

TISSUE DIELECTRIC CONSTANT (TDC) AS AN INDEX OF LOCALIZED ARM SKIN WATER: DIFFERENCES BETWEEN MEASURING PROBES AND GENDERS

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ABSTRACT

An easily measured, non-invasive, quantitative estimate of local skin tissue water is useful to assess local lymphedema and its change. One method uses skin tissue dielectric constant (TDC) values that at 300 MHz TDC depend on free and bound water within the measurement volume. In practice such measurements have been done with a research-type multi-probe, but recently a hand-held compact-probe has become available that may be more clinically convenient. Because most available published data is based on multi-probe measurements it is important to characterize possible differences between devices that unless known might lead to ambiguous quantitative comparisons between TDC values. Thus, our purpose was to evaluate potential differences in measured TDC values between multi-probe and compact-probe devices with respect to probe effective sampling depth, anatomical site, and gender and also to compare compact-probe TDC values measured on women with and without breast cancer (BC). TDC was measured bilaterally on forearms and biceps of 32 male and 32 female volunteers and on 12 female patients awaiting surgery for breast cancer. Results show that 1) TDC values at 2.5 mm depth were significantly less than at 1.5 mm; 2) Female TDC values were significantly less

than male values; 3) TDC values were not different between females with and without BC; and 4) dominant/non-dominant arm TDC ratios were not significantly different for any probe among genders or arm anatomical site. These findings indicate that probe type differences in absolute TDC values are present and should be taken into account when TDC values are compared. However, comparisons based on inter-arm TDC ratios are not statistically different among probes with respect to gender or anatomical location.

Keywords: edema, lymphedema, dielectric constant, lymphedema measurement, skin

There is an important need to be able to conveniently obtain non-invasive quantitative estimates of skin tissue water content in many conditions especially those related to evaluating local edema and lymphedema. One method that is capable of measuring at any anatomical site and has been available for some relies on the measurement of the skin tissue dielectric constant (TDC) at a frequency of 300 MHz. Since the TDC value is largely dependent on the tissue water content, the TDC value itself can be used as index of local tissue water content and its subsequent change that might accompany therapy. In practice, the measurement is done by contacting the skin with a concentric

probe that behaves as an open ended coaxial transmission line into which a very small amount of 300 MHz energy is transmitted to the skin (1-3). One of several different sized probes is connected through a cable to a central control box in which processing of data is done to determine the TDC. In effect, the TDC calculation is based on an analysis of the magnitude and properties of the reflected 300 MHz wave. At this frequency the TDC value is proportional to both the free and bound water within the target volume. Currently TDC measuring devices fall into two categories. One is a multi-probe device in which multiple-sized probes can be connected to the central control unit and provide the potential for measuring TDC to effective skin depths below the epidermis ranging from 0.5 mm to 5.0 mm (4). The multi-probe has been used in a variety of research applications for which extensive data has been published in areas including lymphedema (5-10), irritated and burned skin assessments (11-15) and skin physiology (16-18). More recently a fully portable compact device has been developed that integrates the probe and control box features into a single hand-held apparatus. Such a compact device might be more readily usable in clinical situations in which the multi-probe type measurement system with external probes is prohibited or difficult to implement. However, the relationship between TDC values measured with this new compact system to those measured with the multi-probe system is currently unclear. Clarification of these relationships would facilitate comparisons of TDC data already in the literature and allow for future data comparisons. Since the new compact device has the capability of measuring to only one depth an important aspect of its characterization is to determine its effective measurement depth. Further, since differences in TDC values between male and female (19) and differences between anatomical sites (4,20) have been described, possible effects of such differences on compact probe TDC values need to be

assessed and characterized. Thus, our specific aims were to compare TDC values obtained with the multi-probe device and the compact probe with respect to potential differences in 1) male-female TDC values, 2) effective measurement depth, 3) arm site TDC values and 4) TDC values in females with and without breast cancer.

