Bioimpedance for the spot measurement of tissue density

To cite this article: E S Dylke et al 2013 J. Phys.: Conf. Ser. 434 012054

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Bioimpedance for the spot measurement of tissue density

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Abstract. Long-standing lymphoedema is characterised by tissues changes which are currently not detectable using bioimpedance spectroscopy. It has been suggested that a combination of bipolar and tetrapolar measurements may be used to detect these tissues changes for a single site in the transverse direction. This technique was trialled in a group of control participants with no history of lymphoedema or recent upper limb trauma. Repeated spot measurements were done without removal of electrodes to determine biological variability as well as with removal of electrodes to determine technical reproducibility. The inter-limb spot ratio of the controls was then compared to that of a number of women previously diagnosed with secondary lymphoedema in the forearm. Biological variability was not found to greatly influence repeated measures but only moderate technical reliability was found despite excellent co-efficient of variation for the majority of the measurements. A difference was seen between those with more severe swelling and the controls. This novel technique shows promise in detecting tissue changes associated with long-standing lymphoedema.

1. Introduction

Secondary lymphoedema can occur after a disruption to or obstruction of the lymphatic system [1]. Early stages of the condition are characterised by increases in extra-cellular fluid leading to soft pitting swelling of the limb. Bioimpedance analysis (BIA) has been shown to be more sensitive to changes in these stages allowing treatment to be started earlier than traditional circumference or volume measures [2]. Long standing lymphoedema though, is associated with tissue composition changes where the fluid has been predominantly replaced by a fatty, fibrotic tissue [3]. Conventional tetrapolar BIA measurements are not useful in diagnosis or monitoring at this time [4]. It has been suggested that a combination of bipolar and tetrapolar bioimpedance measurements could be used to overcome this deficiency allowing changes in the tissue to be detected at a single site in the transverse direction (spot measurements) rather than impedance longitudinally along a limb [5].

In order to detect possible tissue changes, a series of six bipolar and tetrapolar bioimpedance measurements could be performed at each location of interest bilaterally [5]. When bipolar impedance is measured using skin electrodes, the measured impedance is that of the body tissues both parallel and perpendicular (transverse) to the longitudinal axis (direction of current flow). In contrast, a tetrapolar electrode arrangement measures the longitudinal component only. The transverse impedance at a single site can then be calculated from the combination of these measurements by simple vector algebra. The ratio of the spot measure resistance of the dominant or affected arm to the non-dominant or unaffected arm is then determined.
The aim of this study was to determine the reliability of this method of spot bioimpedance measurements and to compare measurements in control participants with those from women with secondary lymphoedema.

2. Methods

2.1 Participants: Fifteen healthy females without a history of upper limb lymphoedema or recent upper limb trauma were recruited from the staff and student bodies at the University of Sydney. Five women with upper limb lymphoedema secondary to treatment for cancer were recruited as part of a larger study. Participant details are provided in table 1. Ethical approval was obtained from the University of Sydney’s Medical Human Research Ethics Committees and all participants provided written informed consent.

<table>
<thead>
<tr>
<th>Table 1: Participant characteristics</th>
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<tbody>
<tr>
<td>Control group (n=15)</td>
</tr>
<tr>
<td>-----------------------</td>
</tr>
<tr>
<td>Age (y)*</td>
</tr>
<tr>
<td>Height*</td>
</tr>
<tr>
<td>Weight*</td>
</tr>
<tr>
<td>BMI*</td>
</tr>
<tr>
<td>Dominance (R:L)</td>
</tr>
<tr>
<td>Affected side (R:L)</td>
</tr>
<tr>
<td>Inter-arm circumference difference (cm) ^</td>
</tr>
</tbody>
</table>

*mean (SD), ^ range

2.2 Protocol: Three studies were undertaken to examine the utility of the measurement technique. For all studies, participants were positioned in supine and the skin on their hands, forearms and feet was thoroughly cleaned with an alcohol wipe. Bilaterally, a point 15 cm proximal from the ulnar styloid was then marked on the dorsal forearm. An electrode was placed at this location as well as on standard BIA assessment locations: the 3rd metacarpal phalange joint; in line with the ulnar styloid; between the maleoli on the front of the leg and between the 2nd and 3rd metatarsal phalange joints. Care was taken to ensure good adherence between the electrode and the skin. Measurements were completed using a BIM4 single frequency (50 kHz) impedance meter (SEAC-ImpediMed, Brisbane).

