

Suitability of single tissue dielectric constant measurements to assess local tissue water in normal and lymphedematous skin

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Summary

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Previous reports described the use of average tissue dielectric constant (TDC) measurements to assess local tissue water and its change. Our goal was to determine if a single TDC measurement could be used in place of the average of multiple measurements. The comparison criteria used to test this was the extent to which single and averaged measurements yielded similar TDC values in both normal and lymphedematous tissue. Measurements were made in two groups of women; a control group ($n = 20$) and a group with unilateral arm lymphedema ($n = 10$). In the control group, TDC was measured to multiple depths (0.5–5.0 mm) on both ventral forearms and to a depth of 2.5 mm on the lateral thorax on both body sides. In the lymphedematous group, TDC was measured on both ventral forearms to a depth of 2.5 mm. Results showed that the 95% confidence interval for differences between single and averaged TDC values was less than ± 1 TDC unit and that the limits of agreement between methods was less than ± 2.5 TDC units ($\pm 6.5\%$) for each condition, site and depth measured. This finding suggests that where this level of agreement is acceptable suitable clinical assessments can be made using a single TDC measurement.

Introduction

A variety of methods are available to assess overall limb oedema via metric and volume measures (Casley-Smith, 1994; Karges et al., 2003; Mayrovitz, 2003; Mayrovitz et al., 2005, 2006, 2007a,b), automated methods (Tierney et al., 1996; Stanton et al., 1997; Mayrovitz et al., 2000; Moseley et al., 2002) and electrical impedance type methods (Cornish et al., 1998, 2001, 2002; Ward, 2006).

However, these are not generally suitable to determine local oedema or oedema in body parts other than the limbs. Quantitative assessment of local tissue oedema could provide important and useful information not previously available to help initially assess and to track oedema and lymphedema progression in patients. Recent work has used the tissue dielectric constant (TDC) method to evaluate local tissue water changes during the menstrual cycle (Mayrovitz et al., 2007a,b). Other work has indicated that assessment of local tissue water based on TDC measurements is a useful discriminator for the presence of lymphedema in patients with unilateral postmastectomy lymphedema (Mayrovitz, 2007; Mayrovitz et al., 2008a,b) and to detect changes subsequent to manual lymphatic drainage therapy (Mayrovitz et al., 2008a,b). The working

principle of the TDC method is based on the fact that tissue electrical properties depend on water content which in turn affects the value of the TDC (Nuutinen et al., 2004). Measurement of TDC at a suitable frequency provides an index of relative tissue water (Aimoto & Matsumoto, 1996; Alanen et al., 1998).

In all previous studies, TDC measurements at sites of interest were done in triplicate and then averaged to help reduce measurement variance potentially associated with a single measurement (Mayrovitz, 2007; Mayrovitz et al., 2007a,b, 2008a,b). This strategy is useful, but it also triples the amount of time required for each assessment site. Further, the average of repeated measurements is only better than a single measurement if the results or reproducibility obtained are significantly different between them (Fagan et al., 1988). If the difference between single and averaged triplicate TDC measurements were known, than an informed decision as to which approach to adopt for clinic applications could be made. Thus, our goal was to determine and compare differences between single and triplicate TDC measurements with respect to outcome values obtained.

To provide a reasonably broad characterization of such potential differences, measurements were made at different sites in two groups of women. In a control group of 20 women, measurements were made on the ventral forearm with four

different probes to achieve tissue sampling to four different depths (0.5–5.0 mm). Measurements were also done on the lateral thorax to a depth of 2.5 mm. The second group consisted of 10 women with frank unilateral arm lymphedema that had developed subsequent to breast cancer treatment-related surgery and/or radiation. In this group, ventral forearm measurements were made in both the lymphedematous and non-lymphedematous arms to a single depth (2.5 mm). The null hypothesis to be tested was that there would be no significant difference between single and averaged TDC values.

Methods

Subjects

Two groups of women were evaluated after signing Institutional Review Board approved informed consents. One was a control group of 20 women with ages (mean \pm SD) of 54.6 ± 11.6 years who had no history of arm oedema or lymphedema. The other group consisted of 10 women of ages 71.2 ± 14.1 who had unilateral arm lymphedema subsequent to breast cancer related surgery and/or radiation treatment. The age of the lymphedematous group was significantly greater than the control group ($P < 0.05$).

