Minimum Detectable Changes Associated with Tissue Dielectric Constant Measurements as Applicable to Assessing Lymphedema Status

Harvey N. Mayrovitz, PhD, Alexander Mikulka, MS, and Don Woody

Abstract

Background: Tissue dielectric constant (TDC) measurements are increasingly being used as a tool to help characterize lymphedema features, detect its presence, and assess treatment related changes. Although the underlying physics of this technology has been well described in the literature, there has been little systematic study of in vivo reliability aspects. A central unanswered question is the minimal detectable change (MDC) that, with a given level of confidence, may be ascribed to this technology. Our goal was to address this issue using test-retest measurements from which intraclass correlations coefficients (ICC) and MDC could be estimated.

Methods and Results: Forty volunteers (20 females) aged 19–61 years with body mass indices of 14.7–47 kg/m² and body fat percentages of 12.0%–48.9% were evaluated. Two measurers (M1 and M2) used two different TDC measuring devices (multiprobe and compact) to measure TDC in triplicate sequentially and bilaterally at three locations; anterior forearm, hand palmar mid-thenar eminence, and dorsum mid-web. These measurements were made by each measurer twice constituting test-retest values (T1 and T2). From these measurements ICC and MDC at 95% confidence were determined for each site and probe for absolute TDC values and for inter-side ratios. MDC values for absolute TDC ranged from 2 to 9 TDC units, and for inter-side ratios ranged from 5.3% to 8.0% depending on site and probe. ICC values ranged from 0.765 to 0.982.

Conclusions: The MDC values herein documented may be used to provide guidance to aid interpretation of measured TDC changes or differences in a clinical environment.

Keywords: lymphedema measurement, tissue dielectric constant, measurement reliability, minimum detectable change, minimum detectable difference

Introduction

Tissue dielectric constant (TDC) measurements are increasingly being used as a tool to help characterize lymphedema features, detect its presence, and assess treatment related changes. Although the underlying physics of this technology have been described in the literature, there has been surprisingly little systematic study of in vivo reliability aspects. Because of its use to assess changes in lymphedema status resulting from various forms of therapy and other conditions the question of measurement reliability becomes increasingly important. A central question in this regard relates to the minimal detectable change (MDC) that, with a given level of confidence, may be ascribed to this technology. Our goal was to address this issue by performing test-retest measurements using two different TDC measuring devices from which intraclass correlations coefficients (ICC) and MDC could be estimated thereby providing a guide to aid interpretation of measured TDC changes or differences in a clinical environment.

Methods

Subjects

A total of 40 adult volunteers (20 females and 20 males) participated in this research study. Subjects were recruited from medical students, faculty, staff, and family through word of mouth resulting in a range of ages (19–61 years), body mass indices (14.7–47 kg/m²), body fat percentages...
(12.0%–48.9%), and total body water percentages (38.0%–
62.2%). Respective means and standard deviations (SDs)
were 26.3 ± 6.4 years, 26.0 ± 6.1 kg/m², 25.5 ± 9.1%, and
54.0 ± 5.9%. After explaining the study to potential par-
ticipants, and if they agreed to participate, they signed a
consent form that was approved by the University institu-
tional review board (IRB), and a time for participation was
scheduled. 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. To be eli-
gible for participation, potential subjects needed to be at least
18 years of age with no history of arm or hand edema or
lymphedema or any current skin condition that might impact
the planned measurements. The study was conducted from
January through July of 2018 at Nova Southeastern Uni-
versity.

**Measurers**

TDC measurements (described subsequently) were done
by two medical students who before this study had no ex-
perience using the TDC measuring devices. Operational
procedures were explained by the senior author (H.N.M.),
and they had an opportunity to utilize the devices with
H.N.M. as a subject with feedback provided regarding tech-
nique during a 1-hour training session. Subsequently, the two
measurers, denoted as M1 and M2, as part of their experience
development made all protocol measurements on five test
subjects who would not be part of the main study. The test
data were reviewed by H.N.M. for consistency with a primary
criterion that at least 80% of all triplicate measurements
demonstrated a coefficient of variation of 5% or less. This
criterion was achieved by both measurers.

**Initial study procedures**

Upon entry into a dedicated experimental room, subjects
removed their shoes and socks and stood on a body composi-
tion scale (Tanita Ironman BC558, Segmental Body Com-
position Monitor) to measure their weight, body water
percentage, total body fat percentage, and individual body
compartment fat percentages. Each subject self-reported their
age, height, and dominant hand. After this they sat on a
padded chair to which an arm rest was attached across the
front so that they could comfortably rest their arms. Room
temperature and humidity were recorded at the start of
measurements. Thereafter the TDC measurement protocol
was initiated.

