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# Assessing Lower Extremity Lymphedema Using Upper and Lower Extremity Tissue Dielectric Constant Ratios: Method and Normal Reference Values

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## Abstract

***Background:*** Lower extremity swelling accompanies many conditions, including gynecological surgery and chronic venous dysfunction. Some clinical and quantitative assessment methods exist, but other ways to rapidly assess early lymphedema and track changes are needed. Our goal was to use lower to upper extremity intraside tissue dielectric constant (TDC) ratios with the specific aim of providing normal reference values potentially useful as a comparison measure against which persons at risk for lower extremity lymphedema might be evaluated.

***Methods and Results:*** TDC ratios (calf/forearm, foot/forearm) were measured in 44 young ($25.1 \pm 2.2$ years) and 60 mature ($60.1 \pm 11.5$ years) volunteers equally divided by gender. Foot/forearm and calf/forearm ratios did not differ between genders. For mature, values measured on dominant sides were $1.050 \pm 0.151$ and $1.013 \pm 0.162$, respectively. Lymphedema threshold ratios, calculated as the mean ratio plus twice their respective standard deviations, were for calf/forearm and foot/forearm 1.352 and 1.337, respectively. As an initial test of the thresholds, they were compared to TDC ratios determined in six patients with lower extremity edema due to congestive heart failure.

***Conclusion:*** Based on these findings, it is proposed that a calf/forearm TDC ratio that exceeds 1.35 is suggestive of lower extremity lymphedema and that the calf/forearm ratio could be used to track temporal changes and therapy-related improvements. The test of these conclusions requires future research in which these intraside TDC ratios and thresholds are evaluated in patients with lower extremity lymphedema and venous-related edema. This work provides the reference values for such comparisons to be systematically done.


**Keywords:** lymphedema, lower extremity edema, lower extremity lymphedema, tissue dielectric constant, lymphedema tracking, lymphedema detection

## Introduction

Lower extremity swelling occurs in a host of disparate conditions, including congestive heart failure (CHF),[1,2] primary lymphedema,[3] secondary lymphedema,[4,5] diabetes related,[6,7] kidney[8,9] or liver[10] disease, venous hypertension,[11] and drug induced.[12] Quantitative assessment of such edema or lymphedema is important for determining effectiveness of treatment for traumatically related edema,[13] to detect and track lymphedema in patients who have undergone gynecological[14–16] surgery, and to track CHF progression in which peripheral edema may be one of the early components useful for CHF diagnosis.[17] Although the interstitial aspects of the swelling may be different with very low protein content for CHF-related peripheral edema[18] and high protein content for lymphedema, each is associated with increased fluid content that is a target of measurement.

Clinical assessment of lower extremity edema or lymphedema is largely visual and tactile. A puffy and swollen limb in which the architecture of the skin is smoothed with the absence of surface veins provides visually descriptive evidence of edema presence. The tactile detection part relies on skin pressing usually with nonstandard pressures for usually nonstandard times[19] and observing either indentation depth or how long skin indentation remains after release of the pressure. Based on a combination of 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

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mainly subjective and largely dependent on the evaluator's skill and experience.

There has been some success in creating more objective measures, but most are mainly suitable for evaluating unilateral limb edema or lymphedema when the edema has already progressed to being visually obvious compared to the other limb. Such methods include the measurement of limb volumes using water displacement[20,21] or calculating limb volumes based on multiple perimeter measurements done either manually or electronically,[22,23] and incorporating these girth measurements into a mathematical model representing the limb geometry.[24–26] More recently, bioimpedance spectroscopy (BIS) methods have evolved using single or multiple frequencies in which limb electrical impedance ratios are used to judge the relative edema of an affected limb.[27–29]

This method depends on a lower electrical impedance of the limb with more accumulated fluid volume. BIS measures the entire limb contents (muscle, bone connective tissue, fluid, etc.) and generally is 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).[30–32]

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 that have unilateral lymphedema, interlimb ratios of measured values are reported useful with BIS[29,33] and TDC[34,35] methods. However, even with unilateral cases, in which such interlimb ratios are useful parameters, there is still a need for other discriminatory approaches. Furthermore, since lower extremity edema or lymphedema may develop bilaterally, direct use of interlimb ratios is not applicable.