Measurement device

The device used was the MoistureMeter-D (Delfin Technologies Ltd, Kuopio, Finland). It consists of a probe connected to a control unit that displays the TDC when the probe is placed in contact with the skin. The physics and principle of operation has been well described (Stuchly et al., 1982; Aimoto & Matsumoto, 1996). In brief, a 300-MHz signal is transmitted to the tissue via the probe in contact with skin with the probe acting as an open-ended coaxial transmission line (Alanen et al., 1999). The reflected portion of the incident electromagnetic wave depends on tissue's dielectric constant, which itself depends on the amount of free and bound water in the tissue volume through which the wave passes. Reflected wave information is processed and the relative dielectric constant is displayed. Pure water has a value of about 78.5. Effective penetration depth depends on probe dimensions, with larger spacing between inner and outer conductors causing greater penetration. Four different

dimension probes were used for TDC values on forearms of the control group. Probe effective penetration depths were 0.5, 1.5, 2.5 and 5.0 mm, with corresponding (maximum) probe diameters of 10, 20, 23 and 55 mm with conductor spacing of 1, 3, 5 and 17 mm respectively. Because of clinic time constraints, only the 2.5 mm penetration depth probe was used to assess forearms of the lymphedematous group and the thorax of the control group.

Measurement procedure

Measurements were done with subjects supine after they had been lying for 10 min. Arm measurements were made on volar (ventral) forearms of both arms, of both groups, 6 cm distal to the antecubital crease. Thorax measurements were made on the lateral thorax 8 cm below the axilla on both sides only in the control group. Measurement points were first marked for reference with a dot using a surgical pen. The dot served as the center point for probe placements. For the control group, arm measurements were started with the smallest diameter probe with progression to the largest diameter probe. For all measurements, the probe was placed in contact with the skin and held in position using gentle pressure and values obtained in triplicate-pairs. The first pair was done by measuring one site and then, immediately after, measuring the same site on the other body side (arm or thorax). This procedure was repeated twice more. This alternating method between body sides was employed to help obtain paired values as close in time as possible. The time required to obtain a single measurement, once the probe was placed in contact with the skin, was about 10 s. The elapsed time between sequential measurements at the same site was standardized at 20 s. The time required to obtain a triplicate measurement at a given site was 52.6 ± 1.9 s (mean \pm SD). The elapsed time between the last measurement of one probe and the start of measurements with the next probe in the control group forearm measurements was 60 s.

Analysis

Two parameters were used for comparison; the first TDC value obtained and the average of triplicate TDC values. These parameters are designated as TDC_1 and TDC_{AVG} respectively. For the control group, values for each body side were merged to

Table 1 Tissue dielectric constant (TDC) values for control group.

Depth (mm)	Ventral forearm ($n = 40$)				Lateral thorax ($n = 40$)			
	TDC_1	TDC_{AVG}	95% CI of difference	Correlation R	TDC_1	TDC_{AVG}	95% CI of difference	Correlation R
0.5	36.3 ± 4.6	36.2 ± 4.7	-0.37 to 0.58	0.949				
1.5	34.0 ± 5.3	34.2 ± 4.9	-0.56 to 0.15	0.979				
2.5	23.9 ± 4.0	23.9 ± 4.1	-0.27 to 0.26	0.979	24.1 ± 4.3	24.1 ± 4.1	-0.35 to 0.22	0.978
5.0	21.1 ± 3.4	21.1 ± 3.2	-0.19 to 0.12	0.991				

TDC_1 and TDC_{AVG} are tissue dielectric constant values in relative units for single and average of triplicate measurements. Data entries are mean \pm SD. Differences between TDC_1 and TDC_{AVG} were statistically insignificant at the forearm for all depths and at the thorax.

