Advances in Life Science and Technology
ISSN 2224-7181 (Paper) ISSN 2225-062X (Online)
Vol. 9, 2013

Physics of Bio-electrical Impedance Analysis: Phase Angle and its Application

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Abstract

Bioelectrical impedance analysis is an easy technique to evaluate the changes in the body composition. In BIA a small amount of electric current is passed through the body and from electrical properties of human body, Biological values or quantities are calculated, Human body behaves like electric circuit, it acts like RC series and parallel circuit. Here in this review paper these circuits are discussed and then try to implement them on human body to find the composition of human body. The science of this technique is presented that may be helpful for further research in this field... From BIA Phase angle is calculated. Phase angle is very important in clinical research and it can be used as an indicator of health. Role of Phase angle in different disease like cancer and HIV, and its application to monitor and evaluate the patient condition and its role as a prognostic indicator is discussed in this review article using the studies of different researchers. Phase angle can be used as survival indicator in advance cancer patient and HIV. Phase angle can be used to monitor the malnutrition in patient of HIV.

Keywords: Phase angle, Prognostic indicator, Cancer and HIV, body composition

1. Introduction

In Bioelectric impedance analysis a small amount of current almost 1- 10μA at a frequency of 50 KHz (Normally greater than 10 KHz) passed through the body. The reactance and resistance of the body is measured. (17)Now consider the basic definitions of the current, resistance and capacitor. After that RC circuit will be discussed. Here we review the use of these electrical properties to predict the biological properties of human body, like how with the help of these properties, body cell mass (BCM), Extra cellular mass (ECM), Fat free mass (FFM), Fat mass (FM). Phase angle, Total body water (TBW) are calculated and cab be easily find. (18).Physics of this technique is discussed here to improve the understanding of bioelectrical impedance.

Electric Current

Electric current is defined as the rate of flow of electric charge in any conductor and is measured in amperes .The most common alternating current is sine-wave current and its equation $I=I_m Sin\omega t$

The electric current flows through the human body. The exact path of the electric current is not known, different circuits are proposed to find the path of electric current. Current flows through the fluid of the body by the movement of ions and this movement is opposed by the viscosity so it is considered as a resistor.

Resistor

A resistor is an element which opposes the flow of current and consumes power. When the electric current passes through the resistor, the voltage and current are parallel to each other. Through the capacitor electric current is not proportional to voltage but rate of change of voltage. When electric current passes through resistor energy change to heat.

Capacitor

A parallel plate capacitor consists of two parallel plates, plates are conductors and insulator is placed between them. The insulator between two plates is called dielectric. Permittivity is a property of the dielectric and shows the ability of charges to move under applied electric field. The capacitance of capacitor can be represented according to equation.-1

Capacitance depends upon the area of plates, distance between the plates and permittivity of the medium between the plates. (23)

Equation-1

In capacitor the energy is stored as internal electric field. This electric current will charge the cell membrane, and inner and outer part of cell behaves like capacitor. Impedance of the human body is the combination of reactance and resistance. (17), Capacitance defines cell membrane volume [7]

(1)

$$C = \frac{\varepsilon A}{d}$$

1. RC-Series and Parallel Circuit

When the alternating current passes through the human body it is consider as R-C series circuit and RC parallel circuit, so it is very important to consider RC SERIES AND PARALLEL CIRCUIT. (19)
In series circuit total resistance of the circuit or impedance is finding using the following equation.

