



THE ROLE FOR BIO-ELECTRICAL IMPEDANCE ANALYSIS (BIA) IN CRITICALLY ILL PATIENTS



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The impact of a positive fluid balance on morbidity and mortality has been well established. However, little is known about how to monitor fluid status and fluid overload. This article discusses the different parameters related to bio-electrical impedance analysis (BIA) and their use to monitor fluid status and to guide fluid management in critically ill patients.

Introduction

Bio-electrical impedance analysis (BIA) measures whole body (or regional) impedance, phase angle, resistance, reactance and capacitance, by means of an electric current transmitted at different frequencies (Bioelectrical impedance analysis 1994; Plank et al. 1995). New techniques allow measurement of total body water with separation into extracellular and intracellular water (Janssen et al. 1997). Previous and some recent data suggest that BIA may provide useful information not only in different well-established patient groups (dialysis, AIDS, malnutrition), but also in critically ill patients with burns, trauma and sepsis undergoing fluid resuscitation (Van Biesen et al. 2011; Wabel et al. 2009; Wabel et al. 2008; Plank et al. 2000; Savalle et al. 2011; Kraemer 2006; Kraemer et al. 2006; Streat et al. 1985).

smaller cylinders (one central cylinder and two arms, two legs); 3) body composition is assumed to be homogenous; 4) with absence of individual variation, and 5) without impact of environment (temperature, stress, infusions...). This of course only holds true in an ideal situation that may differ from real life situations, especially in the critically ill. To obtain a good BIA measurement five factors are indispensable: impedance value, height, weight, gender and age. Of these gender and age are the most important in obtaining the highest level of accuracy. BIA allows a four compartment body composition analysis dividing the body into fat, water, mineral and protein components (see Figure 2, page 16) (Foster and Lukaski 1996).

BIA Measurement

Reproducible measurements can be obtained with tetrapolar electrodes with two current electrodes (to drive electricity into the human body) and two detection electrodes (to detect impedance) placed on hands and feet. Tetrapolar techniques provide more reproducible results (Kyle et al. 2004; 2004b). Modern devices also apply multiple frequencies, further improving the reproducibility and accuracy of the results. The frequency is the number of repetitions per second of a complete electric waveform (1 repetition per second is 1 Hz) (Plank et al. 1993; Janssen et al. 1997; Streat et al. 2000). A current with a frequency below 100 Hz will not pass the cell membranes and as such will measure only extracellular water (ECW). Current frequencies above 100 Hz will go through cells and measure total body water (TBW). The intracellular water (ICW) can then be calculated as TBW minus ECW. When electric current passes a cell membrane a time delay occurs, expressed as phase angle. A phase angle of 0 degrees is an indicator of absence of cell membranes, whereas 90 degrees represents a capacitive circuit which consists of only membranes with no fluid. The greater the number of cell membranes the signal has to pass

"The recommendations for fluid monitoring can at best be described as open for discussion and debate"

BIA principle

BIA allows calculation of body composition and volumes by means of a current going through the body considered as a cylinder (see Figure 1, page 16). Details of the principles can be found elsewhere (Bioelectrical impedance analysis 1994; Foster and Lukaski 1996; Kyle et al. 2004a; 2004b). In order to obtain reproducible measurements BIA has to make five assumptions: 1) the human body can be considered as a cylinder; 2) this cylinder consists of five

through, the longer the time delay. A high phase angle hence is consistent with high reactance and a large amount of waste cell membrane and body cell mass (BCM) as seen in healthy individuals, whereas (critically ill) patients tend to have a low phase angle (see Figure 3, page 16) (Savalle et al. 2012; Kyle et al. 2002). Pitfalls one has to take into account during BIA measurement are changing posture (best position being supine), incorrect position of arms (should be next to body), incorrect contact with the electrodes and contact with another person or object during measurement. Other factors that may interfere with BIA measurements that are currently not yet well understood are: infusions with large amounts of normal saline, peripheral oedema, changes in ambient air and skin temperature, sweating, conductance of hospital bed, etc.

BIA Parameters

Table 1 lists the different parameters that can be obtained with BIA. Absolute measurements of impedance, reactance, resistance and capacitance have been highly correlated

to changes in the human body, and have been shown to be good prognostic indicators. Under- and overestimation of dry weight is important, and has been shown to impair the survival and quality of life of haemodialysis patients. Body composition and nutritional assessment of children and adults in clinical settings is important in order to identify potential causes of inadequate nutrition status, including the risk of malnutrition. Performing nutritional assessments in diseased patients enables medics to identify related disorders and to monitor the effects of treatment. The glomerular filtration rate (rate at which waste is removed from our kidneys) is an important indicator of kidney function. Creatinine estimations can also be performed. BIA can obtain information on minerals (bone, soft tissue) and protein content of the body. In some patients assessment of the loss of minerals can be very important. Glycogen mass is the primary storage form of carbohydrates found in the cytoplasm of most cells. Intracellular and extracellular body fluid status in both healthy and diseased patients is of significant importance. Extracellular water (ECW) increases

in different diseases and oedema is the most common sign of ECW expansion. Body cell mass (BCM) is an accurate method of establishing a healthy subject's nutritional status or a patient's degree of malnutrition.

