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COMBINED OPTO-ELECTRONIC PEROMETRY AND BIOIMPEDANCE TO MEASURE OBJECTIVELY THE EFFECTIVENESS OF A NEW TREATMENT INTERVENTION FOR CHRONIC SECONDARY LEG LYMPHEDEMA

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ABSTRACT

Secondary lymphedema of the legs is a common sequela of patients treated for cancer of the reproductive, gastrointestinal, urinary systems and melanoma. From a clinical and research perspective it is of utmost importance to use techniques that objectively quantify leg volume and fluid composition as an indicator of lymphedema severity and response to treatment. Two techniques often used in both the clinical and research setting are leg perometry and multi-frequency bioimpedance. Although both techniques have been extensively validated, this trial aimed to cross correlate both measurement techniques to ascertain whether each or both could be used reliably for measurement of leg lymphedema. These measurements were utilized throughout a clinical trial that assessed the effectiveness of a new home based treatment program in the form of the Sun Ancon Aerobic Exerciser®. This machine delivered both elevation and passive exercise to the legs, with participants using the machine over a three week period during which time their leg volumes were measured using both perometry and bioimpedance. The results demonstrated that leg volume measurements decreased using both perometry and bioimpedance. The reduction in body extracellular fluid as measured by bioimpedance correlated well with a reduction in leg volume as measured by perometry. Bioimpedance also recorded a reduction in weight, which was correlated with the reduction in leg volume as measured by perometry. This trial confirms that perometry and bioimpedance were both effective in independently showing a reduction in leg lymphedema using the Aerobic Exerciser therapy, and that both methods can be reliably used to measure and follow leg lymphedema.

Secondary lymphedema is a chronic and often debilitating disorder of leg swelling, associated with soft tissue changes and subjective symptoms. It has been estimated that 30% (1-4) of patients who undergo surgery and/or radiotherapy for cancer of the gastrointestinal, urinary, reproductive systems or melanoma develop this complication. Considering that this incidence is a significant percentage of those who submit to and survive cancer treatment, it is of upmost importance that measurement techniques that are used not only reliably detect the presence of lymphedema, but that they also accurately reflect changes in response to treatment.

Various measurement techniques are used to assess the severity of a lymphedematous leg and/or its response to treatment. Circumference and volume measurement is

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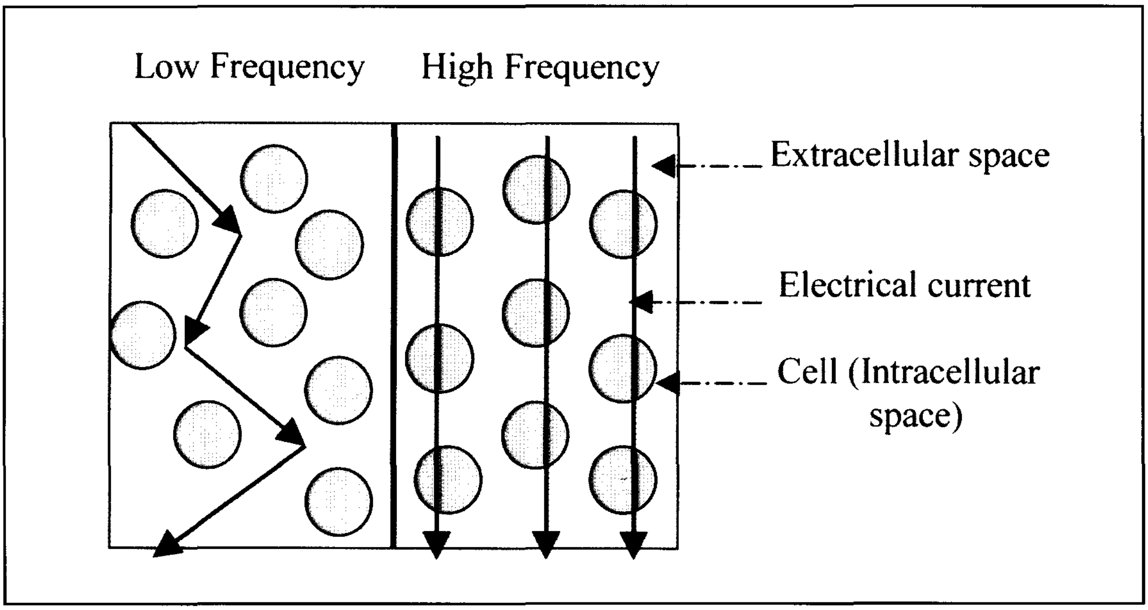

Fig. 1. Conductivity of multi-frequency bioimpedance: Low versus high frequency.

one of the most popular (5). Other techniques to assess lymphedema are perometry and bioimpedance. Although both latter procedures have been extensively validated in various clinical trials, one of the aims of this study was to cross validate and correlate these two methods to ascertain whether both accurately predict fluid and volume changes in response to a new treatment regimen.