It was thus the goal of this research to introduce a new measurement procedure that might be less sensitive to person-to-person variations and to establish a normal reference range of values potentially useful as a comparison measure against which persons at risk for lower extremity lymphedema might be evaluated. 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. More specifically, we sought to provide initial intraside lower to upper extremity TDC ratio reference values as a guide to subsequent assessments of patients in a clinical setting, using a protocol that would be time practical in a busy practice.

To this end, the research proceeded in two phases, the first of which utilized a group of young adults in whom extensive bilateral TDC measurements could be made at multiple upper and lower extremity sites. The specific aims of phase 1 were to determine the extent to which intraside lower to upper extremity TDC ratios differ dependent on (1) skin depth to which TDC measurements was made, (2) anatomical sites used, and (3) intraside used being dominant or nondominant. The second phase consisted of more limited measurements in a group of mature adults with only one body side used with measurements in fewer selected anatomical sites. The specific aim was to provide the needed initial reference ratios in an age group more likely to be representative of the subsequent clinical population.



## Materials and Methods

### Subjects

This research reports on 110 adult volunteer subjects who were evaluated after signing a university institutional review board-approved informed consent. The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Of the 110 subjects, 44 were young adults (YOUNG) with age (mean ± standard deviation [SD]) of 25.1 ± 2.2 years (18–30 years). This group consisted of 22 females with age and body mass index (BMI) of 24.9 ± 2.5 years and 22.3 ± 3.1 kg/m$^2$ and 22 males with age and BMI of 25.3 ± 1.8 years and 26.3 ± 4.1 kg/m$^2$. Sixty of the subjects were mature adults (MATURE) with age of 60.1 ± 11.5 years (35–83 years).

This group consisted of 30 females with age and BMI of 58.0 ± 12.0 years and 27.1 ± 4.6 kg/m$^2$ and 30 males with age and BMI of 62.2 ± 10.7 years and 28.9 ± 4.9 kg/m$^2$. Age did not statistically differ between genders for either group ($p > 0.10$), but BMI of YOUNG males was significantly ($p < 0.001$) greater than YOUNG females, whereas BMI difference between genders of MATURE were not statistically different. YOUNG were recruited mainly from first and second year medical students and MATURE were recruited from various sources, including university faculty and staff. To be considered eligible for inclusion, participants needed to be free of any present or past lower extremity major trauma, skin condition or edema or lymphedema, and not currently taking any medication that had as a side effect the possibility of causing edema.

In addition to YOUNG and MATURE, a small group of six patients (PATIENTS) who had been diagnosed with lower extremity edema secondary to CHF were evaluated. These patients included four males and two females with an age of 82 ± 13.5 years (55–92 years). These patients were evaluated as an initial preliminary test of the edema detection threshold parameters derived from the MATURE data findings to be described.

### Measurements

Measurements were done while participants were supine on a padded examination table with arms resting at their sides and shoes and socks removed. Target skin sites on lower and upper extremities were marked, room temperature and relative humidity were recorded, and skin temperature at each target skin site was measured using an infrared thermometer (Exergen, Watertown Main, Model DX501-RS). Room temperature and relative humidity across all experiments were 23.4 ± 1.1°C and 45.5 ± 6.6%.

After skin temperature measurements, TDC measurements were started after the subject had been supine for at least 5 minutes. TDC was measured using the open-ended coaxial cable method[36–40] that is commercially available as handheld compact devices that measure to approximate depths of 2 mm (MoistureMeterD compact) and 0.5 mm MoistureMeterEpiD compact, both manufactured by Delfin (Kuopio, Finland). This method has been used extensively in a variety of applications[5,30,41–51] with its validity evaluated on arms[32] and legs.[52] Briefly, a 300-MHz signal is transmitted through the probe that is in contact with the skin. Energy reflections depend on the tissue's complex permittivity, which in turn