Validation

Although BIA is a simple, noninvasive, rapid, portable, reproducible, and convenient method of measuring body composition and fluid distribution, it is still unclear whether it is sufficiently accurate for clinical use in critically ill patients (Aghdassi et al. 2001). BIA measures TBW and as such it needs to be validated through comparison with other means of determining TBW or methods (such as densitometry) used to derive the components of the two-compartment model of the body composition, namely fat free mass and body fat. Because BIA disproportionately considers the extremities, the relationship between impedance and TBW can only be empirical (Bioelectrical impedance analysis 1994). This relationship probably exists in most normal subjects and in those with mild disease perturba-

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tions such as mild-to-moderate obesity and other chronic illnesses not producing local fluid accumulation.

The gold standard techniques for measuring body composition and TBW are isotope dilution (labelled deuterium), followed by dual energy X-ray absorptiometry (DEXA), underwater weighing, and air-displacement plethysmography. Abdominal and visceral fat can also be measured with CT and MRI. Previous studies showed varying results and in some cases BIA could not provide additional information (Plank et al. 2005; Beshyah et al. 1995; Bracco et al. 1996; Genton et al. 2002). Total body potassium (TBK) has been found to be linearly correlated with body cell mass (BCM) (Beshyah et al. 1995). Portable methods consist of infrared, skinfold caliper, and dual contact BIA. Tetrapolar BIA falls in between basic and advanced methods. Different studies compared BIA with DEXA showing good correlation. For clinical purposes two devices are available to be used in (critically ill) patients: the Fresenius Medical Care (BCM) Body Composition Monitor (Fresenius Medical Care, Bad Homburg, Germany) (<http://www.bcm-fresenius.com/index.html>) and the Maltron BioScan 920 (Maltron International Ltd, Rayleigh, Essex, UK) (<http://www.maltronint.com/products/bioscan920-2S.php>). However, no head-to-head comparison has been performed in a large sample of critically ill patients.

Clinical Applications

As suggested by ESPEN: "BIA is an important clinical tool for evaluating the metabolic status of ICU patients. It is inexpensive and noninvasive, and it provides useful information concerning altered body composition and membrane potential at the tissue level measured by phase angle, as well as fluid imbalance" (Kyle et al. 2004a; 2004b). From a theoretical point of view the clinical applications for BIA could be numerous: AIDS, muscle wasting, anorexia, postmenopausal women, obesity, pregnancy, Crohn's disease, cystic fibrosis, diabetes, paediatric diseases, enteral and parenteral nutrition, elderly, rheumatoid disease, tropical disease... BIA can be helpful in burn patients, cardiovascular disease, peripheral oedema, gastroenteritis, haemodialysis, CVVH, liver disease, second and third spacing (segmental analysis), lung disease, ARDS, malnutrition, bariatric surgery, postoperative fluid status, renal failure, stroke...

BIA can detect changes in body composition even in the early stages of kidney disease and in patients with cardio-renal syndromes, showing lower resistance, abnormal impedance vectors, reduced phase angle, and higher

total body water together with a lower body cell mass. Importantly, patients do need to have overt signs of overhydration or malnutrition for BIA to detect these alterations (Bellizzi et al. 2006; Aspromonte et al. 2012). These changes in body composition continue during the entire spectrum of chronic kidney disease, being most evident in end-stage renal disease (Dumler and Kilates 2003). In chronic haemodialysis patients multifrequency whole body BIA can give an objective measure of fluid and nutritional status, calculating overhydration within one to two litres (Tattersall 2009). Using BIA as a guide to achieving dry weight results in an improved fluid status and control of blood pressure (Moissl et al. 2013). In peritoneal dialysis patients, who often have a significant residual kidney function, BIA guided fluid management (with measurements performed after draining the intraperitoneal cavity (Arroyo et al. 2014) can help restore diuresis in underhydrated patients and improve tension and weight control in overhydrated patients (Van Biesen et al. 2011; Crepaldi et al. 2009).

Many conditions exist in critical illness (ascites, anasarca, severe peripheral oedema, pleural effusions, the massively overhydrated patient...) where conventional BIA may only provide a poor measure of TBW (Kyle et al. 2004a; 2004b). Therefore, for the time being BIA can only be considered as a research tool in critically ill patients because the TBW-to-FFM ratio is variable and the body impedance-to-TBW ratio may often vary during the above-cited conditions (Bioelectrical impedance analysis 1994; Kyle et al. 2004a; 2004b).

