Whole-body *versus* Segmental Bioelectrical Impedance Analysis in Patients with Edema of the Upper Limb After Breast Cancer Treatment

SEBASTIAN BERLIT[1], JOACHIM BRADE[2], BENJAMIN TUSCHY[1], ETELKA FÖLDI[4], ULRIKE WALZ-ESCHENLOHR[4], HANS LEWELING[3] and MARC SÜTTERLIN[1]

[1]Department of Obstetrics and Gynaecology and [3]Fourth Department of Medicine University Medical Centre Mannheim, Heidelberg University, Mannheim, Germany;
[2]Department of Medical Statistics and Biomathematics, Medical Faculty Mannheim, Heidelberg University, Mannheim, Germany;
[4]Földiklinik, Hinterzarten, Germany

Abstract. *Aim: The purpose of this study was to compare whole-body (50 kHz alternating current) and segmental (5 kHz alternating current) bioelectrical impedance analysis (BIA) in the assessment of manifested edema of the upper limbs. Patients and Methods: Whole-body and segmental BIA were performed in 30 patients with edema of the upper limb following breast cancer treatment. Results: Pearson correlation coefficient comparing both measurements was 0.8891 (p-value <0.0001) with corresponding least squares (r^2) of 0.7904. Conclusion: Whole-body BIA seems to be a suitable method in the assessment of manifested edema of the upper limbs.*

As breast cancer mortality rates in the Western world have significantly declined throughout recent years due to advances in diagnostic and therapeutic approaches, the necessity for adequate management of treatment side-effects, which may have a severe impact on quality of life, is evident. Breast cancer-related lymphedema is an important sequelae whose early detection seems to have a beneficial impact on treatment outcomes, and may prevent progression (1, 2). In this context, bioelectrical impedance analysis (BIA) has increasingly been investigated and was proven to be capable of detecting subclinical edema of the upper limbs (3, 4). BIA is a highly standardized technique, which is fast, non-invasive and therefore well-tolerated by patients. BIA instruments, especially single-frequency devices, are affordable tools and have been proven to be eminently suitable for non-laboratory settings (5). The physical properties of BIA, its measurement variables (resistance, reactance, phase angle) and their significance have been described in many investigations (5-7). Traditionally, resistance (opposition to the electrical current from fluids of the body) is used to analyze edema. The most frequently used BIA is probably whole-body BIA (WBIA), applying a 50-kHz alternating current (AC) as an affordable and easy-to-use method (8). By using an AC of 50 kHz cell membranes are penetrated by the current, leading to a measurement not only of extracellular (ECW) but also of intracellular water (9). Consequently, most investigations evaluating edema of the upper limb *via* BIA use single- or multi-frequency segmental BIA (SBIA) of the upper limbs only in order to calculate resistance at low frequency (0 to 30 kHz), hence ECW. The question is if these relatively new measurement procedures, implying the acquisition of new and more expensive measurement devices with the necessity for additional technical know-how, are so much more accurate compared to WBIA. An advantage of WBIA is the fact that placement of electrodes on the feet and arms is easy to perform, especially in obese patients, and is a more established measurement technique in clinical routine compared to newer BIA methods. In addition, in SBIA, electrodes can be applied to the hands only (instead of the left and right acromion of the humerus) *via* extrapolation, but interpretation of BIA values is demanding, especially when using multi-frequency devices. Foster *et al.* showed that the largest contributors to whole-body resistance are the forearm (28%) and the lower leg (33%), which contribute only 1-2% of the fat-free mass and 1.5-3% of body weight compared with the trunk, which contributes 9% of total resistance and >50% of fat-free mass and body weight (10). Reviewing the literature, there is no disagreement that the

Correspondence to: Sebastian Berlit, MD, Department of Obstetrics and Gynaecology, University Medical Centre Mannheim, Heidelberg University, Theodor-Kutzer-Ufer 1-3, 68167 Mannheim, Germany. Tel: +49 6213832286, Fax: +49 6213835074, e-mail: sebastian.berlit@umm.de

Key Words: Segmental bioelectrical impedance analysis, whole-body bioelectrical impedance analysis, edema of the upper limb, breast cancer.

0250-7005/2013 $2.00+.40

Table I. *Demographic parameters of patients (n=30).*

Variable	Mean	SD	Minimum	Median	Maximum
Age (years)	59.83	12.89	30.00	59.00	84.00
Height (m)	1.64	0.07	1.52	1.63	1.80
Weight (kg)	80.11	19.77	55.60	74.95	139.90
BMI (kg/m^2)	29.99	7.57	19.56	28.42	53.97

SD, Standard deviation; BMI, body-mass index.

