Assessing Free and Bound Water in Skin at 300 MHz Using Tissue Dielectric Constant Measurements with the MoistureMeterD

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13 Assessing Free and Bound Water in Skin at 300 MHz Using Tissue Dielectric Constant Measurements with the MoistureMeterD

Harvey N. Mayrovitz

Key Points

1. Tissue dielectric constant (TDC) measurements using the MoistureMeterD provide a way to assess an individual's local skin-to-fat water rapidly and noninvasively.
2. Assessments can be done in virtually any anatomical site of clinical interest.
3. TDC and thereby relative water can be assessed at different depths, which is a feature that could aid in better characterizing edematous and lymphedematous characteristics.
4. Tracking of changes in lymphedematous status over time is easily and rapidly done.
5. In cases of potential unilateral lymphedema, inter-side TDC ratios may serve as markers of subclinical lymphedema.

Introduction

The MoistureMeterD (MMD) is a multiprobe device (Fig. 13.1) manufactured by Delfin Technologies (Kuopio Finland) that is used to measure skin and upper subcutis tissue dielectric constant (TDC) at a frequency of 300 MHz by touching the skin's surface with a handheld probe for about 10 s (Fig. 13.2). Probe outer diameters range from 10 mm for a 0.5 mm effective measurement depth (Fig. 13.3) to 55 mm for a 5 mm measurement depth. Effective measurement depth is defined as the depth at which the electric field decreases to 1/*e* of its surface field as illustrated in Fig. 13.4 for a 2.5 mm depth measurement probe.

Dielectric constant, also known as relative permittivity, is a dimensionless number equal to the ratio of the permittivity of tissue to the permittivity of vacuum. Because TDC values in part depend on tissue water content, TDC values and their change provide indices of water content and quantitative estimates of water content changes. For reference the dielectric constant of distilled water at 32 °C is about 76. Because the measuring devices operate at a frequency of 300 MHz the measured skin TDC values are sensitive to both free and bound water within the measurement volumes. The vertical dimension for the measurement volume ranges between 0.5 mm and 5.0 mm below the epidermis with the total volume depending on the probe diameter.

Currently available devices come in two flavors. One is the original MMD, the multi-probe version with four separate probes as shown in Fig. 13.1 for effective measurement depths of 0.5, 1.5, 2.5, and 5.0 mm with the largest size probe measuring the deepest. The other device (Fig. 13.5) is a compact version (MMDC) in which the sensor and processing electronics are built into the handheld unit. The MMDC has a bar

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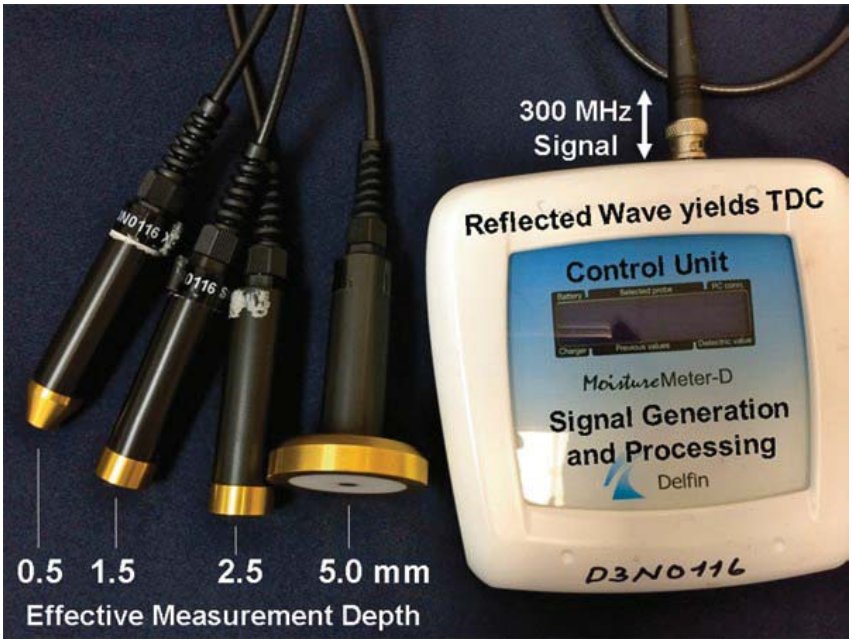

Fig. 13.1 Multiprobe Tissue Dielectric Constant (TDC) device. Effective measurement depth depends on probe construction and dimensions with larger diameter probes penetrating deeper. Operating principle is that a 300 MHz signal is transmitted to the tissue and the reflected wave is processed to obtain the dielectric constant of the tissue volume measured. The TDC is strongly dependent on the free and bound water contained within the measurement volume

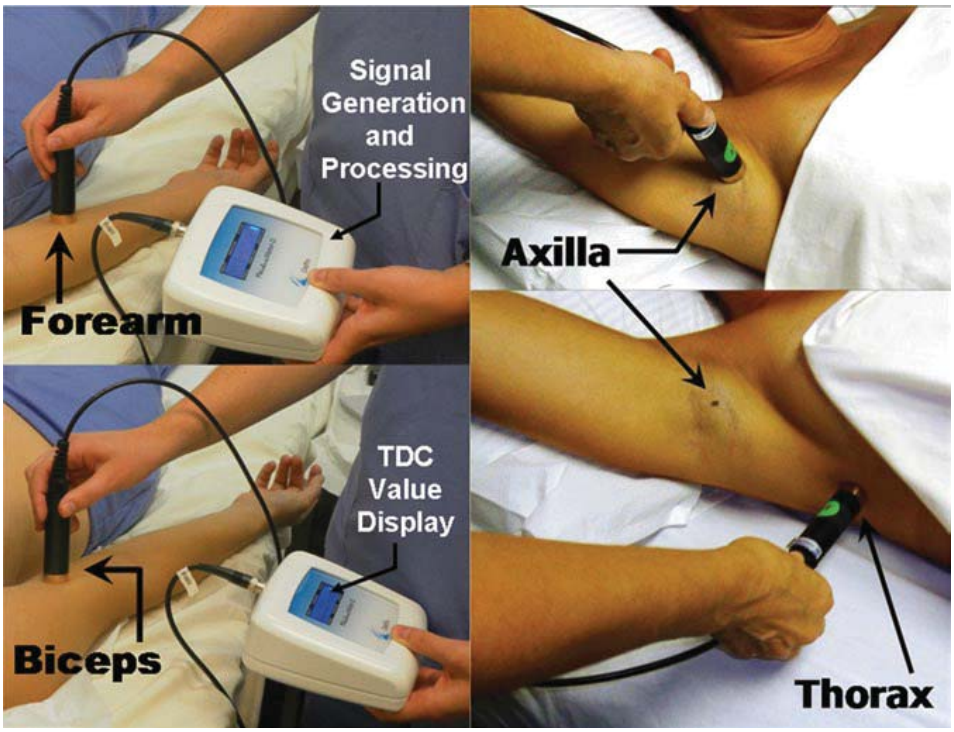

Fig. 13.2 Measuring TDC at multiple sites. Probes can be used to measure TDC at virtually any anatomical site of interest. Here is shown measurements using a probe measuring to an effective depth of 1.5 mm at forearm, biceps, axilla, and lateral thorax. Measurement activates when skin is touched and takes about 10 s

indicator showing the relative amount of contact pressure being exerted on the skin. The MMD and to a lesser extent the MMDC have been used in basic and clinical research studies in which skin tissue water and its change were of interest. Because either probe system can be used in virtually any anatomical location, data and findings are available for multiple anatomical sites on

