

Biophysical measures of skin tissue water: variations within and among anatomical sites and correlations between measures

Harvey N. Mayrovitz*, Maria Bernal, Frances Brilit and Rebecca Desfor

College of Medical Sciences, Nova Southeastern University, Ft. Lauderdale, FL, USA

Background: Biophysical measures to assess that skin water includes stratum corneum hydration via capacitance (SC), dermal water via tissue dielectric constant (TDC), and transepidermal water loss (TEWL). Since skin differs among anatomical sites and tissue depth we sought to determine the site and depth variability of these measures and their relationships.

Methods: Measurements were done at 17 skin sites from forehead to foot in 32 supine healthy women. Measurements included SC at 1.25 MHz, TDC at 300 MHz to depths of 0.5, 1.5, and 2.5 mm and TEWL.

Results: Tissue dielectric constant decreased with increasing depth at forehead, forearm, and calf; increased with depth at palm, thenar eminence and great toe; and was independent of depth at cheek, hand dorsum, thumb pulp, and foot dorsum. SC correlated with TDC at most sites and depths. TEWL cor-

related with TDC at 2.5 mm only at calf sites and thenar eminence.

Conclusions: Results establish parameter ranges for each measure, show that TDC values do not necessarily change with skin depth, and show a significant correlation between TDC and SC values at most sites. These correlations suggest that SC hydration but not TEWL is directly linked to dermal tissue water levels in normal skin.

Key words: transepidermal water loss – TEWL – stratum corneum water – tissue dielectric constant – TDC – SC capacitance – SC moisturization

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PREVIOUS WORK has shown that measurements of tissue dielectric constant (TDC) of human skin at a frequency of 300 MHz are useful indices of local skin-to-fat tissue water (1). The TDC measurement is based on the open-ended coaxial probe method (2–4) that is sensitive to both free and bound water contained within the volume that is measured. The method has been used in a variety of clinically related applications in which assessing skin tissue water and its change were of interest. These include assessing lymphedema (5–8), quantifying lymphedema changes after treatments such as pneumatic compression therapy (9), laser therapy (10), and manual lymphatic drainage (11). Other applications have included characterizing arm tissue water in women with breast cancer prior to treatment (12) and in women with fully developed lymphedema (8), and evaluating changes accompanying weight loss (13), postoperative cardiac surgery (14), skin irradiation (15), skin irritation (16), and the menstrual cycle (17).

Most prior TDC measurements have been made on forearm skin either in healthy persons (18–21) or in persons at-risk for lymphedema (12, 22) or in persons treated for lymphedema (10, 11). In each of these conditions forearm TDC values were found to monotonically decrease as the effective measurement depth was increased from 0.5 mm to 5.0 mm. This depth-dependent decrease has at least in part been attributed to the inclusion of increasing amounts of low-water content fat and other tissues present at greater depths (21). A relevant question not yet systematically addressed is whether this TDC-depth relationship exists for other anatomical areas of clinical interest. Thus one goal of this study was to determine if this relationship is present at varying anatomical locations. The working hypothesis was that sites that tend to have less subcutaneous fat would have less TDC reduction associated with the inclusion of greater tissue depths in the measurement.

A second goal was to determine if the TDC value, which is an index of the amount of local

skin tissue water, is related to the SC and to the amount of transepidermal water loss (TEWL). Even though TEWL values, measured with either open or closed systems (23–27), are usually thought of and used as indicators of skin barrier function (28, 29) the presence of significant anatomical variation in TEWL is documented (30, 31), which has in part been ascribed to variations in corneocyte size structure and arrangement (28, 32). Based in part on the components and dynamics governing TEWL (33–35) we hypothesized that for normal skin, TEWL would be directly related to the amount of skin tissue water. To test this hypothesis, we sought to compare TEWL values with TDC values at different skin depths and also with the stratum corneum (SC) electrical capacitance as an index of SC water. By including multiple anatomical sites (17 in all) we reasoned that there would be a wide range of values from which an assessment of possible TDC-SC-TEWL relationship could be determined.