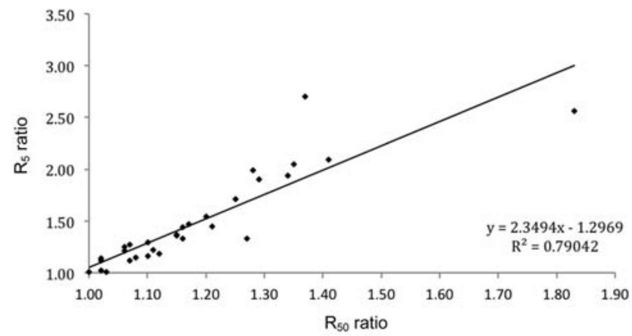

Figure 1. *Regression line of R_5 ratios versus R_{50} ratios according to Pearson's correlation.*

limbs account for most of the whole-body impedance but only a minor fraction of the body volume (10). This raises the question whether in cases of edema of the upper limb, changes in ECW of one arm, as a body compartment constituting approximately one third of whole-body resistance, can be analyzed as accurate *via* WBIA as is performed by SBIA. In a previous study, we showed that WBIA is capable of excluding a developing edema of the upper limb after breast cancer therapy (11). This led to this prospective investigation with the objective of comparing WBIA with SBIA (5 kHz AC) in the assessment of manifest edema of the upper limb.

Patients and Methods

A total of 30 female patients with breast cancer were examined after study approval by the Ethics Committee II of the Mannheim Medical Center, Heidelberg University (2011-341N-MA). Written informed consent was obtained of patients upon recruitment. A standardized questionnaire was used for patients' characteristics taking the following items into account: age, body mass index (BMI), handedness and affected arm. WBIA and SBIA were performed on all patients in one session. A multi-frequency BIA device (Biacorpus RX SPECTRAL; Medical HealthCare GmbH, Karlsruhe, Germany) was used in this study. This instrument is a fully digital, phase sensitive, 4-channel impedance measuring device. Each channel can apply a 5 to 100 kHz AC to measure resistance. WBIA (50 kHz AC) was performed first. Eight electrodes were attached to the participant's hands and feet. The patient was placed supine, limbs slightly abducted and palms pronated flat on the investigator's cot covered with a non-conducting surface. After cleaning the skin areas where the electrodes were to be attached with alcohol swabs, the measurement electrodes were placed on the dorsal surface of the wrist and ankle at the level of the process of the radial and ulnar or fibular and tibial bones. Signal electrodes were attached to the dorsal surface of the third metacarpal bone of hands and feet, so that at least a 5 cm distance was kept between signal and measurement electrodes (12). In this way the resistance of body halves was measured: Right half of body, right arm - right foot: RARF; Left half of body, left arm - left foot: LALF. SBIA was conducted using a 5 kHz AC: The electrodes on the feet were removed and attached to the acromion of the right and left humerus (according to the standard electrode sites for segmental measurement of the arms) (13). The resulting measurements for WBIA and SBIA were automatically transferred to a computer, where they were duly interpreted by the software. The manufacturer's software (BodyComp V 8.3; Medical HealthCare GmbH) was used. The WBIA ratios of resistance values of the affected and unaffected body halves, taking the side of dominance into account, were calculated as:

$$\frac{R_{50}\text{ unaffected body half}}{R_{50}\text{ affected body half}}$$

Concerning SBIA the ratio was modified:

$$\frac{R_{5}\text{ unaffected arm}}{R_{5}\text{ affected arm}}$$

The obtained ratio values then underwent statistical analysis in order to compare both diagnostic approaches. All data were recorded in an Excel datasheet. After careful check for faulty entries and extreme values, the data were transferred into the SAS® environment (Statistical Analysis System, Release 9.2; Cary, NC, USA) for subsequent statistical analysis. Quantitative data are presented as the arithmetic mean and standard deviation (SD) and the median and range; qualitative data as frequencies. Demographic statistics as well as paired *t*-test, Pearson correlation and linear regression analysis were performed as appropriate. A p-value <0.005 was considered significant.

Results

Demographic parameters are given in Table I. Four (13.3%) women were left-handed and edema was localized in the left arm in 13 (43.3%) cases. Raw data of SBIA and WBIA with corresponding ratios are given in Table II; descriptive statistics are provided in Table III.

