $p = 0.1$; paretic X: 6.16 ± 0.55 Ohm, contralateral X: 7.62 ± 0.46 Ohm, $p < 0.001$; paretic θ : $10.97 \pm 0.84^\circ$, contralateral θ : $14.5 \pm 0.82^\circ$, $p < 0.001$; Figure 3a and b).

Anisotropy ratios of resistance, reactance and phase angle were calculated from Configurations 2 and 3. Significant reductions of AR of R and AR of X were observed in the paretic biceps compared to the contralateral side (paretic AR of R: 0.969 ± 0.013 , contralateral AR of R: 1.008 ± 0.011 , $p < 0.02$; paretic AR of X: 0.981 ± 0.066 , contralateral AR of X: 1.114 ± 0.041 , $p < 0.02$). AR of phase angle, however, did not show significant differences between the paretic and contralateral sides (paretic AR of θ : 1.005 ± 0.063 , contralateral AR of θ : 1.098 ± 0.037 , $p = 0.07$; Figure 3c).

D. Clinical Relevance

Clinical assessments of individual subjects were illustrated in Table I. Spearman ρ tests did not confirm any correlations between MAS or MMT and the EIM variables ($p > 0.2$). Similarly, there was no significance found between the other two clinical measures (Fugl-Meyer score and duration since the stroke) and the EIM measures. Note that correlation analysis of the Fugl-Meyer score and MMT was applied only to the 18 subjects who had the assessment.

E. Robustness Analysis

Thirteen subjects were affected in the dominant side and the rest of subjects were affected in the non-dominant side. The differences of impedance between the paretic and contralateral sides were calculated. The resistance demonstrated a range from -13.24% to 47.45% of the differences with an average value of 5.6% . In addition, the differences of reactance and phase angle showed ranges from -67.32% to 55.81% and -64.2% to 69.92% , with averaged values of -19.14% and -24.31% , respectively. Calculation of the CV demonstrated larger variability in the paretic muscle compared with the contralateral side for all impedance parameters (paretic CV for R, X, θ : 0.32, 0.46, 0.4; contralateral CV for R, X, θ : 0.27, 0.31, 0.3).

IV. Discussion

The present study integrated conventional EIM analysis at 50 kHz, multi-frequency analysis, and anisotropy analysis to examine alterations of the intrinsic electrical properties of muscle after a stroke. Impedance analysis based on 50 kHz disclosed substantial reductions in the reactance, phase angle, and anisotropy ratios of resistance and reactance in the paretic biceps brachii muscle compared with the contralateral side.

A. Impedance Analysis

Results from the current study show a significantly lower phase angle in the paretic biceps brachii muscle compared with the contralateral side. Unlike muscle resistance and reactance, phase angle does not represent muscle mass or shape information as those factors cancel out in the calculation. Instead, it is indicative of subtle physiological changes relative to the integrity of cell membranes. For example, reduced EIM phase angle may imply alterations in the distribution and quality of cell membranes and connective tissue of the muscle [25]. Phase angle is also a sensitive biomarker for tracking disease progression in ALS [14], [21], [26]. It was found that EIM phase measured from the most rapidly progressing muscle demonstrated similar decline rate as other severity measures such as handheld dynamometry or the revised ALS Functional Rating Scale [21].

A practical means to understand the cause of reduced phase angle in the paretic muscle is to examine the relationship between reactance and resistance. In the present study, we demonstrated two representative patterns of resistance and reactance relation that may account for decreased phase angle in the paretic muscles (Figure 1 and 2). The first pattern shows larger resistance in the paretic muscle and similar reactance values in the paretic and contralateral muscles across multiple frequencies. In the second pattern, the reactance was smaller in the paretic muscle whereas resistance remained similar in both sides. It seems that either elevated resistance or reduced reactance in the paretic muscle contributes to a reduction of phase angle as long as the other parameter remains similar to the value of the contralateral side. In the ALS animal model and the neuromuscular disease models, decrease of phase angle was often attributable to an elevated resistance coupled with a reduced reactance [21], [30], [31]. Interestingly, it is also observed that low resistance and reactance can lead to a reduction of the phase angle in the animal model as long as the reactance decreases faster than resistance [30].

