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Age-related differences in tissue dielectric constant values of female forearm skin measured noninvasively at 300 MHz

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Background/Purpose: We hypothesized that reported age-related shifts in skin water from less-to-more mobile states would result in increased skin tissue dielectric constant (TDC) values as TDC values depend strongly on water content and state. One aim was to test this hypothesis. Further, as skin-to-fat TDC values are used as a tool for edema and lymphedema assessment, a second aim was to establish reference values suitable for young and older women.

Methods: TDC was measured bilaterally on volar forearm skin in young (20–40 years) and older (≥ 60 years) women. There were four groups with 50, 50, 100, and 50 subjects per age group measured to depths of 0.5, 1.5, 2.5, and 5.0 mm, respectively.

Results: For each age group, TDC values decreased with increasing depth ($P < 0.001$). TDC values at 0.5 and 1.5 mm were greater for older women ($P < 0.001$). At 2.5 mm, there

was no age-group difference ($P = 0.108$). At 5.0 mm the direction of the difference reversed with older TDC values less than the younger ($P < 0.001$).

Conclusion: Results are consistent with age-related shifts in water state from less-to-more mobile and explain depth-dependence differences between age groups. Data also give age-related TDC reference values for assessing local edematous or lymphedematous states.

Key words: skin dielectric constant – skin water – edema – lymphedema – age-related skin changes

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AN EXTENSIVE set of biophysical measurements aimed at characterizing certain age-related changes in men and women (1–5) demonstrated several important features. Stratum corneum (SC) hydration, assessed via electrical capacitance measures at forehead, neck, and forearm, tended to increase with age in females (3) but in males SC hydration decreased or remain unchanged (5). In both genders, reductions in most measures of skin elasticity and distensibility were demonstrated (1, 4). Of particular interest and relevance to the present study is the finding that SC hydration at the volar forearm was greater in the oldest female group (60–80 years) compared to younger (18–39 years). This was found to be true with no apparent age-related difference in female transepidermal water loss (TEWL) (3) although females had significantly greater TEWL values than males at all ages (2). The apparent age-related increase in female SC

hydration has not been explained. Other data based on depth profile measures of volar forearm SC water suggest a tendency for older females to have slightly less percentage water within about 30 μm of the surface, but similar values deeper (6). We believe that an aspect that may be involved is the fact that SC and skin water are largely present as bound water (7) either tightly or loosely bound to macromolecules (8, 9) but shift toward increased percentages of more mobile water with skin aging (10). As bound water (11) has a lower dielectric constant than mobile water (12–14), such a shift if present would be associated with an increase in measured capacitance that could be interpreted as an increase in age-related water content. A shift to a greater proportion of non-hydrogen bound water in photo-aged skin is not restricted to SC and has been reported to be about 30% greater in dorsal forearm skin (epidermis and dermis) (10) with an associated age-related

thinning of dorsal and ventral forearm skin (15). Magnetic resonance imaging of forearm skin has also demonstrated an increase in dermal mobile water in aged females compared to younger females (16, 17) although some other data suggest only a small age-related difference (8).

We hypothesized that a further manifestation of such changes in water state should cause an age-dependent increase in skin tissue dielectric constant (TDC) that would be detectable at depths below the SC in and deeper to the dermis. Thus, one aim of this study was to test this hypothesis by measuring skin TDC values to several skin depths in groups of younger and older women. Further, because skin-to-fat TDC values show promise as a way to characterize skin water changes in a variety of circumstances (18–27) and as a tool for lymphedema assessment (28–32), a secondary aim was to establish reference ranges suitable for use with young and older women.

Methods

Subjects

Female volunteers ($N = 270$), divided into two age groups, young (20–40 years, $N = 165$) and older (≥ 60 years, $N = 105$) with Fitzpatrick's skin types II–IV, separated into four measurement groups (I, II, III, IV), were evaluated after the research nature of the study was explained to them and they had signed an informed consent that was previously approved by the University Institutional Review Board. For each group, TDC measurements (described subsequently) were made at the depths and with the numbers per group as indicated in Table 1. Depending on the specific group, mean ages

ranged from 27.3 to 30.3 years for the young and from 68.9 to 70.5 years for the older group. For all measurement groups age and body mass index were significantly greater in the older group ($P < 0.01$). Prior to participation, subjects were asked not to apply any lotion or creams to their forearms on the day of the scheduled procedure. Subjects with any known skin condition affecting forearm skin, any injury or open wound on either arm, or any prior arm trauma that might have affected tissue water were excluded from participation.

