

ORIGINAL ARTICLE
MISCELLANEOUSPossible applications of normative lower
to upper limb ratios of tissue dielectric
constant to lower extremity edema

Harvey N. MAYROVITZ *, Andrea ALVAREZ, Maria LABRA, Alexander MIKULKA, Don WOODY

College of Medical Sciences, Nova Southeastern University, Fort Lauderdale, FL, USA

*Corresponding author: Harvey N. Mayrovitz, College of Medical Sciences Nova Southeastern University, 3200 S. University Drive, Fort Lauderdale, FL 33328, USA. E-mail: mayrovit@nova.edu

ABSTRACT

Background: Lower extremity edema occurs in many conditions including congestive heart failure, lymphedema, diabetes-related, kidney and liver disease, chronic venous insufficiency with venous hypertension. Clinical edema assessment methods are often subjective and variable. Our goals were to introduce a simple noninvasive measurement procedure potentially useful to characterize lower extremity edema by providing normative values from which edema thresholds might emerge.

Methods: Tissue dielectric constant (TDC) values, as indices of skin-to-fat tissue water, were measured on foot dorsum, lower medial leg and anterior forearm of 88 adults (44 female) with ages ranging from 19-77 years with BMI ranging from 18.3-40.6 kg/m². From these direct measurements lower-to-upper extremity TDC ratios (foot/arm and leg/arm) were determined for each gender. Possible edema threshold ratios were calculated as the mean lower-to-upper ratio to which was added two standard deviations of the overall ratio thereby providing initial thresholds for future testing.

Results: Results showed that at each anatomical site absolute TDC values for males significantly exceed those of females ($P < 0.001$). Male vs. female TDC values were 33.0 ± 5.4 vs. 27.7 ± 4.0 for the forearm, 34.8 ± 6.5 vs. 27.5 ± 4.6 for the leg, and 32.5 ± 6.5 vs. 28.7 ± 5.1 for the foot. In contrast, the foot/arm and leg/arm ratios were similar between genders ranging from 0.990 ± 0.144 to 1.063 ± 0.170 . Corresponding lower extremity to upper extremity threshold ratios ranged from 1.278 for foot/arm to 1.403 for leg/arm. The composite ratios considering both gender ration ($N = 88$) yielded a composite threshold foot/arm ratio of 1.387 and a leg/arm threshold ratio of 1.324.

Conclusions: This assessment method together with the normative ratios and calculated thresholds may aid in rapid detection of lower extremity edema in patients and possibly as a way to quantitatively track changes in edema status with time or treatment. However, the suitability of these thresholds is subject to future validation in persons with clearly defined lower extremity edema for which this report's findings serve as an initial quantitative starting point.

(Cite this article as: Mayrovitz HN, Alvarez A, Labra M, Mikulka A, Woody D. Possible applications of normative lower to upper limb ratios of tissue dielectric constant to lower extremity edema. *Int Angiol* 2019;38:70-5. DOI: 10.23736/S0392-9590.18.04088-9)

Key words: Edema - Diagnostics - Lower extremity - Upper extremity.

Foot, ankle and lower leg edema occurs in a variety of conditions including congestive heart failure (CHF),^{1,2} lymphedema,³ diabetes-related,^{4, 5} kidney^{6, 7} or liver disease,⁸ venous hypertension,⁹ and drug-induced.¹⁰ Quantitative assessment of edema is useful to determine treatment effectiveness in all forms of lower extremity edema including trauma related edema,¹¹ to track lymphedema and to track CHF progression in which peripheral edema may be one of a few components useful for CHF diagnosis.¹² The protein content of CHF-related peripheral edema is reported as very low¹³ so this edema is mainly due to increased interstitial fluid volume caused by elevated capillary filtration pressures. Peripheral edema has also been reported to be predictive of acute renal injury in a manner dependent on the level of assessed edema using edema grades 1-3.¹⁴

The clinical assessment of peripheral edema is largely tactile and visual. A significantly puffy and swollen limb with a smoothing of skin architecture and absence of visualized surface veins is a visual part fairly descriptive of edema presence. The tactile part resides in the pressing of the skin with a non-standard pressure for a non-standard time¹⁵ and observing either the depth of the indentation or how long the skin indentation remains after release of the pressure. Based on a combination of the visual and tactile assessments it is usual to characterize the level of the edema present as 1+, 2+, 3+, or 4+ with the numerical assignment subjectively based and dependent on the skill and experience of the evaluator. There have been some successful efforts to create more objective measures for the assessment of limb edema most of which are mainly suitable for evaluating unilateral limb edema when edema has already progressed to being visually obvious compared to the other limb. Such methods include measuring limb volumes using water displacement or calculating limb volumes based on multiple limb circumference measurements done either manually or electronically^{16, 17} and incorporating these measurements into a mathematical model representing the limb geometry.¹⁸⁻²⁰