METHODS

Subjects and Patients

Sixty-four mostly young and self-described healthy adults participated in this study (32 male and 32 female) along with 12 female patients who were awaiting surgery for breast cancer. Subjects and patients were evaluated after signing a University Institutional Review Board approved informed consent. Healthy subject requirements for participation were that they be at least 18 years of age and have self-reported normal upper extremity function with no history of serious trauma and no self-reported or visual evidence of any abnormal arm skin condition at the time of evaluation. Subjects were advised not to use any form of cream or lotions on their arms on the day of their evaluation. All subjects denied being a current cigarette smoker and none indicated taking any prescribed medication that might be considered as edema producing. Ages (mean \pm SD) for the healthy group were for females; 26.2 \pm 7.7 years (range 18-53 years; median age of 25.0 years) and for males 28.2 \pm 8.2 years (range 19-62 years; median age of 26.0 years). Male-female ages did not significantly differ ($p = 0.331$). Body mass index (BMI) for females was 23.8 \pm 4.8 Kg/m² with a range of 16.8 - 37.0 Kg/m² and a median of 22.4 Kg/m² that was significantly ($p < 0.001$) less than BMI values of males which were 25.3 \pm 3.2 Kg/m² with a range of 20.8 - 37.2 Kg/m² and a median of 24.8 Kg/m². With respect to the entire group (N=64), BMI classification indicates that 5/64 (7.8%) were underweight (BMI <18.5 Kg/m²),

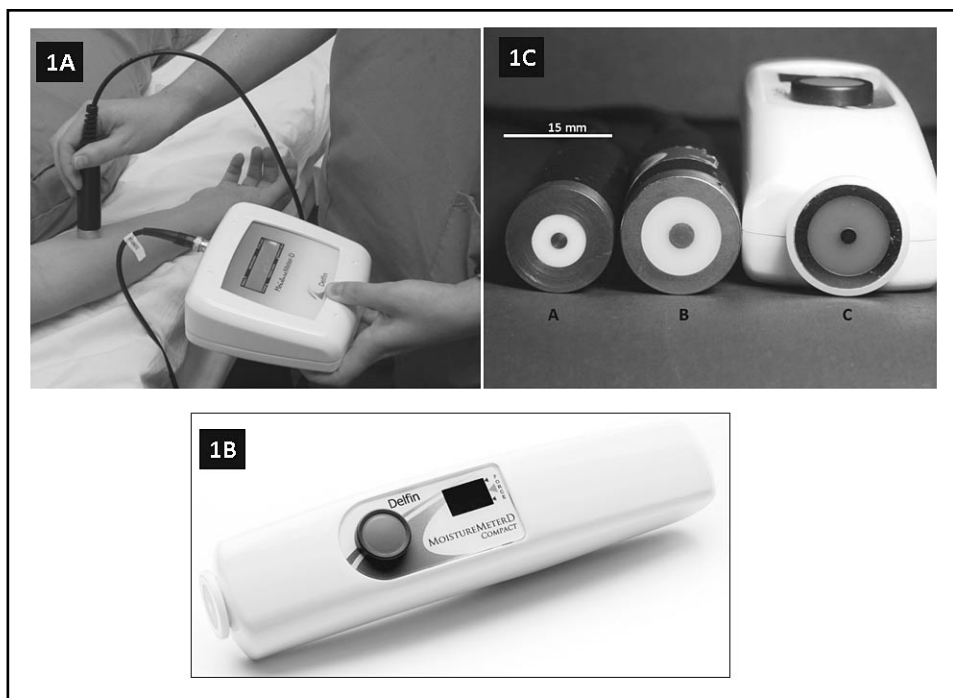


Fig. 1. Measurement devices and probes. 1A) MMD unit with probe in contact with forearm skin; 1B) Compact MMDC unit; 1C) Probes shown from measuring surface end. Probes A and B are used with the MMD unit and have effective measurement depths of 1.5 mm for A and 2.5 mm for probe B. Probe C is the self-contained MMDC unit.

37/64 (57.8%) were normal (BMI <25 Kg/m², 17/64 (26.6%) were overweight (BMI 25-29.9 Kg/m²) and 5 (7.8%) were obese (BMI ≥ 30 Kg/m²). The right hand was the self-reported dominant hand in 42 subjects (65.6%) and the left hand was dominant in 22 subjects (34.4%). Handedness proportions were similar between females and males. Patients included in the breast cancer group were females who had been diagnosed with unilateral breast cancer within two weeks of TDC measurement and were awaiting breast cancer related surgery. Average age was 62.2 ± 12.8 years that was significantly (p<0.001) older than the younger healthy females. Average BMI of the patient group was 29.1 Kg/m² with 4/12 (33.3%) having normal (BMI <25 Kg/m², 4/12 (33.3%) were overweight (BMI 25-29.9 Kg/m²) and 4/12 (33.3%) were obese (BMI ≥ 30 Kg/m²). The self-reported dominant hand in patients was

the right hand in 10/12 (83.3%) and the left in 2/12 (16.6%) of patients. The arm at-risk for lymphedema (the cancer side) was the dominant side in 5/12 (41.7%) of patients.

