Bioimpedance Profiling of the Limbs: Update

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Abstract. Bioelectrical impedance spectroscopy (BIS) is now commonly used to assess breast cancer-related lymphoedema. Typically, the ratio of impedances of the two arms, determined at zero frequency (Z0), is used as a quantitative index of the presence of excess lymph. Measurement uses skin electrodes spanning the whole limb. However, lymphoedema may be highly localised and may involve changes other than simple fluid accumulation, e.g. increased fat and fibrosis, that also give rise to changes in impedance-related parameters such as capacitance. We have previously reported (13th ICEBI, Graz, 2007) a prototype mobile electrode probe that replaces the distal sense electrode which, when moved proximally along the arm, provides an impedance profile. We report here the further development of this technology to incorporate real-time measurement of impedance integrated with a digital measuring wheel. This allows exact synchronisation of impedance with position on the arm. A commercial BIS instrument (ImpediMed SFB7) was modified to collect impedance (R and Xc) data every msec and the mean impedance computed for each 10-mm slice. The apparent resistivity values for arm tissue were used to calculate slice volumes. These computed volumes were compared to equivalent slice volumes from perometry and DXA. The system is being further validated by correlating slice impedance parameters with lean tissue volume determined by pQCT (StraTec XCT 3000), for multiple positions along the arm. Ultimately, it is hoped that such measurements will not only allow localised tissue volume measurement but will also provide information of tissue composition in conditions such as lymphoedema.

1. Introduction

Lymphoedema is a chronic debilitating condition that affects millions world-wide. The most prevalent form is secondary lymphoedema as a consequence of damage to the lymphatic system by, for example, parasitic infection, as in the tropical condition filariasis or, and most commonly in the developed world, as a sequela of damage to the lymph system resulting from treatment for cancer. Reported incidence rates for lymphoedema post-breast cancer vary from 25 to 50% [1]. The condition is characterized by accumulation of lymph fluid in the arm on the affected side leading to swelling, immobility, loss of function and reduced quality of life. Lymphoedema is considered incurable but symptomatic relief may be obtained with drug treatment or surgery but physical therapy, massage and the use of compressive bandaging or garments are most commonly used [2].

Treatment is most effective if introduced at the earliest opportunity and, in turn, is reliant upon early diagnosis of the condition. Since lymph is an extracellular fluid, bioelectrical impedance spectroscopy (BIS) has found a place as the method of choice for early detection of lymphoedema [3]. Typically, the impedance of the at-risk arm is compared to that of the unaffected contra-lateral arm, as a ratio, and this is deemed indicative of the presence of lymphoedema if the ratio exceeds a threshold value (mean + 3 standard deviations) determined in a reference population [4]. This approach, while eminently clinically successful [5], is limited to whole arm measurements whereas lymphoedematous swelling may be localized to a limb segment such as the forearm only. Currently localized lymphoedema is best determined as an abnormally large limb circumference in the region of interest. However simple circumferential measurements may not be specific for lymphoedema and there is no universally accepted criterion presumptive of abnormal swelling. We have previously [6] provided a proof of concept for a BIS method for assessing localized lymphoedema. In the present report we
describe the further development of this methodology and preliminary data validating this approach using peripheral quantitative computed tomography (pQCT) for comparison.

2. Materials and methods

2.1. Theory

The impedance ($Z$) of a homogeneous conductor varies with the length ($l$) of and inversely with the cross-sectional area ($a$) of the conductor:

$$Z \propto \frac{l}{a} \quad (1)$$

thus if a short segment of the arm is considered to approximate a cylinder the impedance of the segment will reflect the segment length, cross-sectional area and the resistivity ($\rho$) of the tissue composition of the segment. The whole arm may be considered to be a series of cylinders of changing cross-section and resistivity due to varying tissue composition connected end-to-end. Therefore, the impedance of the arm measured between a fixed point, e.g. the shoulder, and a continually varying point, e.g. an electrode traversing longitudinally along the arm from a distal point, the wrist, will define an impedance profile along the limb. Since the volume of the intervening segments can be determined from the relationship:

$$Vol = \rho \frac{l^a}{Z} \quad (2)$$

if a value for resistivity is known, then the impedance profile may be determined as a series of segment volumes defined by the linear spatial resolution of the impedance measurement.