yield a total of 40 ($TDC_1 - TDC_{AVG}$) comparison pairs for each of the four depths for arms and 40 comparison pairs for the 2.5 mm depth at the thorax. For the lymphedematous group, oedematous and non-oedematous arms were analysed separately to yield 10 ($TDC_1 - TDC_{AVG}$) comparison pairs for each arm. For each group and depth the difference ($TDC_1 - TDC_{AVG}$) was determined and 95% confidence intervals of differences calculated. This approach to comparing a single measurement to an average of repeated measurements is similar to that done for blood pressure measurements (Fagan et al., 1988). Differences in TDC values among depths for the control group were tested with a general linear model for repeated measures with depth as a within factor. Differences in TDC values between lymphedematous and non-lymphedematous arms in the lymphedematous group were tested with the nonparametric Mann-Whitney U-test. In all cases a P-value <0.05 was set as the criteria for a significant difference. In addition, the agreement between single and averaged measurements was evaluated using the statistical and graphical approach of Bland and Altman (Altman & Bland, 1986). With this method, 95% upper and lower limits of agreement (LOA) are determined by plotting the difference between each measurement-pair ($TDC_1 - TDC_{AVG}$) versus the average of the two measurements ($(TDC_1 + TDC_{AVG})/2$). The upper and lower LOA are calculated as the mean value of the differences ± 2 SD and shown graphically on the same plot. The interval between the upper and lower LOA is expected to contain 95% of the differences between measurements made by the two methods on individual subjects (Bland & Altman, 1999). In addition an estimate of the 95% confidence intervals on the upper and lower LOA are calculated in accordance with the previously established method (Bland & Altman, 2003).

Results

Control group

Tissue dielectric constant values obtained from the first measurement and the average of the repeated measurements were very close at every depth, with differences between them being statistically insignificant as summarized in Table 1. The narrow 95% confidence intervals of the $TDC_1 - TDC_{AVG}$ differences for forearms at all depths and for the thorax to a 2.5-mm depth, illustrate the small difference range between TDC_1 and TDC_{AVG} . As expected, the correlation between single and average values was highly significant ($P < 0.001$). TDC values at forearm and thorax were similar to each other with no significant difference between them ($P > 0.5$). A reduction in TDC values with increasing depth, previously reported using average values (Mayrovitz, 2007), was also seen here with similar depth dependent patterns and statistics as determined by either single TDC values or averages. Both measurement sets showed an overall statistically significant reduction ($P < 0.001$) with TDC values at each depth significantly different from all others ($P < 0.01$). For each measured depth on the forearm and for the 2.5 mm depth on the thorax the difference between single and average values ($TDC_1 - TDC_{AVG}$) versus the

average of the two measurements ($(TDC_1 + TDC_{AVG})/2$) are shown in Fig. 1. The central dashed line is the mean value of the difference, the solid upper and lower lines are located at ± 2 SD from the mean and define the limits of agreement between