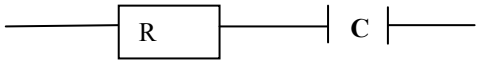


Fig- 1

$$\sqrt{(R^2)} + (-X^2{}_C) \text{-} \qquad \textbf{-(2)}$$

using this equation total impedance of the circuit is calculated
If the parallel circuit is consider then total resistance or impedance of the circuit is calculated a

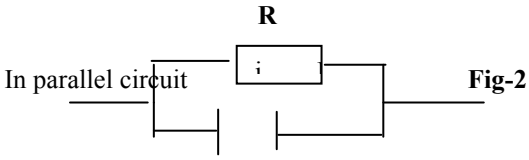


Fig-2

$$Z = \frac{RX_C}{\sqrt{R^2 + X^2{}_C}} \qquad \textbf{------ (3)}$$

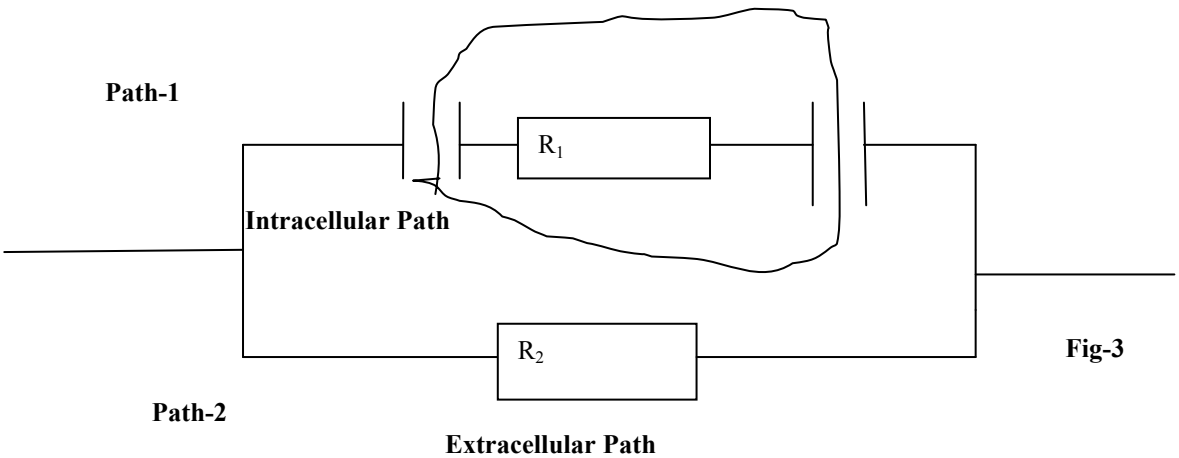


Fig-3

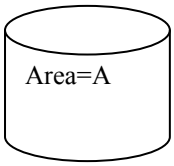
Fig 3-Shows the possible path of electric current, Resistance R_2 represent the extracellular path, and the capacitor and resistance R_1 represent the intercellular path .The outer part of cell is cell membrane and acts like a capacitor. As we know that reactance of capacitor depends on the frequency as shown in the
Equation-4.At high frequency current will pass through the path-1 as reactance is inverse to frequency, Path 1 will offer less resistance at high frequency. At low frequency it will pass through the path 2. But at a particular frequency between low and high, current will pass through the both arms and paths of the circuit. So we can say it's like a band pass filter .The range of this frequency for this band pass filter is 1-10MHz. [17]

Bioelectrical impedance analysis (BIA) measures body components resistance(R) and reactance (X_c) by recording a voltage drop in applied current. Resistance is the restriction to the flow of an electric current, primarily related to the amount of water present in the **tissues (1)**

The resistance of the human body depends on its length and size of the body. As according to the equation

$$R = \rho \frac{l}{A} \quad \text{-----} \qquad \text{- (3)}$$

Human body has resemblance to cylindrical shape as shown in fig below (4).So in cylindrical objects Resistance is directly proportional to length of cylinder and inverse to area of cross-section. Resistance is the extrinsic property of the human body which depends on the size of the human body. But resistivity ρ depends on the nature of the material.
Because in resistivity length and area are Unit quantities and for each material under this condition resistivity depends on the nature of the material. So resistivity is an intrinsic property of the conductor. The resistance of a given sample depends on its geometry (size and shape) and the electrical properties of the conductivity medium. [21]