Resistance and reactance are both inversely related to the cross-sectional area of the muscle and reflect muscle mass and geometry as well as tissue quality [19]. In particular, the resistance is closely related to the content of extracellular and intracellular water and the reactance is mainly influenced by the properties of cell membranes [32], [33]. In the current study, we observed non-significant elevations in resistance but significant decreases of reactance in the paretic muscles at 50 kHz. The findings are similar to previous EIM studies in aging, ALS and myopathy [11], [14], [20], [30], [34]. Increased resistance and reduced reactance are indicative of abnormal muscle fiber structure and membrane integrities, induced by loss of muscle fibers, reduced fiber cross-sectional area, or increased intramuscular fat [14], [20], [30]. Muscle atrophy and changes in fiber-type composition occur in the paretic muscle as a result of disuse or during the process of muscle denervation and reinnervation subsequent to a hemispheric brain lesion [5]–[7], [35]. Paretic lower limb muscles have been observed to have an approximate 20% reduction in muscle area and volume compared to the contralateral side [36]. In addition to loss of muscle mass, excessive intramuscular fat accumulation is found within skeletal muscle in stroke survivors [36], [37]. Such alterations may lead to substantial changes in the conductance and capacitance of the paretic muscle. This study did not measure changes in muscle volume or size, and so it remains unclear how such changes are quantitatively related to the reduced reactance in the paretic muscles.

Dependent edema may occur in stroke survivors as a result of impaired mobility. Increased fluids in the muscle can lead to impedance changes, particularly, a decrease in muscle resistance. In a previous study, a significant reduction of muscle resistance was observed shortly after injection of Botulinum toxin, indicating high sensitivity of the EIM system in detection of local water accumulation [38]. In the current study, muscle resistance in the paretic side is similar or slightly larger than that in the contralateral side. This implies that dependent edema may not occur in the examined muscles.

The reproducibility of the EIM was confirmed in a previous study which repeated measures were applied to three muscles with testing dates 7 to 250 days apart. The results showed high intraclass correlation coefficients and an average of 4.2% of variability for all three muscles [15]. In this study, robustness and variation analysis demonstrated larger coefficients of variation for all impedance variables in the paretic muscle. In addition, the differences of reactance and phase angle between paretic and contralateral sides are remarkable larger than the reported side-to-side differences in the normal subjects [29]. Given that hemiparesis was evenly distributed in the dominant and non-dominant muscles, findings of reduced impedance in this study are more likely associated with muscle structural modifications rather than handedness. Structural modifications could be induced by loss of muscle fibers or fat infiltration as well as changes in the quality of cell membranes post stroke.

The anisotropy of muscle has been established since 1960 and a majority of studies have focused on the resistivity of the tissue [20], [39]. Anisotropy ratios on exposed skeletal muscle are reported to range from 2 to 15 in the literature [39], which are larger than the ratios in our study. Anisotropy ratios vary with electrode size, inter-electrode distance, muscle size, shape, and other compositional factors [40]. It is also found to be influenced by

the frequency and the angular orientation of the electrode with respect to the muscle direction [20], [41]. The relatively smaller electrode size, shorter inter-electrode distance, as well as the surface recording of impedance variables may account for the smaller anisotropy ratios in our study. Reduced anisotropy ratios of resistance and reactance could be associated with loss of muscle fibers and increased fat and connective tissue infiltration [20], [41]. Increased muscle anisotropy in reactance and phase angle were also observed in ALS subjects, possibly due to grouped atrophy as a result of motor unit loss [20].

B. Clinical Relevance and Limitations

The MAS consists of a 6-point ordinal scale to differentiate levels of spasticity [42]. The scale, however, is subjective and tends to cluster in the lower ranges [43]. In our study, a majority of MAS was around 2 or less (18 out of 27). The qualitative nature of the MAS limits the capability to discriminate between individuals [44], [45] and may lead to the insignificant correlations of the study. In addition, evaluation of muscle spasticity or functional recovery involves passive stretching of the muscle or active contractions and movements of the hand and arm. EIM measurements, however, are performed when a muscle is relaxed, which may not characterize functional evaluations of the muscle in a dynamic condition.

