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NOTE

Diurnal changes in local skin water assessed via tissue dielectric constant at 300 MHz

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Abstract

Objective. Skin tissue dielectric constant (TDC) measurements are largely dependent on tissue water content. Because TDC measurements and their inter-side ratios are used for a variety of clinical and research purposes we believe that knowledge of potential TDC diurnal variations could be useful. Because of the strong water-dependency of TDC values, our operative hypothesis was that the absolute TDC measured in upper body areas would progressively decrease during the day whereas TDC values in lower extremities would progressively increase during the day. Our goal was to test this hypothesis and determine the degree of inter-side symmetry. *Approach.* TDC values to a skin depth of 2.0–2.5 mm were self-measured hourly starting at 0800 and ending at 2000 h at four anatomical sites by 12 women who were trained and experienced in the measurement method. Measurements were done bilaterally in triplicate below the eye, mid-cheek, forearm and calf. An assessment of temporal changes in TDC values and inter-side TDC ratios was done via regression and ANOVA. *Main results.* TDC values from the eye, cheek and forearm progressively decreased (correlation coefficient, R, 0.708 to 0.941). Morning-to-night decreases were $11.2 \pm 8.3\%$, $6.8 \pm 5.7\%$ and $5.6 \pm 6.0\%$ respectively. TDC values from the calf progressively increased ($R = 0.864$) with a morning-to-night TDC increase of $9.3 \pm 10.7\%$. In contrast, TDC inter-side ratios (dominant side to nondominant side) were stable over the 13 h monitoring interval with no evidence of significant temporal change. Morning TDC side-averaged values were for the eye, cheek, forearm and calf values averaged 53.8 ± 8.8, 56.7 ± 9.8, 40.6 ± 6.7 and 41.1 ± 4.9 respectively. *Significance.* Three major outcomes of the present study emerge: (1) the findings demonstrate a previously unestablished gravity dependent skin-water shift via TDC measurement, (2) an estimate of time-of-day TDC differences is provided, and (3) the insensitivity of inter-side TDC ratios to time-of-day is demonstrated, thereby providing confidence in TDC ratios obtained at different times of day.

Introduction

Ultrasound measurements made in the morning and then 12 h later suggested diurnal changes in forearm skin water in older persons (Gniadecka *et al* 1994a). Greater changes were found in younger persons, especially in gravitationally-stressed lower limbs, where an unexpected decrease in skin water content was found (Gniadecka *et al* 1994b). These assessments used the concept that more echogenic pixels reflect greater dermal water content. Others used skin thickness measurements to assess morning-to-afternoon 6–7 h diurnal skin water changes of upper versus lower body (Tsukahara *et al* 2001). Such measurements, made in young women and men reveal morning-to-afternoon decreases in upper-body skin thickness (face and arm) but increases in lower-body skin thickness (thigh and calf). Another method to evaluate skin water changes is by measuring the skin tissue dielectric constant (TDC) (Nuutinen *et al* 2004) which, because of its ease of measurement, permits tracking of skin water changes more frequently than would be practical with ultrasound and other imaging modalities. Because TDC measurements are used to assess skin water and its change in a variety of conditions including edema and lymphedema detection and assessment (Nuutinen *et al* 1998, Petaja *et al* 2003, Mayrovitz *et al* 2007, 2015c, 2016c, Lahtinen *et al*

2015) knowledge of its potential diurnal variation would be useful. Based on physiological principles coupled with the limited amount of skin ultrasound data (Gniadecka *et al* 1994a, 1994b, Tsukahara *et al* 2001) the operative hypothesis is that skin water in the upper body would tend to progressively decrease during the day whereas skin water in the lower extremities would tend to progressively increase during the day. The goal of the present research was to test this hypothesis based on data obtained from multiple morning-to-night hourly measurements of TDC and to assess TDC inter-side symmetry.

Methods

Participants

Twelve young healthy adult women participated in this self-measurement study. The women were all first-year medical students who had been trained in the use of the measurement device and had used the device in at least one unrelated research project prior to their current self-measurements. No participant had had a previous facial procedure of any type or had any prior or current skin condition. All participants indicated that they routinely used sunscreen and used anti-aging soaps or creams. No products were applied on the day of the measurements.

