Clin Physiol Funct Imaging (2020) **40**, pp76–82 doi: 10.1111/cpf.12605

Heat-related changes in skin tissue dielectric constant (TDC)

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Summary

The impact of 20 min 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 oedema and lymphoedema. 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 to 41·5 ± 1·3°C increased forearm and thenar eminence skin temperatures to 37·8 ± 0·5 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 min after bandage removal prior to TDC measurements in affected limbs.

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Accepted for publication

Received 4 July 2019;
accepted 25 October 2019

Key words

skin water; sweating; skin permittivity; eccrine glands; lymphoedema; oedema

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; Gabriel *et al.*, 1996; Alanen *et al.*, 1998a; Nuutinen *et al.*, 2004), are useful to detect (Mayrovitz, 2007; Mayrovitz *et al.*, 2009; Mayrovitz *et al.*, 2014), assess (Mayrovitz *et al.*, 2008; Mayrovitz, 2009; Mayrovitz & Davey, 2011) and characterize (Mayrovitz *et al.*, 2015; Koehler & Mayrovitz, 2019; Mayrovitz & Weingrad, 2018) breast cancer treatment-related lymphoedema (BCRL) that is manifest in upper limbs, breast and chest wall. TDC measurements have also proved useful to evaluate oedema and lymphoedema of lower limbs (Jensen *et al.*, 2012; Birkballe *et al.*, 2014; Mayrovitz *et al.*, 2017). The method is noninvasive and easily done by touching the skin with a probe for <10 s. 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

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24·6 ± 2·6 years with similar ages between males versus females (24·9 ± 2·3 versus 24·3 ± 3·0 years, P = 0·378). Age range was 21–32 years. Body mass index (BMI) of the group was 25·5 ± 4·7 kg/m^2 with a range of 18·6–38·3 kg/m^2. There was no statistical difference in BMI between males versus females (26·5 ± 3·9 versus 24·6 ± 5·3 kg/m^2, 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 1 h 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 5 s. 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.*, 1998b). 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 (Nuutinen *et al.*, 2004; Mayrovitz *et al.*, 2009; Jensen *et al.*, 2012; Mayrovitz *et al.*, 2013). 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 Fig. 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 centre of the thenar eminence. The ambient room temperature (TRM) and relative humidity (RH) were

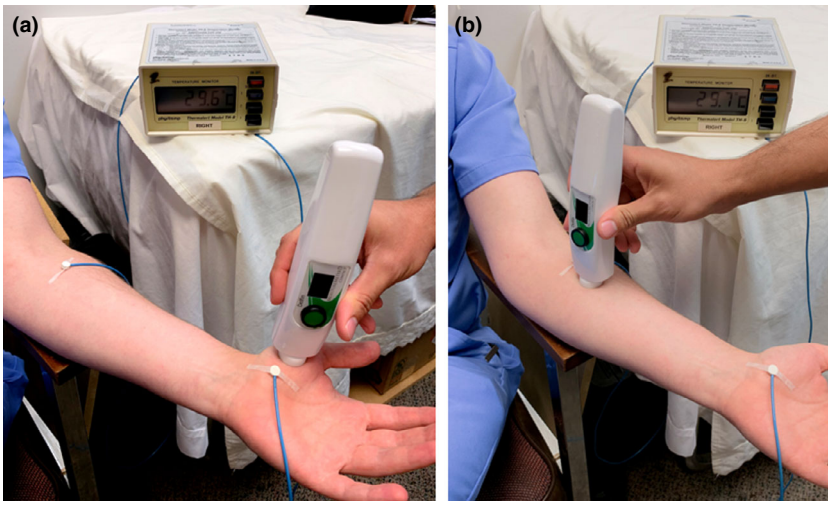

Figure 1 Skin TDC and Temperature Measurement. In (a) TDC is shown being measured on the hand thenar eminence with the skin temperature sensors in place on the forearm and the hand both connected to the temperature measuring device. In (b) TDC is shown being measured on the anterior forearm 5 cm distal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

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 min. 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 min of heating and every 5 min thereafter until 20 min 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 min in the control room a final measurement set was done. Because of the 5 min transit to the control room, this final measurement was made 10 min after the last in-chamber measurement.