Biceps brachii muscle was selected in this study because it is commonly assessed in neurological disorders. Besides, EIM measurements on biceps have demonstrated high reproducibility of test-retest in normal subjects and subjects with ALS [15], [21]. In addition, a significant correlation between EIM and muscle strength has been confirmed in ALS [21]. Strength relevance was not observed in this study. There are a number of factors attributing to the different findings of the two studies. First, strength measurement in our study was based on manual test, which was subjective and had limited accuracy compared with a handheld dynamometer. Second, muscle weakness in stroke involves complicated mechanisms including muscular and neural impairments. In particular, muscle atrophy, motor unit loss or disrupted motor unit recruitment and firing rate can lead to weakness [4], [46], [47]. Third, biceps is less affected compared with the distal muscles in the stroke. Future evaluation of clinical relevance with EIM may focus on more distal muscles such as wrist extensors or tibialis anterior.

To summarize, this study identified significant changes in the intrinsic electrical and anisotropic properties of muscle following a hemiparetic brain lesion. Although these changes were not correlated with the gross clinical assessments of spasticity or functional recovery, they may still provide valuable diagnostic insight into the health of paretic muscles. Future studies that integrate the EIM technique with other electromyography techniques may provide new information on the structural changes of muscle after stroke.

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Biography

Xiaoyan Li received the B.S. degree in electrical engineering from Anhui University, the M.S. degree in biomedical engineering from the University of Science and Technology of China, and the Ph.D. degree in bioengineering from the University of Illinois at Chicago in 2008.

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Le Li received the Ph.D. degree with the Department of Health Technology and Informatics, The Hong Kong Polytechnic University, in 2007. He completed his post-doctoral training with The Hong Kong Polytechnic University in 2010. From 2014 to 2016, he was a Visiting Scientist with the TIRR Memorial Hermann Research Center and the Department of Physical Medicine and Rehabilitation, UTHealth, Houston, USA. He is currently an Associate Professor with the Department of Rehabilitation Medicine, first affiliated hospital, Sun Yat-sen University, Guangzhou, China. His research interests include biosignal processing, neuro-musculoskeletal modeling of normal and spasticity, and musculoskeletal ultrasound application.

Henry Shin received the B.S. and M.S. degrees from the Department of Biomedical Engineering, Northwestern University, in 2013 and 2014, respectively. He is currently pursuing the Ph.D. degree in biomedical engineering with UNC/NC State. He was a Research Coordinator with the NeuroMyo Engineering for Rehabilitation Laboratory, TIRR Memorial Hermann Research Center, from 2014 to 2016. He is interested in

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Sheng Li received the Bachelor of Medicine degree in medicine from Beijing Medical University, Beijing, China, in 1993, and the Ph.D. degree in kinesiology from Pennsylvania State University, University Park, PA, USA, in 2002, and subsequently completed a Post-Doctoral Research Fellowship in neurorehabilitation with the Rehabilitation Institute of Chicago in 2004. He became an Assistant Professor with the University of Montana in 2004. He then returned to residency training from the Department of Physical Medicine and Rehabilitation, The University of Texas Medical School at Houston, from 2009 to 2013. He is currently an Associate Professor with the Physical Medicine and Rehabilitation Department, The University of Texas Medical School at Houston, and an Attending Physician with TIRR Memorial Hermann Hospital.

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References

- [1]. Scherbakov N, von Haehling S, Anker SD, Dirnagl U, and Doehner W, "Stroke induced sarcopenia: Muscle wasting and disability after stroke," *Int. J. Cardiol.*, vol. 170, pp. 89–94, 12 2013. [PubMed: 24231058]

