ORIGINAL ARTICLE

Annals of Agricultural and Environmental Medicine 2013, Vol 20, No 3, 523–527
www.aaem.pl

Altered tissue electrical properties in women with breast cancer – Preliminary observations

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Małecka-Massalska T, Chara K, Gołębiowski P, Władysiuk M, Smoleń A, Kurylcio A, Zuchora B, Zubrzycki J, Orłowska-Kowalik G, Lupa-Zatwarnicka K, Polkowski W. Altered tissue electrical properties in women with breast cancer – Preliminary observations. Ann Agric Environ Med. 2013; 20(3): 523–527.

Abstract

Introduction and objectives: In the United States, breast cancer (BC) is the most common non-skin cancer. In Poland, it is estimated that the number of new breast cancer cases affects about 13,500 women each year. There are many methods for nutritional status assessment. One of them is bioimpedance analysis (BIA). Direct bioimpedance measures (resistance, reactance, phase angle (PA)) determined by bioelectrical impedance analysis (BIA) detectf changes in tissue electrical properties. The study was conducted to investigate whether there are any tissue electrical differences in patients with breast cancer.

Materials and methods: The direct bioimpedance measures determined by bioelectrical impedance analysis (BIA) were performed on 34 patients with BC and 34 healthy volunteers. The measurements were made with ImpediMed bioimpedance analysis SFB7 BioImp v1.55 (Pinkenba Qld 4008, Australia).

Results: Reactance and resistance at 50 kHz was found to be significantly greater in patients with BC than in the control group (53.59° ± 1.53 vs. 47.26° ± 1.25, respectively, p=0.0031; 603.24° ± 15.38 ohm vs. 515.87° ± 11.48 ohm, respectively, p=0.00004).

Conclusion: Pre-surgical patients diagnosed with BC have altered tissue electrical properties. Further observations of a larger patient group would be valuable to calculate survival, validate the prognostic significance of PA, and monitor nutritional and therapeutic interventions in this patient population.

Key words

breast cancer, bioelectrical impedance analysis, phase angle

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]. It is estimated that in Poland the number of new breast cancer cases amounts to about 13,500 women each year [2].

Malnutrition is a frequent manifestation in patients with advanced cancer and is a major contributor to morbidity and mortality [3]. Methods or tools designed to measure and monitor nutritional status can play a dynamitic role in the recovery and quality of life for this patient population. Bioelectrical Impedance Analysis (BIA) has been established as a valuable tool in the evaluation of body composition and nutritional status in the condition of many patients, including cancer [4, 5, 6]. BIA evaluates body components, such as resistance (R) and reactance (Xc) by recording a voltage drop in applied current [7]. Resistance is the opposition to 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 [8]. 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 phase angle (PA).

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Received: 15 February 2012; accepted: 29 December 2012

PA reflects the relative contributions of fluid (indicated by resistance) and cellular membranes (indicated by reactance) in the human body. By definition, PA is positively associated with reactance and negatively associated with resistance [9]. Decreased cell integrity or cell death is suggested by lower PA while large quantities of intact cell membranes may be indicated by a higher PA [10]. By detecting changes in tissue electrical properties, PA has been found to be a prognostic tool, as an indicator of nutritional status, membrane cell function and health marker in patients with liver cirrhosis, acute respiratory failure, end-stage renal disease, human immunodeficiency virus infection, suspected bacteraemia, advanced pancreatic cancer, colorectal cancer, breast cancer and non-small cell lung cancer [10, 11, 12, 13, 14, 15, 16]. 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 and HIV [11, 13, 14, 15, 16].

Objective. The aim of the presented cross-sectional study was to perform bioelectrical impedance analysis to investigate tissue electrical properties in patients diagnosed with BC, prior to surgery. This is the first study to evaluate resistance, reactance and PA among pre-surgical BC patients in Poland.

MATERIALS AND METHOD

Ethical considerations. This study was conducted according to the guidelines set out in the Helsinki Declaration, and all procedures involving human subjects/patients were approved by the Research Ethics Committee of the Medical University in Lublin, Poland. All patients gave their written informed consent as a precondition of participation in the study.

Patients, intervention and outcome measures. Between October 2009 – May 2010, 62 subjects underwent examination of tissue electrical properties. 34 pre-surgical patients with BC were examined: 34 women between the ages of 31–82. Only patients with a histologically confirmed diagnosis of breast cancer were included in the study. All patients were treated at the Department of Surgical Oncology Department of the Medical University in Lublin.

34 healthy subjects (34 women) from the same region and matched by age and gender were selected as the control group (Tab.1, Tab. 2). The group of patients with BC underwent a baseline nutritional assessment, which included subjective global assessment (SGA) and BIA. The control group underwent a baseline nutritional assessment, which included SGA and BIA. 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 3 times in each patient, and the mean values were used. 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.