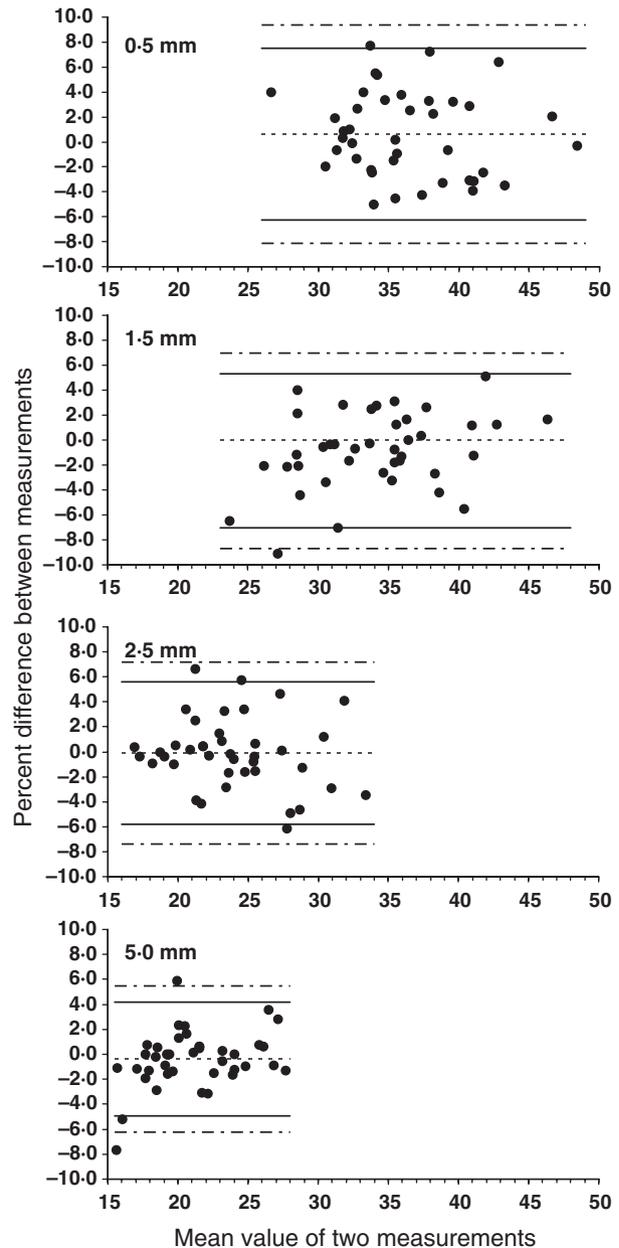


Figure 1 Bland-Altman plots showing differences between single and averaged tissue dielectric constant (TDC) measurements for each penetration depth on the forearm of control subjects. The vertical axis is expressed as the percentage difference between measurements calculated as $100 [TDC_1 - TDC_{AVG} / (TDC_1 + TDC_{AVG}) / 2]$ and the horizontal axis is the mean value obtained using the two methods calculated as $(TDC_1 + TDC_{AVG}) / 2$. The central dashed line is the mean difference between measurement methods and the solid upper and lower lines are located at ± 2 SD from the mean and define the limits of agreement between methods. The line (long-dash, short-dash) above and below the LOA are the upper and lower 95% confidence intervals on the LOA.

Depth (mm)	Non-oedematous arm (n = 10)			Oedematous arm (n = 10)		
	TDC ₁	TDC _{AVG}	95% CI of difference	TDC ₁	TDC _{AVG}	95% CI of difference
2.5	25.0 ± 2.8	25.3 ± 3.0	-0.76 to 0.16	41.0 ± 9.0	41.1 ± 8.8	-0.53 to 0.39

Data entries are mean ± SD. Differences between TDC₁ and TDC_{AVG} for oedematous and non-oedematous arms were statistically insignificant. TDC values for oedematous arms were significantly greater than for non-oedematous arms ($P < 0.001$).

methods and the line (long-dash, short-dash) above and below the LOA are the upper and lower 95% confidence intervals on the LOA.

Lymphedematous group

Similar to the findings for the control group, differences between TDC₁ and TDC_{AVG} values were also insignificantly different from each other for this lymphedematous group as summarized in Table 2. This was true for oedematous and non-oedematous arms although absolute TDC values for lymphedematous arms were significantly greater than for contralateral arms ($P < 0.001$). Correlations between single and averaged values were also high, being 0.998 for the non-oedematous arm and 0.978 for the oedematous arm. Contrastingly, there was no significant relationship between TDC values obtained from the oedematous arm and those

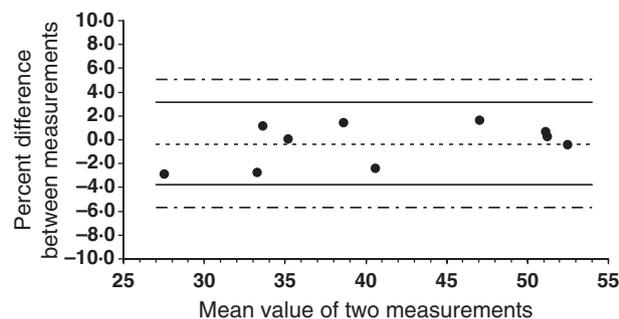


Figure 2 Bland-Altman plot showing differences between single and averaged tissue dielectric constant measurements for lymphedematous arms.

	Depth (mm)	Limit of agreement (LOA)		95% CI of LOA	
		Absolute	%	Absolute	%
Control arms	0.5	±2.50	±6.46	+3.43 to -3.02	+9.37 to -8.12
	1.5	±2.02	±6.16	+2.33 to -2.81	+6.99 to -8.71
	2.5	±1.47	±5.70	+1.82 to -1.91	+7.16 to -7.37
	5.0	±0.90	±4.58	+1.09 to -1.20	+5.46 to -6.20
Lymphedematous arms	2.5	±1.26	±3.49	+1.89 to -2.02	+5.09 to -5.71
Control thorax	2.5	±1.56	±6.22	+1.97 to -1.99	+7.79 to -8.06

CI, confidence interval.