- [2]. Hacke W et al., "Association of outcome with early stroke treatment: Pooled analysis of ATLANTIS, ECASS, and NINDS rt-PA stroke trials," *Lancet*, vol. 363, pp. 768–774, 3 2004. [PubMed: 15016487]
- [3]. Kelly-Hayes M, Beiser A, Kase CS, Scaramucci A, D'Agostino RB, and Wolf PA, "The influence of gender and age on disability following ischemic stroke: The Framingham study," *J. Stroke Cerebrovasc. Diseases*, vol. 12, pp. 119–126, May-Jun 2003. [PubMed: 17903915]
- [4]. Patten C, Lexell J, and Brown HE, "Weakness and strength training in persons with poststroke hemiplegia: Rationale, method, and efficacy," *J. Rehabil. Res. Develop.*, vol. 41, pp. 293–312, 5 2004.
- [5]. Arasaki K et al., "Reduction in the motor unit number estimate (MUNE) after cerebral infarction," *J. Neurol. Sci.*, vol. 250, pp. 27–32, 12 2006. [PubMed: 16904126]
- [6]. Hara Y, Masakado Y, and Chino N, "The physiological functional loss of single thenar motor units in the stroke patients: When does it occur? Does it progress?" *Clin. Neurophysiol.*, vol. 115, pp. 97–103, 1 2004. [PubMed: 14706475]
- [7]. Li X, Fisher M, Rymer WZ, and Zhou P, "Application of the F- response for estimating motor unit number and amplitude distribution in hand muscles of stroke survivors," *IEEE Trans Neural Syst. Rehabil. Eng.*, vol. 24, pp. 674–81, 6 2016. [PubMed: 26168437]
- [8]. Segura RP and Sahgal V, "Hemiplegic atrophy: Electrophysiological and morphological studies," *Muscle Nerve*, vol. 4, pp. 246–248, May-Jun 1981. [PubMed: 7242561]
- [9]. Dattola R et al., "Muscle rearrangement in patients with hemiparesis after stroke: An electrophysiological and morphological study," *Eur. Neurol.*, vol. 33, no. 2, pp. 109–114, 1993. [PubMed: 8467816]
- [10]. Lukaski HC, "Evolution of bioimpedance: A circuitous journey from estimation of physiological function to assessment of body composition and a return to clinical research," *Eur. J. Clin. Nutrition*, vol. 67, no. 1, pp. S2–9, 1 2013. [PubMed: 23299867]
- [11]. Buffa R, Saragat B, Cabras S, Rinaldi AC, and Marini E, "Accuracy of specific BIVA for the assessment of body composition in the United States population," *PLoS One*, vol. 8, no. 3, p. e58533, 2013.
- [12]. Kyle UG, Bosaeus I, de Lorenzo AD, Deurenberg P, Elia M, and Gómez JM, "Bioelectrical impedance analysis—Part I: Review of principles and methods," *Clin. Nutrition*, vol. 23, pp. 1226–1243, 10 2004.
- [13]. Mulasi U, Kuchnia AJ, Cole AJ, and Earthman CP, "Bioimpedance at the bedside: Current applications, limitations, and opportunities," *Nutrition Clin. Pract.*, vol. 30, pp. 93–180, 4 2015.
- [14]. Rutkove SB, Aaron R, and Shiffman CA, "Localized bioimpedance analysis in the evaluation of neuromuscular disease," *Muscle Nerve*, vol. 25, pp. 390–397, 3 2002. [PubMed: 11870716]
- [15]. Rutkove SB, Lee KS, Shiffman CA, and Aaron R, "Test-retest reproducibility of 50 kHz linear-electrical impedance myography," *Clin. Neurophysiol.*, vol. 117, pp. 1244–1248, 6 2006. [PubMed: 16644269]
- [16]. Esper GJ, Shiffman CA, Aaron R, Lee KS, and Rutkove SB, "Assessing neuromuscular disease with multifrequency electrical impedance myography," *Muscle Nerve*, vol. 34, pp. 595–602, 11 2006. [PubMed: 16881067]
- [17]. Matthie JR, "Bioimpedance measurements of human body composition: Critical analysis and outlook," *Expert Rev. Med. Devices*, vol. 5, pp. 239–261, 3 2008. [PubMed: 18331184]
- [18]. Ellis KJ et al., "Bioelectrical impedance methods in clinical research: A follow-up to the NIH technology assessment conference," *Nutrition*, vol. 15, pp. 874–880, Nov-Dec 1999. [PubMed: 10575664]
- [19]. Shiffman CA, Aaron R, Amoss V, Therrien J, and Coomler K, "Resistivity and phase in localized BIA," *Phys. Med. Biol.*, vol. 44, pp. 2409–2429, 10 1999. [PubMed: 10533919]
- [20]. Garmirian LP, Chin AB, and Rutkove SB, "Discriminating neurogenic from myopathic disease via measurement of muscle anisotropy," *Muscle Nerve*, vol. 39, pp. 16–24, 1 2009. [PubMed: 19058193]
- [21]. Rutkove SB et al., "Electrical impedance myography as a biomarker to assess ALS progression," *Amyotrophic Lateral Sclerosis*, vol. 13, pp. 439–445, 9 2012. [PubMed: 22670883]

