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## Bioelectrical impedance analysis in medicine

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### ABSTRACT

The analysis of electrical bioimpedance (BIA) is a non-invasive, low cost and a commonly used approach for body composition measurement and assessment of clinical condition. There are a variety of methods applied for interpretation of measured bioimpedance data and a wide range of utilizations of bioimpedance in body composition estimation and evaluation of clinical status. Bioelectrical impedance analysis is based on knowledge about the electrical properties of human body. The clues are provided here by elementary knowledge of the tissue and cellular structure of the organism and the basis of physics. The amount of electrical resistance (resistance) of a uniform object is directly proportional to its length ( $L$ ) and specific resistance ( $\rho$ ), and inversely proportional to its cross-sectional area ( $A$ ). The impedance ( $Z$ ) is a function of the mentioned resistance and reactance ( $XC$ ), which in turn is inversely proportional to the frequency of the current and the electrical capacity of the system. BIA method can provide a reliable, safe and effective way to study body composition, as well as other parameters resulting from the distribution of water in the body. It can be used in the examination of body composition in both cases: healthy and chronic patients, with particular emphasis on diseases related to metabolism.

**Keywords:** bioimpedance, BIA, impedance analysis, bioelectrical impedance analysis

### 1. INTRODUCTIONS

The analysis of electrical bioimpedance (BIA) is a very reliable, non-invasive, and at the same time safe and effective way to examine body composition in healthy people, as well as

those, who suffers on various types of diseases such as diabetes, hypertension, obesity and others. Bioimpedance analysis consists in measuring the total resultant electrical resistance of the body, which is a derivative of resistance (passive resistance) and reactance (active resistance) using a set of surface electrodes, which are connected to a computer analyzer and using current of a given frequency and intensity. The total amount (TBW), intracellular (ICW) and extracellular (ECW) water in the body, as well as cellular body mass (BCM), and consequently fat (FM) and muscle tissue (FFM) are measured.

BIA allows you to follow changes in body composition during a diet program and adjust your diet and clinical condition.

## **2. MATERIAL AND METHODS**

Bioimpedance analysis is a widely used approach in body composition measurements and patient health assessment systems. Bioimpedance has its source in the properties of electrical tissues that have been known for almost a century and a half - Hermann wrote about them in 1871. In the middle of the twentieth century, the association of bioelectrical impedance measurements with total water in the body was reported by Barnett, followed by Thomasset using two subcutaneous electrodes, and later by Hoffer using four electrodes placed on the skin surface. In the seventies of the twentieth century, Nyboer began pioneering research in the field of impedance plethysmography, in which he pointed to the relationship of changes in the impedance of the human body with changes in pulsatile blood flow in the organs, pulse and breathing. Today on the market there are many devices used to analyze the composition of the body based on BIA, using different configurations of electrodes and different frequencies. There are apparatuses resembling an ordinary household scale with a built-in two-electrode system.

Bioelectrical impedance analysis is based on knowledge about the electrical properties of human body.

The clues are provided here by elementary knowledge of the tissue and cellular structure of the organism and the basis of physics. The amount of electrical resistance (resistance) of a uniform object is directly proportional to its length (L) and specific resistance ( $\rho$ ), and inversely proportional to its cross-sectional area (A). The impedance (Z) is a function of the mentioned resistance and reactance (XC), which in turn is inversely proportional to the frequency of the current and the electrical capacity of the system. In a series connection, the impedance equation has the general form (1)  $Z = \sqrt{R^2 + Xc^2}$ , where all variables are counted in ohms [ $\Omega$ ]; for a parallel connection, the equation has the form (2) :  $Z = \frac{1}{\sqrt{\frac{1}{R^2} + \frac{1}{Xc^2}}}$

Measurement of bioelectrical impedance is performed with the assumption that only the serial connections function in the tested system, which of course is not true, because in the body there are circuits in series as well as in parallel connection. Therefore, the mathematical conversion of the serial to parallel connection is used, which gives the following formula for the bioelectrical impedance of the body: (3)  $Z = \frac{XcR}{\sqrt{Xc^2 + R^2}}$  it can be said in a simplified way, that the bioelectrical impedance of the body is a measure of combined resistance and phase shift of the current, which passes through the body; it is the determination of the size of the hindrance (obstacle) which the body is for the flowing electric current. It is obvious, of course, that the

body is not a homogeneous cylinder, and its resistance and capacitance are variable. This problem can be circumvented by realizing that individual tissues have specific properties in the field of electrical conduction, and that water has a special significance in carrying the electrolyte dissolved in it, and using appropriate mathematical transformations. Fat tissue and extracellular water do not show reactance (capacitive resistance), because they do not behave as capacitors, but they have an active electrical resistance (resistance).