Analysis

Data are presented as mean ± SD unless otherwise stated. TDC differences between genders (female versus male) were tested using the Mann–Whitney U-test and differences between sites (forearm versus 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 analysed 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. Preheated skin temperatures (°C) did not differ between males (n = 12) versus females (n = 12) at forearm (32·2 ± 1·0 versus 32·5 ± 0·9, P = 0·410) or hand (31·5 ± 1·8 versus 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 versus 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 min 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 Fig. 2. Concomitant with the chamber temperature increase, hand and arm skin temperatures increased until 10 min of heating at which time arm and hand skin temperatures levelled off to average temperature of 37·8 and 37·9°C, respectively. Arm and hand skin temperatures measured outside the heat chamber in the control room 10 min 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-min heating interval. During the 10-min recovery interval, arm and hand skin average temperatures decreased by 3·1 and 4·0°C, respectively.

TDC changes during heating

Tissue dielectric constant values measured on the hand were significantly greater (P<0·001) than on the arm at all time

Table 1 Composite temperature and TDC values.

	Temperatures (°C)			TDC Values		
Time (T, min)	Environment	Arm	Hand	Arm	Hand	RH
−5	23·3 ± 1·6	32·3 ± 1·0	31·6 ± 1·4	30·7 ± 4·6	34·7 ± 4·9**	49·6 ± 3·8
0	29·4 ± 2·1	34·5 ± 1·6	34·1 ± 1·2	32·5 ± 4·6	38·7 ± 4·1**	69·7 ± 10·9
5	34·4 ± 2·7	37·2 ± 1·4	36·5 ± 1·2	33·6 ± 5·0	40·6 ± 3·9**	64·6 ± 13·5
10	38·0 ± 2·8	38·0 ± 1·0	37·6 ± 0·8	34·5 ± 5·0	42·1 ± 4·8**	58·3 ± 13·0
15	40·1 ± 2·1	37·9 ± 0·6	37·8 ± 0·5	35·3 ± 5·5	43·3 ± 5·1**	55·4 ± 12·0
20	41·5 ± 1·3	37·8 ± 0·5	37·9 ± 0·4	36·3 ± 5·7	45·1 ± 5·5**	55·6 ± 9·5
30	24·3 ± 2·7	34·7 ± 2·6	33·9 ± 0·8	32·2 ± 4·7	36·6 ± 4·5**	47·1 ± 7·3

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).

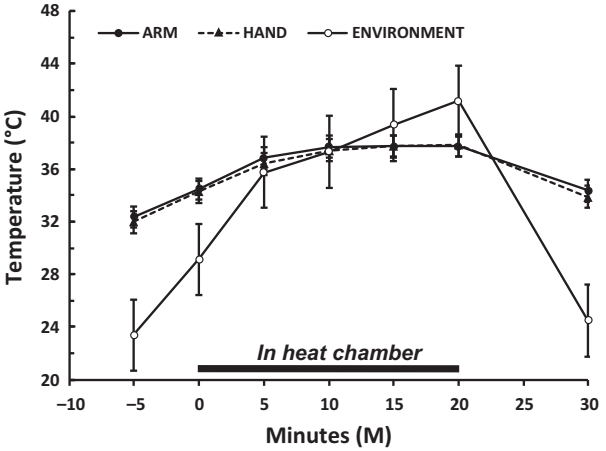

Figure 2 Skin and Environmental Temperatures. Temperatures from 0 to 25 min were with subjects in the heat chamber. Temperatures at −5 and 25 min were outside the heat chamber. Data points are the mean for all 24 subjects. Skin temperature increased and remained above environment temperature for the 1st 10 min of heating. As environmental temperature increased above 37°C at 10 min of heating skin temperature remained essentially constant. All skin temperatures measured in the heat chamber were greater than the baseline (−5 min) temperature (P<0·001). Error bars are ± 1 SD.

points (Table 1). With heating, both arm and hand TDC values increased linearly with time in the heat chamber as shown in Fig. 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 Fig. 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

