# Heat Related Changes in Skin Tissue Dielectric Constant (TDC)

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Heat Related Changes in Skin Tissue Dielectric Constant (TDC)

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SUMMARY

The impact of 20 minutes of whole-body heating (WBH) on the tissue dielectric constant (TDC) of forearm and hand skin was evaluated in 24 young adults. TDC was measured in triplicate at 300 MHz using an open-ended transmission line method in which the effective measurement depth was about 2 mm. TDC measurements are an effective way to assess and track localized edema and lymphedema. The underlying hypothesis was that heat-induced eccrine gland activation would increase TDC values via an increase in fluid within the TDC measurement volume. The goal was to test this concept and to determine the magnitude of the change when environmental temperatures were elevated to near 42°C and to estimate TDC recovery time. The practical aspect of this research is motivated by the fact that patients in whom such measurements are made may arrive at the clinic in various states of sweat gland activation. Thus, knowledge of the effect of such activation on measured TDC values permits better understanding of possible relationships between such activation and TDC values. Results showed that increasing environmental temperature from 23.3±1.6°C to 41.5±1.3°C increased forearm and thenar-eminence skin temperatures to 37.8±0.5°C and 37.9±0.4°C respectively. These changes were associated with increases in TDC at arm from 30.7±4.6 to 36.3±5.7 (18.2%) and at hand from 34.7±4.9 to 45.1±5.5 (30%). Based on calculated TDC recovery rates it is concluded that temperature-related TDC variability can be minimized using a wait-time of at least 15 minutes after bandage removal prior to TDC measurements in affected limbs.

Key Words: skin water, sweating, skin permittivity, eccrine glands, lymphedema, edema
INTRODUCTION

Prior reports have indicated that tissue dielectric constant (TDC) measurements, the values of which are highly dependent on local tissue fluid content (Aimoto & Matsumoto 1996; Alanen, et al. 1998; Gabriel, et al. 1996; Nuutinen, et al. 2004), are useful to detect (Mayrovitz 2007; Mayrovitz, et al. 2009; Mayrovitz, et al. 2014), assess (Mayrovitz 2009; Mayrovitz & Davey 2011; Mayrovitz, et al. 2008) and characterize (Koehler & Mayrovitz 2018; Mayrovitz & Weingrad 2018; Mayrovitz, et al. 2015) breast cancer treatment related lymphedema (BCRL) that is manifest in upper limbs, breast and chest wall. TDC measurements have also proved useful to evaluate edema and lymphedema of lower limbs (Birkballe, et al. 2014; Jensen, et al. 2012; Mayrovitz, et al. 2017). The method is noninvasive and easily done by touching the skin with a probe for less than 10 seconds. However, because such measurements depend on the contents of the tissue volume being measured, the extent to which eccrine sweat gland activation within such regions might affect measured TDC values is unknown. Information of this type is relevant to help achieve an informed interpretation of measured values and changes that might be observed if the state of eccrine activation changes. When activated these glands increase the amount of fluid contained within the TDC measurement area. Thus, we hypothesized that increased eccrine gland activation will result in increased values of TDC. The goal of this research was to test this hypothesis and to determine the magnitude of the increase and estimate its recovery to help interpret both physiological and clinical assessments that are based on TDC measurements.
METHODS

Subjects

Twenty-four medical students (12 females, 12 males) participated in this research after having the study explained to them and then signing an Institutional Review Board approved consent form. The age of the entire group (mean ± SD) was 24.6 ± 2.6 years with similar ages between males vs. females (24.9 ± 2.3 vs. 24.3 ± 3.0 years, p=0.378). Age range was 21 to 32 years. Body mass index (BMI) of the group was 25.5 ± 4.7 Kg/m$^2$ with a range of 18.6 to 38.3 Kg/m$^2$. There was no statistical difference in BMI between males vs. females (26.5 ± 3.9 vs. 24.6 ± 5.3 Kg/m2, p = 0.101). Participant entry requirements were being between 18 and 35 years of age and be willing to refrain from physical/strenuous activity for one hour prior to the start of their participation. Participants with any abnormal skin condition(s), history of diabetes (any form), known cardiovascular abnormality, or sensitivity to heat were not eligible for participation in this study.

