Local tissue water assessed by measuring forearm skin dielectric constant: dependence on measurement depth, age and body mass index

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Background: Tissue dielectric constant (TDC) measured at 300 MHz via the coaxial line reflection method is useful to evaluate local tissue water (LTW) and its change. Because excitation field penetration depth depends on size and geometry of the coaxial probe in contact with the skin, TDC values reflect skin and subcutaneous fat to varying depths depending on the probe used. Because tissue changes that occur with age or body mass index (BMI) may affect tissue water content and its depth distribution, our goal was to use TDC measurements to characterize depth patterns of LTW in normal tissue and to investigate the possible impact of age and BMI.
Methods: TDC was measured to depths of 0.5, 1.5, 2.5 and 5.0 mm on both forearms of 69 healthy women (age: 22–82 years, BMI: 18.7–46.1 kg/m^2).
Results: Independent of age or BMI, TDC values decreased significantly with increasing measurement depth (33.7 ± 5.8 at 0.5 mm to 21.8 ± 3.7 at 5.0 mm) but at all depths dominant and non-dominant TDC values were similar to each other with ratios ranging from 1.025 ± 0.081 at 0.5 mm to 1.017 ± 0.097 at 5.0 mm. TDC values only at 2.5 and 5.0 mm decreased significantly with increasing BMI whereas TDC values only at 0.5 and 1.5 mm increased significantly with age.
Conclusion: The findings indicate that normal TDC values are affected differentially by BMI and age in a depth-dependent manner. Possible explanations are discussed.

Key words: skin water – dielectric constant – tissue water – age

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A NUMBER of investigators have used tissue dielectric constant (TDC) measurements to evaluate local tissue water (LTW) and its change under a variety of conditions including skin irritation (1), skin irradiation (2), hemodialysis (3), post-cardiac surgery changes (4), weight loss (5), menstrual cycle (6) and lymphedema (7, 8). TDC values in these cases were measured at a frequency of 300 MHz via a coaxial line reflection method (9–13) in which the TDC value is dependent on the tissue water content. Because the penetration depth of the excitation field depends on the size and geometry of the coaxial probe that is placed in contact with the skin (11), the TDC value obtained reflects the composite tissue to varying measurement depths depending on the probe used. This feature was exploited in earlier work where measurement depth dependence of LTW in lymphedematous arms over a range from 0.5 to 5.0 mm was investigated (14). Because this depth range includes to variable degrees skin (epidermis+dermis) and subcutaneous fat, it is unclear if tissue changes that occur with age (15–19) or body mass index (BMI) affect tissue water content and its depth distribution. Such information, derived from TDC measurements in normal skin is essentially absent from the scientific literature. Thus the goal of this research was to use TDC measurements to characterize measurement depth patterns of LTW in normal tissue and to investigate the possible impact of age and BMI.

Methods

Subjects
A total of 69 women participated in this study and were evaluated after signing a University Institutional Review Board approved informed consent. Women were chosen for study because

of the interest in the use of the TDC method for lymphedema assessment. To have as broad a sample as possible entry requirements were limited to participants being at least 21 years of age, who had self-reported normal upper extremity function with no history of serious trauma and no upper extremity skin condition. Age (mean $\pm$ SD) was 51.3 ± 18.1 years with a range of 22–82 years and a median age of 54 years. BMI for the group was $27.6 \pm 6.2 \, \text{kg/m}^2$ with a range of 18.7–$46.1 \, \text{kg/m}^2$ and a median of $27.3 \, \text{kg/m}^2$. With respect to BMI classification, none were underweight (BMI $< 18.5 \, \text{kg/m}^2$), 24 (35%) were normal (BMI $< 25 \, \text{kg/m}^2$), 24 (35%) were overweight (BMI 25–$29.9 \, \text{kg/m}^2$) and 22 (30%) were obese (BMI $\geq 30 \, \text{kg/m}^2$). The right hand was the self-reported dominant hand in 62 subjects (90%) and the left hand was dominant in seven subjects (10%). Self-reported ethnicity of participants was Caucasian ($N = 60$) and Hispanic ($N = 9$).

TDC measurement device
The device used in this study to measure TDC was the MoistureMeter-D (Delfin Technologies Ltd, Kuopio, Finland http://www.delfintech.com). 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 has been well described (9, 10, 12, 13, 20). 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 itself acts as an open-ended coaxial transmission line (9, 12). The portion of the incident electromagnetic wave that is reflected 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 relative 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 the present study four different dimension probes were used to characterize depth dependence at the forearm site having effective measurement depths of 0.5, 1.5, 2.5 and 5.0 mm. Corresponding (maximum) probe diameters

were 10, 20, 23 and 55 mm with conductor spacing of 1, 3, 5 and 17 mm, respectively.