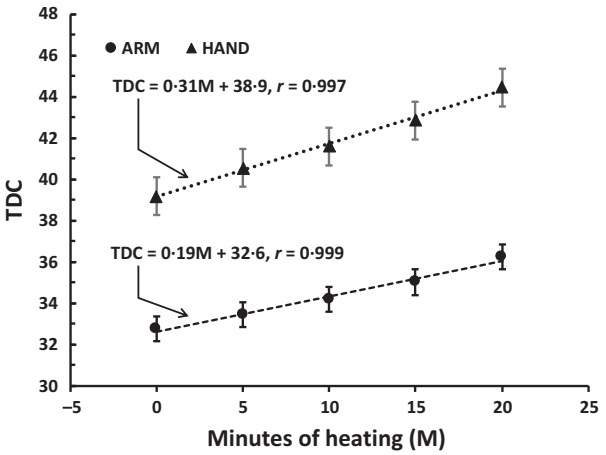

Figure 3 Tissue Dielectric Constant (TDC) of Hands and Arms with Heating. Tissue dielectric constant values increased linearly on arm and hand with increasing time in the heat chamber. Dotted and dashed lines are linear regression equations corresponding to hand and arm, respectively, with their equations indicated in the figure. Tissue dielectric constant values on the hand were significantly greater than on the arm at all temperatures (P<0·001). Error bars are ± 1 SD.

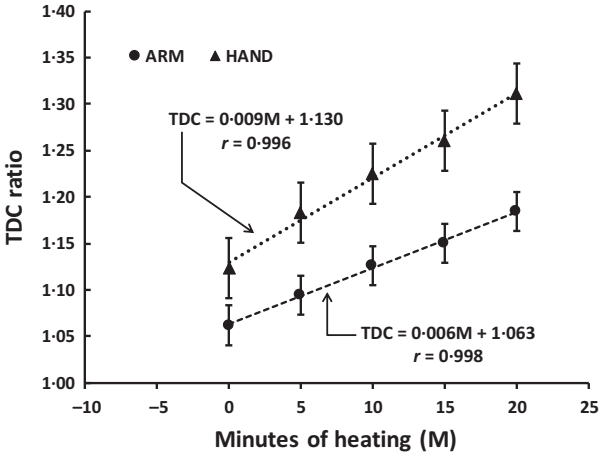

Figure 4 Tissue dielectric constant Values Normalized to Preheating Value. Tissue dielectric constant ratios increased linearly on arm and hand with increasing time in the heat chamber. Dotted and dashed lines are linear regression equations corresponding to hand and arm, respectively, with their equations indicated in the figure. Tissue dielectric constant ratios of the hand were significantly greater than on the arm at all temperatures (P<0·001). Error bars are ± 1 SD.

Fig. 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 Fig. 4. The maximum increase occurred after 20 min 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-min 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/min. If this recovery rate maintains, extrapolated recovery times to preheated TDC control values for arm would be 13·7 min calculated as (36·3–30·7)/0·41 and for hand would be 12·2 min calculated as (45·1–34·7)/0·85.

Gender and site TDC differences

Tissue dielectric constant values were greater in males than females for all temperatures measured on the forearm as shown in Fig. 5. Prior to heating, male versus female TDC values at forearm were 33·2 ± 4·1 versus 28·2 ± 2·7, P<0·001, and at the end of the heating cycle (T = 20 min), these increased, respectively, to 39·5 ± 4·0 versus 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 versus 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

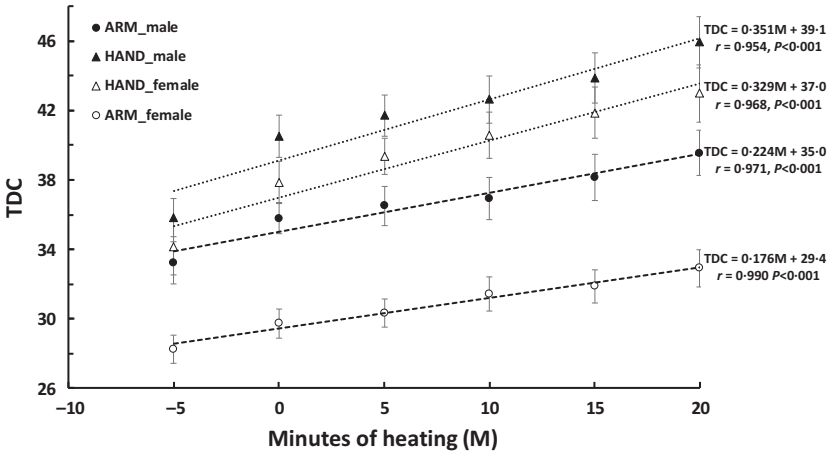

Figure 5 Gender and Site TDC Differences. Figure shows TDC value changes with heating for males and females via their corresponding regression lines and equations. Male values exceed female values at all times at the forearm ($P<0{\cdot}001$) with no gender statistical difference at the hand. Males had 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.

