A Method to Assess Lower Extremity Edema Via Tissue Dielectric Constant Measurements

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ABSTRACT

**Objective:** Foot, ankle and lower leg edema occurs in many conditions including congestive heart failure, lymphedema, diabetes-related, kidney and liver disease and venous hypertension. Current clinical edema assessment methods are subjective and variable. Our goal was to introduce a new rapid, noninvasive measurement procedure that would be less sensitive to person-to-person variation and establish normal reference ranges and edema thresholds.

**Approach:** Ratios of lower-extremity to upper-extremity tissue dielectric constant (TDC) values, as indices of local tissue water ratios were measured in triplicate on foot dorsum, lower medial leg and anterior forearm. Foot/arm and leg/arm TDC ratios were determined for 108 adults with ages ≤30 (N=64) and ≥50 (N=44). Edema ratio thresholds were determined as the mean plus 2SD of each ratio for young and mature groups for females (N=64) and males (N=44).

**Main Results:** Threshold ratios varied by anatomical site, gender and age group. Foot/arm ratios of both young and mature males suggest an edema threshold ratio of 1.29. Contrastingly, leg/arm ratio thresholds for mature males was nearly 12% greater than for young males (1.47 vs. 1.31). Female data indicates a slightly higher threshold for matures (1.49 vs. 1.42). Female foot/arm data indicates a larger mature vs. young threshold ratio (1.50 vs. 1.19).

**Significance:** A new measurement process using TDC ratios to detect and track lower extremity edema rapidly and noninvasively is described. Results provide normal reference values for foot/forearm and leg/forearm TDC ratios and edema thresholds for young and mature persons of both genders. The suitability of these thresholds is subject to future validation 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. This report and data aims to serve as the initial quantitative starting point for such determinations.
INTRODUCTION

Foot, ankle or lower leg edema occurs in a variety of disparate conditions. These include congestive heart failure (CHF) (Yeboah et al., 2016; Breidthardt et al., 2012), primary lymphedema (Christenson et al., 1985), secondary lymphedema (Sawan et al., 2009; Mayrovitz et al., 2008b), diabetes-related (Mayrovitz et al., 2013b; Chao et al., 2012), kidney (Chen et al., 2017; Thanakitcharu and Jirajan, 2014) or liver (Pockros and Reynolds, 1986) disease, venous hypertension (Cesarone et al., 1999), drug-induced (Makani et al., 2011) and other conditions.

Quantitative assessment of peripheral edema is important for many reasons. It is useful to determine effectiveness of treatment for traumatically related edema (Rohner-Spengler et al., 2007) and other conditions. It is also useful to detect and track lymphedema patient status (Mayrovitz et al., 2015c) and CHF progression in which peripheral edema may be one of a few components useful for CHF diagnosis (Roalfe et al., 2012). In most cases, the protein content of CHF-related peripheral edema is reported as very low (Witte et al., 1969) so it is mainly attributable to increased interstitial fluid volume due to 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 lymphedema using edema grades 1-3 (Chen et al., 2016).

The clinical assessment of peripheral edema is largely tactile and visual. A significantly puffy and swollen limb part 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 time (Sanderson et al., 2015) 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 the edema has already progressed to nearly or actually being visually obvious compared to the other limb. Such methods include the measurement of limb volumes using water displacement (Mayrovitz et al., 2005; Sander et al., 2002) or calculating limb volumes based on multiple perimeter measurements done either manually or electronically (Mayrovitz et al., 2000; Sharkey et al., 2017) and incorporating these girth measurements into a mathematical model representing the limb geometry (Casley-Smith, 1994; Mayrovitz, 2003; Taylor et al., 2006). More recently bioimpedance measurement methods have evolved using single frequencies or multiple frequencies in which limb electrical impedance ratios are used to judge the relative edema of the affected limb (Cornish et al., 1999; Ward et al., 1999; Ward et al., 2011b). This method depends on the expected lower electrical impedance of the limb with more accumulated fluid volume. This method incorporates into its measurement the entire limb contents (muscle, bone connective tissue, fluid and etc.) and generally is only used to evaluate an entire limb or substantial portion of a limb. Contrastingly, a method that may be used to assess local tissue water on any body part uses the measurement of tissue dielectric constant (TDC) (Mayrovitz et al., 2008a; Mayrovitz et al., 2013a; Nuutinen et al., 2004).