It is important for the clinician to be aware that the normal ECW/ICW ratio is less than 1. Critically ill patients, especially those with severe sepsis, are prone to develop changes in body fluid distribution with migration of fluid from the intravascular to the extravascular space. Furthermore, the systemic inflammatory response produces changes between the FFM and TBW distribution (Harrison 2010). Raw impedance data can provide information on hydration and cell mass integrity (Barbosa-Silva and Barros 2005).

Plank found that although changes in TBW were similar, patients with peritonitis and sepsis ($n=12$) had higher ECW values compared to those with blunt trauma ($n=18$) (Plank and Hill 2000). In a study on the use of continuous veno-venous hemofiltration to adjust fluid volume excess in 30 septic shock patients with AKI Dabrowski and co-authors found a sustained increase in nonsurvivors (Dabrowski et al. 2014). A similar study in 68 ICU patients with sepsis ($n=51$) compared to patients without sepsis ($n=17$) showed that ECW and FFM hydration were increased in severe sepsis compared to

sepsis (Słotwiński et al. 2013). Changes in tissue physiology and integrity during sepsis may produce changes in electrical properties, as such; the use of raw data obtained with BIA seems promising. Indeed, raw data are not influenced by assumptions that can affect body composition results, and bio-electrical impedance vector analysis provides information on tissue hydration and BCM independent of regression equations, even in overhydrated patients (Nwosu et al. 2013). The study by Słotwiński showed that patients with sepsis had significantly higher raw impedance ($566 \pm 98.66 \Omega$ vs. $423.86 \pm 149.7 \Omega$; $p=0.0003$) and resistance normalised by height ($336.69 \pm 66.9 \Omega/m$ vs. $259.94 \pm 90.9 \Omega/m$; $p=0.00165$) than those with severe sepsis (Słotwiński et al. 2013). The lower mean phase angle of the patients with sepsis laying above 50th percentile in the study by Słotwiński could be related to a low body cell mass and high ECW/ICW ratio, as observed by other investigators (Buffa et al. 2013). A retrospective study comparing BIA data from critically ill patients ($n=15$) with healthy volunteers ($n=25$) showed significant differences in body water composition between patients and healthy individuals (Huygh et al. 2013). In this study patients had higher values for TBW (45 ± 7.7 vs. 38 ± 9.7 Ltr, $p=0.01$), ECW (24.1 ± 5.4 vs. 16.9 ± 5.3 Ltr, $p<0.0001$) and ECW/ICW ratio (1.2 ± 0.2 vs. 0.8 ± 0.2 , $p<0.0001$) while ICW was lower 20.9 ± 3.8 vs. 21.2 ± 5 Ltr, $p=NS$) (Huygh et al. 2013).

Conclusions

BIA is non-invasive and relatively inexpensive. BIA can be performed at bedside, and does not expose to ionising radiation. Modern devices have very limited between-observer variations. However, BIA parameters are population-specific and one must be aware of clinical situations that may interfere with the measurement. BIA allows assessment of TBW, ICW, ECW, ECW/ICW ratio and calculation of volume excess. As such it can help to guide de-resuscitation in patients not transgressing spontaneously from the Ebb to Flow phase of shock (Cordemans et al. 2012). More research is needed in critically ill patients before widespread use of BIA can be suggested in critically ill patients.

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Table 1. Different Parameters That Can Be Obtained With BIA**ABSOLUTE MEASUREMENTS**

- Impedance
- Phase Angle
- Resistance
- Reactance
- Capacitance

DRY WEIGHT

- Dry Weight

BODY COMPOSITION

- Fat %
- Fat Mass
- Fat Free Mass
- Fat Free Mass %
- Body Volume
- Body Density
- Body Mass Index
- Resting Metabolic Rate
- Target Fat (min / max) %
- Target Weight (min / max)
- Target Water (min / max) %

KIDNEY FUNCTION

- Glomerular Filtration Rate
- Creatinine

MINERALS AND PROTEIN

- Total Body Potassium
- Total Body Calcium
- Protein Mass
- Mineral Mass

GLYCOGEN

- Glycogen Mass

FLUID STATUS

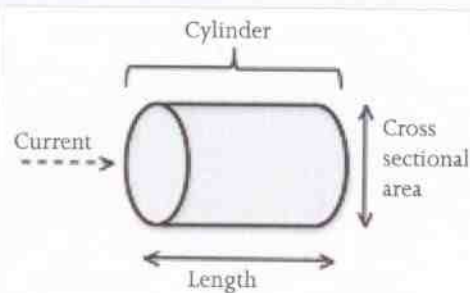
- Extracellular Fluid
- Intracellular Water Volume
- Extracellular Water Volume
- Total Body Water Volume
- Intracellular Water Lt, %
- Extracellular Water Lt, %
- Total Body Water Lt, %
- Extracellular Mass
- Extracellular Solids
- Extracellular / Intracellular Water
- Extracellular Water / Total Body Water
- Intracellular Water / Total Body Water
- Interstitial-Fluid Extravascular
- Plasma-Fluid (Intravascular)