- [22]. Rutkove SB et al., "Cross-sectional evaluation of electrical impedance myography and quantitative ultrasound for the assessment of Duchenne muscular dystrophy in a clinical trial setting," *Pediatric Neurol.*, vol. 51, pp. 88–92, 7 2014.
- [23]. Arnold W et al., "The neuromuscular impact of symptomatic SMN restoration in a mouse model of spinal muscular atrophy," *Neurobiol. Disease*, vol. 87, pp. 116–123, 3 2016.
- [24]. Rutkove SB et al., "Characterizing spinal muscular atrophy with electrical impedance myography," *Muscle Nerve*, vol. 42, pp. 915–921, 12 2010. [PubMed: 21104866]
- [25]. Aaron R, Esper GJ, Shiffman CA, Bradonjic K, Lee KS, and Rutkove SB, "Effects of age on muscle as measured by electrical impedance myography," *Physiol. Meas.*, vol. 27, pp. 953–959, 10 2006. [PubMed: 16951455]
- [26]. Rutkove SB et al., "Electrical impedance myography correlates with standard measures of ALS severity," *Muscle Nerve*, vol. 49, pp. 441–443, 3 2014. [PubMed: 24273034]
- [27]. Sung M, Spieker AJ, Narayanaswami P, and Rutkove SB, "The effect of subcutaneous fat on electrical impedance myography when using a handheld electrode array: The case for measuring reactance," *Clin. Neurophysiol.*, vol. 124, pp. 400–404, 2 2013. [PubMed: 22917581]
- [28]. Hannan WJ, Cowen SJ, Fearon KC, Plester CE, Falconer JS, and Richardson RA, "Evaluation of multi-frequency bio-impedance analysis for the assessment of extracellular and total body water in surgical patients," *Clin. Sci. (London)*, vol. 86, pp. 479–485, 4 1994. [PubMed: 8168344]
- [29]. Rutkove SB, Esper GJ, Lee KS, Aaron R, and Shiffman CA, "Electrical impedance myography in the detection of radiculopathy," *Muscle Nerve*, vol. 32, pp. 335–341, 9 2005. [PubMed: 15948202]
- [30]. Li J, Geisbush TR, Rosen GD, Lachey J, Mulivor A, and Rutkove SB, "Electrical impedance myography for the in vivo and ex vivo assessment of muscular dystrophy (mdx) mouse muscle," *Muscle Nerve*, vol. 49, pp. 829–835, 6 2014. [PubMed: 24752469]
- [31]. Li J, Staats WL, Spieker A, Sung M, and Rutkove SB, "A technique for performing electrical impedance myography in the mouse hind limb: Data in normal and ALS SOD1 G93A animals," *PLoS One*, vol. 7, no. 9, p. e45004, 2012.
- [32]. Shiffman CA and Rutkove SB, "Circuit modeling of the electrical impedance: I. Neuromuscular disease," *Physiol. Meas.*, vol. 34, pp. 203–221, 2 2013. [PubMed: 23353926]
- [33]. Faes TJ, van der Meij HA, de Munck JC, and Heethaar RM, "The electric resistivity of human tissues (100 Hz–10 MHz): A meta-analysis of review studies," *Physiol Meas.*, vol. 20, pp. R1–10, 11 1999. [PubMed: 10593226]
- [34]. Saragat B et al., "Specific bioelectrical impedance vector reference values for assessing body composition in the Italian elderly," *Expim. Gerontol.*, vol. 50, pp. 52–56, 2 2014.
- [35]. Li X, Wang YC, Suresh NL, Rymer WZ, and Zhou P, "Motor unit number reductions in paretic muscles of stroke survivors," *IEEE Trans. Inf. Technol. Biomed.*, vol. 15, no. 4, pp. 505–512, 7 2011. [PubMed: 21478079]
- [36]. Sions JM, Tyrell CM, Knarr BA, Jancosko A, and Binder-Macleod SA, "Age-and stroke-related skeletal muscle changes: A review for the geriatric clinician," *J. Geriatric Phys. Therapy*, vol. 35, pp. 155–161, Jul-Sep 2012.
- [37]. Ryan AS, Dobrovolsky CL, Smith GV, Silver KH, and Macko RF, "Hemiparetic muscle atrophy and increased intramuscular fat in stroke patients," *Arch. Phys. Med. Rehabil.*, vol. 83, pp. 1703–1707, 12 2002. [PubMed: 12474173]
- [38]. Li X, Shin H, Li L, Magat E, Li S, and Zhou P, "Assessing the immediate impact of botulinum toxin injection on impedance of spastic muscle," *Med. Eng. Phys.*, vol. 43, pp. 97–102, 5 2017. [PubMed: 28169197]
- [39]. Gielen FL, Wallinga-De Jonge W, and Boon KL, "Electrical conductivity of skeletal muscle tissue: Experimental results from different muscles in vivo" *Med. Biol. Eng. Comput.*, vol. 22, pp. 569–577, 11 1984. [PubMed: 6503387]
- [40]. Shiffman CA and Aaron R, "Angular dependence of resistance in noninvasive electrical measurements of human muscle: The tensor model," *Phys. Med. Biol.*, vol. 43, pp. 1317–1323, 5 1998. [PubMed: 9623658]
- [41]. Chin AB, Garmirian LP, Nie R, and Rutkove SB, "Optimizing measurement of the electrical anisotropy of muscle," *Muscle Nerve*, vol. 37, pp. 560–565, 5 2008. [PubMed: 18404614]