However, with all of these methods the intrinsic variability in absolute values among subjects makes it difficult to determine true reference values that define thresholds from which early abnormal fluid increases can be detected. For limbs with unilateral edema, inter-limb
ratios of measured absolute values have proved useful both with bioimpedance (Ward et al., 2011a, b) and TDC (Mayrovitz et al., 2017; Mayrovitz et al., 2015b) methods. However, since peripheral edema often develops bilaterally especially in the lower extremities, such inter-limb ratios are not applicable. It was thus the goal of this research to introduce a new measurement procedure that would be less sensitive to person-to-person variations and to establish its normal reference ranges. The measurement method and process to be discussed utilizes ratios of lower extremity to upper extremity TDC values to minimize the effect of variation in absolute TDC values among individuals and to determine the resultant reference thresholds potentially applicable to a range of lower extremity edematous conditions.

METHODS

Subjects

A total of 108 adults participated in this study as volunteer subjects after signing an approved institutional review board informed consent. Subjects were included on the basis of age range. The YOUNG group (N = 64) had ages from 19 to 30 years with mean ± SD ages of 25.1 ± 2.2 years. The MATURE group (N = 44) included subjects with ages ≥ 50 years (62.3 ± 8.4 years; range 50-77 years). The YOUNG group was composed of 42 women and 22 men with respective ages of 24.9 ± 2.3 vs. 25.6 ± 2.1 years. The MATURE group was composed of 22 women and 22 men with respective ages of 61.7 ± 8.5 vs. 62.8 ± 8.5 years. Body mass index (BMI) for YOUNG males was less than for MATURE males (26.5 ± 3.9 Kg/m² vs. 29.9 ± 4.6 Kg/m², p < 0.01) and BMI of YOUNG females was less than for MATURE females (22.7 ± 3.8 Kg/m² vs. 29.1 ± 4.7 Kg/m², p < 0.001). 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.

**Measurements**

Measurements were done while subjects were supine on a padded examination table with their arms resting at their sides and shoes and socks removed. Room temperature and relative humidity of the room in which measurements were done was (mean ±SD) 23.0 ± 1.7 °C and 45.9 ± 7.2% across all experiments. Three target measurement sites were marked on the subject’s 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.

![Figure 1. Tissue Dielectric Constant (TDC) Measuring Sites](image-url)
The first measurements taken were the skin temperatures at each of the sites using an infrared thermometer (Exergen, Watertown Main, Model DX501-RS). Skin temperature (°C) 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. After completing skin temperature measurements, TDC measurements were started after the subject had been supine for between five and eight minutes. The device used for TDC measurements is commercially available (MoistureMeterD Compact, Delfin, Kuopio Finland) that has an effective measurement depth of approximately two mm below the skin surface (Mayrovitz et al., 2015a). The use of TDC values as an index of skin tissue water has been widely reported and validated in the literature (Aimoto and Matsumoto, 1996; Alanen et al., 1998; Athey et al., 1982; Gabriel et al., 1996; Nuutinen et al., 2004). Briefly, the probe acts as an open ended coaxial transmission line through which a 300-MHz signal is transmitted. Reflections depend on the tissue’s complex permittivity, which in-turn depends on the signal frequency and the tissue dielectric 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 hand-held device be placed in contact with the skin for 6-7 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.

Analysis

For purposes of analysis the following definitions were used. Absolute TDC values measured at
the arm, leg and foot are represented as TDC_Arm, TDC_Leg and TDC_Foot respectively. The
lower to upper extremity ratios were calculated as TDC_Foot/TDC_Arm and TDC_Leg/TDC_Arm
with these ratios being defined as TDC_F/A and TDC_L/A respectively. Statistical analyses were
done using SPSS v16. Differences in TDC values between genders and then between age-groups
was tested for at each anatomical site using independent t-tests with a significance level < 0.01
to denote a statistically significant difference. Differences in absolute TDC values among sites
was tested for using a general linear model (GLM) for repeated measures with anatomical site
as the repeated measure and age group as the between subject factor. Threshold TDC ratios
were calculated for each gender and age group 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 threshold would represent a ratio that if exceeded deviates from the
norm sufficiently to represent a high likelihood of edema presence.
RESULTS

Absolute TDC values by Gender

Absolute TDC values measured at each anatomical site in males was found to be greater than that measured at corresponding sites in females (p<0.001) as summarized in table 1. On average, male TDC values measured at arm, leg and foot were respectively 18%, 18% and 13% greater than TDC values measured at corresponding sites of females.

Absolute TDC values by age group

Considering measurements at each anatomical site, TDC values in the young and mature groups were similar to each other with no statistically significant difference detected at any site with all values as summarized in table 1.

Absolute TDC values by Anatomical Site

The GLM analysis, that included all 108 subjects, indicated an overall statistically significant difference in TDC values among anatomical sites (p =0.001) but no significant interaction between site TDC values and age group (p = 0.527). TDC values at forearm and foot dorsum were similar to each other (30.0 ± 5.1 vs. 30.2 ± 5.7) and were both significantly (p =0.008) less than that measured at the leg site (31.7 ± 6.4).