Bioimpedance measurement methods have also evolved that use single or multiple frequencies in which limb electrical impedance ratios are used to judge the relative edema of the affected limb.²¹⁻²³ This method depends on the expected lower electrical impedance of the limb with more accumulated fluid volume. The measurement incorporates all limb contents (muscle, bone connective tissue, fluid) and often is used to evaluate an entire limb or substantial part of a limb. Contrastingly, a method that may be used to assess local tissue water on part of the limb or in fact any external body part location uses the measurement of tissue dielectric constant (TDC).²⁴⁻²⁶

However, with any of these methods, intrinsic variability in absolute values among subjects makes it difficult to determine absolute reference values that define thresholds from which early abnormal fluid increases can be detected or suitably tracked. Further and perhaps more clinically important is the fact that there is no rapid and noninvasive method that can detect early changes in lower extremity fluid prior to visual or gross changes in tissue are present. If such a method were available, it is possible that it could be used as a routine check on lower extremity fluid status as indicated for given suspected or chronic conditions. It was thus the goal of this research to introduce such a simple noninvasive measurement procedure potentially useful to characterize lower extremity edema by providing normative values from which edema thresholds might emerge, reported herein for the first time. The measurement method and process to be discussed utilizes ratios of lower extremity to upper extremity TDC values to eliminate the need for inter-limb comparisons thereby allowing for the possibility to detect early fluid changes in either unilateral or bilateral incipient edema. It should be noted that as of now the method has not been used clinically as the present goal was to develop reference ratios which from which future clinical applications would utilize.