The absolute LOA corresponds to determinations made using absolute differences between TDC values obtained with the two methods and the per cent LOA corresponds to determinations made using the percentage differences between TDC₁ and TDC_{AVG}.

Table 2 Tissue dielectric constant (TDC) values for lymphedematous group.

obtained from the contralateral arm for either single or averaged measurements. The corresponding limits of agreement plot for lymphedematous arms are shown in Fig. 2 with data pertinent to Figs 1 and 2 and the thorax of control subjects summarized in Table 3.

Discussion

The goal of this study was to determine the suitability of using a single TDC measurement to assess local tissue water compared to using the average of multiple measurements. The comparison criteria used to test this was the extent to which single and averaged measurements yielded similar TDC values in both normal and lymphedematous tissue. The results show that the 95% confidence interval for differences between single and averaged TDC values is less than ±1 TDC unit for each condition and all depths measured.

In addition, the limits of agreement analyses further and more precisely define the extent of agreement. In comparing two methods of measurement, the LOA, defined as twice the standard deviation of differences between values obtained by the two methods, establishes an interval in which about 95% of all differences lie. The decision as to whether two methods can be used interchangeably in a clinical setting requires a judgement that is based on whether the magnitude of the LOA is sufficiently small for the clinical purpose of the measurement. Here interchangeability means that either method could reliably be used to measure a patient.

The present results indicate that for the control group, the LOA for different measuring depths on the forearm range between ±6.46% at 0.5 mm depth to ±4.58% at 5 mm depth with an

Table 3 Limits of agreement between single and averaged measurement methods.

intermediate value of $\pm 6.22\%$ at 2.5 mm on the thorax. For lymphedematous arms, TDC values measured to a depth of 2.5 mm on lymphedematous arms show a between methods LOA of $\pm 3.49\%$. Thus the present results define the limits of agreement and indicate that under conditions in which percentage differences of these amounts are acceptable, the single and averaged value measurement approaches are interchangeable.

It should be noted that these findings specifically apply to measurements carried out on the forearm and thorax as these were the anatomical sites that were the focus of this study. These sites were chosen because of their potential relevance to assessments associated with breast cancer treatment-related lymphedema.

The TDC method is simple to use and can provide data from different tissue depths thereby offering possibilities for new basic research investigations. The fact that a single measurement is, within the limits of agreement described, as useful as repeated measurements makes it even more attractive for time conscious clinical assessments. The time saving depends on the number of sites and depths to be evaluated. For example, to evaluate and compare TDC values of a lymphedematous arm to the contralateral non-affected arm at each depth in triplicate requires about 7 min (4 depths \times 2 arms \times 52.6 s). If the thorax is to be included in the clinical evaluation, evaluation time is increased to about 14 min. Using a single TDC measurement would reduce this time by 2/3 to make it less than 5 min. Whether such time savings are useful is a matter to be decided by individual clinicians.

Another major utility derives from the fact that tissue water data can be obtained from any body area as measurements are not limited to limbs as are all other methods. Thus it is possible to assess oedema/lymphedema features in the hand, finger, head, neck, genitalia, chest and ankle and so on which may open up new areas of inquiry.