**TDC measurement**

Two different TDC measuring devices were used, both
manufactured by Delfin Technologies (Kuopio, Finland).
One was the MoistureMeterD using a 2.5 mm effective depth
measuring probe, and the other was the more recently
manufactured version referred to as the MoistureMeter
Compact. TDC measurements were obtained by placing the
probe surface perpendicularly on the subject’s skin with firm
but gentle contact pressure. Measurements were done in
triplicate sequentially and bilaterally at three standardized
locations: (1) the anterior forearm 5 cm distal to the ante-
cubital fossa, (2) the center of the hand palmar thenar emi-
nence, and (3) the hand dorsum mid-web between the thumb
and index finger that was not over bone. The triplicate
measurements at each site were done by alternating between
sides sequentially, starting with the dominant side. The order
of the measurements was hand dorsum to hand palmar to
forearm. After placing the probe on the skin, a measurement
takes about 5 seconds. Anatomical sites were chosen to be
inclusive of sites used related to lymphedema and other TDC-
related measurements.2–6,24,27

The physics of TDC measurements is well described in the
literature.28,32,33,35 Briefly, a very low intensity 300 MHz
signal is transmitted from the probe in contact with the skin
and penetrates the skin to varying depths depending on the
probe used. Some incident energy is reflected to a processing
unit. In the multiprobe device it is a separate unit, and in the
compact device it is self-contained. Based on information
from the reflected wave the processor calculates the real part
of the complex permittivity of the composite tissue being
sampled. This value is the TDC that has a value strongly
dependent on the relative amount of water in the sampled
tissue. The effective penetration depth depends on the probe
design and in the present case the multiprobe effective pen-
etration depth was ~2.5 mm, whereas the compact device
used has a penetration depth of about 2 mm. Effective pen-
etration depth has been defined as that depth at which the
incident energy falls to 37% of its surface value.29

**Procedure**

Two measurers (M1 and M2) and one data recorder par-
ticipated in the protocol. The procedure was for M1 to do the
complete measurement set first using the compact probe with
M2 not present in the experimental room. After M1 com-
pleted the first measurement set M1 left the room and M2
entered and completed the first measurement set with the
compact probe. This process was then repeated with the
measurers using the multiprobe. The combined process of
measuring with the compact and multiprobe was then re-
peated so that M1 and M2 both completed two completed
measurement sets, the first designated as time 1 (T1) and the
second as time 2 (T2). At no time during the measuring
process were M1 and M2 in the experimental room at the
same time and neither knew of the values obtained by the
other. Room temperature and relative humidity of the room
were 22.3°C ± 1.0°C and 52.6% ± 4.1%.

**Analyses**

The MDC is the smallest change or difference that should
be interpreted as being real and was calculated at the 95%
confidence level using the equation

\[ \text{MDC}_{95} = 1.96 \times \text{SEM} \times \sqrt{2} \]

\[ \text{SEM} = \text{SD} \times \sqrt{(1 - \text{ICC})} \]

where SD is the standard deviation of the complete data set for T1 and T2 measurements, and
ICC is the intraclass correlation coefficient. For the present
design the appropriate generalized ICC is ICC_{2,1} calculated
based on a two-way random effects model for absolute
agreement as

\[ \text{ICC}_{2,1} = \frac{(\text{MS}_{S} - \text{MS}_{E})/\text{MS}_{S} + (K - 1)\text{MS}_{E} + K(\text{MS}_{T} - \text{MS}_{E})/n]}{\text{MS}_{E}} \]

In this equation MS_{S} is the subject mean square, MS_{E} is error mean square, MS_{T} is the trials (within)
mean square, n is the number of independent measurements,
and K is the number of measurers. All statistical analyses
were done using SPSS version 16. ICC and MDC values were
determined for the absolute TDC measurements at each site and for each probe and also for the inter-side ratios. Interarm ratios of TDC measurements have been shown to be essentially independent of a person’s handedness.5

Results

TDC values

Table 1 summarizes absolute TDC values and key ratios for each anatomical site measured by both measurers using the multiprobe 2.5 mm depth probe and the compact probe. Initial comparisons of TDC values measured on dominant and nondominant sides during first and second measurement sets (T1 and T2) showed very similar values with no statistically significant difference ($p > 0.3$) between sides or measurement times. Thus, each value in the table includes data of the combined sides and times for a total of 160 measurements (40 subjects $\times$ 2 sides $\times$ 2 measurement times). The main findings with respect to measured TDC values are as follows.