Study one examined the magnitude of subject variability. The series of six bipolar and tetrapolar measurements, as described previously [6], were completed bilaterally, three times in immediate succession without removal of the electrodes followed by a fourth measurement after a period of 15 minutes of rest in five controls. Study two examined the technical reliability of the measurement. The spot measurement technique was again completed three times in succession but all electrodes were removed and replacement before each measurement in a larger control sample which included all subjects from study one (n = 15). Finally, study three compared the data from the controls to those of women with secondary lymphoedema secondary (n = 5). For all of lymphedema participants, the location at 15 cm proximal to the ulnar styloid represented their area of self-reported worst swelling.
For each step of the series of bipolar and tetrapolar bioimpedance measurements, the resistance (R), impedance (Z) and reactance (Xc) was recorded and entered into a spreadsheet which, using Pythagoras’ theory, calculated the R, Z and Xc for the specific location tested (in this case, 15 cm proximal from the ulnar styloid). The inter-limb spot ratio of this point was determined by dividing the resistance on the dominant side by that found for the non-dominant side. For the lymphoedema group, the affected side was compared to the unaffected side.

2.3 Data Analysis: Cronbach’s alpha, a coefficient of reliability,[7] was determined for study one and two to establish the reliability of the inter-limb spot ratios found at each measurement time point. For study 2, the coefficient of variation (CV) for R, Z and Xc for each participant was examined. Finally, a comparison between the control ratios found in study two and that of the lymphoedema group were done using non-parametric independent test as the ratios were not normally distributed.

3. Results

The participants exhibited little biological variability (Cronbach’s alpha = 0.816) between the measurements when the electrodes were not removed. While the technical reliability of the method was only moderate (Cronbach’s alpha = 0.668), the co-efficient of variation for each of the measure was mostly excellent with less than 5% variability for found in 93% of the individual measurements, implying that the reduction in technical reliability may have been caused by errors with individual measurements and not by the technique itself.

The control group was significantly younger and lighter than the lymphoedema group (both \( p < 0.01 \)). All participants had been diagnosed with lymphedema at least 8 months previously (range 8 to 96 months). Three women with secondary lymphoedema had more severe inter-limb differences (>3 cm) at the location of measurement and their inter-limb spot ratio did not overlap with the control group while those with less severe inter-limb differences did (Figure 1). However there was a significant different between the lymphedema group and the controls (Mann Whitney U test \( p < 0.001 \)).

![Figure 1: Inter-limb spot ratio of the controls compared to 5 women previously diagnosed with lymphoedema](image-url)
4. Discussion

This novel technique was found to have acceptable reliability when the electrodes were not removed between measurements. Although the reliability decreased with removal and replacement of the electrodes between measurements, the vast majority of these measurements still exhibited minimal variability. Clinically, therefore, the emphasis when using this technique in its present form, requires stringent attention to the placement and adherence of the electrodes as lack of complete electrode contact in bipolar measurements, such as slight lifting of a corner of an electrode, will affect the measured impedance between the skin and the electrode. This alters the overall measurement increasing error and decreasing the technical reliability, which could be clinically relevant. Furthermore, its present form, the technique is time consuming as a series of six measurements on each arm are necessary before the overall spot impedance can be calculated. Nonetheless, the difference found between those with and without long standing lymphoedema is encouraging and suggests the method’s ability to detect changes in tissue composition.

Further research comparing the method with techniques such as ultrasound or MRI that can directly assess tissue composition are required to confirm these observations. Further determination of its sensitivity in detecting early changes in tissue composition, particularly in women with mild lymphoedema, could assist with treatment decisions. Currently most treatment techniques attempt to mobilise the stagnant fluid in a limb with lymphoedema. If tissue changes have occurred, these techniques are no longer appropriate. Spot measurement of tissue composition could, therefore, play an important role in improving treatments efficacy.

In conclusion, spot BIA shows promise in detecting the tissue changes that occur with long-standing lymphoedema. Further research is necessary to confirm its utility and benefit in treatment decisions.

References