The treatment intervention tested in this trial was a home-based therapy using the Sun Ancon Aerobic Exerciser®. This is a new treatment program where the patient lies supine on the floor and positions their ankles in two molded ankle rests. When the machine is switched on, the ankle rests move from side to side in a sinusoidal fashion delivering both elevation and passive exercise to the legs. Patients were required to use the Sun Ancon Aerobic Exerciser® over a 21 day period during which time the leg volumes were monitored using both perometry and bioimpedance.

The perometer (Perosystems®, Germany) is an opto-electronic imaging device designed for the measurement of limb volume. It consists of a square measuring frame that contains rows of infra-red light emitting diodes on two sides and rows of corresponding sensors on the opposite two sides (6). The patient sits at one end of the perometer with the foot resting centrally on an adjustable support. The frame is then moved along the length of the leg from the ankle to thigh. The limb casts shadows in two planes and using the cross-sectional information obtained, a laptop computer produces a volume picture of the entire leg. Perometry has been rigorously assessed by comparison with other methods (6) and is seen as more accurate than tape measurements (6,7). In various studies it has been shown to be highly reproducible (6), accurate (7-9) and reliable (6,9,10), with one clinical trial quoting an alpha reliability of .9998 (8). It has been tested on both healthy volunteers (7,8,10) and patients with edema-related conditions (7).

Bioimpedance is a non-invasive technique that accurately quantifies both total body fluid and extracellular fluid in extremities, with the capability of also quantifying tissue/lymph fluid changes by distinguishing between the gain or loss of fluid from fat and

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muscle (11). It works on the principle that fat and bone act as insulators of electrical current while electrolytic fluid conducts electricity (11). Bioimpedance measures the resistance to the flow of this current (12-14). Although singular frequency has been traditionally used, multi-frequency is the better method of body fluid analysis because at low frequencies the electrical current only passes through highly conductive extracellular fluid whereas at high frequency it passes through both intra- and extracellular fluid, thereby measuring total fluid impedance (11-13,15) *(Fig. 1)*. Bioimpedance validity in measuring body fluid in both healthy adults and patients has been confirmed (13-20), including in patients with lymphedema (16,21). Multi-frequency is considered reproducible (13,22) with the 8 electrode system more accurate than the traditional 4 electrode system. It also has minimal inter-operator variability (12). Evidence is also accumulating that bioimpedance more accurately distinguishes the ratio of extracellular fluid to intracellular fluid in lymphedema patients than total limb volume measurement (23,24).

With bioimpedance measurements the patient traditionally lies supine on a bed, adhesive electrodes are placed on the posterior wrist and malleolar ankle region and the voltage drop between the two measured. The bioimpedance machine used in this clinical trial was the InBody 3.0® manufactured in Korea by Biospace Ltd. The Inbody 3.0® is a multi-frequency body and segmental analyzer (5kHz-500kHz) where the patient stands erect on electrode footplates and holds electrodes in the hands, resulting in 8 electrode contact sites — the right and left heels, front feet, fingers and thumbs. This arrangement also helps to eliminate discrepancies in electrode placement, standardizing the placement, enhancing the reproducibility and accuracy of the measurements. The InBody 3.0® analyzer's reproducibility has been previously documented with a reliability factor of 0.940 (25).

Information about the individual patient such as name, UR number, age, sex and height can readily be entered into the analyzer via computer keyboard. The machine also takes into account ethnicity, with a setting for Afro-American, Caucasian or Asian populations. Together these factors are thought to improve the accuracy of predicting total body fluid volume (26).

