Annals of Agricultural and Environmental Medicine 2012, Vol 19, No 4, 697-700
www.aaem.pl

Bioimpedance vector pattern in women with breast cancer detected by bioelectric impedance vector analysis. Preliminary observations

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Małecka-Massalska T, Chara K, Smolen A, Kurylcio A, Polkowski W, Lupa-Zatwarnicka K. Bioimpedance vector pattern in women with breast cancer detected by bioelectric impedance vector analysis. Preliminary observations. Ann Agric Environ Med. 2012; 19(4): 697-700.

Abstract

Introduction and objectives: The study was conducted to evaluate soft tissue hydration and mass through pattern analysis of vector plots as height, normalized resistance, and reactance measurements by bioelectric impedance vector analysis (BIVA) in patients with breast cancer.

Materials and methods: Whole-body measurements were made with ImpediMed bioimpedance analysis SFB7 BioImp v1.55 (Pinkenba Qld 4008, Australia) in 68 adult, white, female subjects: 34 adult, white female (age 31-82) patients with breast cancer and 34 healthy volunteers matched by age, gender and BMI as a control group. The measurements were performed prior to oncological and surgical treatment, without the need for active nutritional interventions.

Results: Mean vectors of women with breast cancer versus the healthy women groups were characterized by a slight increase of the normalized resistance and reactance components (separate 95% confidence limits, $p < 0.05$) indicating that there were slight differences of soft tissue hydration and mass.

Conclusion: The results observed in the presented study provide valuable information on the nutritional status of the patient prior to surgery. This quick assessment of the patient nutritional status can allow for early corrective intervention. Further observational research investigating these properties in larger groups would be beneficial to elucidate and/or confirm these findings.

Key words

breast cancer, bioelectrical impedance analysis, bioelectric impedance vector analysis, impedance vector

INTRODUCTION

In the United States, breast cancer is the most common non-skin cancer and the second leading cause of cancer-related death in women [1]. In Poland, it is estimated that the number of new breast cancer cases reaches about 13,500 women each year [2].

There are many methods for nutritional status assessment. One of them is bioimpedance analysis (BIA) and the assessment of direct bioimpedance measures (resistance (R), reactance (Xc) and phase angle (PA)). The use of these raw data has gained popularity in nutrition assessment and monitoring of nutrition status in patients [3]. BIA is based on the principle that a fixed, low voltage, high frequency alternating current introduced into the human body is conducted almost completely through the fluid compartment of the fat free mass [4]. BIA evaluates the body components; resistance (R) and reactance (Xc) by recording a voltage drop in applied current [5]. Resistance is restriction of the flow of an electric current, primarily related to the amount of water present in the tissues. Reactance is the resistive effect produced by the tissue interfaces and cell membranes [5]. Part of the electrical current is stored by the cell membranes, which act as capacitors, creating a resistive force. It is this reactance which causes the current to lag behind the voltage ultimately creating a phase shift, which is quantified geometrically as the angular transformation of the ratio of reactance to resistance, or PA [6].

The BIVA technique is a promising tool which uses 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 at the bedside for assessment and management of body fluids [7]. Bioelectrical impedance vector analysis allows non-invasive evaluation of soft tissue hydration and mass through pattern analysis of vector plots as height, normalized resistance, and reactance measurements [8]. 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's disease [9], in stable and non-stable heart failure patients [10], critically ill and cardiorenal patients [11], haemodialysis patients [12], peritoneal dialysis patients [13] as well as in cancer patients [14, 15].

In healthy populations, the BIVA method has been used in modeling the human body shape [16] and monitoring the variation of the hydrate status in healthy term newborns [17]. In particular, raw BIA measurements measured at 50 kHz, because of its reproducibility quality, has been used to determine the differences in soft tissue hydration and mass [8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18].

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Received: 15 February 2012; accepted: 17 October 2012

MATERIALS AND METHODS

The aim of the presented observational study was to perform bioelectrical impedance analysis to investigate whether the position on the R-Xc plane of impedance vectors from women with breast cancer differed from healthy women, matched by age and BMI.