Tissue dielectric constant measurement method

The dielectric constant, also known as permittivity, is a dimensionless number equal to the ratio of the permittivity of a measured tissue to the permittivity of vacuum. Because TDC values mainly depend on tissue water content, TDC values and their change may provide indices of water content and quantitative estimates of water content changes. For reference, the dielectric constant of distilled water at 32°C is approximately 76. As the measurement frequency is 300 MHz the TDC values are sensitive to both free and bound water. Measuring of the bound water component is important because up to 80–90% of young adult skin water content is bound (7) although this percentage may decrease substantially with skin aging (10).

Measurements of TDC have been used in basic and clinical research studies in which skin tissue water and its change were of interest at various anatomical sites including face (33, 34), breast (25), forearm (21, 35, 36), biceps, axilla and thorax (37), leg and foot (18, 22), and buttocks (38). TDC measurements have also been used to characterize

TABLE 1. Group features and forearm TDC values

	Effective measurement depth							
	Group I (0.5 mm)		Group II (1.5 mm)		Group III (2.5 mm)		Group IV (5.0 mm)	
	Young	Older	Young	Older	Young	Older	Young	Older
<i>N</i>	50	50	50	50	100	100	50	50
AGE (years)	30.3 ± 7.5	69.4 ± 6.9**	29.9 ± 3.7	69.5 ± 6.8**	27.3 ± 6.2	70.5 ± 6.7**	27.5 ± 4.3	68.9 ± 7.2**
BMI (kg/m ²)	24.9 ± 5.3	28.5 ± 6.3*	24.2 ± 5.4	27.8 ± 7.6*	23.9 ± 5.3	28.6 ± 5.9**	23.5 ± 4.6	28.4 ± 6.3**
TDC value	31.6 ± 4.3	37.4 ± 5.5**	30.3 ± 3.3	34.2 ± 4.5**	26.6 ± 4.7	27.6 ± 4.0	25.0 ± 4.5	22.3 ± 3.6**
% TDC difference	18.4		12.9		3.8		-10.8	

BMI, body mass index.

Values are mean ± SD; Older vs. Younger; * $P < 0.01$, ** $P < 0.001$.

TDC values for both groups significantly decrease with increasing depth ($P < 0.001$). Note that the older group TDC values at 0.5 and 1.5 mm depths are greater than for the young group but at the deepest depth the older group value are significantly less than for the young. Percentage Difference is calculated as $100 \times (\text{older} - \text{young})/\text{young}$ for each depth.

and track changes related to lymphedema (29, 30, 39), changes in post-surgical fluid status (27), and assess skin irradiation effects (25).

In use the device generates and transmits a very low power 300 MHz signal into a coaxial probe that is in contact with the skin with the probe acting as an open-ended coaxial transmission line (40). Part of the signal is absorbed, mainly by tissue water, and part is reflected back to a control unit where the complex reflection coefficient is calculated (41, 42) from which the dielectric constant is determined (43, 44). Reflections from the end of this coaxial transmission line depend on the complex permittivity of the tissue which in turn depends 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 the contribution of conductivity to the overall value of the permittivity is small and the dielectric constant is mainly determined by water molecules (free and bound). Consequently, the device includes and analyzes only the dielectric constant that is directly proportional to tissue water content in a manner close to that predicted by Maxwell mixture theory for low water content but a slightly less good prediction for high water content tissues (45). In all cases, TDC is strongly dependent on relative water content with TDC values that decrease with water reductions during hemodialysis (24). Further details including validation and repeatability data are described in the literature (18, 24, 46). Each probe is calibrated against various ethanol–water mixture concentrations each of known dielectric constant values (46).