TDC measurement procedure
TDC measurements were started after a subject was lying supine for 10 min on a padded examination table with arms at her side with hands positioned palm up to expose the anterior surface of both forearms. A standardized measurement site, along the forearm midline located 6 cm distal to the antecubital fossa was marked with a dot to serve as a reference center point for probe placement. A single measurement was obtained by placing a probe in contact with the skin of one arm and held in position using gentle pressure. After about 10 s an audible signal indicated completion of the measurement. The probe was then used to make a measurement on the other arm to complete a measurement pair. This process was continued to obtain triplicate measurement pairs. Alternating between arm sides was used as a way to help obtain paired values as close in time as possible. The order of measurement was from smallest to largest probe (increasing measurement depth) with a 1 min wait between changing probes. For each probe the triplicate measurements were averaged and used to characterize the arm site average TDC value.

Analysis
Differences in TDC values between dominant and non-dominant arms were tested for using paired *t*-tests for each measurement depth with subsequent determinations of the average of both arms and the dominant to non-dominant TDC ratio. Differences in TDC values among measurement depths were tested using a general linear model for repeated measures with measurement depth as the repeated measure. Initial analysis of BMI as a factor was performed using a one-way analysis of variance with BMI class as a between-subjects factor for each measurement depth with the arm average TDC value as the dependent variable. For this analysis, BMI classifications were defined as normal (BMI $< 25 \, \text{kg/m}^2$), overweight (BMI 25–$29.9 \, \text{kg/m}^2$) and obese (BMI $\geq 30 \, \text{kg/m}^2$). Subsequently a full regression analysis of TDC values vs. BMI was carried out. Subject age as a factor was initially tested by stratifying age above and below the median age (54 years) yielding groups of 34 young and 35

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

Depth (mm)	TDC values			
	Dominant arm	Non-dominant arm	Arm ratio	Arm average
0.5	33.9 ± 5.9	33.3 ± 5.9	1.025 ± 0.081	33.7 ± 5.8
1.5	31.8 ± 5.4	31.4 ± 5.2	1.015 ± 0.077	31.6 ± 5.1
2.5	25.5 ± 3.8	25.3 ± 3.8	1.014 ± 0.097	25.4 ± 3.6
5.0	22.0 ± 3.8	21.7 ± 3.6	1.017 ± 0.097	21.8 ± 3.7

Data entries are mean ± SD for $N = 69$ subjects. Absolute TDC values decreased with increasing measurement depth and values at each measurement depth differed significantly from all others ($P < 0.001$). TDC values of dominant and non-dominant arms did not significantly differ at any depth. Arm ratio is dominant to non-dominant and arm average is the average of the two arms. Arm ratio was not significantly different among measurement depths.

older subjects. Arm average TDC values at each measurement depth were used to test for differences between age groups at each depth and to test for overall differences among depths using analysis of variance. Subsequently a full regression analysis of TDC values vs. age was done.

Results

For the entire group of 69 subjects, absolute TDC values as measured on both dominant and non-dominant arms progressively and significantly decreased with increasing measurement depth (Table 1). TDC values at each measurement depth differed significantly from all other depths ($P < 0.001$) with a steep decrease from $31.6 ± 5.1$ at 1.5 mm to $25.4 ± 3.6$ at 2.5 mm (Fig. 1). Despite the decrease in TDC values with depth, dominant and non-dominant arms were insignificantly different from each other for all depths. The average of both arms ranged from $33.7 ± 5.8$ at a measurement depth of 0.5 mm to $21.8 ± 3.7$ at a measurement depth of 5.0 mm. Corresponding dominant to non-dominant arm ratios ranged from $1.025 ± 0.081$ to $1.017 ± 0.097$ with ratios being insignificantly different among depths (Table 1).