In part, because of our interest in the application of the TDC method to the assessment of lymphedema and its early detection a decision was taken to test both hypotheses in healthy females at anatomical sites that would be prone to lymphedema either as a consequence of breast cancer and its treatment (upper limb) or gynecological surgery (lower extremity).

Materials and Methods

Subjects

Female adult volunteer subjects ($N = 32$) participated in this study and were evaluated after signing a University Institutional Review Board approved informed consent. Requirements for participation were that subjects be at least 18 years of age, have no implanted wires or electronic medical devices and have no evidence of any abnormal arm skin condition or open wounds in the vicinity of any face, arm, or leg measurement site. All subjects were asked to not apply any skin cream or lotions on the day of their scheduled experiment. Group age (mean \pm SD) was 33.0 ± 13.9 years (range of 19–77 years) with a median age of 27 years. The group body mass index (BMI) was 24.8 ± 5.4 kg/m² (range 18.3–43.8 kg/m²) with a median of 23.1 kg/m². With respect to the BMI classification, one subject (3%) was underweight (BMI < 18.5 kg/m²), 19

subjects (59%) had a BMI in the normal range (BMI 18.5–24.9 kg/m²), seven subjects (22%) were overweight (BMI 25–29.9 kg/m²), and five subjects (16%) would be classified as obese (BMI > 30 kg/m²). The right hand was the self-reported dominant hand in 30 subjects (94%). No subject reported of being a current smoker or being on any blood pressure medication that might affect fluid volume status. Tests were done with subjects' supine in a quiet experimental room with a room temperature at procedure start of $24.4 \pm 1.4^\circ\text{C}$ and an end temperature of $24.9 \pm 1.2^\circ\text{C}$. Room relative humidity at experiment start was $34.9 \pm 4.7\%$ and at experiment end was $35.1 \pm 4.6\%$.

Measurement devices

Tissue dielectric constant was measured with the MoistureMeter-D (Delfin Technologies Ltd, Kuopio, Finland). It consists of a cylindrical probe connected to a control unit that displays the TDC value when the probe is placed in contact with the skin. The physics and principle of operation have been well described (1–4, 36). In brief, a 300-MHz signal is generated within the control unit and is transmitted to the tissue via the probe that is in contact with the skin. The probe acts as an open-ended coaxial transmission line (2). A portion of the incident electromagnetic wave is reflected that depends on the dielectric constant of the tissue, which itself depends on the amount of free and bound water in the tissue volume through which the wave passes. Reflected wave information is processed within a control unit, and the dielectric constant is displayed. For reference, pure water has a value of about 78.5, and the display scale range is 1–80. The effective measurement depth depends on the probe dimensions, with larger spacing between inner and outer conductors corresponding to greater penetration depths. In this study, three probes were used to achieve effective measurement depth of 0.5, 1.5, and 2.5 mm.

The TEWL was measured using the VapoMeter SWL-2 (Delfin Technologies Ltd). The VapoMeter (27) is battery-operated and contains a humidity sensor housed in a closed chamber within a cylindrical probe that contacts the skin for about 10 s for a TEWL measurement that is reported in water flux units of g/m²/hr. Its use in comparison to open chamber devices has been determined (23, 26). The

relative SC moisturization was based on the SC capacitance (37) and was measured using the MoistureMeter SC-2 (Delfin Technologies Ltd). Skin temperature was measured using an infrared non-contact thermometer (Exergen, Watertown, MA, USA).