- [42]. Bohannon RW and Smith MB, "Interrater reliability of a modified Ashworth scale of muscle spasticity," *Phys. Therapy*, vol. 67, pp. 206–207, 2 1987.
- [43]. Leonard CT, Stephens JU, and Stroppel SL, "Assessing the spastic condition of individuals with upper motoneuron involvement: Validity of the myotonometer," *Arch. Phys. Med. Rehabil.*, vol. 82, pp. 1416–1420, 10 2001. [PubMed: 11588747]
- [44]. Blackburn M, van Vliet P, and Mockett SP, "Reliability of measurements obtained with the modified Ashworth scale in the lower extremities of people with stroke," *Phys. Therapy*, vol. 82, pp. 25–34, 1 2002.
- [45]. Rydahl SJ and Brouwer BJ, "Ankle stiffness and tissue compliance in stroke survivors: A validation of myotonometer measurements," *Arch. Phys. Med. Rehabil.*, vol. 85, pp. 1631–1637, 10 2004. [PubMed: 15468023]
- [46]. Li X, Fisher M, Rymer WZ, and Zhou P, "Application of the F -response for estimating motor unit number and amplitude distribution in hand muscles of stroke survivors," *IEEE Trans. Neural. Syst. Rehabil. Eng.*, vol. 24, no. 6, pp. 674–681, 6 2016. [PubMed: 26168437]
- [47]. Li X, Holobar A, Gazzoni M, Merletti R, Rymer WZ, and Zhou P, "Examination of poststroke alteration in motor unit firing behavior using high-density surface EMG decomposition," *IEEE Trans. Biomed. Eng.*, vol. 62, no. 5, pp. 1242–1252, 5 2015. [PubMed: 25389239]

Fig. 1.