(1) For both measurers and for both probes TDC values were significantly different among anatomical sites ($p < 0.001$) with the forearm having the least TDC value and the hand palm showing the greatest TDC value.

(2) TDC values recorded by the compact probe were statistically different from that recorded by the multiprobe probe at all sites and for both measurers. However, the main difference between probes was recorded at the forearm where the compact probe TDC values exceeded the multiprobe by an average of 16.3% for measurer 1 (M1) and by 16.6% for measurer 2 (M2). At the hand sites the difference between probe values was less than 5% at the hand dorsum and less that 2% at hand palm.

(3) There was an overall statistically significant difference ($p < 0.001$) in TDC values measured by M1 and M2 at each site with percentage differences ranging from 2.0% to 4.3% for the multiprobe and 2.2% to 5% for the compact probe.

Intraclass correlation coefficients ($ICC_{2,1}$) and MDC for absolute TDC value

Table 2 summarizes ICC and MDC values for absolute TDC values for each anatomical site measured by both measurers using the multiprobe 2.5 mm depth probe and the compact probe. The main findings with respect to measured TDC values are as follows.

(1) ICC$_{2,1}$ values had a wide range which when averaged between M1 and M2 had a minimum of 0.765 at the hand dorsum when using the multiprobe and a maximum value of 0.982 at the forearm using the compact device. The corresponding largest and least minimum detectable differences are 9 and 2 TDC units, respectively.

(2) For both the multiprobe and the compact probe the least MDC is observed for measurements on the forearm (4 and 2 TDC units, respectively) and
greatest for measurements on hand dorsum (9 and 4 U, respectively).

(3) For each anatomical site measured the compact probe yielded a smaller MDC value than for the multiprobe.

Intraclass correlation coefficients (ICC$_{2,1}$) and MDC for interarm TDC ratios

Table 3 summarizes ICC and MDC values for dominant to nondominant side TDC ratios for each anatomical site measured by both measurers using the multiprobe 2.5 mm depth probe and the compact probe. The main findings with respect to TDC ratios are as follows.

(1) Average interarm ratios ranged from 0.985–0.986 on the hand palm to 1.000–1.008 on the hand dorsum with all values not differing significantly from a value of one.

(2) For both probes and most anatomical sites the ICC were less compared with corresponding values determined for absolute TDC values (Table 2).

(3) The average MDC for ratios ranged from 0.053 to 0.080 corresponding to MDC% ranging from 5.3% to 8.0% depending on anatomical site and probe used.

Table 2. Reliability Parameters Based on Test-Retest of Absolute Tissue Dielectric Constant Measurements

<table>
<thead>
<tr>
<th>Site</th>
<th>Multiprobe</th>
<th></th>
<th>Compact probe</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M1</td>
<td>M2</td>
<td>Average</td>
<td>M1</td>
</tr>
<tr>
<td>Forearm</td>
<td>0.861</td>
<td>0.935</td>
<td>0.898</td>
<td>0.983</td>
</tr>
<tr>
<td></td>
<td>1.59</td>
<td>1.09</td>
<td>1.34</td>
<td>0.48</td>
</tr>
<tr>
<td></td>
<td>4.42</td>
<td>3.03</td>
<td>3.73 (4)</td>
<td>1.32</td>
</tr>
<tr>
<td>Hand dorsum</td>
<td>0.710</td>
<td>0.820</td>
<td>0.765</td>
<td>0.948</td>
</tr>
<tr>
<td></td>
<td>3.57</td>
<td>2.82</td>
<td>3.20</td>
<td>1.16</td>
</tr>
<tr>
<td></td>
<td>9.91</td>
<td>7.81</td>
<td>8.86 (9)</td>
<td>3.21</td>
</tr>
<tr>
<td>Hand palm</td>
<td>0.892</td>
<td>0.937</td>
<td>0.915</td>
<td>0.944</td>
</tr>
<tr>
<td></td>
<td>1.75</td>
<td>1.34</td>
<td>1.55</td>
<td>1.02</td>
</tr>
<tr>
<td></td>
<td>4.86</td>
<td>3.71</td>
<td>4.29 (5)</td>
<td>2.83</td>
</tr>
</tbody>
</table>

Average, average of M1 and M2 parameters with value in parentheses of the MDC value rounded up to the next whole number; ICC$_{2,1}$, intraclass correlation coefficients; M1 and M2, measurers 1 and 2; MDC, minimal detectable change; SEM, standard error of measurement.