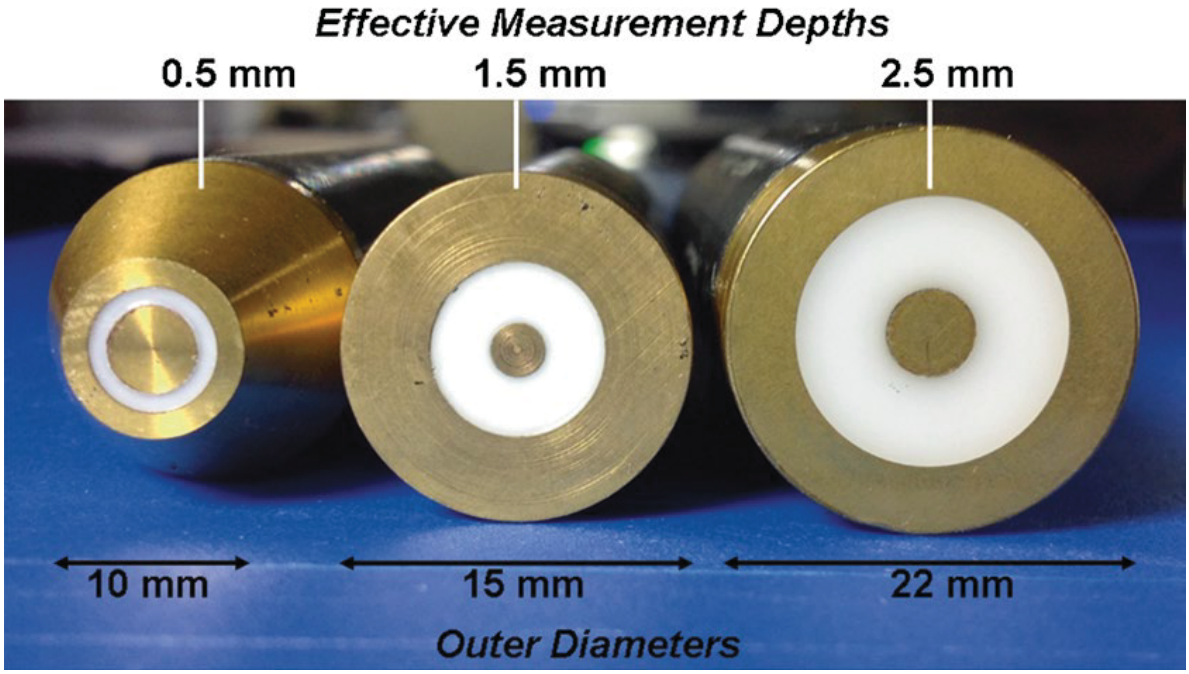

Fig. 13.3 Variation in probe design determines effective measurement depth. TDC measurements are used to assess localized tissue water and its change with the wider probe penetrating more deeply. Choice of probe to use depends on application and available space for placing the probe. The largest effective measurement depth is 5 mm achievable with a probe that has a diameter of 55 mm

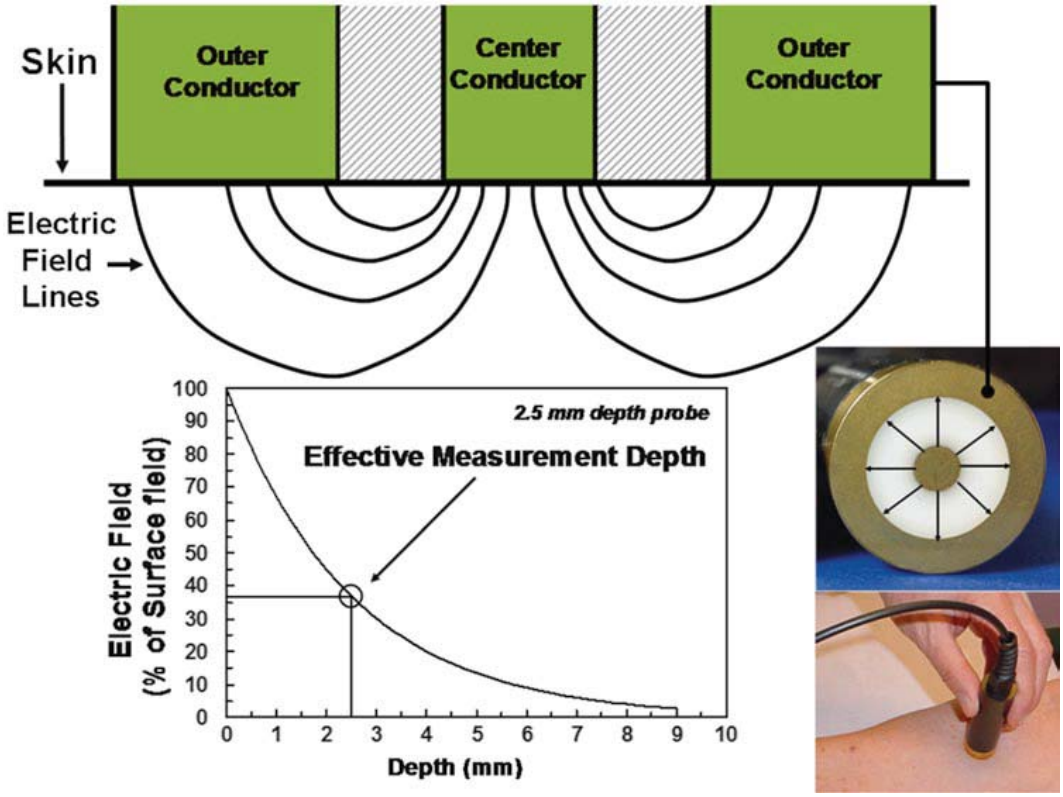

Fig. 13.4 Effective measurement depth concept. Effective measurement depth is defined as that depth at which the electric field produced by the probe on the skin surface is reduced to 1/*e* (36.7 %) of its value. The *electric field lines* are schematically illustrated emanating from and then terminating on the concentric electrodes of the probe