Measurement sites and procedures

A total of 17 anatomical sites were measured sequentially from forehead to toe in the order 1 through 17 as listed in Table 1 and illustrated in Fig. 1. The first measurement set was made with the 2.5-mm TDC probe in which all sites (1–17) were measured sequentially. Then the same sites were re-measured in the same order with the 1.5-mm depth probe and then with the 0.5-mm depth probe. This was followed by the SC measurement sequence, the TEWL sequence and finally the skin temperature sequence. The first measurement was started after a subject had been supine for 10 min. During this time interval, the 17 sites were marked with a surgical pen for reference and re-measurement. Some measurement sites were marked in relationship to measured distances from anatomical landmarks. The anterior and dorsal forearm sites were measured and marked to be 8 cm distal to the antecubital fossa and the anterior, medial, and lateral gaiter sites were marked and measured to be 10 cm proximal to the medial malleolus. The other sites were as indicated in Fig. 1; the forehead site was at mid-forehead

and the cheek site was at mid-cheek. Except for a mid-forehead site all measurements were done on the subject's non-dominant side. The time required to complete all measurements was (mean \pm SD) 55 \pm 6 min (range 42–67 min).

Analyses

To determine the significance of the TDC-depth dependence, TDC values at each depth were treated as within-subject values and tested using a general linear model for repeated measures using the statistical package software SPSS 13. If an overall statistical significance at a P -value <0.01 was found for any anatomical site, then analysis of contrast differences was used to determine the significance of paired differences between depths 0.5 mm and 1.5 mm and between depths 1.5 mm and 2.5 mm. To examine the relationship among parameters and test the hypothesis that TEWL is directly related to the amount of skin tissue water, the correlations among TEWL and the values of SC and TDC were determined for all sites overall. This includes the 17 sites for the 32 subjects amounting to 544 data points as well as correlation analysis for each of the measured sites.

Results

TDC values by depth and site

Three different patterns of TDC-depth dependence were observed as indicated in

TABLE 1. Tissue dielectric constant (TDC) values by depth and site

#	Measurement site	TDC values for different depths			TDC depth significance		
		0.5 mm	1.5 mm	2.5 mm	Overall	0.5 vs. 1.5	1.5 vs. 2.5
1	Forehead (middle)	40.7 \pm 3.4	36.8 \pm 2.7	35.0 \pm 3.6	<0.001	<0.001	<0.001
2	Cheek (middle)	33.4 \pm 6.4	32.5 \pm 3.6	32.2 \pm 4.1	NS		
3	Forearm anterior	29.5 \pm 4.0	28.2 \pm 2.4	24.9 \pm 3.4	<0.001	0.005	<0.001
4	Forearm dorsum	31.4 \pm 3.8	29.2 \pm 2.8	26.6 \pm 3.1	<0.001	<0.001	<0.001
5	Hand palm (thenar)	34.0 \pm 5.6	35.1 \pm 4.5	39.3 \pm 5.1	<0.001	0.042	<0.001
6	Hand palm (center)	31.6 \pm 5.1	32.5 \pm 5.4	34.7 \pm 5.0	<0.001	0.124	<0.001
7	Thumb pulp	36.6 \pm 6.0	36.5 \pm 6.3	36.3 \pm 4.7	NS		
8	Hand dorsum (web)	29.9 \pm 4.4	30.0 \pm 3.4	29.6 \pm 4.3	NS		
9	Hand dorsum (mid)	36.4 \pm 3.4	34.5 \pm 5.4	35.3 \pm 4.1	NS		
10	Medial gaiter	32.4 \pm 5.3	31.4 \pm 5.8	28.2 \pm 4.6	<0.001	<0.001	<0.001
11	Anterior gaiter (shin)	34.7 \pm 4.6	32.6 \pm 3.8	30.1 \pm 4.1	<0.001	<0.001	<0.001
12	Lateral gaiter	36.0 \pm 4.9	33.9 \pm 4.0	33.3 \pm 5.3	<0.001	<0.001	NS
13	Medial peri-malleolus	27.1 \pm 4.6	26.7 \pm 3.6	26.6 \pm 33.5	NS		
14	Foot dorsum (1–2 toe)	27.9 \pm 4.1	28.2 \pm 3.2	28.2 \pm 3.5	NS		
15	Foot dorsum (4–5 toe)	27.7 \pm 3.6	26.7 \pm 2.8	26.9 \pm 3.0	NS		
16	Great toe dorsum	33.0 \pm 5.5	33.6 \pm 4.0	34.0 \pm 4.3	NS		
17	Great toe plantar	31.6 \pm 5.0	33.9 \pm 3.9	38.1 \pm 3.9	<0.001	<0.001	<0.001

Sites listed in the order of their sequential measurement. NS = not statistically significant ($P > 0.05$). TDC = Tissue Dielectric Constant values measured to depths of 0.5, 1.5, and 2.5 mm.