The main group features (mean ± SD) were: age 26.2 ± 1.4 years, body mass index 21.8 ± 2.0 kg m^{-2}, total body fat percentage 29.5 ± 3.5%, total body water percentage 51.9 ± 2.5% and Fitzpatrick skin score 27.5 ± 4.4 (Fasugba *et al* 2014). Body fat and water percentages were determined using bioimpedance measurements at 50 kHz (InnerScan Body Composition Monitor, Tanita model BC558).

Measurement device

The tissue dielectric constant (TDC) was measured at 300 MHz at each skin site using the MoistureMeterD Compact device (MMDC, 1081) manufactured by Delfin Technologies, Kuopio, Finland. The frequency of 300 MHz was intrinsic to the device and was not chosen for some other purpose. The TDC, also known as relative permittivity, is the ratio of the dielectric constant of the measured tissue to that of a vacuum and as a ratio is dimensionless. The MMDC functions as an open-ended coaxial transmission line (Stuchly *et al* 1982, Aimoto and Matsumoto 1996, Alanen *et al* 1998a) and this particular device measures to an effective depth below the skin surface of about 2.0–2.5 mm. The effective depth is defined as the depth at which the excitation field within the tissue is reduced to 1/e of its surface value (Mayrovitz *et al* 2015a). The device displays values as percentage water but the present results give the actually measured TDC value, which for reference, is about 76 for water at 32 °C. At 300 MHz the TDC values are sensitive to both free (mobile) and bound water in the measured volume (Schwan 1965, Pennock and Schwan 1969). Several reports regarding the physics (Stuchly *et al* 1981, Athey *et al* 1982, Aimoto and Matsumoto 1996, Alanen *et al* 1998b, Nuutinen *et al* 2004) and use of TDC measurements are available (Jensen *et al* 2012, Mayrovitz *et al* 2015b, 2016a, 2016b). The device used herein was tested against known values of various ethanol–water concentrations to insure intrinsic accuracy, with data agreeing with published values within ±2.5%. In use, the device is applied firmly but gently perpendicular to the skin for about 8–10 s whereupon the 300 MHz signal generated in the device is transmitted to the tissue with a portion of the incident electromagnetic wave reflected. The reflections depend on the signal frequency and on 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, the contribution of the conductivity to the overall value of the permittivity is small. Consequently, the device includes and analyzes mainly the dielectric constant (TDC) that is directly proportional to tissue water content of the interrogated tissue volume.

Skin measurement sites

Four skin sites were measured on both body sides; two on the face (peri-eye and mid-cheek) as illustrated in figure 1(A), one on the anterior forearm (5 cm distal to the antecubital fossa) as shown in figure 1(B) and one on the medial calf (10 cm proximal to the medial malleolus). The peri-eye site was about 1.5 cm below the lower lid. For brevity, these sites are subsequently referred to as eye, cheek, forearm and calf. At each site TDC measurements were done in triplicate and the average used to characterize the site.

Measurement procedure

Measurements were done on a day when the participant was carrying out their normal studying and household duties with no prior or intervening strenuous exercise. Each skin site was measured hourly starting at 0800 h and continuing to 2000 h for a total of 13 measurement sets. Measurements were done while seated with each set taking less than five minutes. All sites were initially pre-marked with a dot using surgical pen so they could be easily located for sequential hourly measurements. The measurement order was eye, cheek, forearm and calf. At each site the right- and left-hand side measurements were alternated until triplicate measurements were obtained. This alternating side measurement procedure was done to allow more time between successive measurements at the same site thereby helping to minimize possible carry-over effects of the prior measurement. A side-to-side ratio was determined by forming the ratio of the site average TDC value of each person's dominant to non-dominant sides.