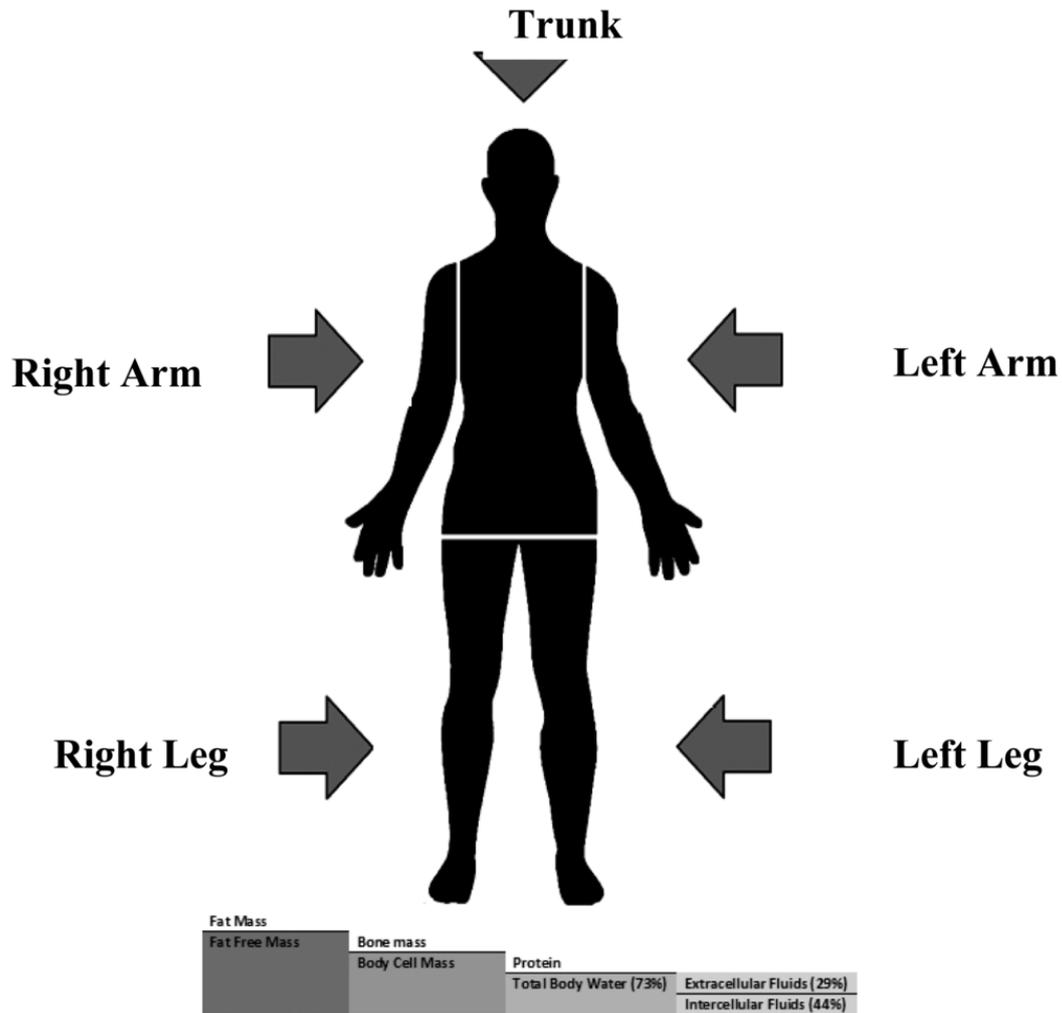


Figure 1. Main body segments and compartments.

