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Bioelectrical Impedance Analysis on the Paretic and Non-paretic Regions of Severe and Mild Hemiplegic Stroke Patients

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ABSTRACT

For many stroke patients undergoing rehabilitation therapy, there is a need for indicator for evaluating the body function in paretic and non-paretic regions of stroke patients quantitatively. In this paper, the function of muscles and cells in paretic and non-paretic regions of severe and mild hemiplegic stroke patients was evaluated using multi-channel bioelectrical impedance spectroscopy. The paretic and non-paretic regions of severe and mild stroke patients were quantitatively assessed by using bioelectrical impedance parameters such as prediction marker (PM), phase angle (Θ), characteristic frequency (f_C), and bioelectrical impedance vector analysis ($BIVA$). The mean values of impedance vector were significantly discriminated in all comparisons (severe-paretic, severe-non-paretic, mild-paretic, and mild-non-paretic). The bioelectrical impedance parameters were proved to be a very valuable tool for quantitatively evaluating the paretic and non-paretic regions of hemiplegic stroke patients.

Key words: Stroke Patient with Upper Extremity Hemiplegia, Bioelectrical Impedance Parameters, Bioelectrical Impedance Vector Analysis (BIVA)

1. INTRODUCTION

Patients surviving from a stroke often have weakness on one side of the body or trouble with moving, talking, or thinking [1]. Most strokes are ischemic strokes which are caused by insufficient blood flow to the brain when blood vessels are blocked by a clot or become too narrow for blood to get through. Brain cells in the area die from lack of oxygen. In another type of stroke, called hemorrhagic stroke, the blood vessel isn't blocked; it bursts, and blood leaks into the brain, causing serious damage. Many stroke patients have a number of devastating disorders such as hemiplegia, motor disturbance, sensory disability, communication disorders, emotional disorders, and cognitive impairment [2]. After stroke, one of the most commonly occurring problems is the limb dysfunction. About 30 to 60% of the stroke patients have serious problems in their lives due to paralysis of the upper and lower extremity [3]. The dysfunction of the limb seriously degrades the quality of life since it causes the challenges of bodily function and everyday life [4]. The long-term goal of rehabilitation

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therapy is to improve the function of body so that the stroke survivor can live as independent as possible. This will help patients suffering from stroke to relearn basic skills like bathing, eating, dressing and walking [5].

The bioelectrical impedance analysis (BIA) measures the body compositions and characteristic of biological tissue or material in a safe, practical, and non-invasive method [6, 7]. BIA depends on the conduction of radio-frequency electric current by the fluid (body water, interstitial fluid, and plasma), electrolytes, and ionic conductivity and permeability of the cell membrane in the body tissue [8]. BIA has been utilized in the diagnosis of diseases as well as evaluate the hydration status, body composition, muscle-fat ratio, degree of obesity, lean balance, lymphedema, and nutritional status of the human body [9].

In this study, severe stroke subjects (N=8) and mild stroke subjects (N=12) were selected to assess the pathophysiological status about paretic and non-paretic regions of the hemiplegic stroke subjects. The body compositions and basic body function such as fat, lean mass, total body water (TBW), body cell mass (BCM), and body metabolic rate (BMR) were measured to assess the paretic and non-paretic regions using bioelectrical impedance spectroscopy (MultiScan5000, Bodystat Ltd., UK). In addition, the bioelectrical impedance parameters such as prediction marker (PM), phase angle (Θ), characteristic frequency (f_c), and bioelectrical impedance vector analysis ($BIVA$) were also utilized to evaluate hydration status, amount of muscle, and function and integrity of cell membrane in paretic and non-paretic regions.

2. THEORY

2.1 Equivalent Circuit of ECF, Cell Membrane, and ICF

Total body water (TBW) accounts for over 60% of the mass of the human body depending on gender, the age, and the obesity. The intracellular fluid (ICF) accounts for approximately 40% of TBW and the extracellular fluid (ECF) approximately 20% of TBW. Further, the interstitial fluid (ISF) accounts for about 75% of ECF and the plasma about 25% of ECF. Although there have a low protein content, the compositions of ISF are similar to those of the plasma. Cells constituting the human organs and tissues are composed of ECF and ICF acting as an electrical conductors, and the cell membranes acting as the electric capacitor [10].

Fig. 1 represents an equivalent circuit of the cell in the human body [11] and Table 1 describes the symbols indicated in Fig. 1.