Length=l

.Reactance is the resistive effect produced by the tissue interface and cell membranes. Reactance is directly related to cell membrane and cell health can be find by considering the value of reactance, Volume of cell membrane can be finding with the value of reactance. While Body fat, total body water, extracellular water is measured with the resistance of human body. Fat tissue cells are not surrounded by cell membranes. [7].In the human body there are 100 trillion cells and size of cell is 10 micron. The mass of one cell is 10^{-12} Kg. There are two main kinds of cells, muscle and fat. Muscle cell have density of about 1.06 times that of water. Fat cell has 0.92 of water. In the cell the cell membrane consists of a layer of non-conductive lipid material between two layers of conductive protein molecules. So it acts like a capacitor. [7]

Reactance causes the current to lag behind the voltage creating a phase shift, which is quantified geometrically as the angular transformation of the ratio of reactance to resistance, or the phase angle. Phase angle reflects the relative contribution of fluid (resistance) and cellular membranes (reactance) of the human body [1].Bioelectrical impedance vector analysis (BIVA) technique is a promising tool, using the pure data obtained by BIA evaluation for the screening and monitoring of nutrition and hydration status. BIVA has the potential to be used as a routine method in the clinical setting for assessment and management of body fluids. Bioelectrical impedance vector analysis allows noninvasive evaluation of soft tissue hydration and mass through pattern analysis of vector plots as height, normalized resistance, and reactance measurement. BIVA has been used to allow detection, monitoring and control of hydration and nutrition status using vector displacement for the feedback on treatment among patients with Alzheimer disease, in stable and constable heart failure, in critically-ill and cardio renal patients and in cancer patients .In healthy populations BIVA method has been used in modeling the human body shape and monitoring the variation of the hydrate status in healthy term newborns. In Particular, Phase angle measured at 50 KHz, because of its reproducibility quality, has been used to determine and predict both the state of health in a healthy population and an altered state observed in the diseased population, with diseased conditions including cancer[2].BIA has been validated for the assessment of body composition and nutritional

status in patient with cancer[2,3]Bioelectrical impedance analysis (BIA) has been established as a valuable tool in the evaluation of body composition and nutritional status in many patients conditions including cancer of lung, cancer of pleura and urethra. [4]
A mathematical view of bioelectrical impedance analysis is explained in Fig-1 below

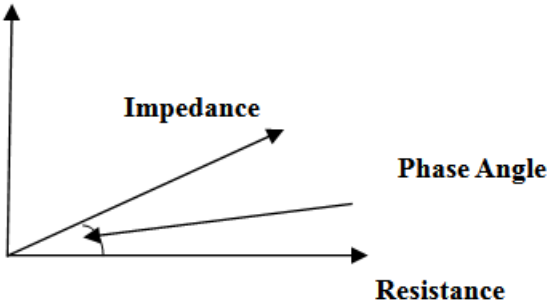


Fig 4[5]

Diagram for Phase angle

$$Tan\theta = \frac{\text{Re}\,ac\tan ce}{\text{Re}\,sis\tan ce} \qquad \textbf{Reactance=}\ \mathbf{X_c}=\frac{1}{2\Pi fc} \quad \textbf{------(4)}$$

Impedance is the frequency- dependent opposition of a conductor to the flow of an alternating electric current. A measure of impedance(Z) is composed of the sum of two vectors, resistance(R) and reactance (A_{ct}), measured at a particular frequency and is described mathematically by the equation $Z^2=R^2+ X_c^2$.[5]

2.1 Fundamental Theory behind the working of Bioelectrical Impedance Analysis

Many authors in their work show the working of BIA on two phenomenons.