In contrast, reactance arises on the cell membrane of tissue with a high water content, which acts as a condenser composed of two covers (conductive hydrophilic fragments of phospholipids directed outside and inside the cell) and a dielectric layer (non-conducting lipophilic fragments directed into the inside of the cell membrane). The resistance causes a voltage drop, while the reactance mainly affects the phase shift of the applied alternating current, represented in vector terms by the phase angle ( $\phi$ ), which is  $R \times C \phi = \arctan$  and ranges from  $-90^\circ$  to  $0^\circ$ . The phase angle assumes only the values in this range, because in a

series connection, the reactance is a vector perpendicular to the resistance, and the impedance is their vector sum with the value calculated from the formula (1). It is known, therefore, that as the current frequency increases (and the reactance decreases), the phase angle and resistance also increase. In turn such values as the resistance of the human body and its electrical capacity are determined based on statistical data for a given population, race, age, sex, health status, etc. For simplicity, instead of the length of the circumference, which would have to be measured from the wrist to the ankle of the leg, where the electrodes were applied, the value of the subject's height is used, taking into account the relevant factors mentioned above. It is also possible to use more accurate anthropometric measurements to determine the mean cross-sectional area of the limbs and torso.

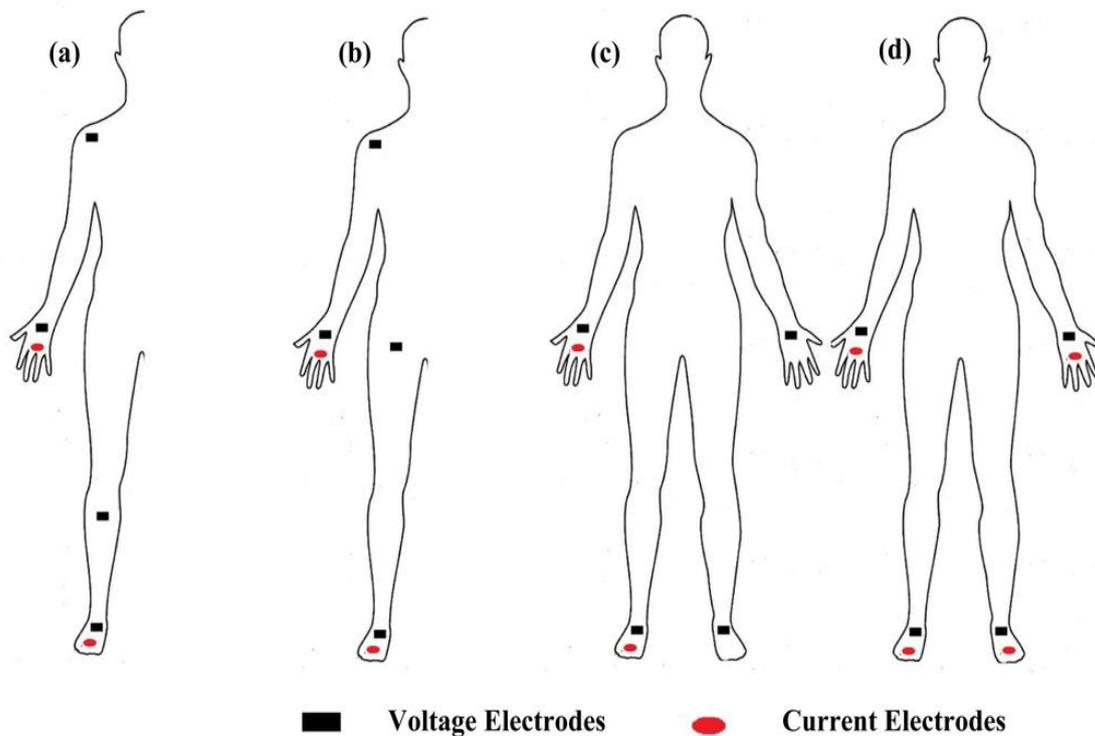


Figure 2. BIA variants

The BIA measuring devices can be divided according to the number of electrodes and on used frequencies. Two, four and even eight-electrodes system is using surface electrodes, with various electrode configurations, e.g. combined leg-leg, leg-arm, hand-hand etc. The most common is the tetrapolar system in the contralateral system, where two the electrodes are placed near the wrist /forearm of the subject, and two next to the ankle of the leg (most of the serious research using BIA uses just such a system). An important factor in the BIA method is using the current frequency.