TDC Ratios and Thresholds

Table 1 summarizes foot/arm and leg/arm TDC ratios for females and males. Within gender groups, there was no statistically significant difference between young and mature groups in either foot/arm or leg/arm ratios. Within the mature female group there was a tendency for a greater foot/arm ratio than in young females (1.093 ± 0.204 vs. 1.001 ± 0.093, p=0.07). This larger mean value for mature females leads to a larger foot/arm threshold value for
the female mature group compared to young females (1.50 vs. 1.19). Contrastingly, foot/arm thresholds for males were quite similar for both young and mature groups (1.29 vs. 1.28) with a rounded threshold of 1.28 based on the combined male group. Leg/arm thresholds for both genders and both age groups tended to be greater than foot/arm thresholds with the exception of the threshold for mature females (1.49) which was similar to the foot/arm ratio (1.50).

<table>
<thead>
<tr>
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<th>FEMALE</th>
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<th>MALE</th>
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<td></td>
<td>YOUNG</td>
<td>MATURE</td>
<td>COMBINED</td>
<td>YOUNG</td>
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<tr>
<td></td>
<td>(42)</td>
<td>(22)</td>
<td>(64)</td>
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<tr>
<td>TDC_Arm</td>
<td>28.2 ± 3.1</td>
<td>27.7 ± 4.9</td>
<td>28.0 ± 3.8</td>
<td>33.9 ± 3.1**</td>
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<tr>
<td>TDC_Leg</td>
<td>30.1 ± 5.7</td>
<td>28.7 ± 5.1</td>
<td>29.6 ± 5.5</td>
<td>34.6 ± 6.4**</td>
</tr>
<tr>
<td>TDC_Foot</td>
<td>28.1 ± 2.7</td>
<td>29.8 ± 6.7</td>
<td>28.7 ± 4.5</td>
<td>33.6 ± 5.7**</td>
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<td>TDC RATIOS</td>
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<tr>
<td>TDC_F/A</td>
<td>1.001 ± 0.093</td>
<td>1.093 ± 0.204</td>
<td>1.032 ± 0.146</td>
<td>0.990 ± 0.143</td>
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<tr>
<td>TDC_L/A</td>
<td>1.067 ± 0.176*</td>
<td>1.061 ± 0.214</td>
<td>1.065 ± 0.188</td>
<td>1.017 ± 0.148</td>
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<td>TDC_RATIO THRESHOLDS</td>
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<tr>
<td>Foot/Arm</td>
<td>1.187</td>
<td>1.501</td>
<td>1.324</td>
<td>1.276</td>
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<tr>
<td>Leg/Arm</td>
<td>1.419</td>
<td>1.489</td>
<td>1.441</td>
<td>1.313</td>
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</table>

Table 1. Composite TDC values and ratios

Table entries are mean ± SD for absolute TDC values and their ratios. * p<0.01 vs. FEMALE of corresponding age-group, ** p< 0.001 vs FEMALE of corresponding age group, † P< 0.01 for differences in foot/arm vs. leg/arm ratios. Absolute TDC values were greater for males than females at all anatomical sites but ratios were similar and not statistically different. Within genders, neither TDC values or ratios differed between YOUNG and MATURE. COMBINED refers to inclusion of both YOUNG and MATURE. THRESHOLDS are the ratios which if exceeded represent a high likelihood of edema.
DISCUSSION

A main goal of this study was to develop a new measurement process that might be useful in the detection and quantitative assessment of lower extremity edema that could be usefully 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 would 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 new information also evolved.

One additional finding is the clear and substantial difference that was observed in absolute TDC values between males and females for both young and mature groups with males showing greater values at the arm and leg ranging from 15% to 21% and nearly 20% greater at the foot of young males. Although some previous work has reported on young 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 and also within a mature group. The prior reported TDC measurements on the forearm (Mayrovitz et al., 2016) 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 was shown to vary somewhat depending on anatomical site, gender and age group. Based on the near agreement in the foot/arm ratio of young and mature males the data suggests a useful threshold ratio for males is 1.29. Contrastingly, even though there was no statistically significant difference in leg/arm ratios between young and mature males, the associated threshold for mature males is nearly 12% greater than for young males (1.469 vs. 1.313) suggesting that separate thresholds should be used for leg/arm ratios for mature and young males (1.47 vs. 1.31). The leg/arm TDC data for females also indicates a slightly higher threshold for mature females (1.49 vs. 1.42). Contrastingly for females, the data indicates a large difference between mature and young foot/arm threshold ratios (1.50 vs. 1.19) that is largely due to the greater standard deviation of the mature ratios.