2.2. Experimental

2.2.1. Subjects. For this proof of concept study, subjects were two healthy control males: subject A, aged 58 y, weighing 78.5 kg and body mass index (BMI) of 25.8 kg/m$^2$ and subject B aged 49 y, weighing 62.3 kg with a BMI of 19.7 kg/m$^2$.

2.2.2. Impedance measurements. Impedance was measured using a modified ImpediMed SFB7 tetrapolar impedance monitor. Measurements were obtained along each arm, commencing at the ulnar styloid process, according the principle of equipotentials [7]. The current drive electrodes were placed at the conventional locations of the base of the fingers and the toes on the side to be measured. A sense electrode (Ag-AgCl gel electrode, 23 x 24 mm, Impedimed, Brisbane) was placed on the anterior surface of the contralateral arm at the mid-point between the ulnar styloid processes. The distal sense electrode (that at the wrist) on the ipsilateral arm was replaced by a 1 cm diameter stainless steel disc electrode that could be slid smoothly along the surface of the skin. The electrode probe also housed a purpose-built rotating disc planimeter that interfaced with the SFB7 firmware to record the distance travelled at 1.58 cm resolution. The modified SFB7 hardware and firmware allowed recording of impedance at a single selected frequency in the range 5 kHz to 1 MHz at a sampling rate of 1 reading per msec. Scans along the arm commenced by locating the probe at the ulnar styloid process and after approximately 3 sec, the probe was slid smoothly along the dorsal skin surface towards the acromion where the probe remained stationary, but still recording, for a further 3 sec. Four to eight replicate scans were performed on each arm. A complete scan required approximately 20 seconds. Measurements were performed at 5 kHz, a frequency appropriate for measurement of extracellular volume, including lymph, only [8]. Electrical conductivity for the probe was assured by a very light application of conductivity gel along the arm prior to measurement.

2.2.3. Tissue volume measurements. Cross-sectional muscle area and fat area were measured by pQCT (XCT 3000 Stratec, Inc., Pforzheim, Germany) on both arms, in 20 slices at 2 cm intervals commencing at a position distal to the shoulder such that the final slice ended at the wrist. The arm
was held horizontal to the body and supported on X-ray transparent bubble wrap in a hemispherical cross-section PVC tube. Each scan took approximately 1 hour. The radiation dose for a single scan was approximately 0.3 µSv, which represents less than 5% of the typical natural background radiation dose acquired each day. Scans were performed according to the manufacturer’s recommendations. Image processing and calculations of numerical values were performed using the manufacturer’s software package (version 5.4, Stratec Inc.). Cross-sectional muscle, bone and fat areas were determined using thresholds of 280 mg/cm$^3$ for bone, 40 mg/cm$^3$ for muscle and -80 mg/cm$^3$ for total tissue area. Adipose tissue area was determined by subtraction. In one subject, total arm volume was also measured by opto-electrical perometry [6].

2.2.4. Data analysis. Although transit speed of the probe was not constant, each scan accumulated a total of 10000 data points, equivalent to approximately 400 data points per 1.58 cm slice. The average resistance for each 1.58 cm slice was computed for each scan and the mean and standard deviation computed across all replicate scans. Since pQCT slices were at each 2 cm interval, the resistance for each equivalent slice was computed by interpolation from the resistance slice data and expressed as ohm/cm for each of the 20 pQCT slices along the arm. Volumes of muscle, bone and adipose tissue for each pQCT slice were computed from the slice thickness and measured tissue areas. The ECF volume of each slice was computed from these volume data assuming hydration factors of 0.73 for muscle and 0.15 for adipose tissue and ECF to total fluid ratios of 0.33 for muscle tissue and 0.4 for adipose tissue [9]. Bone was assumed to contain no ECF. The apparent ECF resistivity of each slice was computed from these values.