Materials and methods

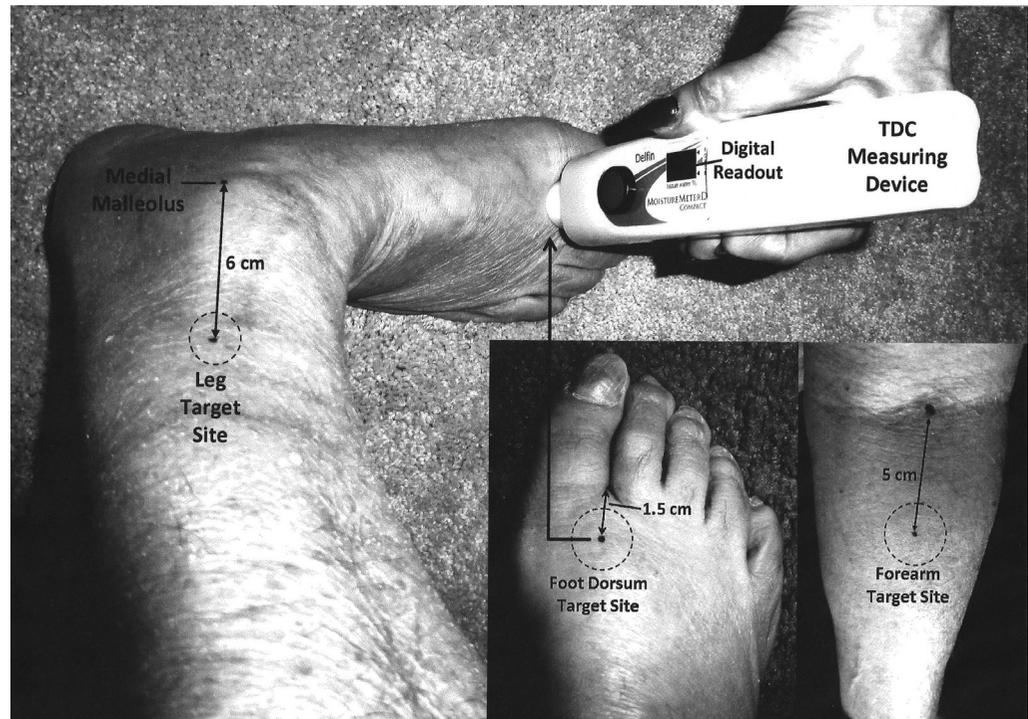
Subjects

A total of 88 healthy adults (44 female), with no evidence of lower extremity edema, participated in this study as volunteer subjects to develop the non-edematous reference leg/arm TDC ratios. Subjects participated after signing an approved Nova Southeastern University (NSU) institutional review board informed consent (#05241606F). To be included subjects needed to: 1) have no history of foot, leg or arm trauma that resulted in sustained swelling; 2) be free of any skin condition or open wound on foot, leg or arm; 3) not be taking any medication known to impact peripheral edema; and 4) not have diabetes. The dominant hand was the right hand in 90% of participants. Female ages (62.3±8.4 years; range 50-77 years) did not differ from males (62.3±8.4 years; range 50-77 years). Body Mass Indices (BMI) were greater in males than females (26.5±3.9 kg/m² vs. 29.9±4.6 kg/m², P<0.01).

Measurements

Measurements were done between the hours of 12:00 to 2:00 p.m. while subjects were supine on a padded examination table with their arms resting at their sides and shoes

Figure 1.—Tissue dielectric constant (TDC) measuring sites. The two lower extremity sites (foot and leg) and the upper extremity forearm site at which TDC values were obtained are shown.



and socks removed. Room temperature and relative humidity of the room in which measurements were done was 23.0 ± 1.7 °C and $45.9 \pm 7.2\%$ across all experiments. Three target measurement sites were marked on the subject's self-reported dominant side as illustrated in Figure 1; the anterior forearm 5 cm distal to the antecubital fossa, the medial lower leg 6 cm proximal to the medial malleolus and on the foot dorsum between the 1st and 2nd toes just proximal to their union.

Skin temperatures at each of the sites was measured first using an infrared thermometer (Exergen, Watertown Main, Model DX501-RS). Skin temperature recorded for the entire group at arm, leg and foot sites was 32.4 ± 1.2 , 31.0 ± 1.4 and 29.9 ± 2.2 respectively. Afterwards, TDC was measured after the subject had been supine for 6 ± 1 minute. The handheld battery-operated device used for TDC measurements was commercially available (MoistureMeterD Compact, Delfin, Kuopio, Finland) with an effective measurement depth of approximately two mm below the skin surface.²⁷ TDC values as indices of skin tissue water has been widely reported and validated in the literature.^{26, 28-31} Briefly, the probe acts as an open-ended coaxial transmission line through which a 300-MHz signal is transmitted. Reflected energy depend on the tissue's complex permittivity, which in-turn depends on the signal frequency and tissue dielec-

tric constant (the real part of the complex permittivity). At the frequency used, the contribution of conductivity to permittivity is small, so TDC is mainly determined by water molecules (free and bound). The device determines the dielectric constant that is proportional to tissue water. As a reference frame, distilled water at a temperature of 32 °C would have a dielectric constant of about 76. The compact device internally converts the measured TDC value to a percentage water, however for consistency to the literature all values herein reported are expressed as the unconverted TDC value. The TDC measurement procedure requires that the device sensor (20 mm diameter) at the tip of the handheld device be placed in contact with the skin for about 5 seconds (Figure 1) whereupon the reading is displayed on the device readout. A built-in pressure sensor allows for reasonably consistent applied pressures to be achieved. Triplicate measurements were taken at each of the three sites, first at forearm, then leg and lastly foot dorsum. The average of the three measurements at each site was used and taken as representative of the site TDC value.

Statistical analysis

For purposes of analysis the following definitions were used. Absolute TDC values measured at arm, leg and foot are TDC_arm, TDC_leg and TDC_foot, respectively.

This document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only one copy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distribute the electronic copy of the article through online internet and/or intranet file sharing systems, electronic mailing or any other means which may allow access to the Article. The use of all or any part of the Article for any Commercial Use is not permitted. The creation of derivative works from the Article is not permitted. It is not permitted to remove, cover, overlay, obscure, block, or change any copyright notices or terms of use which the Publisher may post on the Article. It is not permitted to frame or use framing techniques to enclose any trademark, logo, or other proprietary information of the Publisher.

TABLE I.—Composite tissue dielectric constant (TDC) values and ratios.

Parameter	Female (N.=44)	Male (N.=44)
Absolute TDC values		
Arm	27.7±4.0	33.0±5.4*
Leg	27.5±4.6	34.8±6.5*
Foot	28.7±5.1	32.5±6.5*
TDC ratios		
Foot/arm	1.042±0.160	0.990±0.144
Leg/arm	1.003±0.181	1.063±0.170
TDC ratio thresholds (mean+2SD)		
Foot/arm	1.362	1.278
Leg/arm	1.305	1.403

Values are mean±SD for absolute TDC values and their ratios.
*P<0.001 male vs. female. Thresholds are the ratios which if exceeded represent a high likelihood of edema.