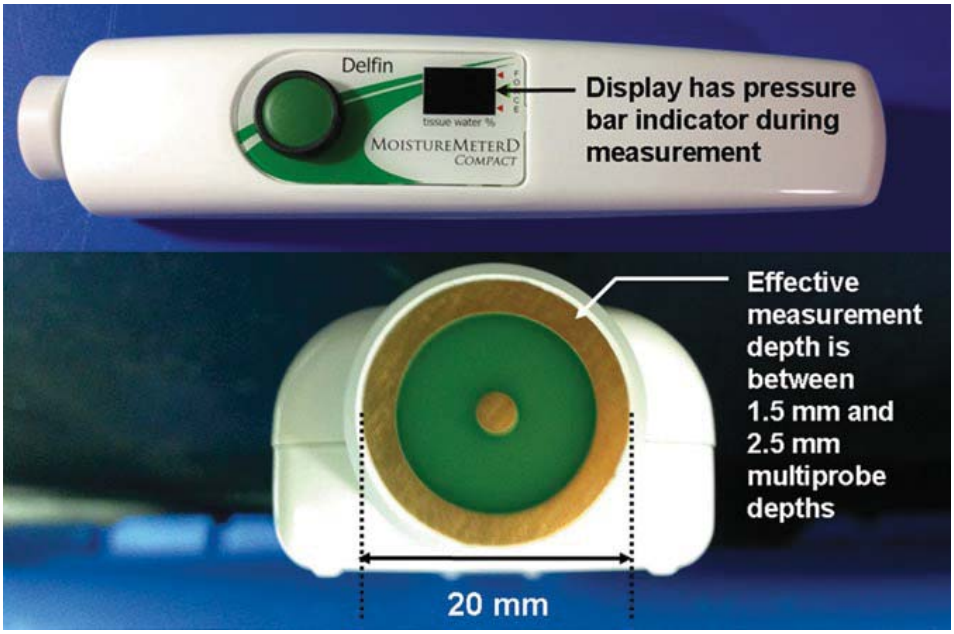

Fig. 13.5 Compact Tissue Dielectric Constant (TDC) measurement device. All functions are built into the single handheld device. Its effective measurement depth is between that of the 1.5 mm and 2.5 mm depth multiprobes and TDC readings would be about 6 % greater than those of the 2.5 mm probe. The display contains a series of *horizontal bars* that when aligned indicate the proper applied pressure. The display reads out in percent water rather than TDC values directly

the upper body including face [1, 2], breast [3], forearm [4–7], biceps, axilla, and thorax [8] and on the leg and foot [1, 9, 10]. One of the most frequent uses to date has been for tracking and possible early detection of subclinical lymphedema in women at-risk for or already having lower extremity lymphedema or upper extremity breast cancer treatment-related lymphedema (BCRL) [11–17]. The method also may have value in differentiating lower extremity lymphedema from lipedema [18], characterizing changes in postsurgical fluid status [19], and assessing skin irradiation effects [3].

Measurement Principles

The control unit (Fig. 13.1) generates and transmits a very low power 300 MHz signal into the probe that is in contact with the skin (Fig. 13.2). The signal is transmitted into the tissue via the probe that acts as an open-ended coaxial transmission line [20]. Part of the signal is absorbed by the tissue, mainly by water, and part is reflected back to the control unit where the complex reflection coefficient is determined [21, 22] from which the dielectric constant is determined [23, 24]. Reflections from the end of this coaxial transmission line depend on the complex permittivity of the tissue which depends 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 and the dielectric constant is mainly determined by water molecules (free and bound). Consequently, the device includes and analyzes only the dielectric constant (TDC) 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 [25]. In all cases TDC is strongly dependent on relative water content with TDC values that decrease with water reductions during hemodialysis [26] and that correlate with whole body water percentages as illustrated in Fig. 13.6 in which forearm TDC

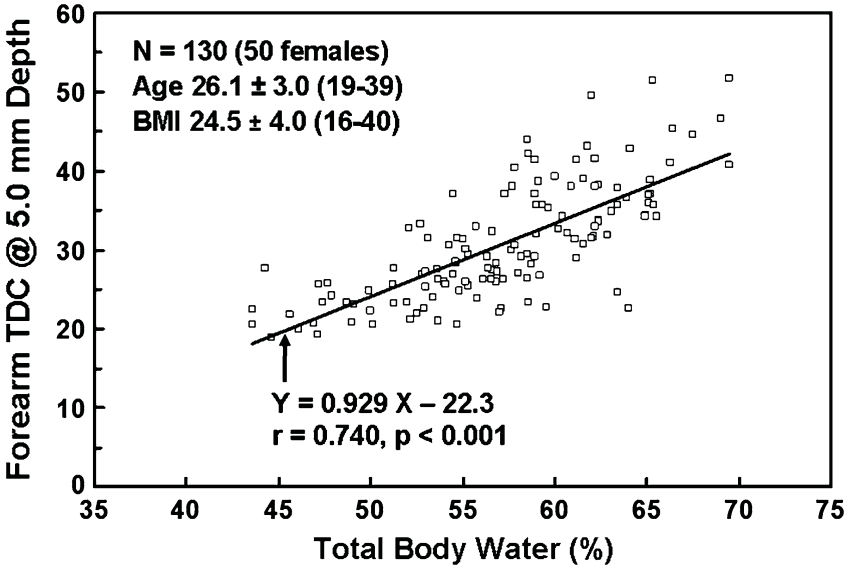

Fig. 13.6 Tissue Dielectric Constant (TDC) values in relation to total body water. TDC values are directly related to percentage of total body water (TBW). TBW was measured via bioimpedance. Relationship between TDC and TBW is illustrated for a 5 mm TDC forearm measurement depth in 130 young adults. The *solid line* is the linear regression equation with parameters as indicated in the figure

values are seen to highly correlate with total body water percentage as determined using bioimpedance measures.

The induced electric field within the tissue falls off exponentially and the effective measurement depth, defined as that depth at which the field is 1/*e* its surface value, depends on the dimensions of the probe [27] with larger dimensions being associated with deeper penetration. If the tissue measurement volume is viewed as being comprised of two layers, one being the skin including stratum corneum, epidermis and dermis with combined skin depth δ, and the other part being the subcutaneous tissue including fat, then it can be shown that measured TDC values depend on dielectric constants of skin (ε_{skin}) and fat (ε_{fat}) and on δ [3, 27]. This relationship can be expressed [2] as $TDC = \left(\varepsilon_{skin} - \varepsilon_{fat}\right)\left(1 - e^{-q\delta}\right) + \varepsilon_{fat}$ in which q is a device constant that depends on probe dimensions and is about 0.82 for the 1.5 mm depth probe. Changes in TDC values largely reflect changes in skin water content because of the normally large fraction of skin water. However, because TDC values also depend on skin thickness (δ) comparisons of absolute water content between individuals or groups should be done with caution. An equation linking percentage of tissue water content (PWC%) to TDC values has been proposed [26] for high water content tissues and is given by PWC% = 100 (TDC – 1)/77.5. The denominator of this equation (77.5) is based on a TDC value for water of about 78.5 at 25 °C. However, since water's dielectric constant depends on temperature, the tissue temperature being measured should be taken into account. For example, at a skin temperature of 34 °C, water's dielectric constant is about 75.2. Table 13.1 lists water dielectric constants for various temperatures. Temperature corrections may result in small TDC changes but under certain circumstances such corrections are useful and easily done. For example if a PWC% reading on the

Table 13.1 Dielectric constant of water versus temperature

Temperature (°C)	Dielectric constant
20	80.1
23	79.0
25	78.5
26	78.0
28	77.3
30	76.6
32	75.9
34	75.2
35	74.9
37	74.2
40	73.2

The most appropriate value for use in converting percentage water to Tissue Dielectric Constant (TDC) when using the compact probe would be to use the skin temperature at which the measurement is being made

compact device was 36 % at a tissue temperature of 34 °C then the true percent water in this tissue would be closer to (77.5/74.2)×36 %= 37.6 %, a value that is approximately 4.4 % greater.

Calibration Procedures

Each device is pre-calibrated by the manufacturer. For the multi-probe system each probe is separately calibrated for a given control unit. If two or more systems are being used, probes should not be interchanged between control units. There may be circumstances when independent calibrations or calibration checks are useful. This can be done by exposing the probe tips to various ethanol–water concentrations and comparing values obtained with known solution dielectric constants. The static dielectric constant for ethanol at 25 °C, averaged from multiple sources, is 24.8. The approximate dielectric constant values for various ethanol–water mixtures that are listed in Table 13.2 may be used to compare values obtained with any probe and if needed take appropriate calibration adjustments into account. An example of a full calibration curve is shown in Fig. 13.7, but only a few ethanol–water mixture concentrations would be sufficient.