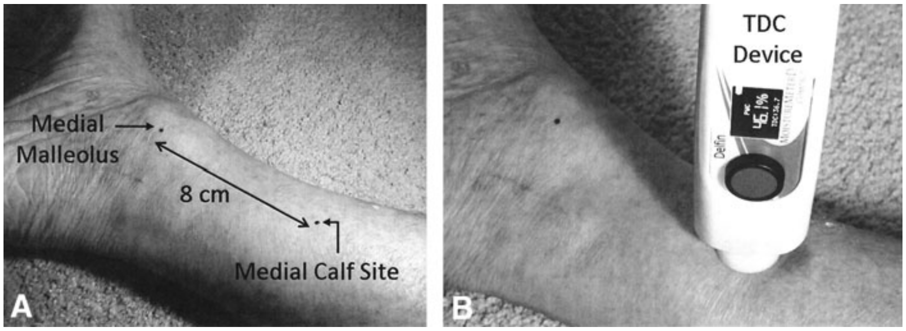


**FIG. 1.** TDC measurement. Medial calf site is shown in **(A)** with the TDC measuring device in position shown touching the skin **(B)**. Values are shown automatically on the display after about 5 seconds of skin contact of the device with the skin. The TDC device shown has an approximate effective measurement depth of 2 mm and was used on all subjects. Not shown are the foot and forearm measurement sites. TDC, tissue dielectric constant.



depends on signal frequency and the TDC (the real part of the complex permittivity).

At 300 MHz, electrical conductivity's contribution 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 frame of reference, distilled water at a temperature of 32°C has a dielectric constant of about 76. Compact devices, used in this study, internally convert the measured TDC value to a percentage water, but for consistency to the literature, all values herein reported are the unconverted TDC value. TDC measurements were made with both devices in YOUNG and only the 2 mm effective measurement depth device in MATURE. Effective measurement depth approximates the depth at which incident electromagnetic field intensity is reduced to 37% of its surface value with factors affecting it previously described.[53,54]

The number of measurement sites and depths used in MATURE was purposefully made less than for YOUNG so that the MATURE measurement set could better simulate a pattern that might actually be used in a busy clinical setting with time constraints. For YOUNG, there were three lower extremity measurement sites (foot dorsum, medial calf, and lateral calf); for MATURE, there were two (foot dorsum and medial calf). The foot dorsum site was between first and second toes just proximal to their union. The calf sites were 8 cm proximal to the center of the corresponding malleolus. For YOUNG, measurements were bilateral; for MATURE, measurements were unilateral on the dominant side. For both groups, the upper extremity measurement site was the anterior forearm 5 cm distal to the antecubital fossa. In YOUNG, an additional site was the hand palm in the center of the thenar eminence. TDC measurements on lower extremity sites were started after completing upper extremity TDC measurements.

The TDC measurement procedure requires that the probe tip be placed in contact with the skin for about 5 seconds, whereupon the value is displayed on the device readout as illustrated for the 2 mm depth probe in Figure 1. A built-in pressure sensor allows for reasonably consistent applied pressures to be achieved. Triplicate measurements were taken at each site and the average of the three was taken as the site TDC value. Absence of pitting edema in MATURE was tested using a standardized localized compression at each lower extremity measurement site.