Measurement procedure

Tissue dielectric constant measurements were made with the MoistureMeterD (MMD, Delfin Technologies, Kuopio, Finland). This device measures skin and the skin-to-fat TDC at a frequency of 300 MHz by touching skin with a small hand held probe for about 10 s. In practice, one of four different probes can be used having outer diameters from 10 mm, for a 0.5 mm effective measurement depth to 55 mm, for a 5 mm measurement depth. Effective measurement depth is defined as the depth at which the 300 MHz electric field decreases to $1/e$ of its surface field. In this study, all probes were used allowing for TDC measurements to

effective depths of 0.5, 1.5, 2.5, and 5.0 mm. Measurements were done with subjects supine on a padded and insulated examination table with arms resting palms up and were started after they had been supine for a minimum of 5 min. Measurement sites were both volar forearms 6 cm distal to the antecubital fossa with each site measured in triplicate. Measurements between right and left arm were alternated until three values per arm were obtained. The average of the three measurements was used to characterize the TDC value of each arm and reported as the average of the two arms. This procedure was done for each of the four effective measurement depths.

Analysis

All statistical tests were done with SPSS (V 13; IBM, Armonk, NY, USA). TDC values at all depths proved to be normally distributed as tested using the Shapiro-Wilks test. Differences in TDC values among depths within age groups were tested using ANOVA with post hoc evaluations of between depth differences done with Bonferroni adjustments. Differences between age groups were evaluated using independent *t*-tests for each depth separately. A *P*-value less than or equal to 0.01 was accepted as significant. This significance level was adopted to reduce type II errors that might arise because of using four independent *t*-tests, one for each depth.

Results

The main numerical experimental results (mean \pm SD) are summarized in Table 1 and the age pattern visualized graphically in Fig. 1 for each effective measurement depth. Results show that within each age group TDC values monotonically decrease with increasing depth ($P < 0.001$). For the young group, TDC values at 0.5 and 1.5 mm depths were not significantly different from each other ($P = 0.441$) but were both greater than TDC values measured at 2.5 and 5.0 mm depths ($P < 0.001$). The 2.5 and 5.0 mm TDC values were not significantly different from each other ($P = 0.113$). For the older group, TDC values at all depths differed from all other depths ($P < 0.001$).

Comparisons of TDC values between age groups at each depth showed a pattern (Fig. 1) in which older values at 0.5 and 1.5 mm depths

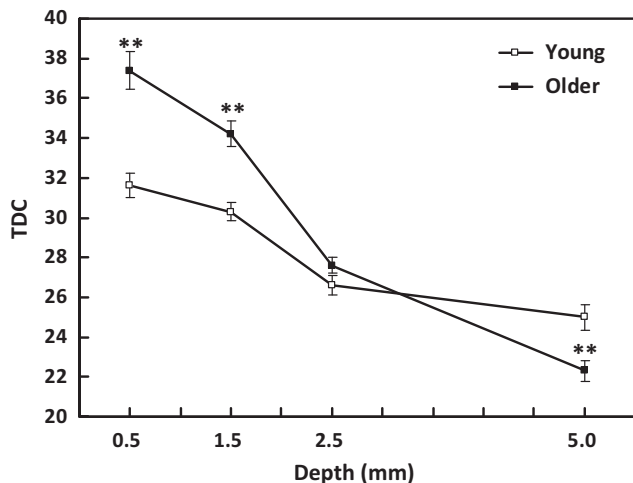


Fig. 1. Age and depth dependence of TDC values. TDC values for young and older groups decrease with increasing depth ($P < 0.001$) with the older group having greater TDC values at the two shallowest depths (0.5 and 1.5 mm) but a lesser value at the deepest depth; $**P < 0.001$ older vs. young groups with no significant difference at an effective depth of 2.5 mm. Error bars are one SEM.

were both significantly greater than the younger group TDC values at corresponding depths ($P < 0.001$). At a depth of 2.5 mm there was no significant difference between age groups ($P = 0.108$), and at a depth of 5.0 mm the direction of the difference reversed with the older group now having TDC values that were less than the younger group ($P < 0.001$). TDC values were significantly correlated with body mass index only for the deepest measurement (5.0 mm) yielding negative correlation coefficients of -0.335 ($P = 0.01$) and -0.301 ($P = 0.05$) for the younger and older groups, respectively.