Study Populations. Between October 2009 – May 2010, BIA examinations of tissue electrical properties were conducted in 68 adult, white, female subjects aged 31-82: 34 patients with breast cancer and 34 healthy volunteers matched by age, gender and BMI as the control group.

Baseline nutritional assessment was performed by Subjective Global Assessment (SGA), which has been widely used to assess nutritional needs and monitor nutrition therapy in the hospitalized population. It is a simple, safe and inexpensive test to administer. BIA was performed by a medical doctor using ImpediMed bioimpedance analysis SFB7 BioImp v1.55 (Pinkenba Qld 4008, Australia). Due to previously published research indicating that exercise influences BIA measurements, in particular the phase angle, this variable was controlled in the presented study. BIA was performed, after a 10-minute rest period. All patients were positioned supine on a bed, with their legs apart and their arms not touching the torso. All evaluations were conducted on the patients' right side by using the 4-surface standard electrode (tetra polar) techniques on the hand and foot. R and Xc were measured directly in ohms at 5, 50, 100, 200 kHz. R and Xc values were measured once in each patient. PA was obtained from the arc-tangent ratio Xc : R. To transform the result from radians to degrees, the result obtained was multiplied by 180°/π. For further analysis, values of R, Xc and PA measured at 50 kHz were taken. Fat mass (kg), as a difference between fat free mass and weight and fat free mass (kg) derived from total body water divided by the hydration constant, were automatically received on the ImpediMed bioimpedance analysis SFB7 BioImp v1.55 equipment.

Bioimpedance. BIA was performed by a medical doctor using ImpediMed bioimpedance analysis SFB7 BioImp v1.55 (Pinkenba Qld 4008, Australia). BIA was performed, after a 10 minute rest period while the patients were lying supine on a bed, with their legs apart and their arms not touching their torso. All evaluations were conducted on the patients' right side by using the 4-surface standard electrode (tetra polar) technique on the hand and foot. R and Xc were measured directly in ohms at 5, 50, 100, 200 kHz. R and Xc values were measured once in each patient. PA was obtained from the arc-tangent ratio Xc : R. To transform the result from radians to degrees, the result obtained was multiplied by 180°/π.

Bioelectrical Impedance Vector Analysis. According to the RXc graph method [19], measurements of R and Xc were standardized by the H subjects (i.e., R/H and Xc/H) and expressed in ohms per meter. By using the bivariate normal distribution of R/H and Xc/H, the bivariate 95% confidence limits for mean impedance vectors of were calculated for cancer patients and healthy subjects (i.e., the limit containing the magnitude and phase angle of the mean vectors with 95% probability). Separate 95% confidence limits indicate a statistically significant difference between mean vector positions on the R-Xc plane, i.e., in their R/H, Xc/H, or both components, or in their magnitude, phase angle or both ($p < 0.05$, which is equivalent to a significant Hotelling T^2test) [19].

Statistical Methods. The results obtained were expressed as mean ± SD. The Shapiro-Wilk (S-W) test was used to assess the distribution conformity of examined parameters with a normal distribution; the Fisher (F) test was used to assess variance homogeneity. For group comparisons of metric data, the Mann-Whitney-U-test was used. A p value < 0.05 was considered statistically significant. Statistical analysis was performed using the computer software STATISTICA v.8.0 (StatSoft, Poland). BIVA was conducted with BIVA software (version 2002).

RESULTS

As previously stated, many research studies refer to the great reproducibility of direct bioimpedance measurements (R, X, PA) at 50 kHz. Due to the logic of this reasoning, our RXc graph method refers to 50 kHz.

The characteristics of the breast cancer patients and the control group with average values of protocol variables are shown in Tables 1-2.