TDC Measurement Devices

The multiprobe device used to measure TDC was the MoistureMeterD (MMD) and the compact device used was the MMD Compacts (MMDC) both manufactured by Delfin Technologies Ltd, Kuopio Finland. The MMD 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 (*Fig. 1A*). The physics and principle of operation have been well described (1-3,21-23). 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 (1,21). 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 the 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 to 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 probes with effective measurement depths of 1.5 mm and 2.5 mm were used for the multiprobe measurements. In the MMDC, the probe is integrated with the main unit and provided with the force sensor for the standardization of the interrater measurements (*Fig. 1B*). The compact device is designed to be a readily-usable portable and pocket-sized device useful for hospitals, research, and treatment units where a quick evaluation of tissue swelling might assist diagnostic or therapeutic procedure. Since the concept of tissue dielectric constant may not be familiar to all potential users the manufacturers chose to have the TDC display of the MMDC show a quantity referred to as the local tissue water (LTW) where the LTW value is derived from the actual TDC measurement according to the formula $LTW(\%) = 100\% \times (TDC - 1)/77.5$. In this way if a measurement were done in a vacuum ($TDC=1$) an $LTW\%$ value of 0% would be shown. If pure water were measured with a TDC value of 78.5 (@ 25°C) the LTW value shown would be 100%. However, in the present paper report MMDC values are given in the same TDC units as the MMD device so that direct comparisons between current TDC values and those in the literature can be easily made. The MMDC probe electrode dimensions are arranged so that the effective penetration depth (i.e., the 37% penetration of the electric field) consists of skin and

upper part of subcutaneous fat. The dimensions of the MMDC electrodes and spacing are similar to that of the MMD probe that has an effective penetration depth of 2.5 mm.

TDC Measurement Procedure

All measurements were done with subjects seated; measurements were started after a 10 minute acclimation rest interval. TDC measurements were made on standardized sites on the anterior part of both forearms and both biceps. The standardized forearm site was along the midline located 6 cm distal to the antecubital crease. The standardized bicep site was 8 cm proximal to antecubital crease. These target measurement sites were marked with dot using a surgical pen to serve as a reference center point for probe placement. In accord with previous assessments (8), a single measurement was obtained at each site by placing the probe in contact with the skin and held in position using gentle pressure. After about 10 seconds an audible signal indicated completion of the measurement. In the healthy subject group TDC measurements at each site were made first with the 2.5 mm depth probe followed by the measurements of the 1.5 mm depth probe and lastly by the compact probe (*Fig. 1C*). TDC measurements in the patient group were made only using the compact probe, but at the corresponding sites used in the healthy group. All TDC measurements in subjects were made by the same investigator (F.B.) and all TDC measurements in patients were made by the same investigator (L.L.). After TDC measurements, arm girth (circumference) at the measurement sites was determined using a tape measure pulled to constant tension using a Gulick-type tape measure (Allegro Medical Supplies, Mesa AZ, USA). All girth measurements on the healthy subjects were made by the same investigator (R.D.) and on patients by (L.L.)

Analysis

TABLE 1
Tissue Dielectric (TDC) Values for Each Probe and Site by Gender

Probe	Forearm		Biceps	
	Female [¶] (N = 32)	Male [¶] (N = 32)	Female [¶] (N = 32)	Male [¶] (N=32)
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 group mean TDC values (mean ± SD) determined as the average of both arms. ** = Male TDC values were greater than corresponding female values (p<0.001) for each probe at each site. ¶ = Male and female TDC values obtained with each probe were significantly greater for males (p<0.001) and each probe value was significantly (p<0.01) different from each other with TDC values monotonically decreasing from the 1.5 mm probe to the compact probe to the 2.5mm probe. Results indicate that the compact probe TDC value lies between the 1.5 and 2.5 mm depth probes.

Dominant and non-dominant arm TDC measurements were averaged to obtain a single averaged TDC value for each of the arm sites (forearm and biceps separately). Possible differences among TDC measurements obtained with 1.5, 2.5, and compact probes on the healthy group were tested using a general linear model (GLM) with repeated measures for each gender. For each probe and site, possible differences between male and female TDC values were tested using independent t-tests with a p-value < 0.01 taken as indicating a significant difference. Possible differences in TDC values between arms were tested directly by comparing dominant vs. non-dominant absolute TDC values (paired t-test). In addition, the ratio of TDC values (dominant/non-dominant) was calculated for each subject and compared by probe, site and gender. To compare compact probe TDC measurements made only on female arms, corresponding anatomical sites on the arms of the female subjects and the patients were analyzed and preliminarily tested for differences using independent t-tests.

