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

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**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 (r²) 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, 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 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
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. WBIA 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:

\[
R_5 \text{ unaffected arm} = -1.30 + 2.35 \times R_5 \text{ affected arm}
\]

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

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
<th>SD</th>
<th>Minimum</th>
<th>Median</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>59.83</td>
<td>12.89</td>
<td>30.00</td>
<td>59.00</td>
<td>84.00</td>
</tr>
<tr>
<td>Height (m)</td>
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<td>0.07</td>
<td>1.52</td>
<td>1.63</td>
<td>1.80</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>80.11</td>
<td>19.77</td>
<td>55.60</td>
<td>74.95</td>
<td>139.90</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29.99</td>
<td>7.57</td>
<td>19.56</td>
<td>28.42</td>
<td>53.97</td>
</tr>
</tbody>
</table>

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

Figure 1. Regression line of \(R_5\) ratios versus \(R_{50}\) ratios according to Pearson’s correlation.
Both intercept \((p\text{-value} < 0.0001)\) and slope \((p\text{-value} < 0.0001)\) were highly significant. Pearson correlation coefficient of \(R_5\) and \(R_{50}\) ratios was 0.8891 \((p\text{-value} < 0.0001)\) 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 sequela 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 \( \text{vs.} \) 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 manifest 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**