NUTRITIONAL STATUS

- Body Cell Mass
- Muscle Mass

Figure 1. BIA Principle

When electric current goes through a cylinder-shaped body the impedance (Z) is related to the length (L) and specific resistivity (p) of the tissue and inversely related to the cross-sectional area (A) of the cylinder. The volume of a cylinder (V) can be calculated as L multiplied with A .



How does bioelectrical impedance analysis calculate volumes?

$$Z = p \cdot LA$$

$$Z = p \cdot LA \cdot LL$$

$$Z = p \cdot L2V$$

Extrapolated to a patient, L stands for the height (in cm) so that the body composition and volume (V) can be calculated as follows:

$$V = p \cdot L2Z$$

where $L2Z$ corresponds to the impedance index that can be calculated with bioelectrical impedance analysis

Figure 2. The Four Compartment Body Composition Analysis With BIA

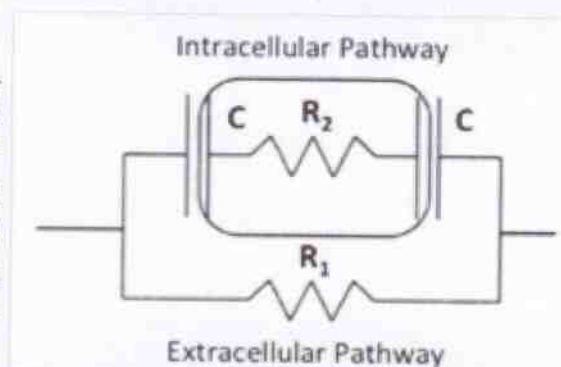
BW			
Standard weight 63.3 (Optimal)			
(57.2-69.9)			
LBM			Body Fat
53.1 (Optimal)			15.2 (Over)
(50.7-54.2)			(9.5-12.7)
SLM	SMM	Minerals	
49.1 (Optimal)	24.0 (Optimal)	4 (Over)	
(47.1-50.2)	(22.0-27.0)	(3.6-3.8)	
TBW	Protein		
38.2 (Optimal)	10.9 (Optimal)		
(36.6-38.9)	(10.1-11.4)		
ICW	ECW		
23.4 (Optimal)	14.8 (Optimal)		
(22.9-25.0)	(13.2-15.3)		

- ICW: Intracellular water (body water that exists inside the cell membrane)
- ECW: Extracellular water (body water that exists outside the cell membrane. Extracellular can be further subdivided into interstitial, lymphatic, trans-cellular fluid and blood)
- TBW: Total body water = ICW + ECW (Body water that exists in- and outside of cell membrane)
- SLM: Soft lean mass = total body water + protein (Skeletal and smooth muscle maintaining body function)
- SMM: Skeletal muscle mass
- LBM: Lean body mass = SLM + minerals
- BW: Body weight = LBM + body fat

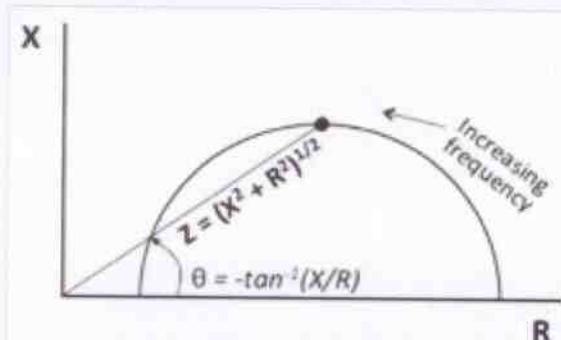
The values in between () are the range of standard body composing constituents. Units are expressed in Litres.

Figure 3. BIA Principles

Panel A. Biological tissues act as conductors or insulators and the flow of current through the body will follow the path of least Resistance (R). Fat Free Mass (FFM) contains large amounts of water and electrolytes and therefore is a better conductor of electrical current than fat and bone, which are poor conductors as they contain low amounts of fluid and conducting electrolytes. The cell membrane of a body consists of a layer of non-conductive lipid (fat, oils and other lipid like substance) material sandwiched between two layers of conductive protein molecules. Cell membranes become reactive elements behaving as capacitors (C) when electrical current is applied.



Panel B. With BIA the Phase angle (θ), the Reactance (X) and the Resistance (R) are measured. Normal Phase angle is $4-15^\circ$. Adapted from Foster and Lukaski.



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