Table 1. Baseline characteristics of breast cancer patient and control group

Characteristic	$\bar{x}$ ± SD (breast cancer patients)	$\bar{x}$ ± SD (control group)	p
n	34	34	
Age at diagnosis (y)	53.88 ± 10.84	53.79 ± 10.18	NS
BMI kg/m^2	26.97 ± 3.99	27.27 ± 7.66	NS
Height (cm)	161.48 ± 7.4	157.44 ± 19.12	NS
Weight (kg)	69.04 ± 12.56	70.07 ± 23.6	NS
R at 50 kHz (ohm)	608.7 ± 84.15	515.35 ± 66.72	**0.000003**
R/H (ohm/m)	377.54 ± 53.86	341.03 ± 127.16	NS
Xc at 50 kHz (ohm)	53.58 ± 8.92	47.01 ± 7.3	**0.001**
Xc/H (ohm/m)	33.28 ± 6.07	31.17 ± 12.42	NS
Phase angle at 50 kHz (°)	5.05 ± 0.66	5.22 ± 0.64	NS
Subjective Global Assessment (SGA)[1]	Well-nourished – 34 (100) Moderately malnourished – 0 (0) Severely malnourished – 0 (0) Not known – 0 (0)	Well-nourished – 34 (100) Moderately malnourished – 0 (0) Severely malnourished – 0 (0) Not known – 0 (0)	

[1] range in parentheses (all such values).

Table 2. BIA measurements and calculated values of the breast cancer patients and control group

Parameter	Value (breast cancer patients)	Value (control group)	p<
n	34	34	
Resistance at 5 kHz (ohm)	683.7 ± 92.3	580.34 ± 73.92	**0.000003**
Reactance at 5 kHz (ohm)	28.8 ± 15.91	25.4 ± 4.36	**0.009**
Phase angle at 5 kHz (°)	2.41 ± 0.39	2.52 ± 0.39	0.28
Resistance at 100 kHz (ohm)	582.72 ± 81.83	493.61 ± 64.09	**0.000005**
Reactance at 100 kHz (ohm)	45.65 ± 7.76	40.36 ± 6.7	**0.004**
Phase angle at 100 kHz (°)	4.51 ± 0.62	4.69 ± 0.63	0.24
Resistance at 200 kHz (ohm)	559.72 ± 79.47	470.48 ± 61.8	**0.000002**
Reactance at 200 kHz (ohm)	41.1 ± 7.74	35.38 ± 5.92	**0.000001**
Phase angle at 200 kHz (°)	4.21 ± 0.6	4.32 ± 0.54	0.46

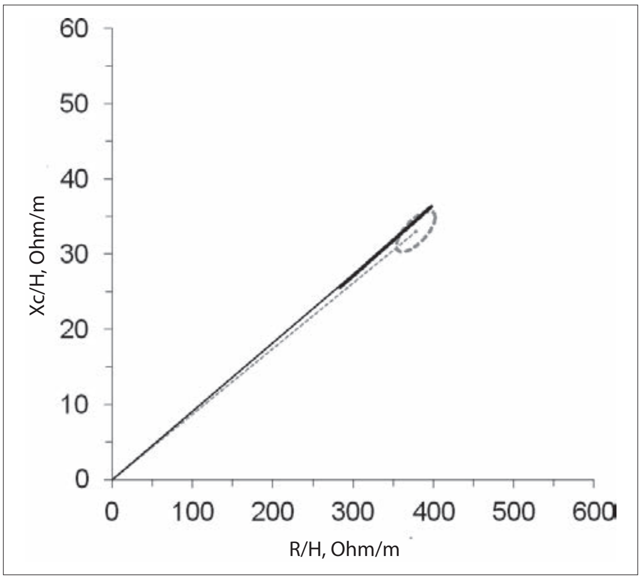

Figure 1. Mean vectors of 95% confidence limits in women with breast cancer (grey dotted line) and control group (solid black line)

Mean vectors of 95% confidence limits in women with breast cancer (grey dotted line) and the control group (solid black line) in Figure 1.

DISCUSSION

Malnutrition is known to be associated with adverse outcomes in cancer patients. In general, patients who have been and/or are being treated for breast cancer have a compromised nutritional status [20]. BIA has been validated for the assessment of body composition and nutritional status in patients with cancer. BIA measures PA, considered to be a global marker of health, although the biological meaning of PA is not fully understood. It reflects body cell mass and is one of the best markers of cell membrane function. It has been observed that decreased cell integrity or cell death is marked by a lower PA, while large quantities of intact cell membranes are marked by a higher PA. PA by definition is positively associated with reactance and negatively associated with resistance. A. Bosy-Westphal et al. [21] emphasizes that age, gender and body mass indices (BMI) are the key determinants of phase angle values.