When subjects were stratified according to BMI classification, there was a trend for TDC values to decrease in the direction from normal (BMI < 25 kg/m^2) to overweight (BMI 25–29.9 kg/m^2) to obese (BMI ≥ 30 kg/m^2) as shown in Table 2. Although this BMI dependent pattern was present at all depths it became significant at a depth of 2.5 mm ($P < 0.01$) and highly significant for a measurement depth of 5.0 mm ($P < 0.001$). For these measurement depths, TDC values of normal weight subjects were significantly higher than for both overweight and obese subjects. There was no significant TDC difference between overweight and obese subjects at any depth. Regression analyses over the full range of BMI
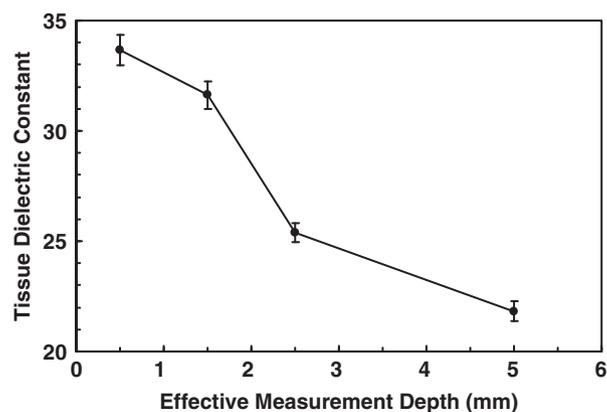

Fig. 1. Tissue dielectric constant (TDC) vs. measurement depth. Values are average of both arms for 69 subjects. Bars are ± 1SEM. TDC values at each measurement depth differed significantly (P < 0.001) from all others.

values confirmed that he greatest association between TDC and BMI is at the 5.0 mm depth for which TDC = -0.302 BMI + 30.2, $r = 0.525$, $P < 0.001$ (Fig. 2). Despite differences in absolute TDC values among depths and between BMI classes, differences in TDC values between arms were minor with dominant to non-dominant arm ratios being close to one and insignificantly different among BMI classes at all depths (Table 3).

When subjects were stratified according to age (above and below the overall 54-year-old median age of the group), the pattern of reduction in TDC values with increasing measurement depth held for each age group (Table 2). However, only for the two shallowest measurement depths (0.5 and 1.5 mm) were TDC values of younger subjects significantly less than for older subjects. The greatest and most significant difference ($P < 0.001$) between young and older subjects was at a 0.5-mm-measurement depth at which arm average TDC values were $31.5 ± 4.7$ and $35.6 ± 5.9$ for young and older subjects, respectively. Regression analyses over the full age range confirmed

TABLE 2. Tissue dielectric constant (TDC) values by body mass index (BMI) and age classification

Depth (mm)	BMI classification			Age classification	
	Normal (N = 24)	Overweight (N = 24)	Obese (N = 21)	Young (N = 34)	Older (N = 35)
0.5	35.0 ± 5.7	33.7 ± 5.4	32.0 ± 6.0	31.5 ± 4.7[‡]	35.6 ± 5.9
1.5	32.6 ± 4.8	31.7 ± 5.3	30.4 ± 5.3	30.0 ± 4.9[†]	33.2 ± 4.9
2.5	27.3 ± 3.4*	24.7 ± 3.6	24.0 ± 3.1	24.8 ± 3.4	25.9 ± 3.8
5.0	24.6 ± 3.6**	20.8 ± 2.5	19.8 ± 2.6	21.7 ± 3.7	21.9 ± 3.5

Data are mean ± SD of the average of the dominant and non-dominant arms. Normal, BMI $<25\,kg/m^2$; Overweight, BMI 25–29.9 kg/m^2; Obese, BMI $>30\,kg/m^2$. Young <55 years, Older ≥ 55 years. TDC values differed significantly among depths ($P<0.001$) for all BMI and Age classifications. Differences among BMI classes were significant for 2.5 and 5.0 mm depths for which TDC values of normal BMI subjects were significantly greater than for overweight or obese subjects:
*$P<0.01$,
**$P<0.001$.
Differences between overweight and obese subjects were not significant at any measurement depth. Differences among Age classes were significant only for the 0.5 and 1.5 mm measurement depths for which the young class values were significantly less:
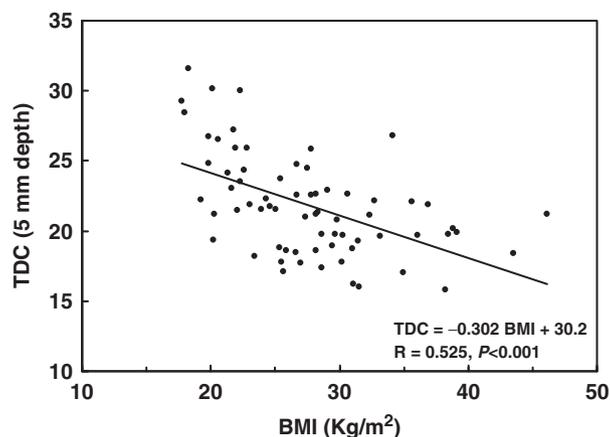[†]$P<0.01$,
[‡]$P<0.001$.