The mean difference (±SD) between both methods was 0.29±0.31; 95% confidence interval=0.18 to 0.41. Pearson correlation gave the following equation:

$$\frac{R_{5}\text{ unaffected arm}}{R_{5}\text{ affected arm}} = -1.30+2.35 \times \frac{R_{50}\text{ unaffected body half}}{R_{50}\text{ affected body half}}$$

Table II. *Handedness, localisation of edema and raw data of segmental and whle-body bioelectrical impedance analysis (BIA) with corresponding ratios (n=30).*

Handedness	Affected arm	Whole-body BIA			Segmental BIA		
		R_{50} RARF	R_{50} LALF	R_{50} unaffected body half / R_{50} affected body half	R_5 RA	R_5 LA	R_5 unaffected arm / R_5 affected arm
Left	Right	342	468	1.37	91	246	2,70
Right	Left	486	364	1.34	302	156	1.94
Right	Left	629	502	1.25	333	195	1.71
Right	Right	448	576	1.29	191	362	1.90
Right	Left	448	245	1.83	335	131	2.56
Left	Left	478	451	1.06	275	220	1.25
Right	Right	291	409	1.41	114	238	2.09
Right	Left	494	462	1.07	291	229	1.27
Right	Right	494	566	1.15	206	282	1.37
Right	Left	425	351	1.21	271	187	1.45
Right	Right	546	578	1.06	257	312	1.21
Right	Right	512	592	1.16	236	313	1.33
Right	Right	472	483	1.02	245	275	1.12
Left	Left	560	509	1.10	253	219	1.16
Right	Right	467	519	1.11	207	253	1.22
Right	Right	401	513	1.28	126	251	1.99
Left	Right	440	506	1.15	208	283	1.36
Right	Left	444	398	1.12	243	206	1.18
Right	Left	538	522	1.03	275	272	1.01
Right	Right	426	459	1.08	233	268	1.15
Right	Right	500	635	1.27	260	347	1.33
Right	Right	604	725	1.20	241	371	1.54
Right	Right	458	535	1.17	184	271	1.47
Right	Right	514	514	1.00	279	283	1.01
Right	Right	394	531	1.35	127	260	2.05
Right	Right	549	562	1.02	304	297	1.02
Right	Left	690	627	1.10	409	318	1.29
Right	Left	530	455	1.16	260	181	1.44
Right	Left	421	413	1.02	199	174	1.14
Right	Left	514	481	1.07	271	243	1.12

R_5, Resistance at 5Khz; R_{50}, resistance at 50kHz, RARF, whole-body measurement from right arm to right foot; LALF, whole-body measurement from left arm to left foot; RA, Segmental measurement of right arm; LA,Segmental measurement of left arm.

Table III. *Descriptive statistics of resistance for whole-body and segmental bioelectrical impedance analysis (n=30).*

Measurement	Mean	SD	Minimum	Median	Maximum	Lower 95% CI for Mean	Upper 95% CI for Mean
R 5 kHz	1.4793	0.4446	1.0100	1.3300	2.7000	1.3133	1.6454
R 50 kHz	1.1817	0.1683	1.0000	1.1500	1.8300	1.1188	1.2445

SD, Standard deviation; CI, confidence interval; R 5kHz, resistance for segmental measurement with 5Khz; R 50kHz, resistance for whole-body measurement with 50kHz.

Both intercept (*p*-value <0.0001) and slope (*p*-value <0.0001) were highly significant. Pearson correlation coefficient of R5 and R50 ratios was 0.8891 (*p*-value <0.0001) with corresponding least squares (r^2) of 0.7904. Figure 1 shows the scatter plot with the regression line.

Discussion

BIA has been increasingly investigated and has been proven to provide accurate relative measurements of lymphedema, as well as functional parameters concerning the emergence of edema of the upper limb (14). For this reason we designed this prospective investigation without a control collective of women without edema of the upper limb. In a cross-sectional investigation, Cornish *et al*. proposed for determination of lymphedema a cut-off ratio using SBIA 1.139 for an affected dominant arm and 1.066 for an affected non-dominant arm (3). Except for four women in our collective, the SBIA R_5 ratios exceeded these established cut-off values. All investigated patients in our study had a clinically manifested edema of the upper limb, verified by circumferential limb measurements. We, therefore, believe that due to the fact that lymphatic drainage and usage of compression garments was performed in all patients, fluctuating lymphedema probably resembled the normal lymph fluid status of the arms. At this point of time, cut-off values for WBIA in the assessment of edema of the upper limb do not exist. In a previous investigation, we showed that WBIA is able to exclude a developing edema of the upper limb (11). To our knowledge, other investigations concerning this sequelae have always used segmental single- or multi-frequency BIA. York *et al*. compared segmental multifrequency BIA to segmental single-frequency BIA in patients with unilateral edema of the upper limb (15). The correlation of impedance ratios (unaffected *vs*. affected limb) comparing different frequencies were calculated. The authors showed that measurements for detection of upper limb lymphedema obtained by segmental single frequency BIA using frequencies in the lower range (less than 30 kHz) and segmental multifrequency BIA at 0 kHz are essentially interchangeable (correlation coefficient =0.987). As expected, comparing measurements of our investigation, WBIA and SBIA are not interchangeable. However, with a correlation coefficient of 0.8891, we have shown that WBIA seems to be a suitable method in the assessment of manifested edema of the upper limb. Further prospective investigations concerning edema appraisal following breast cancer treatment by WBIA, especially with regard to emerging edemas, are needed. In this way, WBIA, as an established and widespread method, could eventually be used as a screening tool for lymphedema after breast cancer treatment without acquisition of new, complex measurement devices.