At low frequencies or near zero, the current does not pass through the film barrier cellular, which acts as an insulator, while at very high levels frequencies, the cell membrane behaves like an almost perfect capacitor, and thus the total body resistance reflects both the volume of the water intra and extra-cellular water. It is worth noting that at 50 kHz, and it is most often

used in BIA devices with one current frequency, the current passes by both cellular: intra- and extracellular fluid, then we get the average weighted their resistances, which, moreover, is crucial to the BIA study, as it the reactance is about 10% of the obtained impedance. There are two main types of BIA devices: using one frequency (SF-BIA) and many frequencies (MF-BIA). The first is considered to be particularly useful in assessment of body composition in healthy people, while the second allows for more accurate analysis of changes in body composition in the body of patients in the postoperative period or o very poor health. SF-BIA devices usually use the mentioned 50 kHz at an intensity of the order of 0.8-1 mA, and MF-BIA cameras use the range 0-500 kHz frequency, although the highest reproducibility of results is noted at in the range 5 kHz - 200 kHz. For the needs of dietary diagnostics, it is usually sufficient the use of one frequency in a tetrapolar system for the entire measurement body (not its single segment, such as the chest or limb, what finds application in the diagnosis of other specialties, e.g. in cardiography impedance or in the assessment of the size of injuries, edema, etc.).

### **3. BIOIMPEDANCE MEASUREMENT BIASING FACTORS**

#### **3. 1. Anthropometric Measurements**

Anthropometric measurements such as weight, height, skin fold thickness, lengths, diameters and circumferences that involves mathematical modules are the main contributors in the estimation of body compartments.

Bioimpedance parameters only without body dimension measurements are considered poor estimators for body composition. Diaz *et al.* concluded that in FM and FFM prediction, resistance and capacitance measurements contribute by 0% – 20%. In contrast, the percentages increase to 11% – 53% after height inclusion, and 22% – 68% after inclusion of Ht<sup>2</sup>/R ratio.

Ward *et al.* presented a validation study to predict BCM and ECF as a portion of TBW without measuring height and using BIA device, the Soft Tissue Analyzer STATM (Akern Sri, Florence, Italy) with a correlation coefficient referenced to the total body potassium counting method is equal to 0.91, 0.82 and 0.89, and a standard estimation error equal of 5.6 kg, 6.3 kg and 1.3 kg for FFM, BCM and ECF, respectively.

#### **3. 2. Gender**

Variations in body composition between male and female were proven in several studies. In body composition prediction, methods based on bioimpedance analysis, and most equations tend to include gender as one of the main determining factors for body compartment assessment.

FFM or lean mass studies show that males have greater FFM than females with different ranges. Kyle *et al.* state that mean FFM for male is 8.9 kg and 6.2 kg for female and fat mass index FMI increases based on age, in females from 5.6 to 9.4 and from 3.7 to 7.4 in males. In a recent study on 1649 healthy children-adults (6–18 years) and 925 adult-elders (19–92 years) using BIA and DXA it was concluded that for all age ranges, males have less fat mass and more fat free mass than females.

TBW averaged 73.2% of fat free mass in the healthy population; however several studies show that males have less TBW than females. Sun *et al.*, stated that in a mixed ethnic groups prediction equation, TBW volume for males start from 1.2 L compared with 3.75 L for females.

Jaffrin *et al.* state that determined TBW resistivity ( $\rho$ ) is on average  $104.3 \pm 7.9 \Omega \cdot \text{cm}$  for men and  $100.5 \pm 7.8 \Omega \cdot \text{cm}$  for women. The values are smaller in men are due to their larger limb cross section.

Due to the different body composition between males and females, gender considerations have a strong impact in estimating body compartments.

### **3. 3. Age**

Aging is defined as a multi-factor changing in the physical and biological activities of the human body that leads to differences in body composition among age groups. When the human body becomes older it leads to a gradual increase in fat mass and spontaneous decrease in lean mass. Fat free mass to fat mass ratio increases gradually in response to increase of age, and a noticeable increment in average weight is seen among the elder population compared with adults associated with increment in fat mass. In some studies, the general body composition prediction equations were unsatisfactory in elderly men over 75 years of age, especially in TBW estimation.