Since the resistance (Rm) and the capacitance (Cm) of cell membrane are connected in parallel, the reactance (X_c) of cell membrane in Fig. 1 can be expressed by Eq. (1):

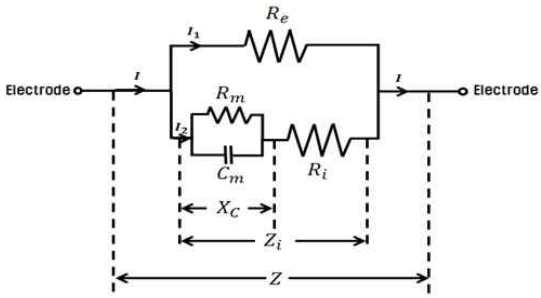

Fig. 1. Equivalent circuit model of cell consisting ECF (R_e), the cell membrane (C_m), and ICF (R_i).

Table 1. Description of symbols indicated in Fig. 1

Symbol	Description
C_m	Capacitance of cell membrane
R_m	Resistance of cell membrane
R_e	Resistance of ECF
R_i	Resistance of ICF
X_c	Reactance of cell membrane
Z_i	Impedance of X_c and R_i
Z	Impedance of Z_i and R_e
I	Current through both ECF and ICF
I_1	Current through only ECF
I_2	Current through both cell membrane and ECF

$$X_C = \frac{1}{\frac{1}{R_m}+j\omega C_m} = \frac{R_m}{1+j\omega R_m C_m} = \frac{R_m}{1+j2\pi f R_m C_m} \quad (1)$$

Impedance (Z_i) of the cell membrane and ICF can be expressed by Eq. 2:

$$Z_i = X_C + R_i = \frac{R_m}{1+j2\pi f R_m C_m} + R_i \quad (2)$$

The total impedance (Z) – which is composed of the reactance (X_C) of cell membrane, the resistance (R_i) of ICF, and the resistance (R_e) of ECF, – can be expressed by Eq. 3:

$$Z = \frac{1}{\frac{1}{R_e}+\frac{1}{Z_i}} = \frac{R_e Z_i}{R_e+Z_i} \quad (3)$$

The reactance (X_C) of cell membrane is dependent on the applied frequency. When the applied frequency is high, the total impedance (Z) is reduced since reactance (X_C) in Eq. 1 is decreased, and Z_i in Eq. 2 is decreased. On the contrary, when the applied frequency is low, Z is increased since the opposite phenomena occur.

2.2 Bioelectrical Impedance Parameters

The prediction marker (*PM*, also impedance ratio) is the ratio of the impedance (*Z*) at 200 kHz to that at 5 kHz. When an alternating current (AC) having a frequency of 5 kHz is applied, the applied AC cannot penetrate the cell membrane and flows in ECF. On the other hand, when an alternating current (AC) having a frequency of 200 kHz is applied, the applied AC has energy enough to penetrate the cell membrane and flows in ICF as well as ECF. Smaller *PM* means more healthy human cells. The *PM* closer to 1.00 represents measly cellular health or excessive amount of fluid [12]. The *PM* is higher in those who subsequently developed edema so that BIA can be utilized as an additional bedside tool with the potential to identify and monitor patients who are susceptible to pathological fluid shifts after major surgery [13]. Higher *PM* values have been associated with postoperative edema [14] worsening renal [15] and cardiac [16] function, and poor nutrition status [17].

The phase angle (Θ) has long been associated with nutritional status and BCM. This parameter is a direct measurement of the functionality of the cell membrane, and recognized as a global health marker in body health assessment [18]. A higher phase angle could mean an increase in BCM or a decrease in fluid, either recovery from infection (or injury) or a reduction of fluid from dehydration. Loss of fat could increase phase angle. On the other hand, a lower phase angle could reflect a loss of BCM, an increase of fluid (rehydrating), and sign of inflammation or infection. Gupta *et al.* demonstrated that phase angle was an independent prognostic indicator in patients with breast cancer and concluded that nutritional interventions targeted at improving phase angle could potentially lead to an improved survival in patients with breast cancer [19].