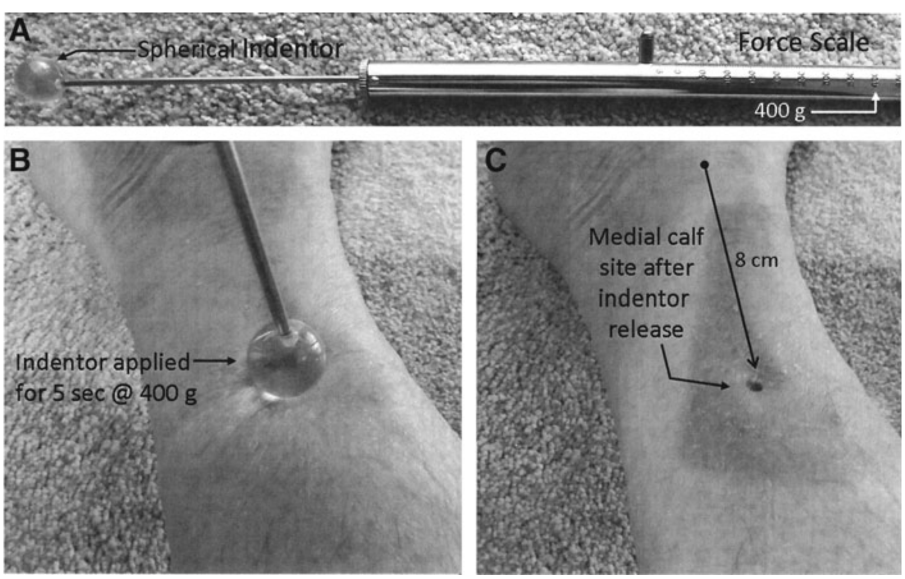


**FIG. 2.** Standardized pitting edema assessment method. Spherical indentor shown in **(A)** is applied to a target site as shown in **(B)** with a force of 400 g for 5 seconds and then released as shown in **(C)**.

Table 1. Tissue Dielectric Constant Values Measured in YOUNG at 2.0 and 0.5 mm Depths

| | YOUNG female (n=22) | | | | | | YOUNG male (n=22) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 2 mm | | | 0.5 mm | | | 2 mm | | | 0.5 mm | | |
| | DOM | NDOM | Ratio | DOM | NDOM | Ratio | DOM | NDOM | Ratio | DOM | NDOM | Ratio |
| $TDC_{ARM}$ | *28.1±3.4 | *27.6±2.9 | 1.020±0.082 | 34.4±5.1 | 34.3±4.3 | 1.011±0.158 | *33.6±2.7 | 33.7±4.5 | 1.012±0.112 | 38.6±5.9 | 36.3±5.5 | 1.067±0.105 |
| $TDC_{HAND}$ | *41.9±9.5 | *42.0±7.6 | 0.995±0.112 | 38.8±7.8 | 37.1±7.3 | 1.051±0.120 | *43.9±7.6 | 42.7±8.6 | 1.043±0.116 | 38.7±6.4 | 38.5±7.5 | 1.017±0.115 |
| $TDC_{LEG-L}$ | 39.6±5.8 | 39.7±6.6 | 1.006±0.114 | 40.9±4.2 | 39.5±5.2 | 1.041±0.067 | 38.0±6.9 | 36.9±5.1 | 1.041±0.199 | 37.0±6.5 | 37.0±6.6 | 1.013±0.161 |
| $TDC_{LEG-M}$ | *33.9±4.2 | *33.3±3.4 | 1.001±0.090 | 38.2±4.4 | 36.7±4.6 | 1.019±0.074 | 34.9±6.0 | 32.1±5.3 | 1.046±0.102 | 37.3±6.8 | 34.4±6.2 | 1.045±0.129 |
| $TDC_{FOOT}$ | 28.4±2.7 | 28.5±3.5 | 1.017±0.066 | 28.6±4.6 | 28.1±4.1 | 1.046±0.085 | 33.3±5.3 | 32.0±5.0 | 1.098±0.173 | 32.1±6.6 | 30.9±6.9 | 1.127±0.176 |

Table entries are TDC values and interside ratios (mean±SD) for DOM to NDOM sides of 22 young females and males. Measurements were at forearm ($TDC_{ARM}$), hand ($TDC_{HAND}$), lateral calf ($TDC_{LEG-L}$), medial calf ($TDC_{LEG-M}$), and foot dorsum ($TDC_{FOOT}$) made to effective depths of ~0.5 and 2 mm. TDC DOM versus NDOM absolute values did not significantly differ from each other at any site as assessed by Wilcoxon signed-ranks paired tests. Interside ratios (DOM/NDOM) also did not statistically differ among sites or between genders or measurement depth.

*TDC values at same anatomical site differed significantly ($p<0.001$) between measurements at 2 and 0.5 mm depths.

DOM, dominant; NDOM, nondominant; SD, standard deviation; TDC, tissue dielectric constant.