Table 13.2 Ethanol–water mixture dielectric constant at 25 °C

% Ethanol by volume	Dielectric constant of ethanol–water mixture
0	78.3
10	73.0
20	67.6
30	62.3
40	56.9
50	51.6
60	46.2
70	40.9
80	35.5
90	30.2
100	24.8

For calibration or calibration checks the Tissue Dielectric Constant (TDC) probe can be exposed to ethanol–water mixtures to determine either calibration factors or to determine how well measured values agree with the values listed in the table

Measurement Procedure

Touching skin with one of the probes of the multiprobe device or touching it with the compact device activates the measurement that is heralded by short distinctive sound. A single measurement takes about 10 s or less to complete with completion signaled by another distinct audible sound. The TDC value is displayed on the control unit of the multiprobe readout. For the compact device the readout is not directly that of the TDC value, but instead it is a calculated percentage water PCW% determined via the equation previously given. If one is using both multiprobe and compact devices, it is useful to convert compact readings to TDC to achieve uniformity of measures for comparison purposes between results obtained from the two systems. The conversion equation that can be used is $TDC = 1 + [(PWC\%)(\varepsilon_{water} - 1)]/100$ in which PWC% is the number displayed on the compact probe (calculated percentage water) and ε_{water} is the dielectric constant of water used by the device for its calculation which is 78.5. For example, a reading of 36 % would correspond to a TDC value of $1 + (36 \times 77.5)/100 = 28.9$.

Short- and Long-Term Measurement Repeatability

One or Multiple Measurements Averaged

TDC measurements taken in triplicate and averaged are the method most frequently employed. However, it has been shown that for TDC measurements on forearms of healthy women and women with BCRL the average difference in TDC value between the first measurement and the average of three sequential measurements to a depth of 2.5 mm is less than ± 1 TDC unit [6]. This suggests that for many purposes a single measurement may be sufficient; however, similar data on other anatomic sites is not yet available.

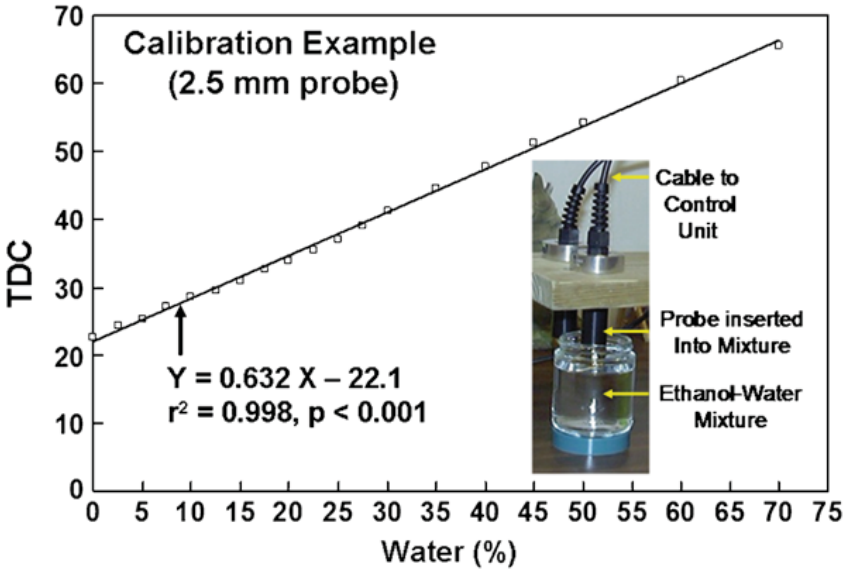

Fig. 13.7 Tissue Dielectric Constant (TDC) probe calibration check using various alcohol-water concentrations. Each probe is calibrated by exposing the probe measuring head to varying ethanol–water concentrations. This figure is for a 2.5 mm effective measurement depth probe and illustrates the essentially linear dependence of the TDC value with water concentration (%Water)

Short-Term Intrarater and Interrater Repeatability

Because some applications use pre- and post-TDC measurements to assess single treatment therapeutic modalities [11, 15] the measurement repeatability over intervals of the order of 60 min are of interest. Intrarater reliability has been assessed based on bilateral forearm TDC measurements to 2.5 mm depth on five subjects at 0, 30, and 60 min by a person with familiarity with TDC measurements. Intrarater repeatability has been assessed using intraclass correlation coefficients (ICC) that broadly express the percentage of variability attributable to true subject variance as opposed to measurement related variability (between-subject variation/total variation). Results revealed a single measure ICC value ($ICC_{2,1}$) of 0.996 with a 95 % confidence interval of 0.96–1.000. Additional tests based on measurements of a minimally trained rater under the same circumstances yielded $ICC_{2,1}$ values 0.999 with 95 % confidence intervals of 0.994–1.000. Interrater reliability ($ICC_{2,2}$) has also been assessed via triplicate measurements made on four subjects at 30 min intervals by two medical students who were minimally trained in TDC measurements. $ICC_{2,2}$ values obtained were quite good at 0.997 with a 95 % confidence interval of 0.988–0.999.

Table 13.3 Intraclass correlation coefficients (ICC) for Tissue Dielectric Constant (TDC) measurements

Measurement site	ICC	95 % Confidence interval
Forearm		
2.5 mm depth	0.962	(0.852–0.994)
1.5 mm depth	0.793	(0.394–0.994)
Leg		
2.5 mm depth	0.945	(0.792–0.991)
1.5 mm depth	0.941	(0.778–0.991)
Foot		
2.5 mm depth	0.887	(0.615–0.982)
1.5 mm depth	0.923	(0.720–0.988)

Measurements were made by two measurers on five subjects with TDC measurements made 1 week apart. Subjects were young healthy adults. Forearm site is on the dominant arm 5 cm distal to the antecubital space. Leg site is on the lateral calf 10 cm proximal to the malleolus. Foot site is mid dorsum of the foot. All measurements were made with subjects supine

Assessments of interrater reliability of TDC measurements made 1 week apart by two other minimally trained medical students yielded reasonable ICC values for both the 2.5 mm and the 1.5 mm depth probes as summarized in Table 13.3 for forearm, leg, and foot. Interobsever agreement of absolute TDC measurements in lower extremities has also been assessed based on measurements of three minimally trained measurers who each measured TDC at calf, ankle, and foot

to a depth of 2.5 mm in 34 healthy women [10]. Results showed average $ICC_{2,3}$ values for ankle and calf at excellent levels of 0.94 at both ankle and calf but a lesser value of 0.77 for the foot.

Long-Term Reliability

Longer term intrarater repeatability has been assessed by measurements of normal control arms in 32 women on six separate occasions by the same therapist over a 24 month period. These women had been diagnosed with unilateral breast cancer and their contralateral arms measured prior to surgery and then at 3, 6, 12, 18, and 24 months post-surgery. Intraclass correlation coefficients ($ICC_{2,1}$) determined for forearm TDC measurements to a depth of 2.5 mm was 0.900 with a 95 % confidence interval of 0.835–0.946.