The characteristic frequency (f_c) is frequency, at which the applied AC flowing through the capacitive path reaches a peak reactance (X_C), and is a useful parameter for evaluating pathophysiological function of cell membrane [20]. When the cell membrane is healthy, f_c is decreased. That is, even though the frequency applied to the cell membranes is lower than 50 kHz (2.12×10^{-10} eV), the ionic conductivity and permeability of the cell membranes can be increased. On the other hand, when the cell membrane is unhealthy, f_c is increased. That is, the ionic conductivity and permeability of the cell membranes cannot be increased although the frequency applied to the cell membranes is higher than 50 kHz. Thus, f_c could be a useful parameter for evaluating the pathophysiological status of the muscles or the cell membrane integrity.

2.3 Bioelectrical Impedance Vector Analysis (*BIVA*)

The BIVA illustrates plot of resistance (*R*) and reactance (X_C) normalized per height as a bivariant vector in the R/H vs. X_C/H graph [21]. The impedance vector (length, direction) in *BIVA* provides a valuable information about hydration sta-

tus, muscle mass and cell membrane integrity. The length of *BIVA* indicates hydration status from fluid overload (decreased resistance, short vector) to exsiccosis, which is insufficient intake of fluids (increased resistance, longer vector) [22].

The direction (migration sideways) of *BIVA* due to low or high reactance indicated decrease or increase of muscle mass in tissues. Significant vector displacement was seen with increasing disease severity [23, 24]. The *BIVA* approach has gained attention as a tool to assess and monitor the hydration and the nutrition status in patients. Moreover, comparison to reference values is possible in *BIVA*; individual vectors can immediately be ranked with regard to tolerance ellipses representing 50%, 75% and 95% of reference values, which allows a detailed classification of vector position. Healthy subjects are usually positioned within the 75% tolerance ellipse [25]. The *BIVA* can be used for routine monitoring of the variation in body fluids, nutritional status of individuals, and for representing a clinically useful procedure [26].

3. METHOD

3.1 Experimental subjects

The experimental subjects were 8 patients (6 females, 2 males) with hemiplegia due to cerebral hemorrhage, and 10 patients (11 females, 2 males) with a mean and standard deviation (± SD) age of 75.85 years (± 8.79 years), an average height of 161.10 cm (± 5.43 cm), an average mass of 55.60 kg (± 6.93 kg), and an average body mass index (BMI) of 21.37 kg/m^2 (± 1.77 kg/m^2). To investigate the correlation between the body compositions and the bioelectrical impedance parameters, 20 subjects were selected as two groups: severe hemiplegic stroke subjects were six females (#2, #4, #10, #11, #19, and #20) and two males (#9, and #13), whereas mild hemiplegic stroke subjects were ten females (#1, #5, #6, #7, #8, #12, #14, #15, #16, and #18) and two males (#3 and #17).

All subjects met the following criteria: 1) had a stroke within last 3 years. 2) were able to move independently for more than 30 min. 3) had sufficient recognition ability to engage in routine communications and follow the directions. Subjects with the following symptom and conditions were excluded in the study: 1) Musculoskeletal diseases or problems with hearing or vision according to the medical records. 2) Complaints of dizziness over last 3 months according to the medical records or during the interview selecting subjects.

Before participating in this study, the purpose and method of the present experiment was sufficiently explained to the subjects, and written informed consents were obtained from each patient. This study was approved by the ethical committee of Inje University Institutional Review Board for Clinical Studies (Document number: 2014250).

3.2 Whole-body impedance measurement

The impedance (Z) measurement was conducted using BIS and applying AC of 800 μA at 50 different frequencies ranging from 5 to 1000 kHz. Impedance parameters (Z, R, X_C, Θ, f_C) as well as body compositions were simultaneously measured at the Medifarm Hospital in Korea between October and November, 2015. Measurement were conducted in the morning after an overnight fast, in the supine position with arms and legs abducted from the body. Eight cutaneous electrodes (Bodystat-0525, UK) were attached to the wrists (left, right) and the ankles (left, right) of 20 stroke subjects with upper extremity hemiplegia. The distance between current applying electrode and voltage detecting electrode was kept at least 5 cm or more.