Table 3. Reliability Parameters Based on Test-Retest of Tissue Dielectric Constant Ratios

<table>
<thead>
<tr>
<th>Site</th>
<th>Multiprobe</th>
<th></th>
<th>Compact probe</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M1</td>
<td>M2</td>
<td>Average</td>
<td>M1</td>
</tr>
<tr>
<td>Forearm</td>
<td>0.786</td>
<td>0.750</td>
<td>0.768</td>
<td>0.816</td>
</tr>
<tr>
<td></td>
<td>0.025</td>
<td>0.032</td>
<td>0.029</td>
<td>0.019</td>
</tr>
<tr>
<td></td>
<td>0.071</td>
<td>0.089</td>
<td>0.080</td>
<td>0.052</td>
</tr>
<tr>
<td></td>
<td>0.994 (0.055)</td>
<td>0.994 (0.064)</td>
<td>0.994 (0.060)</td>
<td>1.001 (0.056)</td>
</tr>
<tr>
<td></td>
<td>1.254</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hand dorsum</td>
<td>0.785</td>
<td>0.838</td>
<td>0.812</td>
<td>0.854</td>
</tr>
<tr>
<td></td>
<td>0.025</td>
<td>0.022</td>
<td>0.024</td>
<td>0.031</td>
</tr>
<tr>
<td></td>
<td>0.068</td>
<td>0.060</td>
<td>0.064</td>
<td>0.086</td>
</tr>
<tr>
<td></td>
<td>1.011 (0.053)</td>
<td>1.005 (0.054)</td>
<td>1.008 (0.054)</td>
<td>1.009 (0.053)</td>
</tr>
<tr>
<td></td>
<td>1.234</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hand palm</td>
<td>0.816</td>
<td>0.895</td>
<td>0.856</td>
<td>0.931</td>
</tr>
<tr>
<td></td>
<td>0.030</td>
<td>0.023</td>
<td>0.027</td>
<td>0.017</td>
</tr>
<tr>
<td></td>
<td>0.083</td>
<td>0.063</td>
<td>0.073</td>
<td>0.047</td>
</tr>
<tr>
<td></td>
<td>0.979 (0.070)</td>
<td>0.990 (0.070)</td>
<td>0.985 (0.070)</td>
<td>0.984 (0.065)</td>
</tr>
<tr>
<td></td>
<td>1.273</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Parameters based on dominant to nondominant side ratios.

Average, average of M1 and M2 parameters; DOM/NDOM, dominant to nondominant side TDC ratio±(SD); Threshold is defined as the mean ratio +3 SD + MSD for a given site and probe.
Discussion

A main goal of this study was to provide useful estimates of the MDC that could be reliably taken to represent a real difference or change when measuring TDC. This undertaking was triggered by the fact that TDC measurements have been widely used and are increasingly being used in a variety of research and clinical studies but until now there has not been a systematic determination of the associated MDC. Without such clarification interpretation of findings is unnecessarily hindered.

The anatomical sites chosen for these measurements and assessments were those that are often used in the evaluation of upper limb edema or lymphedema. So that strictly speaking it is to these sites (forearm and hand) that the MDC estimates apply. Furthermore, because the test subjects were specifically chosen to be free of lymphedema for this reliability study, the extent to which the determined estimates directly apply to persons with lymphedema is unspecified. However, they importantly serve as a lower bound on expected MDC values.

In making these assessments two different TDC measuring devices were utilized. One was a multiprobe device capable of accommodating different probes that measure to differing tissue depths. The other was a compact device that is contained in single handheld device that measures to a single tissue depth. These devices, which are made by the same manufacturer, differed in construction and the depth to which they measured. The multiprobe measured to an effective depth of about 2.5 mm as specified by the manufacturer, whereas the compact probe measured to a depth of about 2 mm as previously determined. These two probes are the ones that are most widely reported in use within the literature.

The fact that absolute TDC values recorded at the forearm were greater when measured using the compact probe was confirmed through the present measurements, with the compact yielding a value of about 4.2 TDC units higher at the forearm. This difference is likely since measuring deeper will include more low-water content subcutaneous fat to be included in the measured volume. The effect would be a lower TDC reading for the 2.5 mm probe.