Fig. 2. Tissue dielectric constant (TDC) vs. BMI. Data points are average TDC values for dominant and non-dominant arms for each subject. Total N = 69. Solid line is linear regression with parameters shown in the inset.

the greatest association between TDC and Age is found at the 0.5 mm depth for which TDC = 0.158 Age + 25.6, $r = 0.490$, $P<0.001$ (Fig. 3). Dominant to non-dominant arm ratios did not differ between ages at any depth (Table 3).

Discussion

The ability to easily and non-invasively assess LTW within skin and subcutis offers a potentially powerful research tool to investigate a variety of physiologically and clinically related conditions in which changes in tissue water are of interest. The TDC method has shown such potential in a number of areas (1, 2, 4–6). Of particular interest to the author is its potential to assess lymphe-dema. Although TDC measurements have already shown some utility in assessing LTW in lymphedematous arms by comparing affected and non-affected arms of the same person (14), reference values for normal arms that take into account age and BMI could potentially enhance this methods utility, possibly extending its use to cases of potential bilateral lymphedema and other bilateral edematous conditions. Thus the goals of this study were to characterize the extent to which LTW within skin and subcutaneous tissue of normal forearms determined by TDC measurements varied by depth from the skin surface and to determine to what extent these values depended on subject age and BMI. The forearm site was chosen because it is an area that is affected by post-mastectomy lymphedema and is an important measurement site for characterizing extent of lymphedema and changes with time or treatment.

Methods considerations
With the current method, a probe in contact with the skin measures a TDC that depends on the electrical properties of all tissues within the effective measurement depth which has been defined as the depth at which the induced electric field falls to $1/e$ of its surface value (3). For the four different sized probes used in the present study this depth includes primarily skin (0.5 and 1.5 mm probes) or skin and subcutaneous fat (2.5 and 5.0 mm probes). Thus all measurements include the low water content stratum corneum, relatively high water content epidermis and

TABLE 3. *Tissue dielectric constant (TDC) arm ratios by body mass index (BMI) and age classification*

Depth (mm)	BMI classification			Age classification	
	Normal ($N = 24$)	Overweight ($N = 24$)	Obese ($N = 22$)	Young ($N = 34$)	Older ($N = 35$)
0.5	1.012 ± 0.068	1.039 ± 0.096	1.024 ± 0.076	1.010 ± 0.063	1.040 ± 0.094
1.5	1.007 ± 0.075	1.003 ± 0.082	1.037 ± 0.072	1.003 ± 0.061	1.027 ± 0.089
2.5	1.024 ± 0.096	1.002 ± 0.103	1.016 ± 0.094	1.008 ± 0.067	1.019 ± 0.120
5.0	1.038 ± 0.127	1.003 ± 0.082	1.008 ± 0.071	0.997 ± 0.074	1.036 ± 0.113

Data are mean $\pm$ SD of dominant to non-dominant arm TDC ratios. Normal, BMI $<25\,\text{kg/m}^2$; Overweight, BMI 25–29.9 kg/m^2; Obese, BMI $>30\,\text{kg/m}^2$. Young <55 years, Older ≥ 55 years. TDC ratios did not significantly differ among depths for any BMI or Age classification or among classes at any depth.
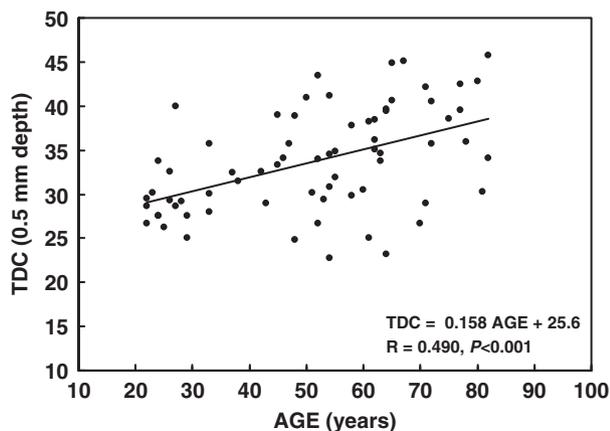

Fig. 3. Tissue dielectric constant (TDC) vs. Age. Data points are average TDC values for dominant and non-dominant arms for each subject. Total N = 69. Solid line is linear regression with parameters shown in the inset.

expression lies in its ability to extract skin values (ε_s) from the measured TDC value provided that skin thickness and the subcutaneous fat dielectric constant are known or estimated. In the present study, however, the focus was on the totally measured TDC value as reflective of all measured tissue components. Thus, reported data are based on probe-specific calibration factors, that take into account the differing field penetrations of the different probe geometries used, that were pre-programmed by the manufacturer within the device's processing unit.