Table 1. Baseline characteristics of breast cancer patients and control group.[1]

Characteristic	Value (breast cancer patients)	Value (control group)
Gender [n (%)] Female	34 (100)	34 (100)
Prior treatment history [n(%)] Newly diagnosed	34 (100)	n/a
Subjective Global Assessment (SGA)	Well-nourished 34 (100) Moderately malnourished 0 (0) Severely malnourished 0 (0) Unknown 0 (0)	Well-nourished 34 (100) Moderately malnourished 0 (0) Severely malnourished 0 (0) Unknown 0 (0)
Age at diagnosis (y)	53.88 ± 10.84 (31–82)[2]	53.79 ± 10.18 (35–75)[2]
Height (cm)	161.48 ± 7.40	157 ± 19.12
Weight (kg)	67.94 ± 12.56	79.07 ± 23.60
BMI kg/m^2	26 ± 3.99	29.61 ± 7.66
Fat mass (kg)	24.39 ± 1.33	25.48 ± 2.23
Fat free mass (kg)	43.37 ±1.1	50.59 ± 1.35
Resistance at 5 kHz (ohm)	684.06 ± 15.83	580.42 ± 12.71
Reactance at 5 kHz (ohm)	28.87 ± 1.01	25.6 ± 0.84
Phase angle at 5 kHz (°)	2.42 ± 0.07	2.53 ± 0.07
Resistance at 50 kHz (ohm)	603.24 ± 15.38	515.87 ± 11.48
Reactance at 50 kHz (ohm)	53.59 ± 1.53	47.26 ± 1.25
Phase angle at 50 kHz (°)	5.05 ± 0,12	5.25 ± 0.11
Resistance at 100 kHz (ohm)	583.02 ± 14.02	493.62 ± 10.99
Reactance at 100 kHz (ohm)	45.67 ± 1.35	40.37 ± 1.15
Phase angle at 100 kHz (°)	4.51 ± 0.11	4.32 ± 0.09
Resistance at 200 kHz (ohm)	559.95 ± 13.61	470.48 ± 10.6
Reactance at 200 kHz (ohm)	39.75 ± 6.37	35.38 ± 1.01
Phase angle at 200 kHz (°)	4.17 ± 0.09	4.44 ± 0.41

Table 1 (Continuation). Baseline characteristics of breast cancer patients and control group.

[1]n = 34; [2]$\bar{x}$± SD; range in parentheses (all such values).

Table 2. Patient and tumour characteristics (n = 34).

Localisation	
Left Breast	18
Right Breast	17
Unilateral	33
Bilateral	1
Neo-adjuvant therapy	
No	30
Yes	4
Tumour histology	
Intraductal	1
Invasive ductal	33
Invasive lobular	1
TNM staging	
Pt	
pTis	1
pT1	23
pT1a	1
pT1b	11
pT1c	11
pT2	11
Pn	
pN0	28
pN0(sn)	27
pN1	7
pM	
pM0	34
pM1	0
Hormone receptor status	
ER+/PR+	25
ER+/PR-	2
ER-/PR+	0
ER-/PR-	8
Grading (G)	
G1	1
G2	29
G3	5
HER 2 status	
HER 2 0	32
HER 2 +3	3

Statistical analysis. The results are 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 with computer software STATISTICA v.8.0 (StatSoft, Poland).

RESULTS

Multi-frequency analysis of resistance, reactance and phase angle at 5, 50, 100 and 200 kHz, were conducted on the BC patients and control group. Nearly all measures at all frequencies were significantly different between BC patients and the control group, except for phase angle (5 kHz, 50 kHz and 100 kHz) (Tab. 3).

There were some differences observed in several anthropometric measured variables between the studied groups, such as height (161.48 ± 7.40 vs. 157 ± 19.12 cm); weight (67.94 ± 12.56vs. 79.07 ± 23.60 kg); fat mass (26 ± 3.99 vs. 29.61 ± 7.66 kg); fat free mass (43.37 ±1.1 vs. 50.59 ± 1.35 kg); BMI (26 ± 3.99 vs. 29.61 ± 7.66 kg/m^2) in BC patients and the control group, respectively. BC patients overall were the same age as the control group. The mean of height of the two groups were also the same. BC patients weighed less, fat mass and fat free mass were all less than the control group. It is unclear whether this is an effect of individual patient variability, or as a result of state of the the disease.

Table 3. BIA measurements and calculated values of breast cancer patients and control group.