Measurements

Tissue dielectric constant (TDC) was measured in triplicate on the anterior forearm and hand thenar eminence of the dominant arm as subsequently described using the MoistureMeterD compact (MMDC, Delfin Technologies, Kuopio, Finland). Each measurement was achieved by touching the probe to the skin with gentle but firm pressure for about five seconds. The average of the triplicate measurements was then calculated and used. The MMDC is a self-contained hand-held device that has a skin contact diameter 20 mm and an effective measurement depth of about 2 mm. Effective
measurement depth is defined as the depth at which the 300 MHz excitation field is diminished to 1/e of its value. The dielectric constant or relative permittivity is a dimensionless number equal to the ratio of tissue permittivity to vacuum permittivity. For reference the dielectric constant of distilled water at 32°C is approximately 76. Because TDC values mainly depend on tissue water they provide quantitative indices of skin water content. Since TDC is measured at 300 MHz its value is sensitive to both free and bound water (Pennock & Schwan 1969). Inclusion of the bound water contribution is important since up to 80–90% of young adult skin water content is bound (Gniadecka, et al. 1998).

The TDC device functions by generating and transmitting a very low power 300 MHz signal into the skin via an effective open-ended coaxial transmission line (Stuchly, et al. 1982). Part of the signal is absorbed, mainly by tissue water, and part is reflected back to permit the calculation of the complex reflection coefficient (Lahtinen, et al. 1997; Lan, et al. 2007) from which the dielectric constant is determined (Alanen, et al. 1998). Reflections depend on the complex permittivity of the tissue which in turn depend on signal frequency and the dielectric constant (the real part of the complex permittivity) and the conductivity of the tissue with which the probe is in contact. At 300 MHz, conductivity contributes little to the overall permittivity value and TDC is mainly determined by free and bound water molecules. Further details including prior uses for skin assessments, validation and repeatability data are described in the literature (Jensen, et al. 2012; Mayrovitz, et al. 2009; Mayrovitz, et al. 2013; Nuutinen, et al. 2004). Each probe is calibrated against various ethanol–water mixture concentrations each of known
dielectric constant values (Mayrovitz 2015). Skin temperatures at forearm and hand sites were measured by surface sensors (SST-1, Physitemp, Clifton NJ, USA) tapped to the skin using paper tape (3M, Micropore) and connected to a control box (Thermalert, Model TH-8, Physitemp). A typical measurement setup showing the temperature sensors in place along with the TDC measurement is shown in figure 1.

Protocol and Sequence

Baseline, preheating measurements were done while subjects were seated in a designated experimental room (control room) located within the College of Medical Sciences. Prior to measurements all subjects drank 8 fluid oz of water. A co-investigator then marked two measurement target sites on the subject’s dominant upper limb. These were located on the anterior forearm 5 cm distal to the antecubital fossa and the hand palm in the center of the thenar eminence. The ambient room temperature (TRM) and relative humidity (RH) were then recorded. Five minutes after limb marking, TDC was measured alternating between forearm and hand until three pairs of measurements were obtained. Thereafter two skin temperature sensors were affixed to the target sites with paper tape and skin temperature (TSK) was measured at each site. These temperature sensors remained in place for the duration of the experiment.

Next, the subject and two co-investigators proceed to the “heat chamber”. The heat chamber was a vehicle that was located on the upper floor of the parking lot. The transit time from the control room to the heat chamber was approximately 5 minutes. The subject sat in the rear with one co-investigator who made the TDC measurements.
with a second co-investigator in the front seat who recorded the data. TRM and RH were
recorded and TDC and TSK measured as done with baseline. All TDC measurements were
preceded by a gentle patting of the skin to remove any surface sweat that might be
present. The vehicle’s heater was turned on and set on high to increase environmental
temperature within the heat chamber. After 5-minutes of heating and every 5-minutes
thereafter until 20 minutes of heating measurements of TRM, RH, TDC and TSK were
made as previously done. After the final in-chamber measurement the subject and the
investigators proceeded back to the control room where after 5-minutes in the control
room a final measurement set was done. Because of the 5 minutes transit to the control
room this final measurement was made 10 minutes after the last in-chamber
measurement.