Lower to upper extremity ratios were calculated as TDC_{foot}/TDC_{arm} and TDC_{leg}/TDC_{arm}. Statistical analyses were done using SPSS v. 16. The distribution of each parameter was tested for normality using the Shapiro-Wilk test for each gender separately. Results of this test showed that the distribution of all male parameters was not significantly different from Normal whereas only the TDC_{arm} and TDC_{leg} parameters were normally distributed by this test. Thus, subsequent tests for gender differences in these two parameters were based on independent non-paired *t*-tests whereas all other gender comparisons were based on the non-parametric Mann-Whitney U-test. Differences in absolute TDC values among sites was tested for using the nonparametric Friedman test. Differences between ratios for the same gender were tested for using the Wilcoxon Signed Ranks test. With all tests a P value <0.05 was taken to indicate a statistically significant difference. Threshold TDC ratios were calculated for each gender by adding to the measured mean value of TDC_{foot}/TDC_{arm} and TDC_{leg}/TDC_{arm} a value equal to twice their respective standard deviations (2SD). This is an arbitrary threshold that represents a ratio that if exceeded would deviate from the norm sufficiently to suggest a high likelihood of lower extremity edema. Other threshold levels could be calculated using the measured values if desired.

Results

Absolute TDC values by gender and anatomical site

Absolute TDC values at each anatomical site in males was greater than that measured at corresponding sites in females (P<0.001) as summarized in Table I. On average, male TDC values at arm, leg and foot were 19.1%, 26.5% and 13.2%,

respectively, greater than TDC values at corresponding sites of females. TDC values among sites were not statistically different for either the female or the male group.

TDC ratios and thresholds

Lower-to-upper limb TDC ratios (foot/arm and leg/arm) for females and males are summarized in Table I. These two ratios do not statistically differ from each other for females (P>0.05) but did for males (P<0.01). However, neither ratio differed statistically between genders. Consequently, an overall ratio that includes both male and female subjects can be calculated for each ratio (N.=88) resulting in ratios of foot/arm and leg/arm of 1.033±0.177 and 1.016±0.154 respectively. If these combined gender data are used to calculate the 2SD threshold for each ratio the result for the foot/arm threshold ratio is 1.387 and for the LEG/ARM threshold ratio is 1.324. For practical purposes these thresholds might be rounded-up to be 1.39 and 1.33, respectively. These values may be compared to the gender and ratio specific thresholds shown in Table I that range from 1.28 to 1.40.

Discussion

A main goal of this study was to investigate the possibility of developing a potentially useful measurement process that might help in the detection and quantitative assessment of lower extremity edema that could be applied in a busy clinical setting. The approach adopted was to utilize lower and upper extremity TDC measurements, as reflective of relative tissue water, to provide normal reference values for foot/forearm and leg/forearm TDC ratios. Such ratios, along with their associated standard deviations, would then form the basis of thresholds such that lower extremity/upper extremity ratios that exceed these thresholds might indicate the likely presence of edema. Because there was virtually nothing known about such measured ratios it was important to include in the measurement process both young and mature subjects of both genders. As a consequence, although a main goal was to establish threshold reference ratios, additional gender related new information also evolved.

One additional finding is the clear and substantial difference that was observed in absolute TDC values between males and females with males showing greater values at arm, leg and foot that ranged from about 13% to 26% greater. Although some previous work has reported on male-female differences in TDC values as measured on the forearm, the data herein is the first to demonstrate this

male-female difference at other anatomical sites. The prior reported TDC measurements on the forearm³² indicated male TDC values to be greater by 14.8% to 22% depending on measuring depth a feature that was potentially related to skin-thickness differences between genders. These forearm differences are consistent with the present findings.