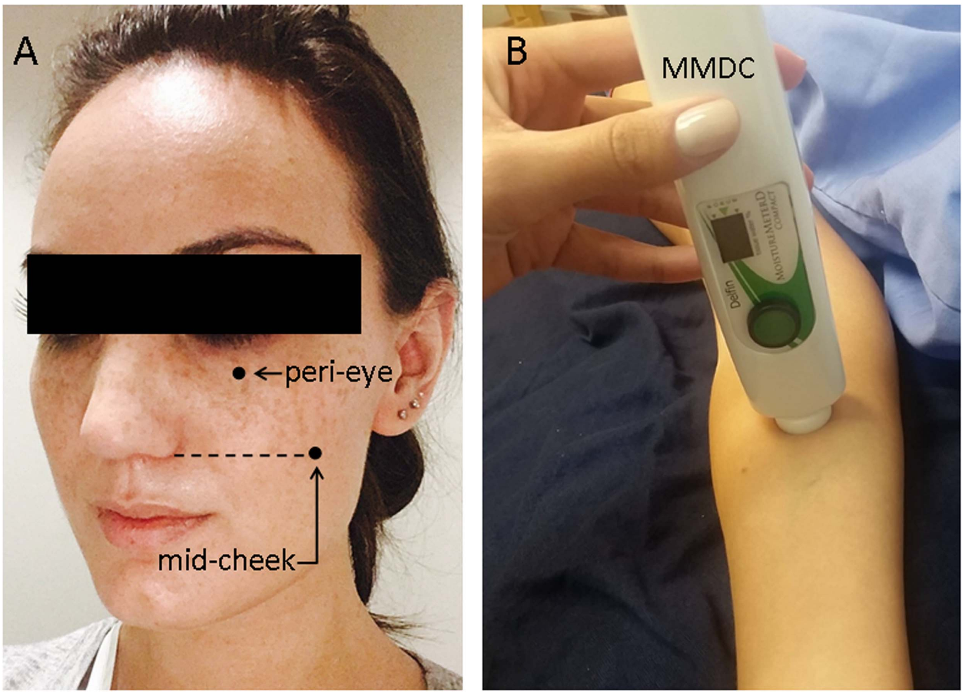

Figure 1. Measurement sites and the measurement device. All tissue dielectric constant (TDC) measurements were bilateral in triplicate. (A) Peri-eye site (about 1.5 cm inferior to the lower eyelid) and mid-cheek are illustrated. (B) TDC measurements on the anterior forearm being made with the MoistureMeterD Compact (MMDC) at a site 6 cm distal to the antecubital fossa. Not shown is the medial calf measurement site located 10 cm proximal to the medial malleolus.

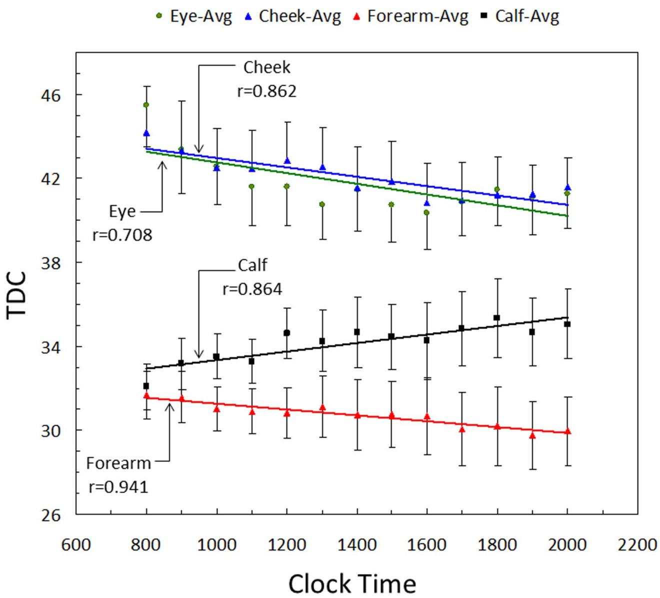

Figure 2. Temporal variation in TDC values. Data points are the mean of the side-to-side TDC averages (Avg) with error bars showing the standard error of the mean (SEM) over all subjects. Lines show linear regression of TDC values upon time of day (clock time) with correlation coefficients (r) as shown. TDC values at all sites showed a statistically significant change with clock time, with eye, cheek and forearm decreasing and only the calf showing a TDC increase from morning to evening.

Results

Measurement repeatability

Triplicate TDC measurements at each site allowed determination of the coefficient of variation (CV%) for each measurement-set as 100 × SD/AVG. These were then averaged over the 13 measurement sets to yield a single CV% for each site (mean ± SD) which were for eye, cheek, forearm and calf locations as follows: 3.25 ± 1.00%, 3.79 ± 1.12%, 2.44 ± 0.96% and 2.47 ± 0.80%. The CV% of eye and cheek measurements were statistically greater than for forearm and calf ($p < 0.01$) likely in part due to the need to use of a mirror to make the facial measurements.