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 versus females as reflected in the regression equation coefficient shown in Fig. 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 oedema and lymphoedema 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 were 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 are 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 min of leg immersion in water maintained at 42°C. These workers also reported an oesophageal 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 min of heating within the chamber suggesting that subjects began to sweat at this point and continued for their remaining 15 min 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 factors (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-min sweating observation interval in which the sweat gland density (activated glands/cm^2) 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/cm^2) and hand palm (518 glands/cm^2). 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 4×10^{-3} 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 lymphoedema 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 subtropical 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 min 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 oedema or lymphoedema. 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 lymphoedema. 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. That 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.

Acknowledgments

The authors should like to thank the volunteer participants in this study without whom this research could not have been completed.

Conflict of interest

All authors declare no conflicts of interest.

References

Aimoto A, Matsumoto T. Noninvasive method for measuring the electrical properties of deep tissues using an open-ended coaxial probe. *Med Eng Phys* (1996); **18**: 641–646.

Alanen E, Lahtinen T, Nuutinen J. Measurement of dielectric properties of subcutaneous fat with open-ended coaxial sensors. *Phys Med Biol* (1998a); **43**: 475–485.

Alanen E, Lahtinen T, Nuutinen J. Variational formulation of open-ended coaxial line in contact with layered biological medium. *IEEE Trans Biomed Eng* (1998b); **45**: 1241–1248.

Birkballe S, Jensen MR, Noerregaard S, *et al*. Can tissue dielectric constant measurement aid in differentiating lymphoedema from lipoedema in women with swollen legs? *Br J Dermatol* (2014); **170**: 96–102.

Crandall CG, Zhang R, Levine BD. Effects of whole body heating on dynamic baroreflex regulation of heart rate in humans. *Am J Physiol Heart Circ Physiol* (2000); **279**: H2486–H2492.

Gabriel S, Lau RW, Gabriel C. The dielectric properties of biological tissues: II. Measurements in the frequency range 10 Hz to 20 GHz. *Phys Med Biol* (1996); **41**: 2251–2269.

Gniadecka M, Faurskov Nielsen O, Christensen DH, *et al*. Structure of water, proteins, and lipids in intact human skin, hair, and nail. *J Invest Dermatol* (1998); **110**: 393–398.

Jensen MR, Birkballe S, Norregaard S, *et al*. Validity and interobserver agreement of lower extremity local tissue water measurements in healthy women using tissue dielectric constant. *Clin Physiol Funct Imaging* (2012); **32**: 317–322.

Koehler LA, Mayrovitz HN. Spatial and temporal variability of upper extremity edema measures after breast cancer surgery. *Lymphat Res Biol* (2019); **17**: 308–315.

Kondo N, Shibasaki M, Aoki K, *et al*. Function of human eccrine sweat glands during dynamic exercise and passive heat stress. *J Appl Physiol* (1985) (2001); **90**: 1877–1881.

Lahtinen T, Nuutinen J, Alanen E. Dielectric properties of the skin. *Phys Med Biol* (1997); **42**: 1471–1472.

Lan CC, Yu HS, Huang SM, *et al*. FK506 induces interleukin-6 secretion from UVB irradiated cultured human keratinocytes via p38 mitogen-activated protein kinase pathway: implication on mechanisms of

tacrolimus-induced skin irritation. *J Dermatol Sci* (2007); **48**: 225–228.

List CF. Physiology of sweating. *Annu Rev Physiol* (1948); **10**: 387–400.

Love AH, Shanks RG. The relationship between the onset of sweating and vasodilatation in the forearm during body heating. *J Physiol* (1962); **162**: 121–128.

Malmberg CJ, Maryott AA. Dielectric constant of water from 0° to 100° C. *J Res Natl Bur Stand* (1956); **56**: 1–8.

Mayrovitz HN. Assessing local tissue edema in postmastectomy lymphedema. *Lymphology* (2007); **40**: 87–94.