With respect to the main goal of the present study, the threshold ratios herein determined based on the mean of the lower/upper extremity TDC ratio plus two standard deviations were shown to vary only slightly depending on anatomical site and gender. The choice of which ratio to utilize clinically depends on which ratio is being employed with specific values available in Table I. It should be noted that these threshold ratios are specifically based on values that are 2SD greater than the measured mean. In certain situations, there may be reasons to use a more conservative estimate by considering thresholds 2.5 or 3.0 SD above the mean. This is a judgement call that in general would be dependent on the application of the measurement and up to the clinician to decide. The present data set provides the basic information from which these other thresholds may easily be determined. Further, the suitability of these thresholds is subject to future assessments as to their applicability in persons with clearly defined lower extremity edema as would be present in persons with edema related complications of congestive heart failure, lower extremity lymphedema and chronic venous hypertension. The present data is aimed at serving as the initial quantitative starting points for such determinations.

Conclusions

This study describes a new measurement process potentially useful to detect and track lower extremity edema rapidly and non-invasively. The approach uses upper and lower extremity TDC measurements to provide normative values for foot/forearm and leg/forearm TDC ratios in persons of both genders. These ratios, along with their associated standard deviations, form the basis of calculated thresholds such that lower extremity/upper extremity ratios that exceed these thresholds would indicate the likely presence of edema. The suitability of these thresholds is subject to future assessments as to their applicability in persons with clearly defined lower extremity edema as would be present in persons with edema related complications of congestive heart failure, lower extremity lymphedema and chronic venous hypertension. The present data is aimed at serving as the initial quantitative starting points for such determinations.

References

- Yeboah J, Bertoni A, Qureshi W, Aggarwal S, Lima JA, Kawel-Boehm N, *et al.* Pedal Edema as an Indicator of Early Heart Failure in the Community: Prevalence and Associations With Cardiac Structure/Function and Natriuretic Peptides (MESA [Multiethnic Study of Atherosclerosis]). *Circ Heart Fail* 2016;9:e003415.
- Breidhardt T, Irfan A, Klima T, Drexler B, Balmelli C, Arenja N, *et al.* Pathophysiology of lower extremity edema in acute heart failure revisited. *Am J Med* 2012;125:1124.e1-8.
- Christenson JT, Hamad MM, Shawa NJ. Primary lymphedema of the leg: relationship between subcutaneous tissue pressure, intramuscular pressure and venous function. *Lymphology* 1985;18:86-9.
- Mayrovitz HN, McClymont A, Pandya N. Skin tissue water assessed via tissue dielectric constant measurements in persons with and without diabetes mellitus. *Diabetes Technol Ther* 2013;15:60-5.
- Chao CY, Zheng YP, Cheing GL. The association between skin blood flow and edema on epidermal thickness in the diabetic foot. *Diabetes Technol Ther* 2012;14:602-9.
- Chen C, Lee J, Johnson AE, Mark RG, Celi LA, Danziger J. Right Ventricular Function, Peripheral Edema, and Acute Kidney Injury in Critical Illness. *Kidney Int Rep* 2017;2:1059-65.
- Thanakitcharu P, Jirajan B. Early detection of subclinical edema in chronic kidney disease patients by bioelectrical impedance analysis. *J Med Assoc Thai* 2014;97(Suppl 11):S1-10.
- Pockros PJ, Reynolds TB. Rapid diuresis in patients with ascites from chronic liver disease: the importance of peripheral edema. *Gastroenterology* 1986;90:1827-33.
- Cesarone MR, Belcaro G, Nicolaidis AN, Arkans E, Laurora G, De Sanctis MT, *et al.* The edema tester in the evaluation of swollen limbs in venous and lymphatic disease. *Panminerva Med* 1999;41:10-4.
- Makani H, Bangalore S, Romero J, Htyte N, Berrios RS, Makwana H, *et al.* Peripheral edema associated with calcium channel blockers: incidence and withdrawal rate—a meta-analysis of randomized trials. *J Hypertens* 2011;29:1270-80.
- Rohner-Spengler M, Mannion AF, Babst R. Reliability and minimal detectable change for the figure-of-eight-20 method of measurement of ankle edema. *J Orthop Sports Phys Ther* 2007;37:199-205.
- Roalfe AK, Mant J, Doust JA, Barton P, Cowie MR, Glasziou P, *et al.* Development and initial validation of a simple clinical decision tool to predict the presence of heart failure in primary care: the MICE (Male, Infarction, Crepitations, Edema) rule. *Eur J Heart Fail* 2012;14:1000-8.
- Witte CL, Witte MH, Dumont AE, Cole WR, Smith JR. Protein content in lymph and edema fluid in congestive heart failure. *Circulation* 1969;40:623-30.
- Chen KP, Cavender S, Lee J, Feng M, Mark RG, Celi LA, *et al.* Peripheral Edema, Central Venous Pressure, and Risk of AKI in Critical Illness. *Clin J Am Soc Nephrol* 2016;11:602-8.
- Sanderson J, Tuttle N, Box R, Reul-Hirche HM, Laakso EL. The Pitting Test: an Investigation of an Unstandardized Assessment of Lymphedema. *Lymphology* 2015;48:175-83.
- 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;13:272-6.
- Sharkey AR, King SW, Kuo RY, Bickerton SB, Ramsden AJ, Furniss D. Measuring Limb Volume: Accuracy and Reliability of Tape Measurement Versus Perometer Measurement. *Lymphat Res Biol* 2018;16:182-6.
- Casley-Smith JR. Measuring and representing peripheral oedema and its alterations. *Lymphology* 1994;27:56-70.
- Mayrovitz HN. Limb volume estimates based on limb elliptical vs. circular cross section models. *Lymphology* 2003;36:140-3.
- Taylor R, Jayasinghe UW, Koelmeyer L, Ung O, Boyages J. Reliability and validity of arm volume measurements for assessment of lymphedema. *Phys Ther* 2006;86:205-14.