Temporal variation in TDC values

Data expressed as the mean of side-to-side TDC averages (figure 2) show that all sites demonstrate a statistically significant change in TDC values from morning through evening. Whereas TDC values at eye, cheek and forearm decreased with increasing clock time ($p < 0.001$), TDC values at calf increased from morning to evening ($p < 0.001$). The corresponding linear regression equations for eye, cheek, forearm and calf are as follows

$$TDC_{EYE} = -0.0032 \times TIME + 58.0, \quad r = 0.708;$$
$$TDC_{CHEEK} = -0.0028 \times TIME + 57.9, \quad r = 0.862$$

$$TDC_{ARM} = -0.0018 \times TIME + 41.9, \quad r = 0.941;$$
$$TDC_{CALF} = 0.0026 \times TIME + 40.2, \quad r = 0.864.$$

Site-to-site differences

Eye and cheek TDC values were similar to each other at 0800 h (53.8 ± 8.8 versus 56.7 ± 9.8, $p = 0.415$, Wilcoxon signed ranks) and though TDC values declined at both sites values remained similar to each other at 2000 h (52.9 ± 7.3 versus 53.4 ± 6.2, $p = 0.760$). Forearm and calf TDC values were similar to each other at 0800 h (40.6 ± 6.7 versus 41.1 ± 4.9, $p = 0.445$) but both were significantly less than either eye or cheek ($p < 0.001$). As the day progressed TDC values at the arm fell but calf values increased so that by 2000 h TDC values at these sites differed significantly (38.4 ± 5.5 versus 44.9 ± 7.3, $p < 0.01$).

Side-to-side ratios

Despite the fact that absolute TDC values all changed during the day, the side-to-side (dominant-to-non-dominant) TDC ratios at each site were relatively unchanged as graphically illustrated in figure 3. Analysis of variance for repeated measures showed no statistically significant difference for TDC ratios among time for any site. Quantitatively, 0800 h vs. 2000 h ratios were: for eye (0.994 ± 0.072 versus 1.003 ± 0.035, $p = 0.386$), for cheek (1.011 ± 0.084 versus 1.006 ± 0.051, $p = 0.799$), for forearm (0.975 ± 0.078 versus 0.995 ± 0.032, $p = 0.125$), and for calf (1.012 ± 0.069 versus 1.006 ± 0.028, $p = 0.859$).

Discussion

Because TDC measurements are used for a variety of purposes (Petaja *et al* 2003, Harrow and Mayrovitz 2014, Lahtinen *et al* 2015, Mayrovitz *et al* 2015b) we believed that knowledge of the potential diurnal variation of this measurement method would be useful. Because the TDC value largely reflects skin water content, the operative hypothesis was that the TDC measured in upper body areas would tend to progressively decrease during the day whereas TDC values in the lower extremities would tend to progressively increase during the day. The present new findings support this concept in that TDC values at the eye, cheek and forearm progressively decreased, whereas TDC values measured at the calf progressively decreased. This general pattern is consistent with skin thickness measurements made in upper and lower body sites in the morning and then 6–7 h later. However, the present work was able to document such changes at multiple sites on an hourly basis and thereby reinforce this general observation. These measurements were accomplished using a hand-held, battery-operated device that was chosen for its ease of use and its potential for rapid clinical measurements of edema and lymphedema.

The overall changes from morning to evening in the present study were not huge, with decreases in peri-eye skin averaging (mean ± SD) 11.2 ± 8.3% with cheek and forearm decreases somewhat less at 6.8 ± 5.7% and 5.6 ± 6.0% respectively. The overall increase in calf TDC values was 9.3 ± 10.7%. These changes may be compared with reported skin thickness changes (Tsukahara *et al* 2001) herein estimated from their table 2B indicating thickness decreases for eye, cheek and arm of 7%, 10% and 12% respectively and an increase of 15% at the calf. These average skin thickness percentage changes are within the standard deviations of the currently measured TDC changes. When absolute TDC values are the measurement quantity of interest the present results provide an estimate of the possible time-of-day differences to be expected.

In contrast to the changes in absolute TDC values, there was no significant change in the side-to-side ratio in measured TDC values at any site during the 13 h monitoring. This new finding is relevant because TDC measurements are sometimes used to assess sequential unilateral changes using inter-side ratios (Lahtinen *et al* 2015, Mayrovitz *et al* 2015b, 2015c) as opposed to absolute values. In principle, this finding implies that such inter-side ratios can confidently be measured at any time of day without concern for time-dependent confounding. This feature would be especially useful in clinical settings in which follow-up measurements on patients are not easily scheduled at fixed times. Of course, this result applies specifically to the anatomical sites herein evaluated but may apply to other sites as well.