1-When the electric current flows through the human body, at low frequency current passes through the extracellular space, so fluid offer resistance to electric current and from resistance, volume of extracellular fluid can be calculated. Body fat, total body water and extracellular water offer resistance to electric current. [7]Mostly the equation used for this purpose is as given below.

$$V = AL = \frac{\rho L^2}{Z} \quad \text{---- (4)}$$

Here V is the Volume (ml); L is the length inter-electrode distance (cm), Z is the impedance (Ohm) and ρ is the resistivity co-efficient (ohm-cm) of tissue fluid. [27]

In most of the BIA literature the about equation used to calculate the TBW volume and total body water is a linear function of $\frac{l^2}{R}$ as shown in the above equation,[24]. But how it used to calculate the volume of fluid, it's not correct, but this equation is applicable only to uniform cylindrical objects of uniform resistivity. But from resistance Volume cannot found until the geometry and electrical properties are known. But the other equations are also given in literature to find the Biological properties of the human body.

With the help of equation (4), ECW, ICW, and TBW water volumes can be predicted by some modification, the resistance at zero frequency and infinite frequency is calculated, at zero frequency current cannot penetrate cell membrane and the resistance R_0 is the resistance of extracellular water (ECW), at infinite frequency current r passes through the cell membrane and hence R_∞ is the resistance of TBW. The resistance of intercellular water (ICW) can be calculated from the measured R_0 and R_∞ .Hence ECW, ICW and TBW water volumes can be predicted from R_0, Ri and R_∞ by equation 4.

R_i, the resistance of intracellular water (ICW) can be calculated from the measured R_0 and R_∞ .[27]

For example the following equation can be used to find the volume of the object if its geometry is known

$$V = \int_0^l \pi r(z)^2 dz. \text{-------} \quad (5)$$

The above equation can be used to calculate the volume if the shape expressed by the function r (z)

So there is no equation that from the resistance volume can be calculated. But experimentally relation exit between the extracellular volume and resistance. So what is the correct method to find the total impedance of the body, the answer is given by Kenneth R Foster in his paper, Whole-body impedance- what does it measure" whole body impedance is determined by the impedance of the distal parts of the limbs near the electrodes.[17]

2-The 2nd rule on which BIA work is also found in many research paper as reactance and capacitance, or reactance is a measure of the volume of cell membrane capacitance is a measure of body cell mass.[7]

2. Phase Angle

The most clinically established impedance parameter is the phase angle. It has gained popularity over the past years since it has shown to be highly predictive of impaired clinical outcome and mortality in a variety of disease. [6] By definition phase angle is positively associated with reactance and negatively associated with resistance. Lower phase angles suggests cell death or decreased cell integrity, while higher phase angles suggests larger quantities of intact cell membranes.[1,28] Phase angle has unique properties, it can be directly measured by BIA device. Phase angle does not need weight, height and other geometrical properties. It is rapid process by which information about the patient nutritional risk .It just take 2 minutes to find the phase angle[9] Phase angle can range from 0 to 90 degrees;0 degrees if the circuit is only resistive(as in a system with no cell membrane) and 90 degrees if the circuit is only capacitive(all membrane with no fluid).A phase angle of 45 degrees would reflect a circuit or body with an equal amount of capacitive reactance and resistance, such as in fresh vegetables[7].The average phase angle for a healthy individual is approximately 6 to 9 degrees, depending on gender and decrease with age, its positive association with physical activity suggests that it might also assess function besides evaluation of body composition.[8] Phase angle has been found to be a prognostic marker in several clinical conditions such as human immunodeficiency virus infection, liver cirrhosis, chronic obstructive pulmonary disease, hemodialysis ,sepsis ,lung cancer[1].Phase angle is one of the direct measures by BIA instrument not requiring body weight and height measurements, and appears to be an objective parameter that is rapid, easy and non-invasive way to provide information about the patients nutritional risk. The biological meaning of Phase angle is not completely understood, [22] but is considered an indicator of cell health with high Phase angle reflecting stronger cell function. Reduced PhA in older subjects has been suggested to reflect a decreased in general health and physical function associated with aging. Recent studies have shown that low PHA, determined by bioelectrical impedance analysis (BIA), is associated with nutritional risk, increased morbidity and mortality in renal disease, HIV, Cancer and surgical patient. [9,].Phase angle provides an index of tissue hydration, cell membrane integrity, and cell mass. [23].Phase angle shows the distribution of water between the extracellular and intracellular spaces, which is indicators of malnutrition. The ECM/BCM index describes the nutritional status.[28]Malnutrition is common in patient with cancer, the cancer and its treatment affect the nutrional status of patient by changing their metabolic function and reducing their food intake [30]Phase angle is used as a nutritional assessment tool in cancer. In research by Digant Gupta it is shown that Phase angle is an indicator of nutritional status in advanced colorectal Cancer. [29]