Analysis

Data are presented as mean ± SD unless otherwise stated. TDC differences
between genders (female vs. male) were tested using the Mann-Whitney U test and
differences between sites (forearm vs. hand) were tested using the nonparametric
Wilcoxon test. Statistical significance was inferred for p-values < 0.01. Changes in TDC
with time in the heat chamber were analyzed for the full group (N =24) using a general
linear model (GLM) and associated regression parameters. All statistical analyses were
done using SPSS version 16.
RESULTS

Temperature changes during heating

Arm, hand and environmental temperatures corresponding to each TDC measurement for males and females combined (N = 24) are shown in table 1. Pre-heated skin temperatures (°C) did not differ between males (n=12) vs. females (n=12) at forearm (32.2 ± 1.0 vs. 32.5 ± 0.9, p = 0.410) or hand (31.5 ± 1.8 vs. 32.5 ± 1.5, p=0.068). The heat chamber temperature, prior to activating the heater, was greater than in the control room (29.4 ± 2.1°C vs. 23.3 ± 1.6°C, p<0.001) since the vehicle was exposed to the outside ambient temperature with no air conditioning. Activation of the heater resulted in the temperature within the chamber to rise to 41.5 ± 1.3°C after 20 minutes of heating.

Chamber temperatures at all time points were significantly greater than in the control room (p<0.001) and displayed an environmental temperature pattern as shown in figure 2. Concomitant with the chamber temperature increase, hand and arm skin temperatures increased until 10 minutes of heating at which time arm and hand skin temperatures leveled off to average temperature of 37.8°C and 37.9°C respectively. Arm and hand skin temperatures measured outside the heat chamber in the control room 10 minutes after leaving the heat chamber (T = 30) were slightly but significantly (p<0.001) greater than initially measured values suggesting a near but incomplete recovery from the prior 20-minute heating interval. During the 10-minute recovery interval arm and hand skin average temperatures decreased by 3.1°C and 4.0°C respectively.
**Tissue dielectric constant (TDC) changes during heating**

TDC values measured on the hand were significantly greater (p<0.001) than on the arm at all time points (Table 1). With heating both arm and hand TDC values increased linearly with time in the heat chamber as shown in figure 3. The rate of TDC increase with heating was about 1.6 times greater on the hand as assessed by the slopes of the corresponding linear regression equations shown in figure 3. To assess the amount of TDC change caused by heat-induced sweat gland activation, the ratio of TDC values measured at various times within the heat chamber to those measured at the initial room temperature was calculated and plotted in figure 4. Simply being exposed to the ambient temperature of the chamber at T=0 (29.4 ± 2.1°C) was associated with 6.2 ± 3.9% and 12.3 ± 8.1% increases in arm and hand TDC values compared to those measured at the initial room temperature (23.3 ± 1.6°C). Activation of chamber heating resulted in a near linear increase in percentage increases in TDC values as shown by the regression lines of figure 4. The maximum increase occurred after 20 minutes of heating that resulted in an 18.4 ± 6.1% increase in TDC for arm and a 31.2 ± 14.5% increase in TDC for hands. During the 10-minute recovery interval (T=20 to T=30), arm and hand skin average TDC values decreased by 4.1 and 8.5 TDC units respectively. These correspond to TDC recovery rates of 0.41 and 0.85 TDC units/minute. If this recovery rate maintains, extrapolated recovery times to pre-heated TDC control values for arm would be 13.7 minutes calculated as (36.3 - 30.7)/0.41] and for hand would be 12.2 minutes calculated as (45.1 – 34.7)/0.85
Gender and Site TDC Differences

TDC values were greater in males than females for all temperatures measured on the forearm as shown in figure 5. Prior to heating male vs. female TDC values at forearm were 33.2 ± 4.1 vs. 28.2 ± 2.7, p< 0.001 and at the end of the heating cycle (T =20 minutes) these increased respectively to 39.5 ± 4.0 vs. 32.2 ± 2.7, p<0.001. At each measurement time the difference between males and females was highly significant (p<0.001). Contrastingly, measurements made on the hand tended to show a slightly higher value for males prior to heating 35.8 ± 3.6 vs. 34.1 ± 5.2, p = 0.378 and were not statistically different at any point in the heating cycle. Based on the slope of regression equations that were determined by including TDC values from the initial measurement through the end of the heating time, there was a slightly greater rate of change in TDC values for males vs. females as reflected in the regression equation coefficient shown in figure 5. This pattern was true at both measured sites (hands and arms) but for both genders the rate of change was greater at the hand than for forearm.
DISCUSSION

One motivating factor for initiating this study stems from the fact that TDC measurements are useful measures of localized edema and lymphedema but are affected by eccrine gland activation in a previously unknown way. A practical impact arises because patients in whom such measurements are made may arrive at the clinic in various states of sweat gland activation. Thus, knowledge of effects of such activation on skin TDC is important and we sought to better understand possible relationships between such activation and TDC values. The underlying hypothesis was that TDC values would increase with increasing heat-induced eccrine gland activation since TDC values are dependent on skin tissue water. However, the magnitude of the effect and the recovery time of such activation was unknown so that clarification was deemed important.