RESULTS

Healthy Subjects

TDC values at effective measurement depths of 1.5 and 2.5 mm using the multiprobe system and TDC values measured with the compact device were all significantly greater in males than females (p<0.001) at both forearm and biceps sites (*Table 1*). Comparisons of differences among probes showed that for males and for females TDC values obtained with each probe were significantly different (p<0.01) from each other with TDC values progressively decreasing from those obtained with the 1.5 mm probe to the compact probe to the 2.5mm probe as summarized in *Table 1*. TDC values for the compact probe in all cases was between the values measured by the 2.5 mm and 1.5 mm depth multiprobe. Percentage differences in TDC values between the compact probe and the 2.5 mm depth probe, calculated as the average of their sum divided by their difference (mean ± SD), were for forearms and biceps respectively 5.4 ± 3.8% and 6.4 ± 5.0% for females, and 5.7 ± 5.0% and 4.7 ± 6.1% for males. These percentage differences were not statistically different between genders and the overall percentage differences (N = 64) between the compact and 2.5 mm probe were respectively for forearm and biceps 5.57 ± 4.43% and 5.61 ± 5.54%.

TABLE 2
Dominant/Non-Dominant Arm TDC Ratios by Gender and Effective Measurement Depth

Probe	Forearm: Dominant/Non-Dominant Arms			Biceps: Dominant/Non-Dominant Arms		
	Female	Male	p-value	Female	Male	p-value
1.5 mm	0.993 ± 0.050	1.030 ± 0.057	0.070	1.000 ± 0.053	1.006 ± 0.053	0.648
Compact	1.000 ± 0.054	1.023 ± 0.064	0.123	1.004 ± 0.064	1.003 ± 0.066	0.966
2.5 mm	0.993 ± 0.051	1.016 ± 0.050	0.075	1.001 ± 0.054	0.996 ± 0.043	0.666
Girth ratio	1.015 ± 0.027	1.0160 ± 0.025	0.930	1.005 ± 0.021	1.008 ± 0.004	0.528

Data entries are Dominant / Non-Dominant arm TDC ratios (mean ± SD) for 32 females and 32 males. There was no significant difference in these ratios between genders or site at any depth nor was there any significant difference among depths for either gender. Results suggest the ratio is a robust parameter with respect to probe type, gender or site.

Despite probe, gender, and depth dependent differences in absolute TDC values, there was no significant difference in absolute TDC values between arms for any probe, gender, or depth. Using the compact probe as an example, female dominant and non-dominant TDC values for forearm were 28.0 ± 1.8 and 28.0 ± 2.1 ($p=0.854$) and for biceps 28.2 ± 2.2 and 28.1 ± 2.0 ($p=0.823$). Corresponding values for males were for forearm 33.9 ± 3.6 and 33.7 ± 3.3 ($p=0.870$), and biceps 34.6 ± 4.0 and 34.5 ± 3.4 ($p=0.787$). Further and importantly, inter-arm TDC ratios (dominant/non-dominant) did not significantly differ with respect to probe, anatomical site or gender as summarized in *Table 2*. This result suggests the such ratios are use for assessment in that they are robust against variations in probe type, depth and gender.

Breast Cancer Patients

TDC values measured in patients with breast cancer using the compact probe showed that even for patients there was no significant inter-arm difference. TDC values (dominant vs. non-dominant) on the forearm were found to be 30.5 ± 4.4 vs. 30.7 ± 4.1 ($p=0.817$) and for biceps were 29.5 ± 3.9 vs. 30.4 ± 3.9 ($p=0.758$). A comparison between these absolute TDC values as measured on

the breast cancer patients were found to be similar to and not significantly different from those measured on the healthy group of 32 female subjects at corresponding anatomical sites. Further, TDC ratios in the breast cancer patients, determined with the compact probe (dominant/non-dominant) at the forearm were 0.994 ± 0.060 and at the biceps were (0.970 ± 0.045) with both ratios being insignificantly different from corresponding ratios determined for the healthy group of females. This result suggests that at least at this early stage the presence of breast cancer did not alter the ratio. The similarity of the ratios also suggests that it may be a tracking parameter that is somewhat robust against age since the breast cancer group was significantly older than the healthy group of females (62.2 ± 12.8 vs. 26.0 ± 7.5 years, $p<0.001$).