However for the forearm this difference is about 16.5%, whereas a prior study reported a difference of about 5.6%. There are several possibilities that may account for this difference. In the prior report the percentage difference was based on the mean difference divided by the average of the values determined by the two probes. In the present study the divisor in the calculation was the value of the 2.5 mm depth. This was used to determine the percentage that the compact exceeded the multiprobe. If percentage difference between the two measurements was determined for the present study a value of 14.2% would be calculated. Another factor that may account for the difference relates to the absolute value determined using the multiprobe. In the present study absolute TDC values measured with the compact probe (31.9 ± 3.5) on the 40 subjects (half female and half male) were similar to that previously reported (31.1 ± 2.6) measured on 64 subjects, also half female and half male. However, the multiprobe TDC values measured in the present study were less than previously measured (27.6 ± 4.3 vs. 29.4 ± 2.7). Such a difference might account for some of the discrepancies and would occur if the current subjects had a greater fraction of hypodermal fat within the measurement volume of the multiprobe. Since this was not measured this plausible reason must for now remain speculative.

Contrastingly, average TDC values at the hand differed by less than 1.0 TDC unit. The smaller probe-related difference might reflect structural differences inherent among anatomical sites. However, despite differences in absolute values measured between probes at the forearm, interarm ratios computed as dominant/nondominant side TDC values proved to be remarkably similar at all sites (Table 2). This suggests that use of either probe would yield comparable results when assessments of interarm ratios were the parameter of interest.

The MDC values summarized in Tables 2 and 3 provide the main reliability outcome of the present study. Because some research and clinical applications may utilize absolute TDC differences while others may use inter-side ratios, MDC is needed separately for each application. The results for the absolute value analysis demonstrate that MDCs are dependent on the anatomical site being evaluated and on the probe being used. For all sites measured, the compact probe had the least MDC value that ranged from 2 TDC units at the forearm to 4 TDC units at the hand dorsum.

At each site the multiprobe demonstrated a greater MDC value that ranged from 4 TDC units at the forearm to 9 TDC units at the hand dorsum. The explanation for the difference in MDC values between these two probes is speculative but probably involves at least two factors. The standard compact device has an included pressor sensor, not present in the multiprobe device, which might allow for a more uniform application pressure which in turn may have yielded a greater intraclass correlation coefficient value. In addition, because the compact probe measures to a lesser depth than the multiprobe, minor differences in contact pressure during the measurement might have less effect on the measured TDC value. This follows since a lesser depth measurement probe includes proportionately more of the homogeneous high-water content dermal region as opposed to possibly including different proportions of dermis and low-water content hypodermis as would be the case for the deeper measurement probe.

In contrast to probe-dependent MDC differences associated with absolute TDC values, probe differences in MDC were less clear as applied to interarm TDC ratios (Table 3). The compact probe average MDC was less than for the multiprobe at forearm and hand palmar but greater at the hand dorsum. Overall the MDC value for interarm TDC ratios ranged from 0.053 to 0.080. These MDC values may be used for lymphedema assessments in two separate ways. When comparing a prior measured interarm ratio to a measurement taken later or after treatment, a change in ratio needs to be greater than the MDC values specified in Table 3 to be considered a possibly real change. For example, if a presurgery interarm ratio (at-risk/contralateral) of 1.065 was measured at the forearm, using the multiprobe, then anything less than a subsequently measured ratio less than 1.065 + 0.080 or 1.145 should not be considered as a real change at the 95% confidence level. If the compact probe were being used, its smaller MDC leads to a threshold of 1.065 + 0.067 = 1.132. Similar calculations could be done for other anatomical sites of interest.

MDC values determined for interarm ratios may also help specify threshold ratios to detect lymphedema. Such thresholds have been calculated as those values that exceed normal...
reference ratio averages by at least 3 SDs. For forearm these range between 1.26–24 and 1.2938 and for hand dorsum are 1.23 for a 2 SD threshold or 1.32 for a 3 SD threshold.6 Threshold values based on the present more limited data set and calculated using the 3 SD threshold using site-dependent and probe-dependent MSD values added ranged between about 1.23 and 1.27, values similar to those previously reported.

Acknowledgments

The authors thank the many study participants without whom this research could not have come to fruition.

Author Disclosure Statement

No competing financial interests exist.

References


Address correspondence to:
Harvey N. Mayrovitz, PhD
College of Medical Sciences
Nova Southeastern University
3200 South University Drive
Ft. Lauderdale, FL 33328
E-mail: mayrovit@nova.edu