Semi-log plot of an example of impedance parameters from a representative stroke subject (S1), who showed larger resistance and similar reactance values in the paretic muscle across multiple frequencies. Each side had three trials of impedance values with the paretic side marked as red solid lines or dots and the contralateral side as black dashed lines or 'x'. Frequency was in a logarithmic scale. (a) Resistance (R). (b) Reactance (X). (c) Linear relationship of resistance and logarithm of frequency. Paretic: $R = 82.2 - 9.8 * \log_{10}(\text{freq})$, $r^2 = 0.96$, $p < 0.0001$; contralateral: $R = 73.64 - 9.54 * \log_{10}(\text{freq})$, $r^2 = 0.94$, $p < 0.0001$; variable 'freq' represents the frequency, (d) Phase angle (θ).

Fig. 2.

Impedance parameters from another representative stroke subject (S2), who showed similar resistance but smaller reactance values in the paretic muscles at multiple frequencies. Each side had three trials of impedance values with the paretic side marked as red solid lines or dots and the contralateral side as black dashed lines or 'x'. Frequency was in a logarithmic scale. (a) Resistance (R). (b) Reactance (X). (c) Linear relation of resistance and logarithm of frequency. Paretic: $R = 48.09 - 6.23 \cdot \log_{10}(\text{freq})$, $r^2 = 0.97$, $p < 0.0001$; S2 contralateral: $R = 54.37 - 7.66 \cdot \log_{10}(\text{freq})$, $r^2 = 0.89$, $p < 0.0001$; variable 'freq' represents the frequency, (d) Phase angle (θ).

Fig. 3.

Comparisons of impedance variables and anisotropy ratios between paretic and contralateral muscles at 50 kHz. (a) Paretic R: 32.06 ± 1.96 Ohm, contralateral R: 30.36 ± 1.57 Ohm, $p = 0.1$. Paretic X: 6.16 ± 0.55 Ohm, contralateral X: 7.62 ± 0.46 Ohm, $p < 0.001$. (b) Paretic θ : $10.97 \pm 0.84^\circ$, contralateral θ : $14.5 \pm 0.82^\circ$, $p < 0.001$. Paretic slope: -8.79 ± 0.55 Ohm/Hz, contralateral: -9.15 ± 0.39 Ohm/Hz, $p = 0.21$. (c) Anisotropy ratios (AR) of impedance. Paretic AR of R: 0.969 ± 0.013 , contralateral AR of R: 1.008 ± 0.011 , $p < 0.02$. Paretic AR of X: 0.981 ± 0.066 , contralateral AR of X: 1.114 ± 0.041 , $p < 0.02$. Paretic AR of θ : 1.005 ± 0.063 , contralateral AR of θ : 1.098 ± 0.037 , $p = 0.07$.

TABLE I

Subject Clinical Information

ID	Duration (m)	MAS	FM	MMT	Stroke location
1	12	1+	52	4	R lentiform nucleus acute infarct
2	16	0	16	2	R MCA infarct
3	88	1	47	4	R MCA infarct
4	52	1+	5	0	L basal ganglia hemorrhage
5	51	0	4	0	R MCA hemorrhage
6	158	0	21	2	L basal ganglia infarct
7	86	1+	13	1	L basal ganglia infarct
8	75	1+	17	2	L MCA infarct
9	41	1	40	2	R basal ganglia hemorrhage
10	64	1	39	4	L MCA hemorrhage
11	164	0	24	3	R basal ganglia hemorrhage L basal ganglia and thalamic
12	101	1	40	3	infarct
13	88	2	28	3	L MCA infarct
14	24	1+	18	2	Not available
15	60	1+	11	1	R basal ganglia infarct
16	18	3	7	0	L MCA infarct
17	42	2	55	4	Not available
18	23	3	16	2	Left MCA infarct
19	42	1+			Not available
20	93	3			L MCA infarct
21	106	2			Not available
22	21	3			Not available
23	15	4			R pons infarct
24	12	1+			R MCA infarct R frontal lobe and basal ganglia
25	34	3			hemorrhage
26	22	0			R MCA infarct
27	312	3			Not available

MAS: Modified Ashworth Scale, FM: Fugl-Meyer upper limb assessment MMT: Manual Muscle Testing R: right; L: left MCA: Middle Cerebral Artery

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