MATERIAL AND METHODS

Thirty three patients with secondary lymphedema (28 women and 5 men) aged 39-88 years (mean 59 years ± 13 years) were recruited into the clinical trial. Each was required to have an accurate diagnosis of secondary lymphedema. The study was approved by the Flinders Medical Centre Clinical Research Ethics Committee, South Australia, Australia. Each patient used the Sun Ancon Aerobic Exerciser® in their own home morning and evening for three weeks adhering to the following regimen: days 1-2: 5 minutes per session, days 3-7: 8 minutes per session, and days 8-21: 12 minutes per session. Participants were asked to fill out a log book so that compliance to the treatment regimen was validated. As part of the trial each patient was measured with perometry and bioimpedance to monitor leg volume and fluid changes in relation to the treatment program.

Key volume measurements were taken before beginning the trial (baseline), at weekly intervals for three weeks and then at 1 month post treatment. Where possible perometry and bioimpedance measurements were taken at the same time of day, a week apart, in the same clinic with a constant ambient temperature. Each measurement was performed by the same operator well trained in the techniques. The bioimpedance machine has a self-calibration program that was activated each day before measurement sessions. Circumstances that could have had an impact upon the swollen leg and therefore the readings, such as menstruation, were also recorded before each measurement.

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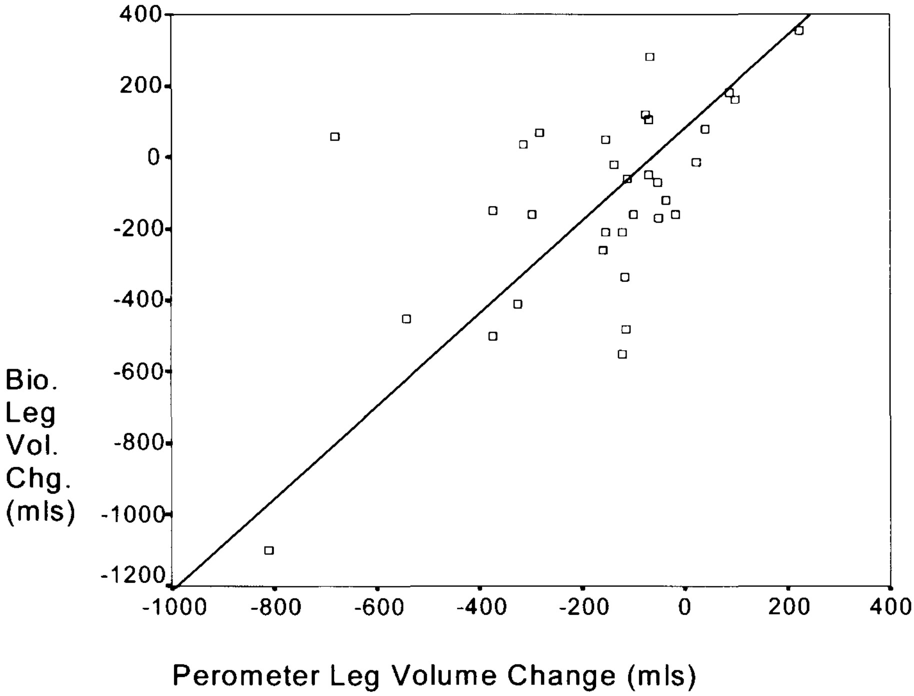

Fig. 2. Perometry leg volume change versus bioimpedance leg volume change.

Perometry

Before trial commencement the patient's data, including name, address, UR number and date of birth was entered into the laptop computer, which was connected to the perometer. This created a file under the patient's name so that each measurement could be stored and accessed from the same file. The patient removed their shoes and any item of clothing (such as support stockings, socks, skirt or trousers) that might interfere with the perometer taking an accurate leg measurement. The patient then sat in a chair and held their leg out horizontally with the foot resting on an adjustable support. The operator ensured that the leg was centrally positioned and not at an angle (horizontally or vertically) and then moved the perometer frame in a smooth motion from the ankle to the top of the thigh and back again. The patient then removed the lymphedematous leg, and the measurement was repeated on the contralateral leg. Each measurement took approximately 1 minute. The information taken was then relayed to a laptop computer, which determined the circumference and the volume of the leg. Once repeat measurements were performed, a volume versus time graph for each leg for circumference and volume was constructed giving an accurate indication of the effectiveness of the treatment regimen.

Bioimpedance

Before trial commencement, each subject had his or her height measured with a linear height scale without shoes to the nearest 0.5cm. This height was then used each time the patient underwent bioimpedance analysis.