During the past decade, several studies have investigated the role of PA as a prognostic tool and indicator of nutritional status and cell membrane function in various disease conditions, including cancer. The prognostic role of PA in cancer patients is most evident in the relationship between survival and PA value. M. C. Barbosa-Silva et al. [6] have stated that PA seems to be the best indicator of cell membrane function, as related to the ratio between extracellular and intracellular water.

The importance of PA values has been demonstrated in a variety of diseased states. In patients with liver cirrhosis, PA equal to or less than 5.4° was associated with shorter survival, in comparison to PA greater than 5.4 [22]. M. Ott et al. [23] observed that a PA value of less than 5.3° was considered to be the most important single predictor of survival. A. Schwenk et al. [24] pointed out that PA values could be used as a marker of malnutrition in HIV-infected patients. In patients, diagnosed with stage IV pancreatic cancer, PA above the median cut-off of 5° was associated with improved survival [25]. In a study by D. Gupta et al. [26] it was observed that PA values in patients with stage IV colorectal cancer, an above the median cut-off of 5.6° was associated with better survival. Gupta et al. [27] also reported that advanced lung cancer patients with a mean PA value of less than or equal to 4.5 degrees had a significantly shorter survival than those with a PA greater than 4.5 degrees.

The presented study was undertaken to investigate whether a BIA-derived phase angle could predict survival in breast cancer.

Previous studies, e.g. Gupta et al. [28], were conducted on a case series of 259 histologically confirmed breast cancer patients, and demonstrated that the phase angle is a strong predictor of survival in breast cancer after controlling for the effects of stage at diagnosis and prior treatment history. The limitations of this study relate to the BIA technique and retrospective study design; therefore, because of its retrospective nature, it relies on data not primarily intended for research.

In the presented study, the BC patient group PA was 5.05°, a value that was not statistically significantly lower ($p = 0.3$) than in the control group (5.05 ± 0.66 vs. 5.22 ± 0.64, respectively). This result is in opposition to that presented by Gupta et al. [28]. The explanation for the result in the presented study may be due the small size of the selected group.

BIVA allows non-invasive evaluation of soft tissue hydration [8]. In the presented study, it was observed that there was no significant difference vector distribution in either the women with breast cancer or the healthy control group. The vector displacement of women with breast cancer and healthy subjects was characterized by a slight increase of Xc component and R component (Fig. 1).

Resistance was significantly ($p=0.000003$) greater in patients with BC than in the control group (608.7 ± 84.15 ohm vs. 515.35 ± 66.72 ohm, respectively). As may be recalled, resistance is the restriction of the flow of an electric current, primarily related to the amount of water present in the tissues. In the presented small study population of BC patients, it was observed that there was a smaller distribution of water between the extra- and intra-cellular compartments, and that there was a greater resistance of the electric current, due to the smaller distribution of water in these patients. Surprisingly, reactance at 50 kHz was found to be significantly ($p=0.001$) greater in patients with BC than in the control group (53.58° ± 8.92 vs. 47.01° ± 7.3, respectively). Reactance, as previously explained, is the resistive effect produced by the tissue interfaces and cell membranes [6]. By definition, PA is positively associated with reactance and negatively associated with resistance [9]. This could mean that the cell membrane was in a better condition in the BC population than in the control group. However, the SGA results presented here indicated that 100% of this group was well nourished. On that point, according to all the available information on PA, BIA was compatible with the nutritional assessment of cancer patients.

In healthy populations there are considerable differences between phase angle reference values. U. G. Kyle et al. [29] found that in the Swiss population, PA values were higher in men than in women. M. C. Barbosa-Silva et al. [30] also demonstrated a difference of PA reference values between genders. T. Malecka-Massalska et al. [31], however, did not detect any difference in bioelectric impedance vector analysis between Taiwanese and Polish college students. The reason for this might also be due to the small size of the studied groups. Since we are aware of the variability of reference PA values in different populations, establishing one for the Polish population would be useful. One limitation of the presented study is this lack of established PA reference values for the Polish population, and the observed variability of national PA values.

