Estimation of limb adiposity by bioimpedance spectroscopy in lymphoedema

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Abstract. Lymphoedema is a chronic debilitating condition that may occur in approximately 25% of women treated for breast cancer. As the condition progresses, accumulated lymph fluid becomes fibrotic with infiltration of adipose tissue. Bioelectrical impedance spectroscopy is the preferred method for early detection of lymphoedema based on the measurement of impedance of extracellular fluid. The present study assessed whether these impedance measurements could also be used to estimate the adipose tissue content of the arm based on a model previously used to predict whole body composition. Estimates of arm adipose tissue in a cohort of women with lymphoedema were found to be highly correlated (r > 0.82) with measurements of adipose tissue obtained using the reference method of dual energy X-ray absorptiometry. Paired t-tests confirmed that there was no significant difference between the adipose tissue volumes obtained by the two methods. These results support the view that the method shows promise for the estimation of arm adiposity in lymphoedema.

1. Introduction

Lymphoedema is a chronic debilitating condition occurring in approximately 25% of women post treatment for breast cancer. It results from inadequate functioning of the lymphatic system that leads to accumulation of lymph fluid, an extracellular fluid (ECF) [1]. As the condition worsens, cellular infiltration of the fluid occurs (“stagnation”) including development of fibrosis and accumulation of lipid material which may also present as a specific condition known as lipedema [2]. In addition, obesity is a common co-morbidity with lymphoedema. Over the past two decades, bioimpedance spectroscopy (BIS) has found an important clinical role in the early detection of lymphoedema due to its ability to quantify ECF as a change in impedance measured at a low, ideally zero, frequency [3].

The aim of this study was to assess whether the bioimpedance protocol used for assessment of unilateral breast cancer-related lymphoedema could be adapted to estimate concurrently arm adiposity.

2. Experimental

2.1 Participants. Studies were performed in 21 women, 16 of whom had clinically ascribed unilateral lymphoedema (LE) and 5 who had undergone axillary node surgery for cancer but had no diagnosis of lymphoedema (non-LE), and 5 male healthy control participants. Participants were all enrolled in...
larger research programs approved by the University of Sydney or the University of Queensland Medical Human Research Ethics Committees.

2.2 Protocol. Bioimpedance measurements were performed on both arms along four consecutive 10-cm segments commencing at the ulnar styloid using an SFB7 (ImpediMed, Brisbane) bioimpedance spectrometer. Current drive electrodes (Ag-AgCl, ImpediMed) were located on the hand at the 3rd metacarpal phalange joint and on the foot between the 2nd and 3rd metatarsal phalange joints. Voltage sense electrodes were at 10-cm intervals along the dorsal surface of the arm commencing in-line with the ulna styloid. Impedance was measured, in triplicate, at 256 discrete current frequencies in the range 4-1000 kHz. The impedance of the whole arm, wrist to shoulder, was also determined according to the principle of equipotentials. Impedance data were analysed according the Cole model using Bioimp version 4.8.0.0 (ImpediMed Ltd) and the resistance at 10 kHz extracted. Arm circumference was measured at each electrode location to 0.1 cm resolution using a flexible tape. The height of each participant was recorded (to 0.1 mm) using a wall-mounted stadiometer.

Each participant at the time of the impedance measurements underwent a whole-body dual-energy X-ray absorptiometry (DXA) scan. Nine subjects were scanned using an Hologic Explorer instrument; the remainder using a Norland XR36 scanner. The tissue composition (fat mass (FM), bone mineral content (BMC) and lean mass (LM)) of the whole arm and each 10 cm segment was determined for each arm. DXA provides tissue masses; these were converted to volumes using the density factors of Brorson et al. [2].

2.3 Calculation of tissue adipose content from impedance measurements. The method is based on that described by Biggs et al. [4]. Briefly, the model assumes that both skeletal muscle (lean tissue) and fat are conductive while other tissues are non-conductive and that the total resistance of a body segment is the sum of fat and lean resistances according to Kirchoff’s law.

\[
\frac{1}{R_{\text{total}}} = \frac{1}{R_{\text{fat}}} + \frac{1}{R_{\text{lean}}} \tag{1}
\]

Equation (1) can be re-written taking into account the relationship between resistance, segment volume (length, L, x cross-sectional area, A) and resistivity, \(\rho\), as

\[
\frac{1}{R_{\text{total}}} = \frac{A_{\text{fat}}}{L \cdot \rho_{\text{fat}}} + \frac{A_{\text{lean}}}{L \cdot \rho_{\text{lean}}} \tag{2}
\]

Since total segmental cross-sectional area equals the sum of the conductive and non-conductive tissue areas and substituting and rearranging equation 2 gives

\[
\frac{1}{R_{\text{total}}} = \frac{A_{\text{conductive}} \cdot \rho_{\text{fat}} - A_{\text{fat}} \cdot \rho_{\text{fat}} + A_{\text{fat}} \cdot \rho_{\text{lean}}}{\rho_{\text{lean}} \cdot \rho_{\text{fat}} \cdot L} \tag{3}
\]