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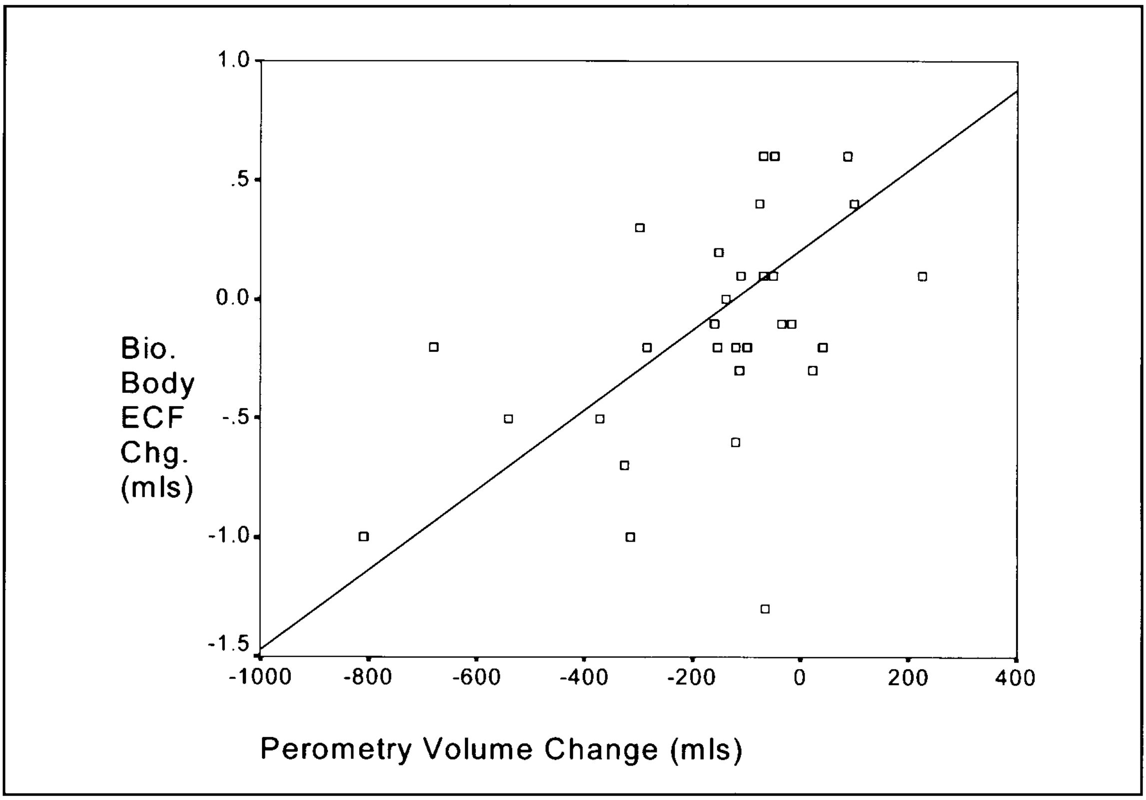

Fig. 3. Perometry leg volume change versus bioimpedance body extracellular fluid.

Before a bioimpedance measurement was undertaken, the patient removed shoes, stockings or socks and wet-wiped the soles of their feet and the palms of their hands, which maximized skin to electrode contact and electrical conductivity. The patient then stood on a footplate and held hand electrodes with the operator ensuring their correct placement. The patient also held their arms out horizontally so that they did not make contact with the body as this can disturb the electrical current and field.

Once on the machine, the patient's data were entered into the computer with leg fluid measurement taking approximately 2 minutes, at which time a printout was produced which detailed the patient's measurements including muscle and fat mass, total body water (both intracellular and extracellular) and the fluid contained within each body segment, namely arms, trunk and legs.

Analysis

Perometry and bioimpedance data were analyzed by comparing initial baseline measurements with the final measurement taken after three weeks of treatment. This arrangement provided a figure of change (either loss or gain) over this interval. The data were then analyzed using SPSS and Pearson correlation analysis.