Parameter	Value (breast cancer patients)	Value (control group)	p<
N	34	34	
Resistance at 5 kHz (ohm)	684.06 ± 15.83	580.42 ± 12.71	**0.000008**
Reactance at 5 kHz (ohm)	28.87 ± 1.01	25.6 ± 0.84	**0.03**
Phase angle at 5 kHz (°)	2.42 ± 0.07	2.53 ± 0.07	0.17
Resistance at 50 kHz (ohm)	603.24 ± 15.38	515.87 ± 11.48	**0.00004**
Reactance at 50 kHz (ohm)	53.59 ± 1.53	47.26 ± 1.25	**0.003**
Phase angle at 50 kHz (°)	5.05 ± 0,12	5.25 ± 0.11	0.19
Resistance at 100 kHz (ohm)	583.02 ± 14.02	493.62 ± 10.99	**<0.000001**
Reactance at 100 kHz (ohm)	45.67 ± 1.35	40.37 ± 1.15	**<0.000001**
Phase angle at 100 kHz (°)	4.51 ± 0.11	4.32 ± 0.09	**<0.000001**
Resistance at 200 kHz (ohm)	559.95 ± 13.61	470.48 ± 10.6	**<0.000001**
Reactance at 200 kHz (ohm)	39.75 ± 6.37	35.38 ± 1.01	**<0.000001**
Phase angle at 200 kHz (°)	4.17 ± 0.09	4.44 ± 0.41	0.07

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, the results of the presented study are illustrated only for, figures below 50 kHz (Fig. 1–2).

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 [17]. BIA has been validated for the assessment of body composition and nutritional status in patients with cancer. BIA measures PA which is considered to be a global marker of health. The biological meaning of PA is not well 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 lower PA, while large quantities of intact cell membranes are marked by higher PA. PA, by definition, is positively associated with reactance and negatively associated with resistance. Bosy-Westphal et al. [18] emphasizes that age, gender and body mass index (BMI) are the key determinants of phase angle values.

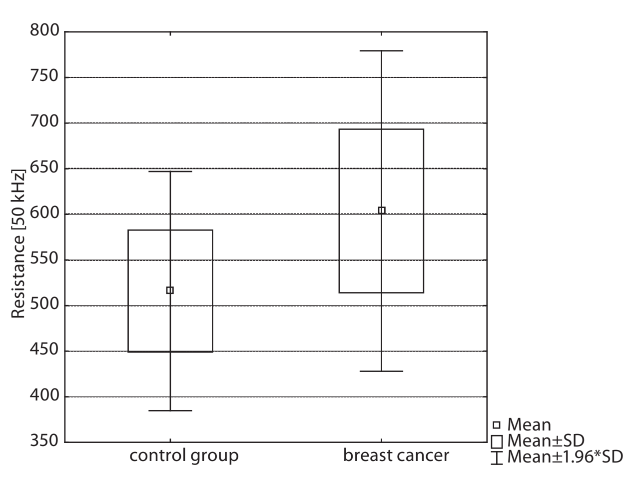

Figure 1. Resistance in women with breast cancer and the control group.

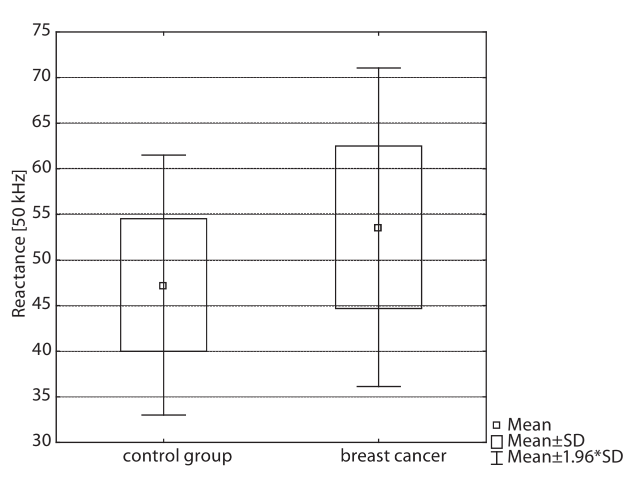

Figure 2. Reactance in women with breast cancer and the control group.

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. Barbosa-Silva et al. [8] 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 with 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 [10]. Ott et al. [11] observed that PA value of less than 5.3° was considered to be the most important single predictor of survival, while Schwenk et al. [12] 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 [13]. In a study of Gupta et al. [14] it was observed that PA values in patients with stage IV colorectal cancer, those above the median cut-off of 5.6° was associated with better survival. Gupta et al. [16] 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 the BIA-derived phase angle could predict survival in breast cancer.