DISCUSSION

The main findings of the present study may be summarized as follows.

- (1) TDC values in healthy male arms are significantly greater than in healthy female arms.
- (2) TDC values for both genders are less at deeper effective measurement depths.

- (3) TDC values measured with the compact probe are between those measured to 1.5 and 2.5 mm depths and exceed the 2.5 mm probe depth value by about 5.6%.
- (4) Inter-arm TDC values and ratios (dominant/non-dominant) did not significantly differ with respect to probe, site, or gender in healthy male and female subjects or between healthy females and those with breast cancer
- (5) Absolute TDC values and inter-arm ratios measured with the compact probe in breast cancer patients did not significantly differ from those measured in younger healthy females.

Gender Differences

The present finding of a greater TDC value in male arms is consistent with previous work in which a 13% greater TDC value was found in male arms at an effective measurement depth of 1.5 mm (19) and also found to be 5.6% greater in forehead skin of males similarly measured to a depth of 1.5 mm (17). Further, the present new result shows that this gender difference is also present to even deeper effective depths of at least 2.5 mm. As has been previously argued, this difference may be partially explained on the basis of gender differences in skin thickness at the measured sites (17,19). Differences in fat content between genders may also contribute to the lesser TDC value measured among females.

Effective Depth Differences: Differences in TDC values obtained among the different probes, with the 1.5 mm probe yielding the highest value and the 2.5 mm probe the least, is largely explained by the fact that electric fields of the 2.5 mm probes extend further into the tissue thereby including more subcutaneous fat in their measurement volume (24) in which the water content of the fat tissue is much lower than in the dermis (25,26). However, the fact that inter-arm TDC ratios did not differ among probes and therefore depths at forearm or biceps suggests that side

dominance has little effect on relative TDC measurements. This implies no intrinsic correction for handedness would be needed for such localized tissue water assessments. These results are also consistent with earlier measurements covering depths from 0.5 to 5 mm (27). A potentially important consequence of this independence of TDC value, being essentially the same on dominant and non-dominant arms, is that when MMD or MMDC devices are used in clinical situations where only one side is at risk for tissue edema or swelling (like breast cancer related lymphedema), then any of the probes can be used to assess lymphedema without taking into account the patient's side dominance as has been advocated for devices using whole arm bioimpedance or bioelectric spectroscopy (28).

Instrumental Differences

As noted, the instrumental difference of the MMD TDC values using the 2.5 mm probe as compared to the MMDC device was about 5.6%. In part this difference may be explained by the slight difference in the electrode construction associated with the difference of the dimensions of the outer electrode (*Fig. 1C*) which has a slightly smaller contact area with the skin in the MMDC device. The average differences between the TDC values measured by the MMD (2.5 mm probe) and the MMDC here determined are of the same order as the short (2%) and longer term (5%) coefficients of variation of TDC values reported for skin (29). Further, the percentage differences are well within the limits of the normal variation in TDC values among normal individuals as found in the present study, ranging from 8.6% to 11.2% depending on site and gender, and for those reported in the literature for upper and lower limbs (27,30,31). However, because of the differences shown herein, it is important that the specifics of the instrument and probe used in any study should be reported to enable subsequent and retrospective comparisons of absolute measured TDC

data. Finally, although the present results indicate differences in measured absolute TDC values for different electric field penetration depths, different measurement sites, and different genders, inter-arm TDC ratios were not found to be different by device, penetration depth, or gender. This suggests that such ratios are rather robust parameters in assessing potential unilateral changes.

Study Limitations

One limitation on the present study was that most of the measurements were done on young healthy persons whereas the most likely application of the TDC method would be to measure and track tissue water or lymphedema changes in an older population. This limitation is partially offset by the measurements made within the older group of patients and consistency of findings within this group and in comparison to the younger healthy group. A second limitation might be that only 12 patients were included for the healthy subject-breast cancer comparison. Partially offsetting this limitation is the fact that TDC values obtained even in this smaller group were consistent with those obtained in the larger healthy group. However, a more extensive undertaking in which the compact probe were applied to a larger group of women may be indicated to further solidify the reference values. Finally, it should be pointed out that no actual patients with lymphedema were evaluated in this study because the primary goal was to investigate potential intrinsic differences between multiprobe and compact devices in their application and values. This goal we believe was well achieved. A future study to track sequential changes utilizing the compact TDC probe would seem to be an important subsequent undertaking.

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