There are several potential limitations of the present study that may impact the generalizability of its findings. Firstly, the data were obtained via self-measurement. This should not be a major limiting factor since all measurers were very well trained in the procedure and had been using the measurement method in at least one other research study so were experienced. Measurements on the face (eye and cheek) needed the aid of a mirror and variability in that area was somewhat higher than on the arm or leg. However, the coefficient of variation among all measurers was less than 4%.

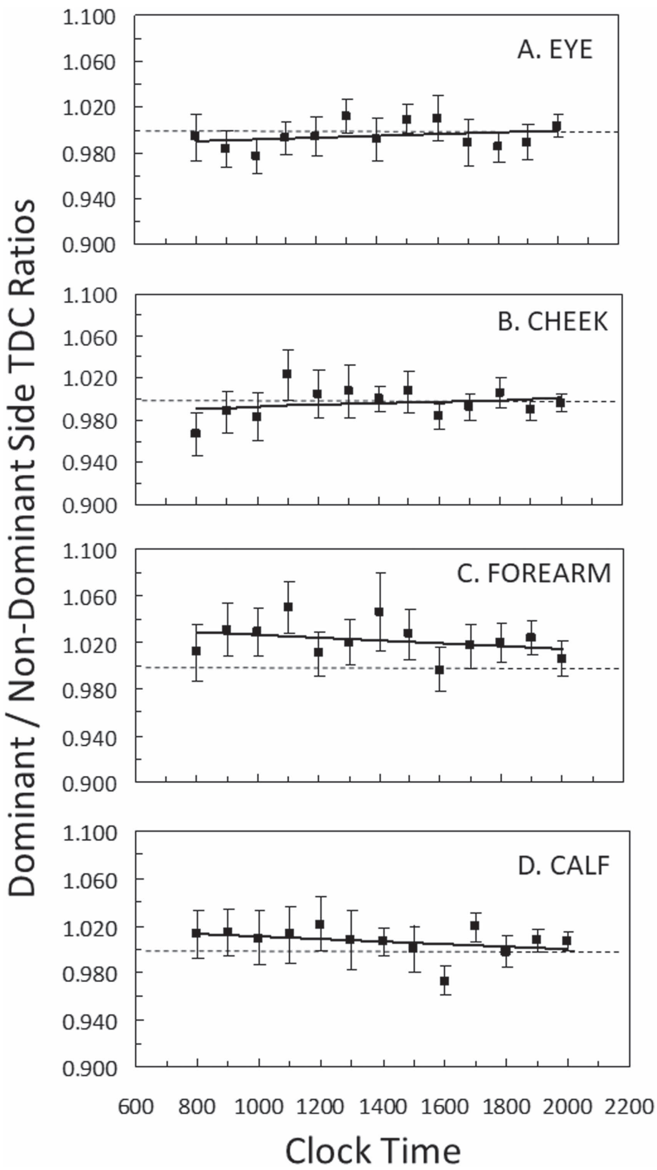

Figure 3. Inter-arm TDC ratios. Data points are the mean values of the dominant to non-dominant side TDC ratios for each site with SEM error bars. The dashed line represents a ratio of 1. Although the absolute values at each site change with the hour of the day, the ratio does not significantly change.

A second potential limitation is the number and uniformity of the studied group, which comprised of 12 young healthy women. Because the study design required hourly measurements over an extended period it was necessary to utilize subjects that were well trained in the measurement method and available and willing to volunteer to participate. It turned out that these combined criteria were met by the young adult females included in this study. These facts dictated the number of subjects from which data could be obtained. Because the basic pattern of changes was seen in all subjects it is likely that no significant alteration in the overall pattern would emerge with a larger number of subjects. The fact that the group participants were female and young implies that the data herein reported strictly apply to that demographic. Because TDC measurements are most often made in women, the gender limitation is not likely restrictive. However, because differences in absolute skin TDC values have been shown to be both gender (Mayrovitz *et al* 2016a) and age (Mayrovitz *et al* 2016b, 2017) dependent, it may be that absolute TDC values at the presently measured sites would be somewhat different in males of the same age and in older females. In addition, because the full impact of age on inter-side symmetry is not well established, extension of the present findings to older individuals should be done with that fact in mind.

Conclusion

Three outcomes of the present study emerge. (1) The findings demonstrate a previously unestablished gravity dependent skin-water shift via TDC measurement. (2) An estimate of time-of-day TDC differences is provided. (3) The insensitivity of inter-side TDC ratios to time-of-day is demonstrated, thereby providing confidence in the TDC ratios obtained at different times of day.

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The author declares no conflict of interest.

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