Factors Effecting Measured TDC Values

Effective Measurement Depth

Depending on the anatomical site, measured TDC values will vary with generally higher values at lesser depths and lesser values at greater depths. This dependence is not necessarily linear as illustrated by measurements made on the anterior forearm of a large group of women (Fig. 13.8). For this data set the TDC averaged between both arms decreased according to a nonlinear power regression equation given by $TDC = 32.44\,\delta^{-0.185}$ in which δ is measurement depth. This observed pattern is at least in part due to the inclusion of increasing amounts of low water content fat in the measurement volume with increasing depth [8]. Although this pattern is

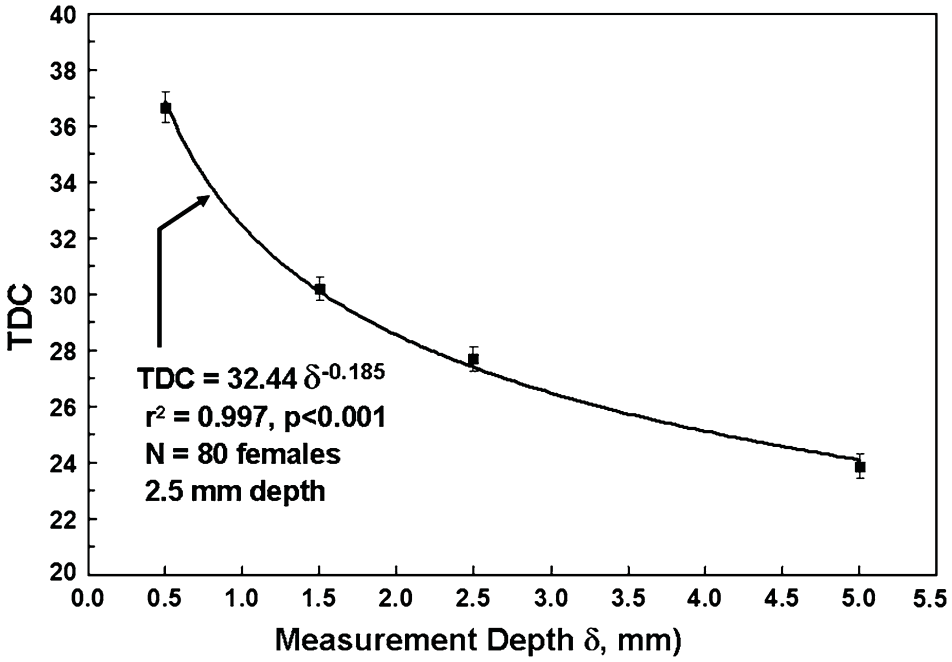

Fig. 13.8 Tissue Dielectric Constant (TDC) measurement depth-dependence: pre-surgery. Data points are pre-surgery mean TDC values for 80 patients with individual patient TDC values calculated as the average of both forearms. Error bars are ± 1 sem. *Solid line* is nonlinear (power-law) regression with the equation $TDC = 32.44\,\delta^{-0.185}$ determined based on 80 TDC measurements at each depth. *Inset* shows at-risk/control arm ratio with associated SD

Table 13.4 Site variations of Tissue Dielectric Constant (TDC) values

	TDC at indicated effective measurement depths		
Measurement site	0.5 mm	1.5 mm	2.5 mm
Forehead[a]	40.7 ± 3.4	36.8 ± 2.7	35.0 ± 3.6
Cheek	33.4 ± 6.4	32.5 ± 3.6	32.2 ± 4.1
Forearm[a] (Anterior)	29.5 ± 4.0	28.2 ± 2.4	24.9 ± 3.4
Thenar Eminence[a]	34.0 ± 5.6	35.1 ± 4.5	39.3 ± 5.1
Hand (Dorsum)	36.4 ± 3.4	34.5 ± 5.4	35.3 ± 4.1
Calf[a] (Medial)	32.4 ± 5.3	31.4 ± 5.8	28.2 ± 4.6
Peri-malleolar (Medial)	27.1 ± 4.6	26.7 ± 3.6	26.6 ± 3.5
Foot (Dorsum)	27.9 ± 4.1	28.2 ± 3.2	28.2 ± 3.5
Great Toe (Dorsum)	33.0 ± 5.5	33.6 ± 4.0	34.0 ± 4.3
Great Toe[a] (Plantar)	31.6 ± 5.0	33.9 ± 3.9	38.1 ± 3.9

Data (mean ± SD) is for 32 females (33.0 ± 13.9 years) with BMI of 24.8 ± 5.4 kg/m^2. All measurements are with subjects supine. Forearm and hand values are for the dominant arm

[a]TDC values were significantly different among depths ($p < 0.001$)

Table 13.5 Tissue Dielectric Constant (TDC) variations along nondominant forearm

	TDC measurement depth	
Distance distal to the antecubital crease	2.5 mm	1.5 mm
4 cm	26.3 ± 2.8	28.5 ± 2.5
8 cm	27.4 ± 3.4	29.4 ± 2.7
12 cm	28.4 ± 3.7	30.1 ± 2.5

Values are mean ± SD for 30 young adult females with average age of 27.4 ± 6.5 years and body mass index (BMI) of 22.9 ± 3.4 kg/m^2. TDC values at 1.5 mm depth were all greater than corresponding values at 2.5 mm depth ($p < 0.001$). The small TDC increase with increasing distance from the antecubital crease is statistically significant ($p < 0.001$)

commonly observed in tissues such as forearm and biceps it may be different in other anatomical sites. For example no significant difference in TDC values was detected among depths of 0.5, 1.5, and 2.5 mm on the cheek or the dorsum of hand or foot [1]. Contrastingly, significant differences in TDC values as a function effective measurement depth were observed for forehead; forearm; and medial, lateral, and anterior gaiter areas of the leg [1].

Anatomical Site Variations

Not unexpectedly TDC values depend on the anatomical site being measured. There appears to be no specific guiding principle that will predict which anatomical site for a given effective measurement site will have a particular value range. Table 13.4 summarizes some absolute TDC values previously measured [1] at various sites and effective depths for a group of 32 healthy women. Local TDC values may also vary slightly depending on the exact location of the measurement. The range of such potential variations has been assessed on the forearm of 30 healthy females [5] with triplicate measurements along and on either side of the forearm midline at various distances (Z, cm) from the antecubital crease for a total of nine separate sites. Mean TDC differences between adjacent longitudinal sites along the midline separated by 4 cm ranged from 0.7 to 4.2 % for 2.5 mm depth and 0.4 to 3.1 % for 1.5 mm depth. Variations among adjacent sites 1.2 cm distant from the midline in the medial direction ranged from 0.0 to 1.8 % for 2.5 mm depth and from 0.8 to 2.4 % for 1.5 mm depth. Table 13.5 summarizes absolute TDC values measured along the forearm midline [5]. For the 2.5 depth probe the regression equation was $TDC = 0.26Z + 25.2$ ($r^2 = 0.999$) and for 1.5 mm depth $TDC = 0.20Z + 27.7$ ($r^2 = 0.994$).

Gender and Age as Factors

Comparisons of TDC values measured to a depth of 1.5 mm in young adult males and females [2, 28] indicates that TDC values measured at the forehead, cheek, and forearm are all significantly greater in males than in females ($p < 0.001$). On average male TDC values were found to be about 13 % greater than females on the forearm [28] and about 5.6 % and 9.5 % greater on the forehead and cheek respectively [2]. These TDC differences may be related to male–female differences in skin thickness or to actual differences in water content. In either case male–female differences should be considered in any protocol that includes both genders.