Conclusion

WBIA seems to be a suitable method in the assessment of manifest edema of the upper limbs.

References

1 Stout Gergich NL, Pfalzer LA, McGarvey C, Springer B, Gerber LH and Soballe P: Preoperative assessment enables the early diagnosis and successful treatment of lymphedema. Cancer *112(12)*: 2809-2819, 2008.

2 Szuba A and Rockson SG: Lymphedema: Classification, diagnosis and therapy. Vasc Med *3(2)*: 145-156, 1998.

3 Cornish BH, Chapman M, Hirst C, Mirolo B, Bunce IH, Ward LC and Thomas BJ: Early diagnosis of lymphedema using multiple frequency bioimpedance. Lymphology *34(1)*: 2-11, 2001.

4 Ward LC, Dylke E, Czerniec S, Isenring E and Kilbreath SL: Confirmation of the reference impedance ratios used for assessment of breast cancer-related lymphedema by bioelectrical impedance spectroscopy. Lymphat Res Biol *9(1)*: 47-51, 2011.

5 Ridner SH, Dietrich MS, Deng J, Bonner CM and Kidd N: Bioelectrical impedance for detecting upper limb lymphedema in nonlaboratory settings. Lymphat Res Biol *7(1)*: 11-15, 2009.

6 Lukaski HC, Johnson PE, Bolonchuk WW and Lykken GI: Assessment of fat-free mass using bioelectrical impedance measurements of the human body. Am J Clin Nutr *41(4)*: 810-817, 1985.

7 Baumgartner RN, Chumlea WC and Roche AF: Bioelectric impedance phase angle and body composition. Am J Clin Nutr *48(1)*: 16-23, 1988.

8 Kyle UG, Bosaeus I, De Lorenzo AD, Deurenberg P, Elia M, Manuel Gomez J, Lilienthal Heitmann B, Kent-Smith L, Melchior JC, Pirlich M, Scharfetter H, Schols AM and Pichard C: Bioelectrical impedance analysis-part II: Utilization in clinical practice. Clin Nutr *23(6)*: 1430-1453, 2004.

9 Thomasset A: Bio-electric properties of tissues. Estimation by measurement of impedance of extracellular ionic strength and intracellular ionic strength in the clinic. Lyon Med *209*: 1325-1350, 1963 (article in French).

10 Foster KR and Lukaski HC: Whole-body impedance-What does it measure? Am J Clin Nutr *64(3 Suppl)*: 388S-3896, 1996.

11 Berlit S, Brade J, Tuschy B, Hornemann A, Leweling H, Eghardt V and Sütterlin M: Comparing bioelectrical impedance values in assessing early upper limb lymphedema after breast cancer surgery. In Vivo *26(5)*: 863-867, 2012.

12 Cornish B: Bioimpedance analysis: Scientific background. Lymphat Res Biol *4(1)*: 47-50, 2006.

13 Cornish BH, Jacobs A, Thomas BJ and Ward LC: Optimizing electrode sites for segmental bioimpedance measurements. Physiol Measure *20(3)*: 241-250, 1999.

14 Cornish JL and van den Buuse M: Regional expression of c-Fos in rat brain following stimulation of the ventral tegmental area. Neurosci Lett *220(1)*: 17-20, 1996.

15 York SL, Ward LC, Czerniec S, Lee MJ, Refshauge KM and Kilbreath SL: Single frequency *versus* bioimpedance spectroscopy for the assessment of lymphedema. Breast Cancer Res Treat *117(1)*: 177-182, 2008.

Received May 19, 2013
Revised June 16, 2013
Accepted June 18, 2013