4. RESULTS AND DISCUSSION

4.1 Body composition of paretic and non-paretic regions in severe and mild hemiplegic stroke patients

Table 2. Body compositions of the study population

	MN	MP	SN	SP
Fat [%]	34.70 ± 3.21	39.6 ± 5.28	41.85 ± 6.23	45.55 ± 4.54
LM [%]	65.26 ± 9.32	60.26 ± 2.06	59.15 ± 6.23	54.45 ± 4.60
TBW [%]	48.30 ± 8.79	40.26 ± 6.47	41.43 ± 3.88	35.60 ± 2.23
BCM [kg]	21.29 ± 5.93	17.83 ± 2.54	15.03 ± 3.08	11.60 ± 2.48
BMR [kcal]	1305.20 ± 208.23	1138.19 ± 193.35	1131.25 ± 137.10	1085.91 ± 113.91

Legend
MN: Mild Non-paretic, MP: Mild Paretic, SN: Severe Non-paretic, SP: Severe Paretic, LM: Lean Mass, TBW: Total Body Water, BCM: Body Cell Mass, BMR: Basal Metabolic Rate

Of the 20 participating subjects, 12 (60%) classified as mild stroke subjects and 8 (40%) were classified as severe stroke subjects. Data on body composition for paretic and non-paretic regions of severe and mild stroke subjects with upper extremity hemiplegia are listed in Table 2. The lean mass, TBW, BCM, and BMR in severe hemiplegic subjects were lower than those in mild hemiplegia subjects, while fat in severe hemiplegia subjects was higher than that in mild hemiplegic subjects. In severe and mild hemiplegia stroke subjects, lean mass, TBW, BCM, and BMR in paretic region were lower than those in non-paretic region, whereas fat in paretic region was higher than that in non-paretic region.

4.2 Bioelectrical impedance parameters

The PM was significantly larger in mild paretic (MP) than in mild non-paretic (MN) and then increased further in severe non-paretic (SN) and severe paretic (SP) in Fig. 2. The mean SD of PM in paretic regions of severe and mild hemiplegic stroke subjects were 0.9200.864 ± 0.013 (MP), and those in non-paretic regions of severe and mild hemiplegic stroke subjects were 0.881 ± 0.024 (SN) and 0.843 ± 0.013 (MN). Therefore, the mean SD of PM in paretic regions were higher than those of PM in non-paretic regions. For example, among 38 individuals undergoing major abdominal surgery, preoperative PM measured by an MF-BIA device (QuadScan 4000, Bodystat) was significantly higher in the 20 participants who developed postoperative edema compared with individuals who did not develop edema later on (0.81 ± 0.03 vs 0.78 ± 0.02; P = .015) [14]. Accordingly, PM in paretic regions of severe strokes subjects was much higher than that of subjects suffering from postoperative edema. These findings suggest that PM can be utilized in evaluating the paretic and non-paretic regions of hemiplegic stroke patients with upper extremity receiving rehabilitation.

Phase angle (Θ) was lower in MP than MN and reduced further in SN and SP in Fig. 3. The mean ± SD of phase angle (Θ) in paretic region of severe and mild hemiplegic stroke subjects were 2.30 ± 0.27 (SP) and 4.01 ± 0.32 (MP). On the other hand, the mean of phase angle (Θ) in non-paretic region

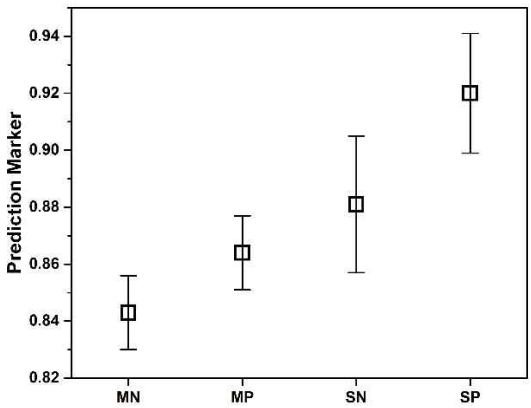

Fig. 2. Significantly larger PM in paretic and non-paretic regions of severe stroke subjects (SP and SN) compared with that in paretic and non-paretic region of mild stroke subjects (MP and MN).

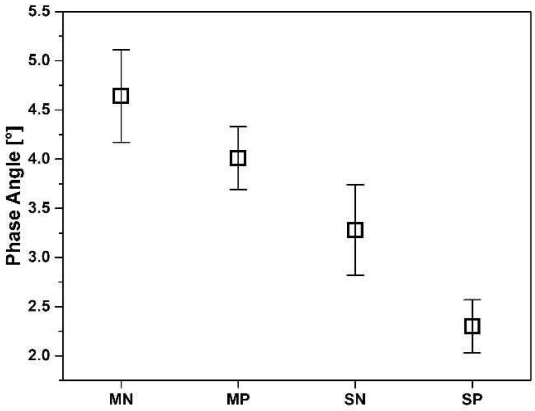

Fig. 3. Significantly smaller phase angles (θ) in paretic and non-paretic regions of severe stroke subjects (SP and SN) compared with those in non-paretic region of mild stroke subjects (MP and MN).