The role of age has been investigated by comparing forearm TDC values at multiple depths in two groups of women divided by age above and below 55 years [12]. The results showed that to depths of 0.5 mm and 1.5 mm the older group TDC values were significantly greater than for the younger group but for the deeper depths of 2.5 mm and 5.0 mm there was no detectible difference. Table 13.6 summarizes the comparative TDC values.

Table 13.6 Age as a factor in Tissue Dielectric Constant (TDC) values

	Forearm TDC values	
Measurement depth (mm)	Younger ($N=34$)	Older ($N=35$)
0.5	31.5 ± 4.7	35.6 ± 5.9**
1.5	30.0 ± 4.9	33.2 ± 4.9*
2.5	24.8 ± 3.4	25.9 ± 3.8
5.0	21.7 ± 3.7	21.9 ± 3.5

Entries are forearm TDC mean ± SD determined as the average TDC values of the dominant and nondominant arm in 69 females with ages below 55 years (younger) and equal to or greater than 55 years of age (older). **$p<0.001$ vs. younger, *$p<0.01$ vs. younger

Body Fat Percentage as a Factor

TDC values tend to decrease with increasing body fat percentage and also to decrease with the percentage of arm fat. This feature is illustrated in Fig. 13.9 that is based on whole body and segmental body composition measurements via bioimpedance in 130 subjects. The fat dependence is greater when the effective measurement depth is greatest since for this condition the contribution of the low water content fat to the overall measurement is also greatest.

Vascular Factors

The potential impact of skin blood flow and vascular volume on TDC values has been investigated by measuring arm TDC values under various test conditions [4]. Arm vascular volume and skin blood flow was changed using an upper arm cuff inflated to 50 mmHg as illustrated in Fig. 13.10 with TDC measurements before and after inflation. Changes in skin blood flow were

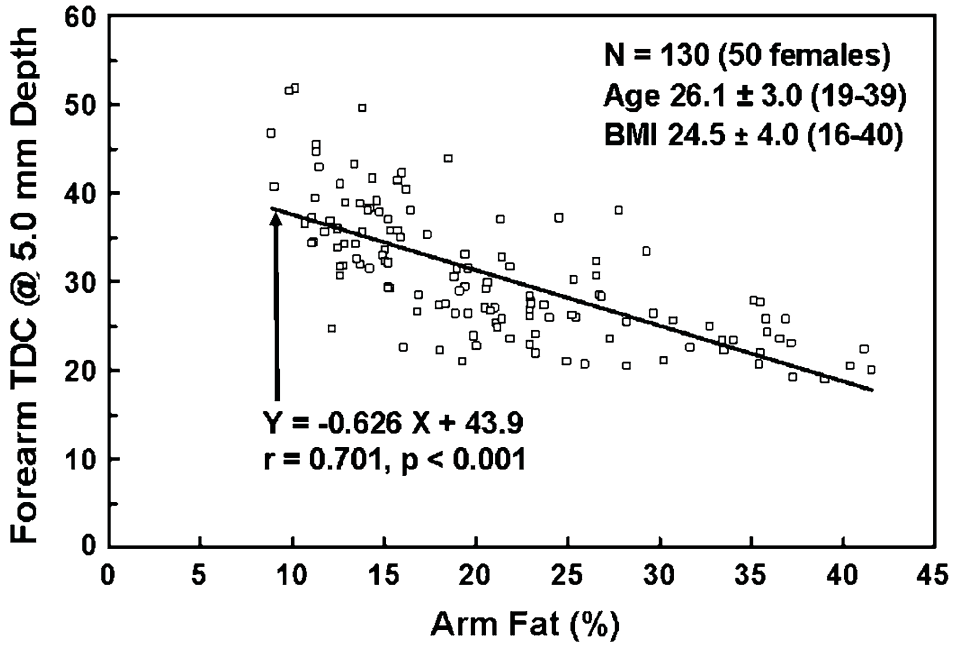

Fig. 13.9 Tissue Dielectric Constant (TDC) values in relation to percentage of fat in the arm. In contrast to a direct dependence on total body water, there is an inverse relationship between TDC values and total body fat percentage. TDC values to a depth of 5 mm are shown in relation to arm fat percentage determined via segmental bioimpedance. *Solid line* is linear regression equation with parameters shown in the figure

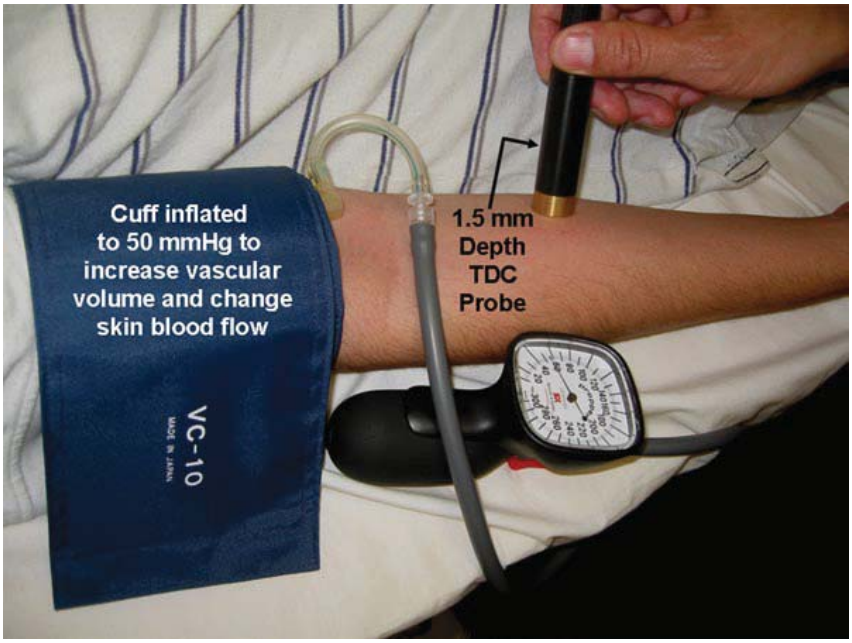

Fig. 13.10 Setup to assess vascular volume effects on Tissue Dielectric Constant (TDC). Forearm TDC measurement with a probe having an effective measurement depth of 1.5 mm is illustrated. Cuff around the upper arm is used to increase vascular volume and reduce blood flow. TDC measurements made before and during cuff inflation

also produced via changes in arm position ranging from horizontal positioning to arm elevated above the head. Illustrative results of such perturbations on skin blood flow measured via laser Doppler methods are shown in Fig. 13.11. As anticipated the various maneuvers caused significant vascular volume and blood flow changes but only minor effects on measured TDC values in the range of ±3 %. This suggests that vascular changes in most conditions are of minor importance vis-à-vis measured TDC values. However, from a technical viewpoint one should avoid placing the measuring probes directly over visible blood vessels.

Hormonal Factors

Because at least one anticipated application of the TDC method is the evaluation of edema and lymphedema in female patients the potential impact of hormonal influences associated with the menstrual cycle are of interest. This issue has been addressed via TDC measurements in premenopausal and postmenopausal women with premenstrual measurements made at three time points in the monthly cycle [7]. Results as summarized in Table 13.7 showed that forearm TDC values were not significantly different over the menstrual cycle at any measurement depth.