Measurement depth dependence
A finding with respect to measurement depth dependence was the significant decrease in TDC values with increasing depth in both dominant and non-dominant arms for all subjects (Table 1). Such dependence is consistent with the variation in tissue constituents and their water content with depth below the skin surface because TDC values obtained from greater measurement depths are increasingly influenced by deeper tissue constituents such as subcutaneous fat and its lower relative water content (10, 20). Although TDC values at each measurement depth significantly differed from all others, the largest change was observed to occur between a measurement depth of 1.5 and 2.5 mm (Fig. 1). This finding may be explainable by considering skin thickness features in relation to measurement depth. Measurements of skin thickness on the volar forearm of women using high frequency ultrasound indicate that skin depth to the subcutis interface ranges between 0.75 and 1.25 mm (26–29). These data are consistent with and would largely explain the large TDC difference between 1.5 and 2.5 mm and the smaller difference between 2.5 and 5.0 mm measurement depths for the following reason. The 2.5 and 5.0 mm measurement

dermis and for the larger probes also the relatively low water content subcutaneous fat. Although the stratum corneum represents a fairly well-defined laminae, skin layers are less clear and there is a gradual transition from below the corneum to basal cell layers in which water content increases from about 20% to about 70% (21). Dermal superficial papillary and deep reticular regions may differ slightly in their water content (22, 23) but is about 70%. Water content of subcutaneous fat is reported as about 10% (24). Thus the TDC value obtained reflects to varying degrees the differing water contents within the measurement volume. Quantitative aspects of this dependency have been described based on analysis of a two-layer model composed of an upper skin layer and lower fat layer (11, 25). Accordingly the TDC value was shown to be expressible in terms of skin and fat dielectric constants (ε_s and ε_f), skin (epidermis and dermis) depth δ and probe-specific calibration factors q as $TDC = (\varepsilon_s - \varepsilon_f)(1 - e^{-q\delta}) + \varepsilon_f$. The utility of this

depths include in their sampling volumes both skin (epidermis and dermis) and portions of subcutis containing relatively less water content than dermis, whereas measurement depths of 0.5 and 1.5 mm include mostly or exclusively skin. Further, because subcutis depth, measured from dermal–subcutis interface to fascia, is about 7.5 mm in ventral forearms (27), the slightly less TDC value recorded to 5.0 mm compared with 2.5 mm may be explained by the relatively greater proportion of low water content subcutis included in the 5.0 mm depth sampling volume.

TDC value dependence on BMI

Although there was a tendency for TDC values at each measurement depth to decrease with increasing subject BMI (Table 2), it was at the deepest measurement depths (2.5 and 5.0 mm) for which this dependency was significant, with the dependency at 5.0 being highly significant (Fig. 1). One interpretation of this finding is that with increasing BMI there is an associated increase in the relative fat content within the TDC measurement volume that, because of its relatively lower water content, causes TDC values to be reduced. Such changes in fat content would be expected to be greatest within the lower dermis and hypodermis and have their greatest effect on TDC values that are obtained from the deeper measurement depths.

TDC value dependence on age

Older persons demonstrated increased TDC values than younger persons only at the shallowest measurement depths (0.5 and 1.5 mm) with measurements to a depth of 0.5 mm showing the greatest and most significant difference (Table 2 and Fig. 3). This finding suggests that skin tissue water as assessed by TDC tends to increase with increasing age. It is a somewhat surprising finding because dermal glycosaminoglycans that serve to bind up to 1000 times their volume in water (30) have been reported to be significantly reduced in aged human skin (31) with parallel reductions in water content as measured in rat skin (32). Despite this, the present results are consistent with previous reports, in which magnetic resonance imaging demonstrated greater amounts of mobile water in the upper dermis of aged skin as compared with younger skin (23) and a report that describes dermal water depots moving closer to the skin surface with increasing

age (19). Although age-related decreases in relative dermal fat content might also explain the greater water content found in the present subjects, such age-related changes are not supported by available evidence (33). Further, the age dependence it is not explained by BMI differences because there was no significant correlation between subject age and BMI. Future additional investigative effort to further study this aspect would appear warranted.

Acknowledgement

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