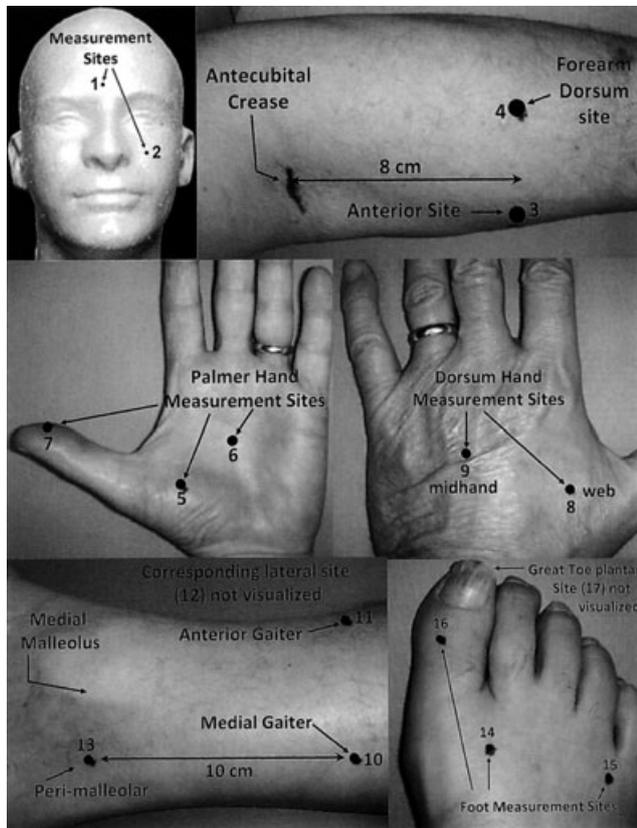


Fig. 1. Illustrating the 17 measured sites numbered in the order of their sequential measurement.

Table 1. At nine of the measured sites (52.9%) there was an overall significant ($P < 0.001$) change in TDC value with increasing effective measurement depth from 0.5 mm to 1.5 mm to 2.5 mm. Six of these sites (35.3%) showed a significant monotonic decrease in TDC values. These sites included the forehead, both forearm sites, and the three calf (gaiter) sites. Contrastingly, at three sites (17.6%) there was a monotonic increase in TDC values with increasing depth. This pattern occurred at both of the palmer hand sites and at the great toe plantar site. The remaining eight sites showed no significant change in TDC value with effective measurement depth. These sites were the cheek, both hand dorsum sites, the three foot dorsum sites, and the thumb pulp site.

Relationship among parameters

TDC-SC Relationship: Considering measurements at all sites ($N = 544$ data points) there was a highly significant ($P < 0.001$) correlation between SC and TDC values at depths of 0.5 mm, 1.5 mm, and 2.5 mm with respective correlation

coefficients of 0.604, 0.568, and 0.424. These results indicate that SC moisturization as measured by SC capacitance is most closely correlated to tissue water within the epidermis + dermis that corresponds to that included in the TDC measurement depths of 0.5 and 1.5 mm. Examination of individual sites showed that the SC measure of stratum corneum water was significantly correlated with TDC values at most measured sites. For a measurement depth of 1.5 mm the great toe plantar (site 17) displayed the greatest SC-TDC correlation (0.786). Non-significant correlations were recorded for each of the calf sites. The complete listing of the SC-TDC correlations for a 1.5-mm depth are shown in Table 2 which is arranged in descending order of correlation coefficient values. Sites of maximum and minimum correlations varied slightly by TDC measurement depth. For example, at a measured TDC depth of 0.5 mm the correlation coefficients ranged from a high of 0.803 ($P < 0.001$) at the thumb pulp and medial peri-malleolar sites to a least value of 0.369 ($P < 0.05$) at the forehead site. For the 2.5-mm TDC-depth measurement the high and low correlations were 0.742 at the thenar eminence ($P < 0.001$) and 0.354 for the anterior gaiter site ($P < 0.05$).