Diabetes Mellitus (DM)

Given the incidence of diabetes and its possible impact on skin physiology, awareness of possible impacts on skin tissue water is useful. This aspect has been investigated by comparing TDC values at multiple depths in forearm and foot dorsum in persons with and without diabetes mellitus [9]. Forearm TDC values tended to be slightly greater at all depths for the DM group but did not reach statistical significance. Contrastingly TDC values measured on foot dorsum were on average about 15 % greater in persons with DM. Absolute TDC values for persons with and without DM are summarized in Table 13.8. Although average foot TDC values were significantly ($p<0.05$) greater for the DM group, inter-foot TDC ratios were similar at all depths with no significant differences between groups.

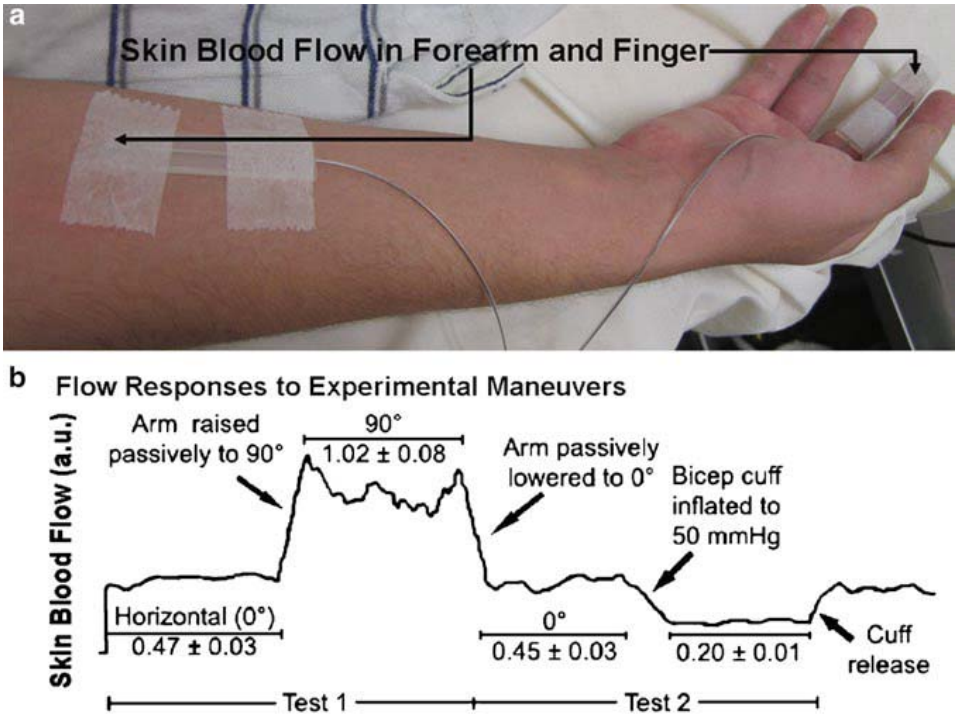

Fig. 13.11 Skin blood flow changes during experimental maneuvers. (**a**) Location of laser Doppler probes on forearm and finger to measure skin blood flow. (**b**) Typical example of blood flow changes associated with the various maneuvers. Forearm TDC is measured in triplicate near the end of each maneuver

Table 13.7 Menstrual cycle as a factor in Tissue Dielectric Constant (TDC) values

	Day of menstrual cycle		
TDC measurement depth (mm)	4	12	22
0.5	27.7 ± 3.6	27.8 ± 2.7	26.8 ± 3.4
1.5	26.6 ± 2.5	26.8 ± 2.8	25.7 ± 2.9
2.5	25.6 ± 3.3	25.6 ± 3.0	25.2 ± 2.8
5.0	20.8 ± 3.8	21.4 ± 3.2	21.3 ± 4.1
Hormones (pmol/L)			
Estradiol	5.7 ± 1.5	11.8 ± 6.8	3.4 ± 1.0
Progesterone	105.7 ± 35.9	138.3 ± 64.4	266.8 ± 220.4

Entries are mean ± SD with each depth measured in triplicate and averaged. TDC values are measured on the dominant arm forearm. TDC values did not significantly differ among cycle day for any depth. Estradiol concentration at day 12 was significantly greater than for either day 4 or day 22 ($p < 0.05$). Progesterone concentrations at day 22 were significantly greater than for either day 4 or day 12

Breast Cancer

Earlier published work evaluated TDC values at four strategic anatomical sites in women diagnosed with unilateral breast cancer [8]. These sites, forearm, biceps, axilla, and lateral thorax, were measured, and values obtained were compared to those obtained from a control group of women. Subsequently forearm TDC values were compared among three groups of women with groups classed as (1) healthy controls, (2) with breast cancer but prior to surgery, and (3) those patients who had developed BCRL [13]. The most current data available for these comparisons is for TDC measurements made in 80 women who were diagnosed with unilateral breast cancer and who were evaluated prior to their surgery. A summary of TDC values for the at-risk (cancer) side and for the contralateral (healthy) side as well as at-risk/contralateral side ratios are shown in Fig. 13.12.

Table 13.8 Diabetes Mellitus (DM) as a factor in Tissue Dielectric Constant (TDC) values

	TDC values	
TDC site and depth	NODM	DM
Forearm		
0.5 mm	32.4 ± 3.7	34.3 ± 4.6
1.5 mm	30.2 ± 2.7	32.0 ± 3.6
2.5 mm	27.5 ± 3.3	29.1 ± 3.9
Foot		
0.5 mm	28.4 ± 4.8	31.9 ± 3.7*
1.5 mm	28.9 ± 32.5	32.5 ± 5.9*
2.5 mm	29.1 ± 4.1	33.3 ± 6.4*

Entries are mean ± SD for 18 persons with and 18 persons without DM. * indicates significantly different from NODM ($p < 0.05$). Forearm TDC values decrease with increasing depth ($p < 0.001$), but foot dorsum values are not different among depths

Side-to-side TDC values did not significantly differ for any site, but differences among sites were significant ($p < 0.001$) with each site being significantly different from any other site. Contrastingly, side-to-side TDC ratios did not differ among measured sites.

Lymphedema

The presence of clinical lymphedema is associated with a significant increase in TDC values [13, 17] with affected arm values having average TDC values between 44 % to 65 % greater than contralateral arm values depending on the effective measurement depth [17]. Further, TDC values have been observed to decrease with various forms of therapy in lymphedematous legs [14, 15] and in arms and legs [11] by amounts ranging between 10 % and 16.8 % for legs and 8.2 % for arms. Table 13.9 summarizes the most recent data for TDC values measured at 2.5 mm depth in arms of 80 women with BCRL, in 80 women with breast cancer (BC) but no lymphedema and in 80 women without breast cancer (NOBC). TDC values of the lymphedematous arm greatly exceed TDC values obtained from contralateral arms. In patients with BCRL, contralateral arm TDC values are not significantly different from those measured in patients with breast cancer without lymphedema or in healthy women free of breast cancer.