Previous studies, such as a study by Gupta et al. [15], were conducted on a case series of 259 histologically-confirmed breast cancer patients. It demonstrated that the phase angle is a strong predictor of survival in breast cancer after controlling the effects of the stage at diagnosis, and prior treatment history. Limitations of the presented study relate to the BIA technique and retrospective study design, and because of its retrospective nature relies on data not primarily meant for research.

In BC patient group in the presented study, PA was 5.05° and this value was not statistically significantly lower (p=0.13) than in the control group (5.05 ± 0,12 vs. 5.25 ± 0.11, respectively). Surprisingly, reactance at 50 kHz was found to be significantly (p=0.0031) greater in patients with BC than in the control group (53.59° ± 1.53 vs. 47.26° ± 1.25, respectively) – reactance is the resistive effect produced by the tissue interfaces and cell membranes [8]. 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 of the presented study indicate that 100% (Tab. 1) of this group was well nourished. On that point, all available information on PA, the BIA was compatible with the nutritional assessment of the cancer patients.

Resistance was significantly (p=0.00004) greater in patients with BC than in the control group (603.24° ± 15.38 ohm vs. 515.87° ± 11.48 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 in these patients there was a greater resistance of the electric current due to the smaller distribution of water in.

In healthy populations, there are considerable differences between phase angle reference values. Kyle et al. [19] found that in a Swiss population, PA values were higher in males than in females. Barbosa-Silva et al. [20] also demonstrated the difference of PA reference values between genders. Since the variability of reference PA values in different populations is known, establishing one for the Polish population would be useful. The lack of established PA reference values for the Polish population, and the observed variability of national PA values, may be one limitation of the presented study.

To the best of our knowledge, this is the first study to evaluate resistance, reactance and PA among pre-surgical BC patients. The study was largely restricted to newly-diagnosed patients (only 4 patients had previous treatment history). The results observed provide valuable information on the nutritional status of the patient prior to surgery. In the opinion of the authors of the presented study, further research with a larger sample size could support the presented results, provide an avenue for early nutritional intervention and corrective nutritional replacement, ultimately combined with oncology intervention leading to increased survival, in this patient population. Clinical relevance of this information will be to provide in the future by cut-off percentiles of bioelelctrical phase angle which might be predictable in functionality, quality of life, and mortality in patients. However, this requires a larger group of patients.

Evaluating resistance, reactance and PA among pre-surgical BC patients can provide a quick, simple and reproducibly means to determine nutritional status. This quick assessment in nutritional status of the patient can allow for early corrective intervention.

CONCLUSION

Pre-surgical patients diagnosed with BC have altered tissue electrical properties. Reactance and resistance at 50 kHz was found to be significantly greater in patients with BC than in the control group. Phase angle (PA) measured during the study, at 50 kHz was found to be not statistically significant. Further observations of a larger patient group would be valuable to calculate survival, validate the prognostic significance of PA, and monitor nutritional and therapeutic interventions in this patient population.

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 zlosliwe w Polsce w 2006 roku. Centrum Onkologii- Instytut, Warszawa, 2008 (in Polish).
3. Sarhill N, Mahmoud FA, Christie R, Tahir A. Assessment of nutritional status and fluid deficits in advanced cancer. Am J Hosp Palliat Care 2003; 20: 465–473.
4. Desport JC, Preux PM, Bouteloup-Demange C, Clavelou P, Beaufrère B, Bonnet C, Couratier PP. Validation of bioelectrical impedance analysis in patients with amyotrophic lateral sclerosis. Am J Clin Nutr. 2003; 77: 1179–1185.
5. Pencharz PB, Azcue M. Use of bioelectrical impedance analysis measurements in the clinical management of malnutrition. Am J Clin Nutr. 1996; 64: 485S-488S.
6. Simons JP, Schols AM, Westerterp KR, ten Velde GP, 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.
7. Zarowitz BJ, Pilla AM. Bioelectrical impedance in clinical practice. DICP, Ann Pharmacother. 1989; 23: 548–555.
8. 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.
9. Baumgartner RN, Chumlea WC, Roche AF. Bioelectric impedance phase angle and body composition. Am J Clin Nutr. 1988; 48: 16–23.
10. 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.
11. 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. 2005; 9: 20–25.
12. Schwenk A, Ward LC, Elia M, Scott GM. Bioelectrical impedance analysis predicts outcome in patients with suspected bacteremia. Infection. 1998; 26: 277–282.

13. 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.
14. Gupta D, Lammersfeld CA, Burrows JL, Dahlk SL, Vashi PG, Grutsch JF, Hoffman S, Lis CG. Bioelectrical impedance phase angle in clinical practice: implications for prognosis in advanced colorectal cancer. Am J Clin Nutr. 2004; 80: 1634–1638.
15. 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.
16. 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.
17. 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.
18. 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.
19. 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.
20. 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.