Mayrovitz HN. Assessing lymphedema by tissue indentation force and local tissue water. *Lymphology* (2009); **42**: 88–98.

Mayrovitz HN. Assessing free and bound water in skin at 300 MHz using tissue dielectric measurements with the MoistureMeterD. In: *Lymphedema: Presentation, Diagnosis, and Treatment Springer* (eds Greene AK, Brorson H, Slavin SA) (2015) pp. 133–148. Springer International Publishing Switzerland, New York.

Mayrovitz HN, Davey S. Changes in tissue water and indentation resistance of lymphedematous limbs accompanying low level laser therapy (LLLT) of fibrotic skin. *Lymphology* (2011); **44**: 168–177.

Mayrovitz HN, Weingrad DN. Tissue dielectric constant ratios as a method to characterize truncal lymphedema. *Lymphology* (2018); **51**: 125–131.

Mayrovitz HN, Davey S, Shapiro E. 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* (2008); **41**: 87–92.

Mayrovitz HN, Davey S, Shapiro E. Suitability of single tissue dielectric constant measurements to assess local tissue water in normal and lymphedematous skin. *Clin Physiol Funct Imaging* (2009); **29**: 123–127.

Mayrovitz HN, Weingrad DN, Davey S. Local tissue water in at-risk and contralateral forearms of women with and without breast cancer treatment-related lymphedema. *Lymphat Res Biol* (2009); **7**: 153–158.

Mayrovitz HN, Bernal M, Carson S. Gender differences in facial skin dielectric constant measured at 300 MHz. *Skin Res Technol* (2012); **18**: 504–510.

Mayrovitz HN, Guo X, Salmon M, *et al*. Forearm skin tissue dielectric constant measured at 300 MHz: effect of changes in skin vascular volume and blood flow. *Clin Physiol Funct Imaging* (2013); **33**: 55–61.

Mayrovitz HN, Weingrad DN, Davey S. Tissue dielectric constant (TDC) measurements as a means of characterizing localized tissue water in arms of women with and without breast cancer treatment related lymphedema. *Lymphology* (2014); **47**: 142–150.

Mayrovitz HN, Weingrad DN, Lopez L. Patterns of temporal changes in tissue dielectric constant as indices of localized skin water changes in women treated for breast cancer: a pilot study. *Lymphat Res Biol* (2015); **13**: 20–32.

Mayrovitz HN, Grammenos A, Corbitt K, *et al*. Young adult gender differences in forearm skin-to-fat tissue dielectric constant values measured at 300 MHz. *Skin Res Technol* (2016); **22**: 81–88.

Mayrovitz HN, Volosko I, Sarkar B, *et al*. Arm, leg, and foot skin water in persons with diabetes mellitus (DM) in relation to HbA1c assessed by tissue dielectric constant (TDC) technology measured at 300 MHz. *J Diabetes Sci Technol* (2017); **11**: 584–589.

Nuutinen J, Ikaheimo R, Lahtinen T. Validation of a new dielectric device to assess changes of tissue water in skin and subcutaneous fat. *Physiol Meas* (2004); **25**: 447–454.

Pennock BE, Schwan HP. Further observations on the electrical properties of hemoglobin-bound water. *J Phys Chem* (1969); **73**: 2600–2610.

Sato K, Sato F. Individual variations in structure and function of human eccrine sweat gland. *Am J Physiol* (1983); **245**: R203–R208.

Stuchly MA, Athey TW, Samaras GM, *et al*. Measurement of radio frequency permittivity of biological tissues with an open-ended coaxial line: Part II - Experimental Results. *IEEE Trans Microw Theory Tech* (1982); **30**: 87–92.

Taylor NA, Machado-Moreira CA. Regional variations in transepidermal water loss, eccrine sweat gland density, sweat secretion rates and electrolyte composition in resting and exercising humans. *Extrem Physiol Med* (2013); **2**: 4.

Wilson TE, Cui J, Crandall CG. Absence of arterial baroreflex modulation of skin sympathetic activity and sweat rate during whole-body heating in humans. *J Physiol* (2001); **536**: 615–623.

Wilson TE, Cui J, Crandall CG. Effect of whole-body and local heating on cutaneous vasoconstrictor responses in humans. *Auton Neurosci* (2002); **97**: 122–128.