TABLE 2. SC-TDC correlations by site at a TDC measurement depth of 1.5 mm

#	Measurement site	r-value	P-value
17	Great toe plantar	0.786	0.001
6	Hand palm (center)	0.779	0.001
7	Thumb pulp	0.773	0.001
13	Medial peri-malleolus	0.724	0.001
5	Hand palm (thenar)	0.669	0.001
16	Great toe dorsum	0.588	0.001
2	Cheek (middle)	0.545	0.001
15	Foot dorsum (4-5 toe)	0.529	0.002
14	Foot dorsum (1-2 toe)	0.439	0.009
9	Hand dorsum (mid)	0.415	0.018
1	Forehead (middle)	0.384	0.031
3	Forearm anterior	0.374	0.035
8	Hand dorsum (web)	0.371	0.037
4	Forearm dorsum	0.358	0.044
11	Anterior gaiter (shin)	0.322	0.072
12	Lateral gaiter	0.257	0.155
10	Medial gaiter	0.063	0.524

Measurement sites listed in descending order of SC-TDC correlation coefficient (r-value). TDC = Tissue Dielectric Constant values measured to a depth of 1.5 mm; P-value = significance of the correlation coefficient. Lower extremity gaiter sites are not significant. Sites with P-value <0.05 are marginally significant. Sites with P-values <0.01 are considered highly significant.

TEWL-TDC relationship

The TEWL values ranged from a maximum average value of 48.9 ± 25.8 at the thumb pulp to a minimum site average of 8.1 ± 5.4 at the forearm. Table 3 summarizes all measured parameter values arranged in descending order of TEWL. Analysis showed that there was an overall significant correlation ($P < 0.001$) between TEWL and TDC values measured at 0.5 mm, 1.5 mm, and 2.5 mm with correlation coefficients of 0.200, 0.341, and 0.430, respectively. This result, which takes into account all sites measured ($N = 544$ measurements), would seem to be consistent with a TEWL dependence on TDC and also indicates that the strongest correlation is with the effective water content contained within the deepest measurement depth of 2.5 mm. However, when individual sites were analyzed ($N = 32$ per site) it was found that the overall highly significant correlation between TEWL and TDC at 2.5-mm depth was mainly attributable to significant ($P < 0.01$) correlations at only four sites. These sites were the hand thenar eminence and the medial, lateral, and anterior gaiter sites. The corresponding TEWL-TDC correlation coefficients for these sites were 0.468, 0.513, 0.443, and 0.430, respectively. Only at the hand palm and thenar eminence sites was a significant ($P < 0.001$) correlation between TEWL and SC values demonstrated with correlation coefficients of 0.636 and 0.743, respectively.

Discussion*TDC as a function of skin depth*

The TDC-depth findings of the present study serve to dispel the notion that TDC values invariably decrease with increasing measurement depth. Previous work (8, 21, 22) in which TDC measurements were made at various depths on the forearm did show monotonically decreasing TDC values that were attributed to the inclusion of increasing amounts of low-water content subcutaneous fat. Currently obtained TDC values are consistent with this pattern for the forearm and have also revealed a similar pattern for forehead and for all three calf sites. Contrastingly, at hand palm and great toe plantar sites TDC values were found to increase with increasing measurement depth. Although there is no firm explanation for this reverse pattern it is consistent with the possibility that at these glabrous skin sites TDC values reflect the increasing water content of the more deeply lying eccrine sweat glands that tend to have their greatest density in palm and plantar skin regions. This possibility is reinforced by the fact that at the deepest depth measured (2.5 mm) the greatest TDC values among all sites were found at the hand palm (39.3 ± 5.1) and great toe plantar surface (38.1 ± 3.9).