There were two major new aspects revealed by the present work. Firstly, the impact of whole-body heating on measured TDC values over a wide range of environmental temperatures was quantitatively characterized. Although impacts of whole-body heating on skin blood flow (Wilson, et al. 2002), arm blood flow (Love & Shanks 1962) and other parameters (Crandall, et al. 2000) have been reported, the present data on TDC effects is unique. Average skin temperatures achieved at the end of heating in this study (38°C) was similar to that achieved (37.9°C) by whole body heating via a water perfusion suit protocol (Wilson, et al. 2001). Studies of heat-related increases in sweating have shown heat effects to be due to combined increases in sweat gland activation density and sweat output per gland (Kondo, et al. 2001). These workers found a
near linear increase in sweat gland output measured on forearm subsequent to 60 minutes of leg immersion in water maintained at 42°C. These workers also reported an esophageal temperature associated with the onset of sweating to be 36.8°C with a corresponding skin temperature of 35.8°C. As applicable to the present study, this same skin temperature was achieved after 5 minutes of heating within the chamber suggesting that subjects began to sweat at this point and continued for their remaining 15 minutes in the chamber. Clear visual evidence of sweating was observed in all subjects.

A clear difference in forearm TDC values between genders was noted prior to heating and throughout the heating cycle with males having significantly greater TDC values at the forearm. This male-related greater value for TDC value is consistent with previously reported larger male values (Mayrovitz, et al. 2012) and has been attributed to a greater thickness of the male dermis at this anatomical site among other factor (Mayrovitz, et al. 2016). Contrastingly, measurements on the hand thenar eminence have not previously been systematically reported so the fact that these TDC values are more alike among genders is a new observation.

Once sweating began, forearm and hand skin temperatures herein measured remained relatively constant in a way similar to that observed during a 20-minute sweating observation interval in which the sweat gland density (activated glands/cm²) increased from about 18 at the sweating threshold to about 80 (Kondo, et al. 2001). These values may be compared to those summarized (Taylor & Machado-Moreira 2013) as maximum values at forearm (104 glands/cm²) and hand palm (518 glands/cm²).
Although eccrine gland properties are individually variable, average features are reported as 3.5 mm long coils with an average diameter near 40 μm, a volume of $4 \times 10^{-3} \text{ mm}^3$ (Sato & Sato 1983) and a skin surface opening with a diameter of about 70 μm (List 1948).

With increasing numbers of these eccrine glands being activated it is to be expected that the fluid volume within the tissue being measured would increase and the TDC value measured would increase as was observed in the present study. The increase in TDC would not have occurred directly by the increased skin temperature since there is an inverse relationship between the dielectric constant of water and its temperature (Malmberg & Maryott 1956). Based on the temperature dependence they reported, an increase in forearm skin temperature from baseline (32.3°C) to the end of heating (37.8°C) would result in a decrease in water's dielectric constant from 76 to 74. In fact, TDC was shown to increase not decrease. Further such small changes in water dielectric constant would have minor effects on measured TDC values. Further since the skin was patted dry prior to each TDC measurement the possible impact of skin surface wetness contributing to the elevated TDC values is not likely significant. Thus, the conclusion is that the elevation in TDC values, although not large, is mainly attributable to increased numbers of activated eccrine glands. This causes the TDC measurement to include larger volumes of free fluid that accumulates within the activated eccrine glands within the TDC epidermal-dermal-hypodermal measured volume.

A second new finding arising from this work is the estimation of the probable impact that eccrine gland activation has on TDC values in a clinical environment. Patients
requiring TDC assessments to evaluate or track their lymphedema status may arrive for such evaluations having previously being exposed to elevated outside temperatures and often with compression bandages in place. This is especially true in geographic areas with climates such as that in Florida and other sub-tropical areas and during some summer months in almost all geographic regions. This combination of heat and bandaging leads to eccrine gland activation of varying extent thereby affecting interpretation of TDC measurements. The present work does not fully account for such changes but does provide adequate data to offer likely bounds on the impact and recovery time needed to minimize eccrine activation related variability. Based on the recovery rates calculated from the relatively high heating levels herein used as heat-stimuli, a wait time of 15 minutes should be sufficient to minimize variability in TDC values attributable to heat-induced variations in TDC values. If a patient were wearing bandages on the affected limb then this wait time should start immediately after bandage removal.