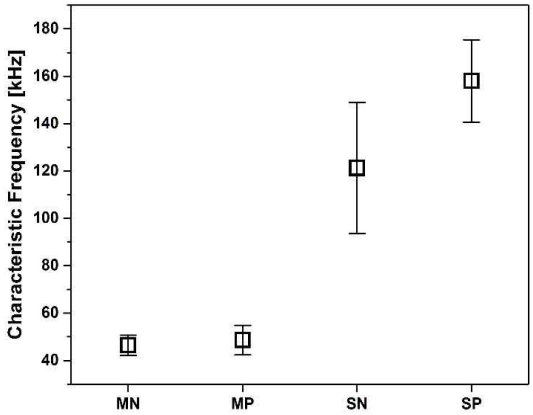

Fig. 4. Significantly larger characteristic frequency (f_c) in severe regions (SP and SN) compared with mild non-paretic (MN) region.

of severe and mild hemiplegic stroke subjects were 3.28 ± 0.46 (SN) and 4.64 ± 0.47 (MN). Therefore, the mean ± SD of Θ in paretic regions was lower than those of PM in non-paretic regions. The mean ± SD (2.30 ± 0.27) of Θ in paretic region of severe stroke patients (SP) with upper extremity were significantly small when compared to those (7.43 ± 0.98° and 7.05 ± 1.1.58°) for males and females on 42 healthy subjects between the age group of 18 to 50 yrs [27]. For example, a higher Θ indicates a proportionally greater reactance for a given resistance, which has been interpreted to suggest more intact cell membranes and higher BCM. In contrast, the low has been interpreted to indicate cell loss and decreased cell integrity and BCM [28]. Θ was reported to be significantly positively correlated with BMI (r=0.011, P<0.001). The reason that severe stroke subjects have low Θ is likely to have less amount and low quality of muscle in paretic region as well as low TBW and BCM. Θ, as a superior prognostic marker, should be considered as a screening tool for the identification of risk patients with impaired nutritional and functional status [29].

The characteristic frequency (f_c) was significantly larger in the severe stroke patients (SN and SP) than in the mild stroke patients (MN and MP) in Fig. 4. The mean ± SD of characteristic frequencies (f_c) in paretic region of severe and mild hemiplegic stroke subjects were 158.00 ± 17.36 kHz (SP) and 48.60 ± 6.25 kHz (MP). On the other hand, the mean ± SD of characteristic frequencies (f_c) in non-paretic region of severe and mild hemiplegic stroke subjects were 121.25 ± 27.67 kHz (SN) and 46.40 ± 4.27 kHz (MN). Therefore, the mean ± SD of f_c in paretic regions were higher than those of f_c in non-paretic regions. f_c could be a useful clinical parameter because it changes with the reactance (X_c) of cell membranes [30]. Since the cell membranes in severe hemiplegic stroke subjects were unhealthy, the applied AC having low frequency (< 50 kHz) was not able to pass through the cell membrane but the applied AC having high frequency (158.00 ± 17.36 kHz in paretic regions and 121.25 ± 27.67 kHz in non-paretic regions) had energy enough to pass through the cell membrane and then flowed in both ECF and ICF.

Fig. 5 shows the descriptive statistics for $BIVA$ with the R/H - Rc/H diagram for paretic and non-paretic regions of 8 severe hemiplegic stroke subjects (females: #2, #4, #10, #11, #19, #20, males: #9, #13) and 12 mild hemiplegic stroke subjects (females: #1, #5,. #6, #7, #8, #12, #14, 18, males: #

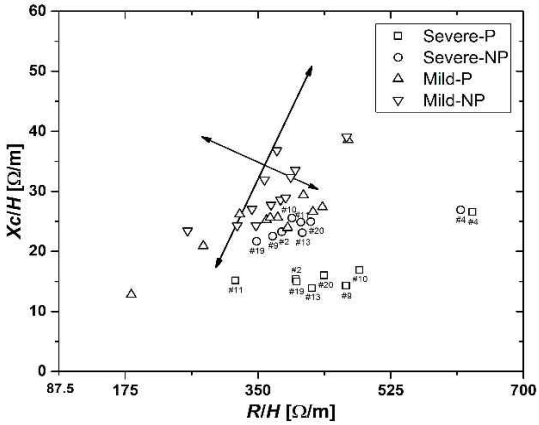

Fig. 5. BIVA graph for paretic and non-paretic regions of severe stroke patients (N=8) and mild stroke patients (N=12) with upper extremity hemiplegia.