Several studies were conducted using the BIA method on children adults, and elders. In children, the BIA method using the Deurenberg equation, underestimates body fat as determined by DXA. It however achieved a better correlation than the skin fold method. Muscle mass loss among the elderly reduces the fat free mass at a certain age, followed by decreases in total body water and bone mass. Marja *et al.* reported that in 75-year-old Swedes, average fat free mass index was 15.6 and 18.3; and body fat index was 11.0 and 8.6 for women and men, respectively, compared to the DXA method.

### **3. 4. Ethnic Groups**

Body composition varies among different races and ethnic groups due to the environment, nutrition factors, culture and anthropometric measurements that include body conformation. There is also difference in limb length, body structure, body size and that lead to variation in body fat percentages among different ethnic groups which may lead to prediction errors (3%).

The 23 majority of bioimpedance measurement studies have been done on Caucasian subjects, Kotler *et al.* and Sun *et al.* have included African American and Hispanic subjects in their studies. Kim *et al.* assessed the segmental lean mass among Koreans, Schulz *et al.* assessed the fat free mass among Germans and compared it to the American and Swiss population. Siváková *et al.* studied the clinical applications of BIVA on Slovaks. Nigam *et al.* had performed a comparative study among two different Indian races, whereas Saragat *et al.* obtained specific BIVA reference values for the Italian healthy elderly population in order to construct the specific tolerance ellipses to be used for reference purposes for assessing body composition in gerontological practice and for epidemiological purposes. Validation of bioimpedance measurements among different ethnicities is thus needed due to differences in body composition among certain populations.

### **3. 5. Measurements Protocols and Posture**

Simplicity and the economic acceptance of bioimpedance analysis method for body composition estimation have increased the need to unify the protocols and procedures of bioimpedance measurements in order to retrieve robust data. For the foot to ankle measurement method, bioimpedance measurements performed in a supine position with abduction of the

upper limbs to 30 degrees and lower limbs to 45 degrees for 5 to 10 min. studies show that when the posture changes from a standing to a supine body position, the ECV decreased in the arms by 2.51% and legs by 3.02%, but increased in the trunk by 3.2%. Fasting for at least 8 hours and bladder voiding before measurements are recommended as consumption of food and beverages may decrease impedance by 4–15  $\Omega$  over a 2–4 h period after meals and that causes an error (<3%). Body anthropometric measurements should be retrieved prior of the test and for scale or foot to foot bioimpedance analyzer weight retrieved automatically.

Electrodes should be placed on the pre-cleaned metacarpal and metatarsal phalangeal joints with a distance in between of at least 5 cm without skin lesions at the location of the electrodes. In some studies skin temperature should be counted. Subjects under test should not perform any exercise activities before measurements that could lead to errors in assessed resistance and reactance equal to 3% and 8% respectively. Roos *et al.* concluded that the error in total body water prediction range from 1 to 1.5 L figured out after laying at rest for one hour.

### **3. 6. Electrode Shape and Measurement Error**

In bioimpedance analysis, the geometrical structure of electrode has a strong impact on elementary data retrieved during the measurement process. In bioimpedance analysis electrodes are defined as isoelectric materials with a negligible voltage drop along the connectors. The minimum numbers of electrodes required to perform the bioimpedance measurements are two, one for current injection with the assumption of zero potential difference and the other for collecting the voltage drop with a negligible current flow and is more affected by position.

The tetrapolar electrode approach become widely used for whole bioimpedance measurements because of the uniformity of current distribution compared to monopolar electrodes, and the usage of more than two potential collecting electrodes or octapolar electrode method were used for segmental bioimpedance studies to assess compartments in different body segments.

Ag-AgCl electrodes are now used in most bioimpedance measurements because it has a well-defined DC potential with electrolyte gel to minimize the gap impedance between skin and electrodes. Circular and rectangular electrode shapes with a contact area greater than 4  $\text{cm}^2$  are the most commonly used shapes. Buendía *et al.* investigated the impact of electrode discrepancy on BIS measurements and concluded that mismatched potential electrode causes 4% overestimated measurements in resistance at zero and infinite frequency because of an imbalanced electrical field distribution addressed the artifacts caused by inaccurate distance between electrodes in four electrode measurement methods performed on a 17.5 cm segment of the thigh area. That study reported that the values of resistance and reactance were four times larger when the current injecting electrodes were placed 2.5 cm from the sensing electrodes. Scharfetter *et al.* stated that capacitance between different body segments and earth, and capacitance between the signal ground of the device and earth cause a significant false dispersion in the measured impedance spectra at frequencies >500 kHz.