The present study is not without limitations. Firstly, the study population was young and did not have edema or lymphedema. Thus, rates of change of TDC values with heating and the time to recover, apply to young adults. Recovery times may be different in older persons or in persons with lymphedema. This should be studied in a future undertaking. However, the present protocol would not be suitable for such groups but would best be conducted using a proper heat chamber in which patients could be evaluated in a bit less stressful and more controlled manner. Which points to a second limitation of the present study; use of the vehicle heating system to produce whole body
heating. This was a practical approach done in the absence of such a standard heat chamber. However, this approach met the needs for evaluating the young healthy group resulting in similar skin temperature patterns of studies using water perfusion body suits. Future studies are being planned to evaluate such patients using other heating methods but with the aid of the present findings to guide such initiatives.

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Conflict of Interest

All authors declare no conflicts of interest
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Table 1. Composite Temperature and TDC Values

Initial (T = -5) and final (T = 30) measurements were made in an experimental room with all other measurements made in the heat chamber. Table entries are mean ± SD for N = 24 subjects. RH is relative humidity. Skin temperatures and TDC values at all time points after initial measurements were statistically greater (p<0.001) than initial values at T=-5. Arm temperatures did not statistically differ from hand temperatures but TDC values differed at all time points (** = p<0.001).

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<th>Hand</th>
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<th>RH</th>
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<td>-5</td>
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<td>32.3±1.0</td>
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<td>69.7±10.9</td>
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<td>40.6±3.9**</td>
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<td>43.3±5.1**</td>
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<td>36.6±4.5**</td>
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FIGURE LEGENDS

Figure 1. Skin TDC and Temperature Measurement
In A, TDC is shown being measured on the hand thenar eminence with the skin temperature sensors in place on the forearm and the hand both connected to the temperature measuring device. In B, TDC is shown being measured on the anterior forearm 5 cm distal to the antecubital fossa.

Figure 2. Skin and Environmental Temperatures
Temperatures from 0 to 25 minutes were with subjects in the heat chamber. Temperatures at -5 and 25 minutes were outside the heat chamber. Data points are the mean for all 24 subjects. Skin temperature increased and remained above environment temperature for the 1st 10 minutes of heating. As environmental temperature increased above 37°C at 10 minutes of heating skin temperature remained essentially constant. All skin temperatures measured in the heat chamber were greater than the baseline (-5 minutes) temperature (p<0.001). Error bars are ± 1 SD.

Figure 3. Tissue Dielectric Constant (TDC) of Hands and Arms with Heating
TDC values increased linearly on arm and hand with increasing time in the heat chamber. Dotted and dashed lines are linear regression equations corresponding to hand and arm respectively with their equations indicated in the figure. TDC values on the hand were significantly greater than on the arm at all temperatures (p<0.001). Error bars are ± 1 SD.
Figure 4. TDC Values Normalized to Pre-heating Value

TDC ratios increased linearly on arm and hand with increasing time in the heat chamber. Dotted and dashed lines are linear regression equations corresponding to hand and arm respectively with their equations indicated in the figure. TDC ratios of the hand were significantly greater than on the arm at all temperatures (p<0.001). Error bars are ± 1 SD.

Figure 5. Gender and Site TDC Differences

Figure shows TDC value changes with heating for males and females via their corresponding regression lines and equations. Male values exceed female values at all times at the forearm (p<0.001) with no gender statistical difference at the hand. Males had a slightly increased rate of TDC change at both sites but the magnitude of TDC and their rate of change were greater on the hand for both genders. Error bars are ± 1 SEM.
FIGURE 1
FIGURE 2

![Graph showing temperature changes over time with different symbols representing arm, hand, and environment. The graph indicates temperature in degrees Celsius (°C) on the y-axis and minutes (M) on the x-axis. The graph includes a note indicating "In heat chamber." ]
FIGURE 3

TDC = 0.31M + 38.9, r = 0.997

TDC = 0.19M + 32.6, r = 0.999
FIGURE 4

TDC = 0.009M + 1.130
r = 0.996

TDC = 0.006M + 1.063
r = 0.998
FIGURE 5

- $TDC = 0.351M + 39.1$, $r=0.954$, $p<0.001$
- $TDC = 0.329M + 37.0$, $r=0.968$, $p<0.001$
- $TDC = 0.224M + 35.0$, $r=0.971$, $p<0.001$
- $TDC = 0.176M + 29.4$, $r=0.990$, $p<0.001$

Minutes of Heating (M)

TDC