This was achieved by compressing the test area with spherical indentor using a standard force of 400 g utilizing a self-made calibrated device pictured in Figure 2. The spherical plastic indentor head (1.25 cm diameter) was pressed against the skin at a gram-force of 400 g for 5 seconds and released. The absence of pitting was determined by visual inspection and touch. The presence of pitting edema in PATIENTS was verified also using this device. After force release, the recovery of any pitting was timed up to 60 seconds. If recovery had not occurred by 60 seconds postrelease, the patient was verified to have significant edema.

### Analysis

For analysis purposes, the following definitions were used: TDC values at forearm, hand, medial calf, lateral calf, and foot dorsum are denoted as $TDC_{ARM}$, $TDC_{HAND}$, $TDC_{LEG-M}$, $TDC_{LEG-L}$, and $TDC_{FOOT}$, respectively. The ratio of TDC values measured at a lower extremity site to those measured at the forearm were calculated as $TDC_{FOOT}/TDC_{ARM}$, $TDC_{LEG-M}/TDC_{ARM}$, and $TDC_{LEG-L}/TDC_{ARM}$ and lower extremity to hand TDC ratios were calculated as $TDC_{FOOT}/TDC_{HAND}$, $TDC_{LEG-M}/TDC_{HAND}$, and $TDC_{LEG-L}/TDC_{HAND}$. All ratios were calculated for YOUNG and $TDC_{FOOT}/TDC_{ARM}$ and $TDC_{LEG-M}/TDC_{ARM}$ were calculated for MATURE.

For YOUNG, intraside ratios were determined for the self-reported dominant side and nondominant side, whereas for MATURE, they were determined only for the dominant side. For YOUNG, differences between dominant and nondominant side values and ratios for each gender and each TDC measurement depth were tested using nonparametric Wilcoxon signed-ranks paired tests. To account for the multiplicity of sites tested (five) a $p$-value of <0.01 was taken as evidence of a statistically significant difference. For both groups, differences in TDC ratios among anatomical sites were tested for using a general linear model for repeated measures with site overall values as the repeated measure. Threshold TDC ratios were calculated by adding to the mean value of a lower extremity/upper extremity a value equal to twice their respective SDs (2SD). This threshold would theoretically represent a ratio that if exceeded would deviate from the norm sufficiently to represent a probable edema presence. All statistical analyses were done using SPSS v16.

## Results

### TDC values and interside ratios of YOUNG

TDC measurements on YOUNG were done mainly to determine (1) if gender differences were to be expected, (2) if dominant or nondominant sides were better for use in the MATURE group, and (3) if there were differences in values or ratios to be expected dependent on tissue depth measured. Table 1 summarizes these results for the absolute TDC values and for interside ratios (dominant/nondominant) measured to approximate effective depths of 2 and 0.5 mm at each anatomical site on dominant and nondominant sides of females and males. At a depth of 2 mm, the measurement includes epidermis, dermis, and some hypodermis. At a depth of 0.5 mm, the measurement includes epidermis and some dermis.

Table 2. MATURE and YOUNG Tissue Dielectric Constant (TDC) Values and Intraside TDC Ratios

| | *MATURE* | | | | *YOUNG* | | | |
|---|---|---|---|---|---|---|---|---|
| | *Female (n = 30)* | *Male (n = 30)* | p | $T_{SKIN}$ | *Female (n = 22)* | *Male (n = 22)* | p | $T_{SKIN}$ |
| $TDC_{ARM}$ | 28.9 ± 4.1 | 33.4 ± 3.8 | <0.001 | 32.1 ± 1.5 | 27.8 ± 3.1 | 33.7 ± 3.7 | <0.001 | 32.3 ± 1.2 |
| $TDC_{LEG\text{-}M}$ | 29.4 ± 4.7 | 35.8 ± 5.2 | <0.001 | 30.3 ± 1.7 | 33.6 ± 3.8 | 33.5 ± 5.7 | 0.516 | 31.5 ± 0.9 |
| $TDC_{FOOT}$ | 29.4 ± 4.5 | 33.3 ± 4.9 | 0.002 | 29.5 ± 2.8 | 28.4 ± 3.1 | 33.5 ± 5.7 | <0.001 | 29.7 ± 2.1 |
| $TDC_{LEG\text{-}M}/TDC_{ARM}$ | 1.022 ± 0.154 | 1.078 ± 0.150 | 0.151 | | 1.137 ± 0.177 | 1.113 ± 0.176 | 0.601 | |
| $TDC_{FOOT}/TDC_{ARM}$ | 1.021 ± 0.156 | 1.006 ± 0.170 | 0.716 | | 1.015 ± 0.143 | 0.995 ± 0.113 | 0.656 | |