Errors in bioimpedance measurements are caused by many factors such as motion, mis-positioning, connector length and fabrication errors. Moreover, the diversity of the commercially available bioimpedance analyzers cause a wide range of fluctuations in measurements between the devices. Thus the calibration of the components inside a bioimpedance analyzer such as signal generator, sensing apparatus, scales of weight and height and electrical interference should be conducted to ensure the reliability of the bioimpedance analyzers. Applications of Bioimpedance Analysis in Clinical Status Monitoring and Diagnosis

of Diseases Bioimpedance analysis in healthcare practice contributes to the estimation of body compartments to assess the regular change in nutrition status in in-patients and to monitor nutritional risk in out-patients.

Most of the body composition assessment methods like BMI techniques, skin fold method and underwater weight measurements is used to estimate fat mass and fat free mass, however bioimpedance analysis can estimate FM and FFM in addition to total and particular body fluids which is very helpful for disease prognosis. The National Health and Nutrition Examination Survey program in United States included bioimpedance analysis in the third NHANES program between 1999 and 2004 to assess the health and nutritional status of adults and children because of a general frustration with the dependability of the skin fold thickness method to estimate FM and FFM, especially in subjects with higher amount of segmented fat. Observation of body compartment fluctuations like fat free mass, fat mass and total body water from normal limits are considered as key factors to be used in bioimpedance analysis in healthcare applications. Abnormal loss in lean body mass and unbalanced shifts in body fluids are the most measured parameters to be used to assess the healthiness of the human body. Analysis of bioimpedance parameters has been used in several studies to estimate and analyze the changes in disorders of different kind of diseases. Norman *et al.* stated that phase angle is an essential predictor of clinical status. Pichler *et al.* stated that estimation of body fluids using BIS was slightly better than anthropometric methods among healthy and diseased. Table 1 contains some of the applications of bioimpedance analysis in disease diagnosis that are organized according to the organ systems of human body, diseases or abnormalities diagnosed based on bioimpedance parameters, and comments on how these factors are applied to determine the health condition. Bioimpedance analysis is a common method used for estimating body composition among healthy and diseased subjects in research and clinical trials. This review has focused on the theoretical and the fundamentals of bioimpedance analysis. Thus it may have some limitations, where possible important studies on the applications of bioimpedance analysis in diagnostic of diseases and the related shifts in bioimpedance parameters may have been missed.

#### **4. SAFETY OF USING BIA**

Research using BIA can be considered completely safe for body. The current frequencies don't cause nerve irritation nor myocardium, and the current is completely harmless, because the higher the frequency of the current, the safer it is e.g. the lethal intensity it is 100 mA at 0.5 kHz (as in a home electric socket), and already at 5 kHz the mortality threshold is only 1000 mA. In addition, the threshold of perceived current on human being is 1-1.5 mA, so the current used in the measurement of 0.8-1 mA is virtually imperceptible. There are no known cases of effects side that could be associated with the BIA study. Additionally, the use of low-voltage batteries or energy sources minimizes considerably risk of infestation. The last factor to be considered during conducting the test BIA, is the effect of the BIA apparatus on other devices emitting the field electromagnetic and vice versa. This problem has not been convincingly so far loose. Until this issue is cleared up, people who have implanted heart defibrillator are revived BIA test, because even a small current can disrupt the operation of the device. It is believed, however, that the BIA study is safe for people with an implanted pacemaker.

## 5. CONCLUSIONS

Summary according to the data presented above, the BIA method can provide a reliable, safe and effective way to study body composition, as well as other parameters resulting from the distribution of water in the body. It can be used in the examination of body composition in both cases: healthy and chronic patients, with particular emphasis on diseases related to metabolism. The results of the BIA study are influenced by factors depending on the correct selection of the BIA variant used and the operation of the device, as well as the appropriate preparation of the subject.

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