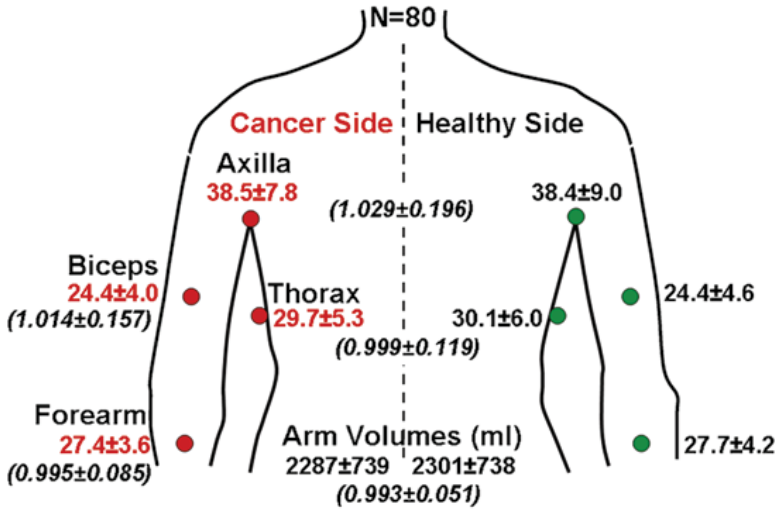

Fig. 13.12 Tissue Dielectric Constant (TDC) reference values from patients with breast cancer prior to surgery. TDC values, measured to a 2.5 mm depth, are given as mean ± SD and in parenthesis is the ratio of at-risk side (cancer side) TDC values to the contralateral side (healthy side) values. Volumes are the arm volumes. Side-to-side values did not differ for any site but TDC values among sites were significantly different one from another ($p < 0.001$)

Table 13.9 Tissue Dielectric Constant (TDC) values for women with and without breast cancer related lymphedema

	Tissue Dielectric Constant (TDC)		
Group[a]	Affected (A) side	Control (C) side[b]	TDC ratio (A/C)
NOBC ($N=80$)	26.8 ± 4.9	26.4 ± 4.7	1.001 ± 0.050
BC ($N=80$)	24.8 ± 3.3	24.9 ± 3.8	0.998 ± 0.082
BCRL ($N=80$)	42.9 ± 8.2**	26.0 ± 4.0	1.663 ± 0.319[§]

Data entries are TDC mean ± SD measured on forearms to an effective depth of 2.5

[a]For breast cancer (BC) and lymphedema (BCRL) groups affected (A) sides refers to at-risk arms and lymphedema arms respectively; control sides are contralateral arms. For the group without breast cancer (NOBC) side A corresponds to the dominant arm and side C corresponds to the nondominant arm

[b]Control side TDC values are not significantly different among groups

** TDC values of BCRL affected arms were significantly greater than for BC or NOBC groups ($p<0.001$). For BC and NOBC groups, TDC values were insignificantly different between paired-arms and between groups yielding similar A/C ratios

[§]A/C ratios for the LE group were significantly greater than for either the BC or NOBC groups ($p<0.001$)

Multiprobe Versus Compact Probe as a Factor in TDC Values

All reported TDC measurements so far are based on use of the multiprobe system (Fig. 13.1). Because of construction and design feature differences of the compact TDC probe (Fig. 13.5) an assessment of comparative TDC values produced by the different devices is useful. For that purpose TDC values obtained with the compact probe were compared with the multiprobe system for probes to depths of 1.5 mm and 2.5 mm in forearms and biceps of 32 males and 32 females. Results of this comparison are summarized in Table 13.10. The compact device measurements were found to be between the 1.5 mm and 2.5 mm measurements. Including both male and female values, compact device values are 5.6 % to 5.8 % higher than the 2.5 mm probe.

Table 13.10 Compact versus multiprobe Tissue Dielectric Constant (TDC) values

	Forearm		Biceps	
Probe	Female	Male	Female	Male
1.5 mm	30.9 ± 2.7	35.7 ± 3.4**	31.3 ± 2.5	36.6 ± 3.3**
Compact	28.2 ± 2.0	33.9 ± 3.2**	28.3 ± 2.0	34.4 ± 3.3**
2.5 mm	26.7 ± 2.3	32.0 ± 3.2**	26.5 ± 2.4	32.9 ± 3.7**

Data entries are TDC values (mean ± SD) determined as the average of both arms for 32 males and 32 females. ** = Male TDC values were greater than corresponding female values ($p<0.001$) for each probe at each site. The compact probe TDC values lie between the 1.5 and 2.5 mm depth probes and exceed the 2.5 mm depth probe by 5.6 % to 5.8 %

Potential Use of TDC for Early Lymphedema Detection

Based on the normal variance in TDC values among persons it is possible to develop criteria potentially useful to aid in the detection of early incipient lymphedema in persons at risk of developing unilateral arm lymphedema. To this end TDC bilateral forearm and biceps measurements were made to a depth of 2.5 mm in 103 women (60.6 ± 13.2 years) who had been diagnosed with breast cancer. Measurements were made prior to their scheduled surgery to eliminate surgery as a variable. Because of the relative site independence of inter-arm TDC ratios, inter-arm TDC ratios were chosen as the potential detection parameter and determined as the ratio of TDC values measured on the at-risk arm to the TDC value measured on the contralateral arm. This ratio is designated by the symbol γ and is for the forearm $\gamma_{forearm}$ and for the biceps as γ_{biceps}. A summary of these measurements is shown in Table 13.11. Theoretical lymphedema detection thresholds might be based on $\gamma+2.5$ SD (includes 99.4 % of cases) or on $\gamma+3.0$ SD (includes 99.9 % of cases). A determination of the number of patients that exceed the $\gamma+3.0$ SD threshold was investigated in the course of tracking 104 different patients evaluated on average 26.3 ± 17.5 months post-surgery. Ten patients (9.6 %) exceeded the forearm threshold and six (5.8 %)

Table 13.11 Arm Tissue Dielectric Constant (TDC) values and ratios for breast cancer patients prior to treatment

Site	At-risk arm	Control arm	γ	γ+2.5 SD	γ+3.0 SD
Forearm TDC	25.7±3.8	25.8±4.1	1.003±0.097	1.243	1.291
Biceps TDC	23.3±4.5	23.3±4.7	1.012±0.143	1.369	1.441

Entries are mean±SD for TDC values and at-risk/control arm ratios (γ) for 103 patients with age of 60.6±13.2 years. Forearm site is 6 cm distal to the antecubital crease and the bicep site is 8 cm proximal. Theoretical lymphedema detection thresholds might be based on γ+2.5 SD (includes 99.4 % of cases) or γ+3.0 SD (includes 99.9 % of cases)

exceeded the biceps threshold. Further, patients reporting at least one lymphedema-related symptom (N=34, 32.7 %) also had a significantly greater value for γ_{biceps} than patients with no symptoms (1.113±0.335 vs. 1.001±0.119, p=0.014) and also had a greater value for γ_{forearm} (1.100±0.231 vs. 1.026±0.129, p=0.038). Although these findings are encouraging vis-à-vis threshold detection, the concept remains theoretical at this time while awaiting outcomes of ongoing prospective sequential studies.

Conclusion

Measurements of the tissue dielectric constant (TDC) of the skin are a noninvasive, rapid, and reliable way to assess skin-to-fat relative water content and its change at almost any anatomical site. As described, the method has a well-documented physical basis and has a fairly extensive background of use in a variety skin sites and has been investigated for use in several conditions including lymphedema evaluation. The ability to measure water rapidly and locally provides the advantage of tracking changes in anatomical sites of particular interest either for pretreatment and posttreatment reasons or for longer-term follow-up assessments. In addition, the method allows for easy tracking of those anatomical sites deemed to be particularly at risk of developing lymphedema or those sites that on clinical examination already appear slightly edematous. Investigations into the use of TDC measures for early detection of incipient lymphedema have indicated significant potential, but studies are as yet incomplete and thresholds not yet validated.

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