TDC values are mean ± SD. Measurements were at forearm ($TDC_{ARM}$), medial calf ($TDC_{LEG\text{-}M}$), and foot dorsum ($TDC_{FOOT}$) made to an effective depth of ~2 mm. MATURE TDC values are based on their dominant side; YOUNG TDC values are based on data from their combined dominant and nondominant sides. Intraside ratios for both groups ($TDC_{LEG\text{-}M}/TDC_{ARM}$ and $TDC_{FOOT}/TDC_{ARM}$) are for dominant sides. *p*-Values apply to gender comparisons within groups. $T_{SKIN}$ is skin temperature (°C) measured at TDC measurement sites. $T_{SKIN}$ progressively decreased from forearm to leg to foot ($p < 0.001$), but did not statistically differ between genders or groups.

Results of the analyses indicate that for both measurement depths, dominant versus nondominant TDC values do not significantly differ between genders (Wilcoxon signed-ranks paired tests). There were, however, differences in TDC values among sites that depended on which anatomical site was considered. For both genders, TDC values obtained at the forearm and hand to a depth of 2 mm differed significantly from those measured to a depth of 0.5 mm ($p < 0.001$). However, the direction of the differences was not the same. At forearm, TDC values measured to a depth of 2 mm were less than for those measured to a depth of 0.5 mm, whereas at the hand, the 2 mm depth value was greater. Despite these various differences in absolute TDC values, whether by site or by depth, the interside ratios dominant/nondominant did not statistically differ among sites for either gender or measurement depth.

### *TDC values and intraside ratios of MATURE and YOUNG*

TDC measurements made on MATURE were mainly done to obtain the needed normal TDC values and reference ratios in an age group more likely to be seen clinically for either lower extremity lymphedema or chronic edema. Based on our TDC measurement experience in the YOUNG, it was decided to utilize the 2 mm depth probe in the MATURE group. This decision was based on ease of use and coefficient of variation data. The absence of a difference in TDC values between DOM and NDOM in the young indicated that we could choose either the dominant or nondominant side to focus on for the MATURE measurements. A random flip of a coin decided the issue to be the dominant side.

Table 2 summarizes these results for absolute TDC values ($TDC_{ARM}$, $TDC_{LEG\text{-}M}$, and $TDC_{FOOT}$) and intraside ratios ($TDC_{LEG\text{-}M}/TDC_{ARM}$ and $TDC_{FOOT}/TDC_{ARM}$) for MATURE and also YOUNG groups for comparison. MATURE values are based on their dominant side whereas YOUNG values are based on combined dominant and nondominant sides. In MATURE, absolute TDC values of males exceeded those of females at each measured site by amounts ranging from 13.3% at the foot, 15.6% at the forearm, and 21.7% at the medial leg.

In YOUNG, absolute TDC values of males exceeded those of females at foot and forearm by 17% and 21.2%, respectively. Despite these absolute value differences, the intraside ratios did not significantly differ between genders for either MATURE or YOUNG. Combined intraside ratios (male and female, $n = 60$) for MATURE were 1.050 ± 0.151 for $TDC_{LEG\text{-}M}/TDC_{ARM}$ and 1.013 ± 0.162 for $TDC_{FOOT}/TDC_{ARM}$. Corresponding intraside ratios for YOUNG ($n = 44$) were 1.124 ± 0.176 and 1.004 ± 0.128, respectively. The distribution of these ratios was not significantly different from Gaussian as determined by the Shapiro–Wilk test for normality, with all significance levels >0.900. Based on mean values of MATURE distributions and their SDs, the 2SD threshold for lower extremity lymphedema as would be determined by $TDC_{LEG\text{-}M}/TDC_{ARM}$ is 1.352 and as would be determined by $TDC_{FOOT}/TDC_{ARM}$ is 1.337.