It should be noted that these threshold ratios are specifically based on values that are 2SD greater than the measured mean. In certain situations, a more conservative estimate may wish to be used 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 noninvasively. The approach uses upper and lower extremity TDC measurements to provide normal reference values for foot/forearm and leg/forearm TDC ratios in young and mature 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.

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REFERENCES

Aimoto A and Matsumoto T 1996 Noninvasive method for measuring the electrical properties of deep tissues using an open-ended coaxial probe Med Eng Phys 18 641-6


Casley-Smith J R 1994 Measuring and representing peripheral oedema and its alterations Lymphology 27 56-70


Chao C Y, Zheng Y P and Cheing G L 2012 The association between skin blood flow and edema on epidermal thickness in the diabetic foot Diabetes Technol Ther 14 602-9


Christenson J T, Hamad M M and Shawa N J 1985 Primary lymphedema of the leg: relationship between subcutaneous tissue pressure, intramuscular pressure and venous function Lymphology 18 86-9

Gabriel S, Lau R W and Gabriel C 1996 The dielectric properties of biological tissues: II. Measurements in the frequency range 10 Hz to 20 GHz Phys Med Biol 41 2251-69


Mayrovitz H N 2003 Limb volume estimates based on limb elliptical vs. circular cross section models Lymphology 36 140-3

Mayrovitz H N, Davey S and Shapiro E 2008a 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 28 337-42

Mayrovitz H N, Davey S and Shapiro E 2008b Localized tissue water changes accompanying one manual lymphatic drainage (MLD) therapy session assessed by changes in tissue dielectric constant inpatients with lower extremity lymphedema Lymphology 41 87-92

Mayrovitz H N, Fasen M, Spagna P and Wong J 2017 Role of handedness on forearm skin tissue dielectric constant (TDC) in relation to detection of early-stage breast cancer-related lymphedema Clin Physiol Funct Imaging

Mayrovitz H N, Grammenos A, Corbitt K and Bartos S 2016 Young adult gender differences in forearm skin-to-fat tissue dielectric constant values measured at 300 MHz Skin Res Technol 22 81-8

Mayrovitz H N, Guo X, Salmon M and Uhde M 2013a Forearm skin tissue dielectric constant measured at 300 MHz: effect of changes in skin vascular volume and blood flow Clin Physiol Funct Imaging 33 55-61
Mayrovitz H N, McClymont A and Pandya N 2013b Skin tissue water assessed via tissue dielectric constant measurements in persons with and without diabetes mellitus *Diabetes Technol Ther* **15** 60-5

Mayrovitz H N, Sims N, Litwin B and Pfister S 2005 Foot volume estimates based on a geometric algorithm in comparison to water displacement *Lymphology* **38** 20-7


Mayrovitz H N, Weingrad D N, Brlit F, Lopez L B and Desfor R 2015a Tissue dielectric constant (TDC) as an index of localized arm skin water: differences between measuring probes and genders *Lymphology* **48** 15-23


Nuutinen J, Ikaheimo R and Lahtinen T 2004 Validation of a new dielectric device to assess changes of tissue water in skin and subcutaneous fat *Physiol Meas* **25** 447-54

Pockros P J and Reynolds T B 1986 Rapid diuresis in patients with ascites from chronic liver disease: the importance of peripheral edema *Gastroenterology* **90** 1827-33

Rohner-Spengler M, Mannion A F and Babst R 2007 Reliability and minimal detectable change for the figure-of-eight-20 method of measurement of ankle edema J Orthop Sports Phys Ther 37 199-205


Sanderson J, Tuttle N, Box R, Reul-Hirche H M and Laakso E L 2015 The Pitting Test; an Investigation of an Unstandardized Assessment of Lymphedema Lymphology 48 175-83


Thanakitcharu P and Jirajan B 2014 Early detection of subclinical edema in chronic kidney disease patients by bioelectrical impedance analysis J Med Assoc Thai 97 Suppl 11 S1-10


Ward L C, Dylke E, Czerniec S, Isenring E and Kilbreath S L 2011b Reference ranges for assessment of
unilateral lymphedema in legs by bioelectrical impedance spectroscopy *Lymphat Res Biol* 9 43-6

Witte C L, Witte M H, Dumont A E, Cole W R and Smith J R 1969 Protein content in lymph and edema
fluid in congestive heart failure *Circulation* 40 623-30

Pedal Edema as an Indicator of Early Heart Failure in the Community: Prevalence and
Associations With Cardiac Structure/Function and Natriuretic Peptides (MESA [Multiethic Study
of Atherosclerosis]) *Circ Heart Fail* 9 e003415