3, #17). The mean impedance vectors of *BIVA* differed significantly in all comparisons (severe-paretic: SP, severe-non-paretic: SN, mild-paretic: MP, and mild-non-paretic: MN). The mean positions of *BIVA* in SN and SP were significantly displaced compared with those in MN and MP. The impedance vectors of *BIVA* in severe stroke subjects with upper extremity hemiplegia migrated sideway downward due to reduced BCM (also muscle mass) and cell membrane integrity compared with those of mild stroke patients with upper extremity hemiplegia. In addition, the positions of impedance vectors in paretic regions were below than those in non-paretic regions in severe and mild hemiplegic stroke subjects. A similar phenomena that X_C/H in paretic regions of severe stroke patients was significantly reduced was reported in BIVA diagram aimed at the elderly with malnutrition and impaired functionality [31, 32].

Evaluation of functional statue in hemiplegic stroke subjects after stroke has been mainly performed in indirect method through the rehabilitation assessment tools such as hand grip strength [33], manual function test (MFT) developed by Sakai [34], and activities of daily living (ADL) using the modified Barthal index (MBI) [35]. However, these methods are quite subjective because it is difficult to obtain an accurate evaluation value and its test results also vary widely depending on the ability and skill of the examiner. According to our previous published paper, assessment of paretic and non-paretic regions of stroke subjects with upper extremity hemiplegia using bioelectrical impedance parameters agreed quite well with that using conventional assessment tools [36]. In addition, bioelectrical impedance parameters provide rehabilitation evaluator with the information about muscle strength and pathophysiological function for paretic and non-paretic regions of stroke hemiplegic patients. Therefore, more subjects are categorized by gender, age, and body mass index (BMI), etc., BIA could be clinically valuable tool capable of evaluating paretic and non-paretic of stroke patients and monitoring over the rehabilitation processes [37].

5. CONCLUSION

Study on the bioelectrical impedance analysis (BIA) has been performed for a long time by many researchers, and researchers mainly carried out the body composition and the physiological properties of the tissue using the single frequency (SF) BIA. However, bioelectrical impedance measurement applying the multi frequency (MF) using BIS for severe and mild stroke subjects with upper extremity hemiplegia have not been carried out substantially. Accordingly, the aim of this study is a quantitative assessment of paretic and non-paretic regions of severe and stroke subjects with upper extremity hemiplegia using MF-BIS.

In this study, the paretic and non-paretic regions of severe and mild stroke subjects with upper extremity hemiplegia were quantitatively distinguished using impedance parameters (PM, Θ, f_c, $BIVA$). Using these impedance parameters, results for paretic and non-paretic regions of subjects with upper extremity stroke are summarized as follows. First, lean mass, TBW, BCM, and BMR in paretic

region were lower than those in non-paretic region, whereas fat in paretic region was higher than that in non-paretic region. Second, the mean ± SD of PM in paretic regions was higher than those of PM in non-paretic regions. Third, the mean ± SD of Θ in paretic regions was lower than those of PM in non-paretic regions. Fourth, the mean ± SD of f_c in paretic regions was higher than those of f_c in non-paretic regions. Fifth, the mean impedance vectors of $BIVA$ differed significantly in all comparisons (severe-paretic: SP, severe-non-paretic: SN, mild-paretic: MP, and mild-non-paretic: MN). The mean positions of $BIVA$ impedance vectors in SN and SP were significantly displaced compared with those in MN and MP.

However, the number of severe and mild stroke subjects with upper extremity hemiplegia was limited in the experiments. When the subjects are categorized by gender, age, and disease states, and the bioelectrical impedance measurement are performed for long time intervals in the rehabilitation therapy, bioelectrical impedance characteristics could be effectively distinguished in paretic and non-paretic regions of severe stroke patients as a more confident manner.

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