For the eight measured sites that showed no change in TDC value with increasing measurement depth, five were on skin dorsum, including

TABLE 3. Biophysical parameter values by site

#	Measurement site	Temp	TEWL	SC	TDC 0.5	TDC 1.5	TDC 2.5
7	Thumb pulp	31.2 ± 2.4	48.9 ± 25.8	48.1 ± 28.6	36.6 ± 6.0	36.5 ± 6.3	36.3 ± 4.7
6	Hand palm (center)	33.2 ± 1.6	48.0 ± 37.7	32.9 ± 35.3	31.6 ± 5.1	32.5 ± 5.4	34.7 ± 5.0
5	Hand palm (thenar)	32.4 ± 1.6	37.4 ± 23.0	33.5 ± 25.4	34.0 ± 5.6	35.1 ± 4.5	39.3 ± 5.1
17	Great toe plantar	27.1 ± 3.5	29.9 ± 8.5	30.1 ± 17.8	31.6 ± 5.0	33.9 ± 3.9	38.1 ± 3.9
8	Hand dorsum (web)	31.9 ± 1.8	19.3 ± 6.3	19.1 ± 10.3	29.9 ± 4.4	30.0 ± 3.4	29.6 ± 4.3
1	Forehead (middle)	34.1 ± 0.7	18.3 ± 9.4	70.5 ± 28.9	41.2 ± 12.5	37.1 ± 3.2	35.3 ± 4.3
16	Great toe dorsum	28.5 ± 2.8	14.8 ± 7.2	24.0 ± 14.9	33.0 ± 5.5	33.6 ± 4.0	34.0 ± 4.3
2	Cheek (middle)	33.1 ± 1.0	13.1 ± 7.1	55.0 ± 27.5	33.4 ± 6.4	32.5 ± 3.6	32.2 ± 4.1
14	Foot dorsum (1–2 toe)	29.7 ± 2.1	12.5 ± 7.1	15.8 ± 14.4	27.9 ± 4.1	28.2 ± 3.2	28.2 ± 3.5
9	Hand dorsum (mid)	32.3 ± 1.6	11.7 ± 4.6	31.3 ± 15.0	36.4 ± 3.4	34.5 ± 5.4	35.3 ± 4.1
15	Foot dorsum (4–5 toe)	29.4 ± 2.1	10.7 ± 4.7	13.6 ± 11.6	27.7 ± 3.6	26.7 ± 2.8	26.9 ± 3.0
13	Medial peri-malleolus	30.8 ± 1.7	10.4 ± 5.5	10.0 ± 8.9	27.1 ± 4.6	26.7 ± 3.6	26.6 ± 33.5
12	Lateral gaiter	32.0 ± 1.5	10.0 ± 5.5	19.6 ± 10.8	36.0 ± 4.9	33.9 ± 4.0	33.3 ± 5.3
10	Medial gaiter	31.2 ± 1.1	9.0 ± 6.5	21.0 ± 14.8	32.4 ± 5.3	31.4 ± 5.8	28.2 ± 4.6
11	Anterior gaiter (shin)	31.5 ± 1.0	9.0 ± 6.6	24.8 ± 13.1	34.7 ± 4.6	32.6 ± 3.8	30.1 ± 4.1
3	Forearm anterior	32.5 ± 1.0	8.2 ± 4.9	32.9 ± 15.0	29.5 ± 4.0	28.2 ± 2.4	24.9 ± 3.4
4	Forearm dorsum	31.8 ± 0.8	8.1 ± 5.4	24.8 ± 12.9	31.4 ± 3.8	29.2 ± 2.8	26.6 ± 3.1