3.1 Phase angle as Prognostic indicator in different diseases

Prognosis, characterized as the usual course of disease, is an uncertain process that integrates clinical data derived from biomedical tests and physician experience to predict possible future outcomes of a treatment for an individual with cancer .Physician accuracy of prognosis is limited and statistically based methods are too imprecise for individual patient use, and accuracy at present is limited to the last 30 days of life when the potential for positive impact is significantly reduced. Prognosis includes an assessment of the presence and severity of disease, the effectiveness of treatment, frailty or vitality, and timing of non-acute death in chronic disease.[10]

Given the close correlation between phase angle and nutritional as well as functional status it is not surprising that a high predictive potential of the phase angle has been reported by many studies. Compared to healthy subjects, a low phase angle frequently occurs in sick patients correlating with disease severity. It has consequently been shown to be predictive of impaired prognosis(mortality, disease progression, incidence of postoperative complications, length of hospital stay) in pancreatic, colorectal, breast and lung cancer as well as in HIV/AIDS, liver cirrhosis, renal insufficiency on peritoneal-or haemo-dialysis and amyotrophic lateral sclerosis, systemic sclerosis, bacteraemia/sepsis and surgical patients.[6]Loss of body weight and wasting of lean body mass are leading symptoms of the advanced stages of HIV infection. Early in the epidemic it was proposed that malnutrition may be an important cofactor of disease progression. [1] Changes in body composition have been a central feature of HIV infection and AIDS since the beginning of the epidemic, wasting, characterized by loss of both lean tissue and fat, has been the most common clinical alternation and was once nearly universal in advanced AIDS. Current laboratory measures, molecular and genetic markers, radiological imaging studies, and physical examination are generally limited in their prognostic abilities. Therefore, an imminent need exists for a more accurate and reliable approach to supplement currently used measurements in the prognosis of cancer patients and end of life decision making. [10] Phase angle has been used to predict cell mass; for this reason, it has been used as a nutritional indicator in adults and children. Some authors have studied the role of phase angle as a prognostic indicator. A positive association was shown between phase angle and survival in patient with HIV-positive AIDS, with lung cancer, undergoing hemodialysis and who are critically ill. Some authors suggested that phase angle could be an important tool for evaluating clinical outcome for monitoring disease progression and may be superior to other serum or anthropometric nutritional indicators.[11]Phase angle also shows the property of cell membrane that is related to fluidity [25]Phase angle can be used to monitor fatty acid supplementation aimed at addressing abnormalities in cell membranes that occur in SCD(Sickle cell disease)[24] .Table 1 gives an overview on studies demonstrating the prognostic impact of low phase angle in various disease settings. However, most authors generated phase angle cut-offs in comparison with a healthy control group. A major drawback of this method is that these cut-offs are not necessarily transferable to other populations and might thus not be applicable in general clinical setting. [6]

Table 1[6]

Studies on prognostic impact of phase angle [6, 13, 14, 15, 16, and 17]

Study population	N	Cut-off value	BIA device	Clinical outcome of patients below cut-off value
HIV/AIDS HIV[6] HIV	 75 469	 5.6 5.3	 101,RJL,Systems 2000-1,Data input	 Decreased survival parameter estimate in LR test Increased progression of disease
Tumor Disease,[6] Lung Cancer	63	4.5	101.RJL System	Decreased Survival
Coloretal Cancer[6]	52	5.57	101Q RJL System	Decreased survival
Pancreatic Cancer[16]	58	5.08	101Q,RJL System	Decreased Survival
Breast Cancer[6]	259	5.6	101Q,RJL System	Decreased Survival
Lung Cancer,[6]	165	5.3	101Q,RJL Systems	Decreased Survival