To the best of our knowledge, this is the first study evaluating whether there is a difference in the position on the R-Xc plane of impedance vectors from Polish women with breast cancer, and healthy women matched by age and BMI. The presented study was largely restricted to newly diagnosed patients (only 4 patients had previous treatment history), although the results observed provide valuable information on the nutritional status of the patient prior to surgery.

Further research with a larger sample size could, however, support the obtained results, provide an avenue for early nutritional intervention and corrective nutritional replacement, and ultimately combined with oncology intervention lead to increased survival in this patient population.

CONCLUSION

The bioelectric impedance vector analysis (BIVA) technique is a useful tool for the screening and monitoring of nutrition and hydration status among women with breast cancer. Rapidly available, non-invasive, BIVA may offer objective measures to improve clinical decision-making and predict outcomes. Monitoring vector displacement trajectory towards the reference target vector position may represent useful feedback in support therapy planning of individual patients before surgery in patients with breast cancer. Mean vectors of women with breast cancer versus the healthy women were characterized by a slight increase in the normalized resistance and reactance components. Further observational research investigating these properties in larger groups would be beneficial for elucidating and/or confirming these findings.

Ethical Approval

The research complied with the policy of the Journal on Ethical Consent.

Acknowledgements

The authors wish to thank Professor Antonio Piccoli, University of Padua, Italy, for kindly providing the BIVA Software 2002.