Discussion

Investigations of potential age-related differences in skin properties have previously focused on a variety of skin parameters including skin thickness (15, 47–51), TEWL (2, 3, 52, 53), mechanical properties (1, 4, 54–59), pH and sebum content (60–62) and SC properties, and water content (6, 8, 61, 63–66). To our knowledge the present is the first systematic investigation and report of age-related differences in skin-to-fat TDC values between young and older females. A major new finding based on these TDC measurements of volar forearm skin in a large number of females is that the magnitude and direction of differences between age groups depends on the depth of the tissue included in the measurement.

For shallower depths, that included tissue volumes to 0.5 and 1.5 mm below the skin surface, TDC values were greater for older females. Differences between age groups disappeared when measurements were to depths of 2.5 mm. At an effective measurement depth of 5.0 mm, TDC values were now greater for the younger females. The greater TDC values of the older females measured at the shallower depths is consistent with the previously noted age-related shift in water state from mostly bound water to more mobile water with increasing age. This would be predicted as mobile water has a greater dielectric constant than bound water. The fact that the greatest difference between older and younger females occurs at the shallowest depth of 0.5 mm (18.4%, Table 1) and decreases to 12.9% at 1.5 mm depth is explainable by considering the tissue type included in the two measurement depths. TDC measurements to a depth of 0.5 mm would include all of the epidermis and a portion of the dermis, whereas measurements to a depth of 1.5 mm would include the dermis and also include a portion of hypodermis with its low water content fat. Because the shift in water state occurs in epidermis and dermis, the expected increased TDC value that would be associated with more mobile water would be blunted by including greater amounts of fat-rich hypodermis. This process could also explain the non-significant difference in TDC values between age groups at a measurement depth of 2.5 mm as at this depth there is a large fraction of the total tissue volume attributable to hypodermis thereby diminishing the net effect of the increase in dermal TDC value of the older group.

The reversal of the TDC difference at the deepest depth (5.0 mm) is not fully explainable based on a shift in water state. However, other factors may be involved. From volar forearm dermal thickness values reported (50) for the age range of female subjects evaluated in the present study, a reduction in average thickness of 0.95 mm (age 20–40 years) to an average of 0.85 mm (age 60–90 years) occurs with similar thickness reductions reported by others (15). By itself this change would favor a lesser TDC value in older females as percentage wise, less high content dermal water would be included in a fixed-depth measurement volume. Thus, the cross-over herein observed at the deepest measurement depth (5.0 mm), characterized by

a lesser TDC value in the older group, might be explained by this process because at this depth the large percentage of low TDC value hypodermis might overwhelm the impact of the change in water state within a now thinner dermis.

In addition to providing insights into factors affecting TDC measurements and differences between age groups, the present data also provide a substantial reference set of TDC values for each effective measurement depth. As already noted, forearm TDC measurements have shown potential for characterizing and possibly detecting early onset lymphedema (28, 32, 67) because of the strong dependence of skin TDC on water content. The present data provide a set of non-edematous forearm skin reference values that could be used to aid in detecting edema or lymphedema presenting in forearms. This could be done by determining the departure of measured values from the reference set herein contained specific to the age-range group of the patient being evaluated and the depth of the measurement. For that purpose

a multiple of the SD presented in Table 1 would be added to the corresponding TDC mean value to arrive at a threshold value above which the presence of edema or lymphedema is likely to be present. For example, if TDC measurements were made to a depth of 2.5 mm, a value exceeding a 2.5 SD threshold (99.5% of cases would be less than this value) would likely represent the presence of edema or lymphedema. For the data herein obtained, these thresholds are 38.3 and 37.7 for the younger and older age groups, respectively. Other thresholds can be computed and used in a similar manner depending on the degree of diagnostic conservatism desired.

In summary, the present TDC measurement results; (i) are consistent with the hypothesis of an age-related shift in the water state from less-to-more mobile, (ii) help explain the depth-dependence differences between ages, and (iii) provide for the first time age-related TDC reference values for use in assessing local edematous or lymphedematous states that manifest in forearms.

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