Further rearrangement provides a quotient (Q) which relates the segmental fat to the sum of fat plus lean which can be calculated from

\[
Q = \frac{\rho_{\text{lean}} \cdot \rho_{\text{fat}} \cdot L}{A_{\text{conductive}} \cdot R_{\text{total}} \cdot (\rho_{\text{lean}} \cdot \rho_{\text{fat}})} - \frac{\rho_{\text{fat}}}{\rho_{\text{lean}} \cdot \rho_{\text{fat}}} \tag{4}
\]

Segmental volumes and cross-sectional areas were calculated from the circumferential measurements for each 10 cm segment assuming that the segments can be represented as truncated cones. For the whole arm, the wrist to shoulder length, L, was calculated, based on published anthropometric data, as 0.33 x the participant’s height with a circumference equivalent to that of mean
segmental circumferences. The cross-sectional of the conductive tissue was calculated as the difference between total cross-sectional area and non-conductive area derived from measurements of bone area by pQCT [5]; resistivity values were those quoted by Biggs et al. [4], i.e. 5000 Ohm.cm for adipose tissue and 120 Ohm.cm for lean tissue. Thus the volume of adipose tissue was calculated from the total segment volume and the adiposity quotient, Q, derived using equation 4.

2.4 Data analysis. Segmental adipose tissue volumes computed from impedance measurements were compared to those measured by DXA by concordance correlation analysis and the significance of differences using a paired t-test.

3. Results
The mean bioimpedance inter-arm ratio for the participants with lymphoedema was 1.20, exceeding the established threshold values confirming the presence of lymphoedema in these participants. The mean overall volume, measured by DXA, of the affected arm was 17.5 ± 16.8% larger than that of the unaffected arm for these participants with similar increases in both adipose (18.7 ± 21.2%) and lean (17.7 ± 21.4%) tissues; comparable data (dominant:non-dominant arm) for the 5 female control participants were impedance ratio, 1.02, volume excess, 10.9 ± 8.5%; adipose tissue excess, 14.7 ± 12.2% and 3.7 ± 12.6% increase in lean respectively. The comparable values for the 5 control male participants were an impedance ratio of 1.03 and a volume excess of 5.2 ± 9.4%. Excess adipose volume was 22.2 ± 10.9% and excess lean volume 0.5 ± 10.9%.

Pooled data for adipose volume of all segments estimated from impedance was strongly correlated with the DXA measurements, \( r_c = 0.82 \) (\( P < 0.001 \)), Fig 1.

![Figure 1](image)

**Figure 1.** Correlation of segmental adipose tissue volume estimated by impedance with that measured by DXA. Legend: ---, the line of identity; ▼, unaffected or non-dominant arm for controls; ○, affected or dominant arm.

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For the lymphoedema participants only, segmental adiposity estimated from impedance was equally strongly correlated \((P < 0.001)\) with the DXA measurements for both the affected arm and the contralateral control arm, \(r = 0.82\) and \(r = 0.86\) respectively. Poorer correlations were found for whole arm measurements; \(r = 0.67\) and \(r = 0.75\) respectively.

There was no significant difference in segmental adipose tissue volume estimated by impedance compared with that measured by DXA, \(303 \pm 160\) and \(291 \pm 177\) ml respectively. Mean of all segmental adipose volumes were larger for the affected limbs of the lymphoedema participants only, again with no significant difference between the impedance and DXA measurements, \(345 \pm 175\) and \(341 \pm 178\) ml respectively. Similarly the mean adipose volume of the whole arm estimated by impedance was not significantly different to that measured by DXA, \(1545 \pm 465\) and \(1636 \pm 742\) ml respectively.

4. Discussion
This study demonstrates the feasibility of estimating arm adipose tissue content from impedance measurements simultaneously with measurement of the excess fluid accumulation characteristic of the presence of lymphoedema. The presence of excess body fat or frank obesity is a common co-morbidity in women with lymphoedema.

Although, the protocol for impedance measurements is the same as that currently used for measurement of lymph accumulation, in order to estimate adipose volume additional anthropometric measurements are required. The cross-sectional areas of the non-conductive and conductive tissues of the arm need to be determined from arm length and circumference measurements. Since the arm is not a simple cylinder, the arm was divided into 10-cm segments approximating truncated cones and the adiposity of these discrete segments estimated. These were found to be not significantly different to those measured using the reference technique of DXA. Although this procedure of segmenting the arms is in common clinical use for calculation of arm volume in lymphoedema assessment, it adds substantially to the number of measurements required and the time taken may be inconvenient to the patient and clinician. Therefore, the possibility that total arm adiposity could be similarly estimated from whole arm measurements only was investigated. Again the results were encouraging in that no significant differences in adiposity values were observed. The precision of limb impedance measurements is well established [3]; further work is required to determine if better anthropometric measurements could improve further accuracy of the method.

In conclusion, the method has the potential to extend the application of impedance assessment of lymphoedema from measuring fluid accumulation to simultaneous measurement of adipose tissue volume; clinical utility, however, remains to be established in larger scale clinical trials.

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