### *TDC values and intraside ratios of PATIENTS*

TDC measurements made on PATIENTS were done to obtain an initial test of the ‘‘theoretical’’ threshold ratios as

Table 3. PATIENT Intraside Tissue Dielectric Constant Ratios

| *Subject* | *Age (years)* | *Sex* | *BMI (kg/m²)* | $TDC_{LEG\text{-}M}/TDC_{ARM}$ | $TDC_{FOOT}/TDC_{ARM}$ |
|---|---|---|---|---|---|
| 1 | 92 | Male | 26.5 | 1.364 | 0.998 |
| 2 | 87 | Male | 22.1 | 1.602 | 1.318 |
| 3 | 84 | Female | 33.3 | 1.698 | 1.310 |
| 4 | 55 | Female | 55.2 | 1.589 | 1.511 |
| 5 | 86 | Male | 29.7 | 1.304 | 1.261 |
| 6 | 88 | Male | 27.1 | 1.880 | 1.871 |

Data are for six test patients with diagnosis of congestive heart failure, who had leg site pitting edema that did not recover the 400 g loading release fully by 60 seconds. Ratios are for the dominant side, which for all patients was their right side. TDC measurements were made using the 2 mm depth probe.

determined for the MATURE group. Although the PATIENTS did not have either lymphedema or venous-related edema, their clearly evidenced edema provided an initial test for the thresholds.

Table 3 summarizes features and intraside ratios for the test group of six PATIENTS. Except for one patient (#4), all were older than the MATURE average age and except for one other patient (#2), they were either overweight or obese as judged by their BMI values. In all, but one patient (#5), the leg-to-arm TDC ratio ($TDC_{LEG\text{-}M}/TDC_{ARM}$) exceeded the corresponding 2SD reference threshold (1.352), but the foot-to-arm ratio ($TDC_{FOOT}/TDC_{ARM}$) exceeded the threshold (1.337) in only two patients.

## Discussion

The main goal off this work was to provide suitable intraside TDC ratios to serve as reference thresholds against which persons with lower extremity lymphedema might be compared for the purpose of detection or tracking their condition. These data indicate that the two intraside TDC ratios herein evaluated (foot-to-arm and leg-to-arm) are similar in their numerical values and lead to similar threshold ratios potentially suitable to detect or quantify lower extremity lymphedema whether unilateral or bilateral. The edema detection ability of these thresholds that was tested in a small group of patients with CHF-related lower extremity edema favored the leg-to-arm TDC ratio. It would seem that this might also be true for patients with lower extremity lymphedema (venous disease-related edema) in that the lower leg is frequently involved, whereas foot swelling is not always evident.

Thus, based on these findings, we would propose that a leg/arm TDC ratio that exceeds 1.35 is suggestive of the presence of lower extremity lymphedema. Furthermore, we would propose that a reduction in this ratio could be used to track therapy-related improvements. It is to be emphasized that the validity of these concepts needs to be assessed by future research in which these, and perhaps other intraside TDC ratios, are evaluated in patients with lower extremity lymphedema or venous-related edema, which have been firmly established since the reference values herein determined are by design obtained from persons without either lymphedema or edema.

Beyond the ''theoretical'' nature of these thresholds, additional potential limitation of the approach relates to the fact that although well-defined anatomical sites were used to generate the reference ratios, the ratios and associated thresholds are strictly limited to tissues at and around those sites. If a patient's lower extremity lymphedema was manifested at sites not affecting the calf, then it is unlikely that the specific ratios herein determined would be as useful. However, magnetic resonance imaging assessments of calf subcutaneous tissue suggests that in fact, the calf is a good site for lower extremity lymphedema staging.[55]

In summary, a new method to quantitatively assess lower extremity lymphedema is proposed, which utilizes lower to upper extremity TDC ratios to judge lymphedema presence or changes with treatment. This report provides a possible set of reference values that may prove to be useful for that purpose, but a full judgment of the method's usefulness awaits future research with the threshold values being assessed in the presence of documented lower extremity lymphedema.

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## Author Disclosure Statement

No competing financial interests exist.

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