REFERENCES

1. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. CA Cancer J Clin. 2005; 55: 74–108.
2. Wojciechowska U, Didkowska J, Zatonski W. Nowotwory złośliwe w Polsce w 2006 roku. Warszawa: Centrum Onkologii- Instytut, 2008.
3. Bosy-Westphal A, Danielzik S, Dörhöfer RP, Later W, Wiese S, Müller MJ. Phase angle from bioelectrical impedance analysis: population reference values by age, sex, and body mass index. JPEN 2006; 30: 309-316.
4. Simons JP, Schols AM, Westerterp KR, ten Velde GP and Wouters EF. The use of bioelectrical impedance analysis to predict total body water in patients with cancer cahexia. Am J Clin Nutr. 1995; 61: 741-745.
5. Zarowitz BJ, Pilla AM. Bioelectrical impedance in clinical practice. DICP. Ann Pharmacother. 1989; 23: 548-555.
6. Barbosa-Silva MC, Barros AJ. Bioelectrical impedance analysis in clinical practice: a new perspective on its use beyond body composition equations. Curr Opin Clin Nutr Metab Care. 2005; 8: 311-317.
7. Piccoli A. Bioelectric impedance measurement for fluid status assessment. Contrib Nephrol. 2010; 164: 143-52.
8. Toso S, Piccoli A, Gusella M, Menon D, Crepaldi G, Bononi A, Ferrazzi E. Bioimpedance vector pattern in cancer patients without disease versus locally advanced or disseminated disease. Nutrition 2003; 19: 510-4.
9. Buffa R, Mereu RM, Putzu PF, Floris G, Marini E. Bioelectrical impedance vector analysis detects low body cell mass and dehydration in patients with Alzheimer's disease. J Nutr Health Aging. 2010; 14: 823-7.
10. Gastelurrutia P, Nescolarde L, Rosell-Ferrer J, Domingo M, Ribas N, Bayes-Genis A. Bioelectrical impedance vector analysis (BIVA) in stable and non-stable heart failure patients: a pilot study. Int J Cardiol. 2011; 146: 262-4.
11. Peacock WF. Use of bioimpedance vector analysis in critically ill and cardiorenal patients. Contrib Nephrol. 2010; 165: 226-35.
12. Nescolarde L, Piccoli A, Román A, et al. Bioelectrical impedance vector analysis in haemodialysis patients: relation between oedema and mortality. B Physiol Meas. 2004; 25: 1271-80.
13. Piccoli A. Italian CAPD-BIA Study Group. Bioelectric impedance vector distribution in peritoneal dialysis patients with different hydration status. Kidney Int. 2004; 65: 1050-63.
14. Toso S, Piccoli A, Gusella M, Menon D, Crepaldi G, Bononi A, Ferrazzi E. Altered tissue electric properties in lung cancer patients as detected by bioelectric impedance vector analysis. Nutrition 2000; 16: 120-124.
15. Malecka-Massalska T, Smolen A, Zubrzycki J, Lupa-Zatwarnicka K, Morshed K. Bioimpedance vector pattern in head and neck squamous cell carcinoma. J Physiol Pharmacol. 2012; 63: 101-4.
16. Kim CH, Park JH, Kim H, Chung S, Park SH. Modeling the human body shape in bioimpedance vector measurements. Conf Proc IEEE Eng Med Biol Soc. 2010; 3872-4.
17. Margutti AV, Monteiro JP, Camelo JS Jr. Reference distribution of the bioelectrical impedance vector in healthy term newborns. Br J Nutr. 2010; 104: 1508-13.
18. 18. Floriańczyk B, Grzybowska L, Marzec Z. Metallothionein and manganese concentrations in breast cancer and mastopathic tissues. J Pre-Clin Clin Res. 2011; 5(2): 63-65.
19. Piccoli A, Rossi B, Pillon L, Bucciante G. A new method for monitoring body fluid variation by bioimpedance analysis: the RXc graph. Kidney Int. 2004; 46: 534.
20. Rock CL, Demark-Wahnefried W. Nutrition and survival after the diagnosis of breast cancer: a review of the evidence. J Clin Oncol. 2002; 20: 3302–3316.
21. Bosy-Westphal A, Danielzik S, Dörhöfer RP, Later W, Wiese S, Müller MJ. Phase angle from bioelectrical impedance analysis: population reference values by age, sex, and body mass index. JPEN 2006; 30: 309-316.
22. Selberg O, Selberg D. Norms and correlates of bioimpedance phase angle in healthy human subjects, hospitalized patients, and patients with liver cirrhosis. Eur J Appl Physiol. 2002; 86: 509-516.
23. Ott M, Fischer H, Polat H, Helm EB, Frenz M, Caspary WF, Lembcke B. Bioelectrical impedance analysis as a predictor of survival in patients with human immunodeficiency virus infection. J Acquir Immune Defic Syndr Hum Retrovirol. 1995; 9: 20-25.
24. Schwenk A, Ward LC, Elia M, Scott GM. Bioelectrical impedance analysis predicts outcome in patients with suspected bacteremia. Infection 1998; 26: 277-282.
25. Gupta D, Lis CG, Dahlk SL, Vashi PG, Grutsch JF, Lammersfeld CA. Bioelectrical impedance phase angle as a prognostic indicator in advanced pancreatic cancer. Br J Nutr. 2004; 92: 957-962.
26. Gupta D, Lammersfeld CA, Burrows JL, et al. Bioelectrical impedance phase angle in clinical practice: implications for prognosis in advanced colorectal cancer. Am J Clin Nutr. 2004; 80: 1634-1638.
27. Gupta D, Lammersfeld CA, Vashi PG, King J, Dahlk SL, Grutsch JF, Lis CG. Bioelectrical impedance phase angle in clinical practice: implications for prognosis in stage IIIB and IV non-small cell lung cancer. BMC Cancer 2009; 9: 37-42.
28. Gupta D, Lammersfeld CA, Vashi PG, King J, Dahlk SL, Grutsch JF, Lis CG. Bioelectrical impedance phase angle as a prognostic indicator in breast cancer. BMC Cancer 2008; 8: 249-255.
29. Kyle UG, Genton L, Slosman DO, Pichard C. Fat-free and fat mass percentiles in 5225 healthy subjects aged 15 to 98 years. Nutrition 2001; 17: 534-541.
30. Barbosa-Silva MCG, Barros AJD, Wang J, Heymsfield SB, Pierson RN Jr. Bioelectrical impedance analysis: population reference values for phase angle by age and sex. Am J Clin Nutr. 2005; 82: 49-52.
31. Malecka-Massalska T, Smolen A, Madro E, Surtel W. Bioimpedance vector pattern in Taiwanese and Polish college students detected by bioelectric impedance vector analysis: Preliminary Observations. Sci World J. 2012, Article ID 684865, doi:10.1100/2012/68486.