RESULTS

When the volume change of the affected leg(s) as measured by both perometry and bioimpedance was compared, there was a

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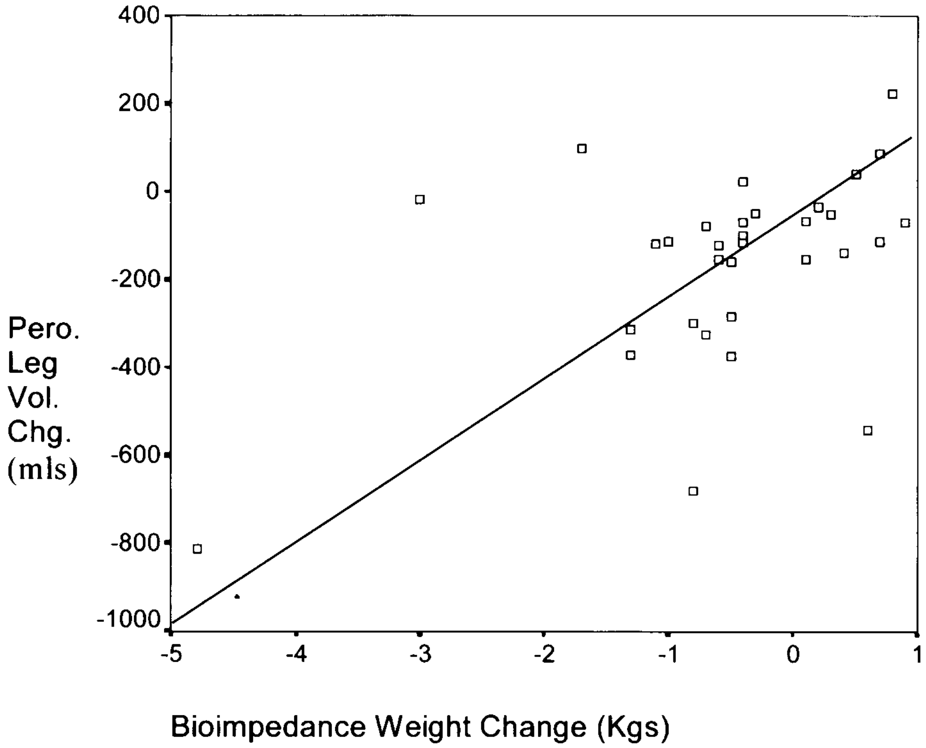

Fig. 4. Perometry leg volume change versus weight change as measured by bioimpedance.

good correlation (r=0.611) which was highly significant (p< 0.000) *(Fig. 2)*.

The leg volume change as measured by perometry also correlated with the change in whole body extracellular fluid change as measured by bioimpedance with a correlation of r=0.495 and significance of p<0.004. The loss in extracellular fluid volume as determined by bioimpedance was reflected in leg volume loss as measured by perometry *(Fig. 3)*.

The loss of fluid as reflected in leg volume change also correlated with weight change as measured by bioimpedance. (Correlation of r=0.478 and significance of p< 0.006.)

The Bioimpedance machine also demonstrated internal consistency with the change in body extracellular fluid correlating with the change in leg volume (r=0.427, p< 0.015) and the change in weight correlating with the change in leg volume (r=0.601, p< 0.000) *(Fig. 4)*.

DISCUSSION

This clinical trial demonstrated that there are good correlations between perometry and multi-frequency bioimpedance measurements and that the bioimpedance machine had internal consistency. Bioimpedance measures both intracellular and extracellular fluid, giving an accurate measurement of pure fluid changes in each segment (limb), whereas perometry measures other components such as changes in cells and fiber. Thus, bioimpedance is a more accurate assessment of limb fluid change while perometry provides an accurate determination of total limb volume

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change. Both, however, are equally valid in reflecting leg volume changes and can be used sequentially in both the clinical and research setting.

Both techniques accurately measured the leg volume that occurred in response to the newly introduced treatment regimen in the form of the Aerobic Exerciser. The fact that leg volume, body extracellular fluid volume and weight reduction were significantly and well-correlated demonstrated that the new treatment intervention was having a beneficial effect on leg lymphedema.

There are, however, potential drawbacks with both measurement techniques. With perometry the patient must be able to abduct the hips and hold the leg horizontally for approximately 1 minute. With bioimpedance, the patient needs to stand upright for 2 minutes and have all limbs intact (no amputees) for accurate measurement. Although several patients had limited mobility, they were still able to undergo these measurement techniques.

Both perometry and bioimpedance are non-invasive, relatively easy and quick methods to assess secondary lymphedema. As shown in this clinical trial, using both together provided an accurate and in-depth picture of the complex condition of secondary leg lymphedema and how it responds to treatment.

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