A study conducted in patient with advanced with advanced lung cancer stratified the patient cohort by the mean phase angle of 4.5 degrees. Interestingly, patients with phase angle less than or equal to 4.5 degrees had a significantly shorter survival than those with phase angle greater than 4.5 degrees .In another study it is shown that in stage IV colorectal cancer patients, phase angle above the median cut-off 5.6 was associated with better survival. [12, 13] Similarly, in stage IV pancreatic cancer, phase angle above the medium cut-off of 5 was associated with improved survival [12, 14]. .In patient with liver cirrhosis, phase angle was speculated to be a

marker of clinically relevant malnutrition characterized by both increased extracellular mass and decreased body cellular mass. In advanced lung cancer, phase angle was speculated to be an indicator of altered tissue electrical properties. [15]Malnutrition is a frequent sign in patients with advanced non-small cell lung cancer (NSCLC) and is a major contributor to morbidity and mortality. Malnutrition is characterized by changes in cellular membrane integrity and alternations in fluid balance. As a result, measurement of body composition is an important component of overall nutritional evaluation in cancer patients. [12] In spite of lack of standardized cut-off values, phase angle seems to play an important role as a marker of morbidity and mortality in a wide range of disease conditions, with higher phase angle reflecting a general indicator of wellness. [15]

2.2 Phase Angle as a Predictive marker in HIV

Weight loss and malnutrition are important symptoms that occur more than 90% patients of HIV during the disease. [26], malnutrition is an important factor for disease progression [16] It is a common test in HIV care.

Phase angle describes the relation between the 2 vector components of impedance of the human body to an alternating electric current. Because the current passes only through the ionized water compartments within the body, the volume of TBW can be estimated from resistance. Reactance reflects the ability of cell membrane to act as perfect capacitors. Therefore, phase angle is an indicator of the distribution of water between the intra and extra-cellular spaces. A high phase angle corresponds to a low ECW-ICW ratio. Expansion of ECW and loss of ICW are typical features of systemic illness [16] the relation of measured impedance to body composition is indirect and not fully clarified, Phase angle describes the relation between the 2 vector components of impedance (reactance and resistance) of the human body to an alternating current .Because the current passes only through the ionized water within the body, the volume of TBW can be find from resistance.

Phase angle is an indicator of the distribution of water between the intra-and extracellular spaces.(20)AND LOSS OF ICW are symptoms of illness.(20)The result of some studies shows that the strong ability of the Phase angle to predict survival and clinical progression in HIV-infected patients,(20)Alternation in cell membrane is common in cancer and HIV infection. A low phase angle indicates of cell membrane breakdown and less ability of cells to store energy. Phase angle shows the condition of cell membrane, low phase angle shows cell death and high value of phase angle shows good condition of cell membrane. [31]

5. Conclusion

BIA is an important technique which is used to find the body composition. It has advantage over the other techniques, and useful information is obtained about the body composition in patients of different disease like cancer and HIV. Its basic theory on which it work is not yet cleared even empirically it is clear that it is used to find the body cell mass and other quantities but the science that work behind this technique is not yet completely or 100% known. More work is required in this field to find the exact path of current through the human body.
From the review of literature and review of basic principles of Bioelectrical impedance analysis it is clear Phase angle is very important prognostic tool in different diseases and a universal health marker .Phase angle can be used as a prognostic tool in various clinical situation. It can be used as a marker of survival in HIV patient and in cancer .It is easy method to monitor the condition of patient in various diseases .High value of Phase angle indicates good health of patient. Patient with low value of phase angle has shorter survival than patient with high value of Phase angle in cancer and HIV...Phase angle also a general indicator of health.

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