Measurement sites listed in descending order of measured TEWL value. Entries are mean \pm SD. Temp, skin temperature ($^{\circ}\text{C}$); TEWL, Transepidermal water loss ($\text{g}/\text{m}^2/\text{hr}$); SC, stratum corneum relative moisturization value; TDC 0.5, TDC 1.5, and TDC 2.5, Tissue Dielectric Constant values measured to depths of 0.5, 1.5, and 2.5 mm.

both hand sites and the three foot sites. The two remaining non-depth-dependent sites were the thumb pulp and the peri-malleolar area. Although we have no definitive explanation for the absence of a depth-dependent TDC value at these sites it may be that lesser amounts of subcutaneous fat typically associated with these areas is partly responsible. Whatever the reason turns out to be, measured-TDC values at these sites suggest a reasonably uniform skin tissue water content within a skin depth up to about 2.5 mm.

Parameter relationships

The concomitant measurements of SC, TEWL, and TDC, which was unique to the present study, revealed a wide range of values for each parameter. TDC values represented the least site-to-site variations and TEWL values represented the greatest variation among sites. Such variations in values over the large anatomical range covered in the present study are perhaps to be expected in that significant differences even at marginally different sites on the forearm have been reported for TEWL (38) and TDC (19).

With regard to TEWL values, it has been argued that differences in TEWL values among anatomical sites are related to the size of stratum corneum corneocytes and the number of cell layers (29, 32). Accordingly face skin with its smaller size corneocytes and less cell layers than for forearm skin should have greater TEWL values (32). The present TEWL data are consistent with this concept to the extent that measured TEWL values of the cheek were about 1.6 times greater than those measured at either forearm site. However, a significant correlation between TEWL and TDC was demonstrated only at the three calf sites and the thenar eminence, and then only with TDC measurements to a depth of 2.5 mm. These findings do not strongly support our initial working hypothesis that TEWL values are generally affected by the level of the localized TDC or SC value. Rather it appears that a positive relationship between TEWL and either TDC or SC occurs only at a few sites.

In the present study, the strongest relationship among the measured biophysical

parameters at a given site was between the SC water-content measurement and TDC. Except for the three gaiter sites a positive correlation was demonstrated at all sites. For a TDC-measurement depth of 1.5 mm the significant SC-TDC correlations ranged from 0.786 at the great toe plantar surface to 0.358 at the forearm dorsum. A significant SC-TDC correlation is consistent with the fact that the TDC measurement reflects the combined water contents of the stratum corneum, viable epidermis and the dermis and is also consistent with various models of skin water dynamics (34, 35, 39). The absence of a significant SC-TDC correlation at any of the three calf sites may be influenced by significant positive correlations between TEWL and TDC at these three sites. If the permeability to water at these sites were high, then SC water content would be less of an influencing factor thereby possibly explaining the absence of a significant TDC-SC correlation. Although site variations in skin permeability have been described (29, 31) specific data on the site-specific permeability differences of the calf is not conclusive so this aspect would be in need of further study.

In conclusion, these findings help establish parameter value ranges for each measured biophysical quantity, show that TDC values do not necessarily change with skin depth, and show that for most sites there is a significant correlation between TDC values and SC values. These correlations suggest that SC hydration is directly linked to dermal tissue water levels. Although such a relationship is consistent with skin structure-function considerations, it is thought that the present work is the first to provide direct evidence of such a possible relationship. In contrast to the SC-TDC linkage, we found little evidence linking TEWL to either SC or TDC values. This may indicate that in normal skin TEWL at most sites is not importantly dependent on dermal and sub-dermal hydration. Finally, these findings suggest that the substantial variation in the biophysical parameter values among sites needs to be prudently considered in the design and interpretation of any comparative study involving different skin sites.

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Address:
Harvey N. Mayrovitz
Professor of Physiology
College of Medical Sciences
Nova Southeastern University
3200 S. University Drive
Ft. Lauderdale, FL 33328
USA
Tel: +954 262 1313
Fax: +954 262 1802
e-mail: mayrovit@nova.edu