3. Results and Discussion
Typical, and essentially identical, impedance profiles, along both the left and right arms, for subject A are presented in figure 1. The overall coefficient of variation (CV) between replicate impedance scans averaged 7% but was notably higher in the region of the wrist and shoulder. Poorer reproducibility (typical CV of 15%) was obtained for ventral surface scans.

The calculated apparent ECF resistivities for the 20 pQCT slices were: for subject A, mean resistivity was 25.2 ± 3.9 ohm.cm and 25.5 ± 2.5 ohm.cm for subject B. Recalculating the resistivities assuming that the arm was represented as a single cylinder yielded slightly higher values of 27.9 and 27.3 ohm.cm respectively. These computed resistivity values are remarkably similar despite clear differences in tissue composition and overall size of the arm between each subject (figure 2), e.g. percentage muscle masses were 62.7% and 83.7% for subjects A and B respectively. This lends confidence to the view that the method is providing a robust measure of apparent ECF resistivity largely independent of tissue composition and geometry. The mean computed resitivities for each subject were used to predict the ECF volume for each slice of the other subject and these predicted values compared to those determined by pQCT. These data are presented in figure 2. The predicted ECF profile for each subject closely corresponds to that determined by pQCT. The correlations
between the measured pQCT ECF volume for each slice with those predicted from impedance were
0.89 and 0.93 for subjects A and B respectively. For subject A, total ECF volume was 338.9 ml
determined from impedance and 332.8 ml by pQCT. Corresponding values for subject B were 306.4
ml and 299.8 ml respectively.

Figure 2. Tissue volume profiles of the left arms for two subjects with differing tissue composition.
Predicted ECF volume profile is presented for comparison with that determined by pQCT. For
subject A, the correspondence between computed total pQCT tissue volume and volume measured
by perometry is also shown.

4. Conclusion
The impedance probe provides a practical method for determining the impedance profile of a limb.
Measurement of limb ECF volume by tracer dilution is not feasible. However, pQCT provides an
independent method for ECF determination that allows calculation of apparent ECF resistivity,
facilitating prediction of ECF volume from impedance measurements. These studies are being
extended to the assessment of arms of women with expanded ECF volume due to lymphoedema.

References
[1] Warren AG, Brorson H, Borud LJ and Slavin AS 2007 Lymphedema a comprehensive review
Ann. Plast. Surg. 59 464–72
[2] Moseley A, Carati C and Piller N 2007 A systematic review of common conservative therapies
for arm lymphoedema secondary to breast cancer treatment Ann. Oncol. 18 639-46
[3] Ward LC 2009 Early detection of lymphoedema: is BIS ready for prime time as the gold
standard measure? J. Lymphoedema 4 52-6.
[4] Ward LC 2006 Bioelectrical impedance analysis: proven utility in Lymphedema risk assessment
and therapeutic monitoring Lymphat. Res. Biol. 4 51-6
[5] Schonholz SM 2009 Preoperative assessment enables the early detection and successful
treatment of lymphedema Cancer 115 909
[6] Ward LC, Kilbreath SL, Lee M-J and York SL 2007 Bioimpedance profiling of limb
lymphoedema Proc. XIII Int Conf Electrical Bioimpedance & VIII Conf on Electrical
Impedance Tomography (Graz, Austria, 29 August - 2 September) IFMBE Proc 17 624-7
[7] Cornish BH, Jacobs A, Thomas BJ, and Ward LC 1999 Optimizing electrode sites for segmental
bioimpedance measurements Physiol. Meas. 20 241-50
[8] Ward LC, Piller N and Cornish BH 2001 Single or multiple frequency bioelectrical impedance
analysis for the assessment of lymphoedema? Proc. XI Int Conf on Electrical Bio-Impedance
(Oslo, Norway,17-21June 2001) Eds. S Grimnes, O Martinsen and H Bruwal. pp373-6
[9] Roche AF, Heymsfield SB and Lohman TG, Eds. 1996 Human Body Composition (Champaign:
Human Kinetics Press)