References

- Aimoto A, Matsumoto T. Noninvasive method for measuring the electrical properties of deep tissues using an open-ended coaxial probe. *Med Eng Phys* (1996); **18**: 641–646.
- Alanen E, Lahtinen T, Nuutinen J. Measurement of dielectric properties of subcutaneous fat with open-ended coaxial sensors. *Phys Med Biol* (1998); **43**: 475–485.
- Alanen E, Lahtinen T, Nuutinen J. Penetration of electromagnetic fields of an open-ended coaxial probe between 1 MHz and 1 GHz in dielectric skin measurements. *Phys Med Biol* (1999); **44**: N169–N176.
- Altman DG, Bland JM. Comparison of methods of measuring blood pressure. *J Epidemiol Community Health* (1986); **40**: 274–277.
- Bland JM, Altman DG. Measuring agreement in method comparison studies. *Stat Methods Med Res* (1999); **8**: 135–160.
- Bland JM, Altman DG. Applying the right statistics: analyses of measurement studies. *Ultrasound Obstet Gynecol* (2003); **22**: 85–93.
- Casley-Smith JR. Measuring and representing peripheral oedema and its alterations. *Lymphology* (1994); **27**: 56–70.
- Cornish BH, Ward LC, Thomas BJ, Bunce IH. Quantification of lymphoedema using multi-frequency bioimpedance. *Appl Radiat Isot* (1998); **49**: 651–652.
- Cornish BH, Chapman M, Hirst C, Mirolo B, Bunce IH, Ward LC, Thomas BJ. Early diagnosis of lymphedema using multiple frequency bioimpedance. *Lymphology* (2001); **34**: 2–11.
- Cornish BH, Thomas BJ, Ward LC, Hirst C, Bunce IH. A new technique for the quantification of peripheral edema with application in both unilateral and bilateral cases. *Angiology* (2002); **53**: 41–47.
- Fagan TC, Conrad KA, Mayshar PV, Mackie MJ, Hagaman RM. Single versus triplicate measurements of blood pressure and heart rate. *Hypertension* (1988); **11**: 282–284.
- Karges JR, Mark BE, Stikeleather SJ, Worrell TW. Concurrent validity of upper-extremity volume estimates: comparison of calculated volume derived from girth measurements and water displacement volume. *Phys Ther* (2003); **83**: 134–145.
- Mayrovitz HN. Limb volume estimates based on limb elliptical vs. circular cross section models. *Lymphology* (2003); **36**: 140–143.
- Mayrovitz HN. Assessing local tissue edema in postmastectomy lymphedema. *Lymphology* (2007); **40**: 87–94.
- Mayrovitz HN, Sims N, Macdonald J. Assessment of limb volume by manual and automated methods in patients with limb edema or lymphedema. *Adv Skin Wound Care* (2000); **13**: 272–276.
- Mayrovitz HN, Sims N, Litwin B, Pfister S. Foot volume estimates based on a geometric algorithm in comparison to water displacement. *Lymphology* (2005); **38**: 20–27.
- Mayrovitz HN, Sims N, H CJ, Hernandez T, Greenschner A, Diep H. Hand volume estimates based on a geometric algorithm in comparison to water displacement. *Lymphology* (2006); **39**: 95–103.
- Mayrovitz HN, Brown-Cross D, Washington Z. Skin tissue water and laser Doppler blood flow during a menstrual cycle. *Clin Physiol Funct Imaging* (2007a); **27**: 54–59.
- Mayrovitz HN, Macdonald J, Davey S, Olson K, Washington E. Measurement decisions for clinical assessment of limb volume changes in patients with bilateral and unilateral limb edema. *Phys Ther* (2007b); **87**: 1362–1368.
- Mayrovitz H, Davey S, Shapiro E. Localized tissue water changes accompanying one manual lymphatic drainage (MLD) therapy session assessed by changes in tissue dielectric constant in patients with lower extremity lymphedema. *Lymphology* (2008a); **41**: 87–92.
- Mayrovitz HN, Davey S, Shapiro E. Local tissue water assessed by dielectric constant: anatomical site and depth dependence in women prior to breast cancer-related surgery. *Clin Physiol Funct Imaging* (2008b); **28**: 337–342.
- Moseley A, Piller N, Carati C. Combined opto-electronic perometry and bioimpedance to measure objectively the effectiveness of a new treatment intervention for chronic secondary leg lymphedema. *Lymphology* (2002); **35**: 136–143.
- Nuutinen J, Ikaheimo R, Lahtinen T. Validation of a new dielectric device to assess changes of tissue water in skin and subcutaneous fat. *Physiol Meas* (2004); **25**: 447–454.
- Stanton AW, Northfield JW, Holroyd B, Mortimer PS, Levick JR. Validation of an optoelectronic limb volumeter (Perometer). *Lymphology* (1997); **30**: 77–97.
- Stuchly MA, Athey TW, Samaras GM, Taylor G. Measurement of radio frequency permittivity of biological tissues with an open-ended coaxial line: Part II – Experimental results. *IEEE Trans Microw Theory Tech* (1982); **30**: 87–92.
- Tierney S, Aslam M, Rennie K, Grace P. Infrared optoelectronic volumetry, the ideal way to measure limb volume. *Eur J Vasc Endovasc Surg* (1996); **12**: 412–417.
- Ward LC. Bioelectrical impedance analysis: proven utility in lymphedema risk assessment and therapeutic monitoring. *Lymphat Res Biol* (2006); **4**: 51–56.