21. Cornish BH, Jacobs A, Thomas BJ, Ward LC. Optimizing electrode sites for segmental bioimpedance measurements. *Physiol Meas* 1999;20:241–50.
22. Ward L, Cornish BH, Paton NI, Thomas BJ. Multiple frequency bioelectrical impedance analysis: a cross-validation study of the inductor circuit and Cole models. *Physiol Meas* 1999;20:333–47.
23. Ward LC, Dylke E, Czerniec S, Isenring E, Kilbreath SL. Reference ranges for assessment of unilateral lymphedema in legs by bioelectrical impedance spectroscopy. *Lymphat Res Biol* 2011;9:43–6.
24. Mayrovitz HN, Davey S, Shapiro E. Local tissue water assessed by tissue dielectric constant: anatomical site and depth dependence in women prior to breast cancer treatment-related surgery. *Clin Physiol Funct Imaging* 2008;28:337–42.
25. Mayrovitz HN, Guo X, Salmon M, Uhde M. Forearm skin tissue dielectric constant measured at 300 MHz: effect of changes in skin vascular volume and blood flow. *Clin Physiol Funct Imaging* 2013;33:55–61.
26. Nuutinen J, Ikäheimo R, Lahtinen T. Validation of a new dielectric device to assess changes of tissue water in skin and subcutaneous fat. *Physiol Meas* 2004;25:447–54.
27. Mayrovitz HN, Weingrad DN, Brilit F, Lopez LB, Desfor R. Tissue dielectric constant (TDC) as an index of localized arm skin water: differences between measuring probes and genders. *Lymphology* 2015;48:15–23.
28. Aimoto A, Matsumoto T. Noninvasive method for measuring the electrical properties of deep tissues using an open-ended coaxial probe. *Med Eng Phys* 1996;18:641–6.
29. Alanen E, Lahtinen T, Nuutinen J. Measurement of dielectric properties of subcutaneous fat with open-ended coaxial sensors. *Phys Med Biol* 1998;43:475–85.
30. Athey TW, Stuchly MA, Stuchly SS. Measurement of radio frequency permittivity of biological tissues with an open-ended coaxial line: Part I. *IEEE Trans MTT* 1982;30:82–6.
31. Gabriel S, Lau RW, Gabriel C. The dielectric properties of biological tissues: II. Measurements in the frequency range 10 Hz to 20 GHz. *Phys Med Biol* 1996;41:2251–69.
32. Mayrovitz HN, Grammenos A, Corbitt K, Bartos S. Young adult gender differences in forearm skin-to-fat tissue dielectric constant values measured at 300 MHz. *Skin Res Technol* 2016;22:81–8.

Conflicts of interest.—The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Acknowledgements.—The authors would like to thank all of the volunteer participants without which this research would not have been possible.

Manuscript accepted: December 21, 2018. - Manuscript received: September 21, 2018.

This document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only one copy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distribute the electronic copy of the article through online internet and/or intranet file sharing systems, electronic mailing or any other means which may allow access to the Article. The use of all or any part of the Article for any Commercial Use is not permitted. The production of derivative works from the Article is not permitted. It is not permitted to remove, cover, overlay, obscure, block, or change any copyright notices or terms of use which the Publisher may post on the Article. It is not permitted to frame or use framing techniques to enclose any trademark, logo, or other proprietary information of the Publisher.