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Spatial and Temporal Variability of Upper Extremity Edema Measures After Breast Cancer Surgery

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Abstract

Background: Tissue dielectric constant (TDC), as an index of local tissue water, and girth measurements are quantitative methods to measure and characterize lymphedema.
Objective: To describe the spatial and temporal variability in arm girth and TDC values in women surgically treated for breast cancer and to describe the relationship between these measures.
Methods and Results: This was a prospective longitudinal study that observed 36 women for 78 weeks after breast cancer surgery with lymph node removal. Arm circumferences and TDC values, as indices of local tissue water, were measured on both arms at multiple sites at postsurgery weeks 2, 4, 12, and 78 in women undergoing surgical breast cancer treatment with one or more axillary lymph nodes removed. TDC and girth values remained relatively uniform from visit-to-visit for both at-risk and contralateral control arms with no overall statistically significant difference in values ($p > 0.05$). There was a strong inverse correlation between arm girth and the TDC value in both the at-risk and control arms ($p < 0.001$). Overall, there was no statistically significant difference in TDC interarm ratios among visits or anatomical sites. TDC values for at-risk and control arms tended to significantly decrease with increasing distance from the wrist ($p < 0.001$).
Conclusion: TDC arm values and girth measures remained relatively uniform in women after breast cancer surgery. The fact that TDC values are higher distally than proximally provides new information from which TDC measurements may be interpreted and also provides a better understanding of arm spatial variability in relation to girth measures.

Keywords: lymphedema, breast, TDC, tissue dielectric constant, girth measures

Introduction

Lymphedema after treatment for breast cancer may occur in the at-risk hand or arm, trunk, or affected breast with a frequency reported to range from 6% to 65%.[1] Assessment of the early occurrence and tracking of such breast cancer-related lymphedema (BCRL) is important to initiate timely treatment and possibly guide lymphedema therapy. Several quantitative methods are available to assess overall arm volume changes due to lymphedema,[1–3] but rapid noninvasive assessments of localized edema are frequently done using arm girths or tissue dielectric constant (TDC) measurements that are largely dependent on tissue water.

Prior work using TDC measurements of the arm has shown that measured values vary somewhat depending on the arm location at which the TDC measurements are made.[2–9] The literature demonstrates that TDC measures are higher distally than proximal measures in nonlymphedematous arms,[3] which may be due to the increased fatty tissue proximally having a lower water content. However, there has been no systematic evaluation of the spatial variability of TDC values obtained at arm sites that correspond to those routinely clinically measured for girth assessments.

In addition, prior reports of site variability were mostly restricted to a single time point so that potential temporal changes in TDC values among various spatial sites are currently unknown and the relationship of TDC values with corresponding arm girth values at any time point is also unknown. Such information is important clinically as it aids in interpreting TDC value changes and also may help our

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understanding of the factors that contribute to such spatial and temporal variability.

The two main goals of this work are 1) to describe the spatial and temporal variability in TDC values in women treated for breast cancer at sequential times after their breast surgery, and 2) to describe the relationship of these TDC values with other assessment parameters, the patient's breast cancer treatment, and treatment-related complications.

Materials and Methods

Design

This prospective study with a repeated measures design evaluated 36 women at 2, 4, 12, and 78 weeks, respectively, designated as visits 1, 2, 3, and 4 after breast cancer surgery: 36 women completed the first three visits and 32 women completed all four visits in the study. This study was approved by the University of Minnesota Internal Review Board in accordance with the ethical standards on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. All women were recruited from the Masonic Cancer Breast Center and written consent was obtained. This study was a subanalysis of the original study on axillary web syndrome.[10,11]

Participants

Inclusion criteria consisted of female surgical breast cancer patients (lumpectomy, mastectomy, and/or contralateral prophylactic mastectomy) who underwent removal of more than one lymph node and consented to participate in the study. Women with history of shoulder surgery, breast cancer, deep vein thrombosis, shoulder dysfunction, or diagnosis of bilateral breast cancer were excluded from the study. Table 1 depicts the participant characteristics.

Table 1. Participant Characteristics

Characteristic	*Mean*
Age (years)	56.3 ± 9.6 [35–73]
BMI (kg/m^2)	27.0 ± 6.0 [17.8–45.1]
Dominant arm = right, *n* (%)	31 (86.1)
Cancer side = right, *n* (%)	15 (41.7)
Cancer side = dominant side, *n* (%)	20 (55.5)
Tumor quadrant location, *n* (%)	
Upper lateral	23 (63.9)
Upper medial	8 (22.2)
Lower lateral	4 (11.1)
Lower medial	1 (0.25)
Breast surgery procedure, *n* (%)	
Lumpectomy	18 (50.0)
Unilateral mastectomy	11 (30.6)
Bilateral mastectomy	7 (20.4)
Node procedures	
Sentinel lymph node biopsy, *n* (%)	28 (77.8)
Axillary lymph node dissection, *n* (%)	8 (22.2)
Nodes removed	5.4 ± 7.1 [1–32]
Patients with ≥one positive node, *n* (%)	4 (11.1)
Patients with radiation, *n* (%)	22 (61.1)
Patients with chemotherapy, *n* (%)	16 (44.4)
Patients with seroma, *n* (%)	12 (33.3)
Patients with lymphedema treatment, *n* (%)	12 (33.3)

Age, BMI, and nodes removed are expressed as mean ± SD with range in brackets []. All other parameters are expressed as number of patients with percentages in parentheses ().

BMI, body mass index.

Measurement devices

A nonstretch flexible tape measuring device with a tension gauge (Fabrication Enterprises, White Plains, NY) was used to measure circumferences on the arm. A tension gauge measuring device has shown to be more reliable than a standard tape measuring device.[12] The MoistureMeter D (Delfin Technologies Ltd., Kuopio Finland; www.delfintech.com) was used to measure TDC on the arms. Based on previous literature, the M25 size transducer head was used in this study.[5,13] The M25 head is ~10 mm in radius and measures to a depth of ~2.5 mm. The transducer emits a 300 MHz electromagnetic wave into the tissue and the wave returns to the transducer head. The information travels from the transducer through a coaxial cable to the device's base unit. The value shown in the unit's display is reflective of the local water content. The TDC value ranges from 0 to 80 with higher values indicating higher water content. For reference, a value of 0 indicates no water and distilled water is around 76 at 32°C–34°C. An interarm TDC ratio is calculated using the formula TDC affected/TDC unaffected. An interarm TDC ratio of >1.26 is suggestive of lymphedema. Further description of this device can be found in previous publications.[5,9,14–18]

Measurement protocol

Lymphedema measures were taken with individuals lying supine with the palm facing upward and arm slightly abducted to access the medial arm. Girth measurements were taken first followed by TDC measures. Marks were made with a marking pen on the medial side of the arms bilaterally from 0 to 40 cm measuring at 8 cm increments distal to proximal starting at the ulnar styloid. TDC measures were taken once at each site, bilaterally on the medial side of the arm in the same location as the incremental 8 cm marks (Fig. 1). The at-risk side was measured followed by the contralateral side for both girth and TDC measures.

Although this was a prospective observational study without intervention, part of the study written and verbal lymphedema education were provided by the first author (L.K.) at the 12-week visit (visit 3) after surgery. Individuals in the study followed the normal plan of medical care determined by their medical providers. Referral for lymphedema treatment occurred only if an attending medical provider initiated a referral.

Data analysis

Temporal variability in TDC and girth values at each measured arm site were initially assessed using a general linear model (GLM) for repeated measures with visit as the repeated measure. This analysis was done for each arm (at-risk and control) for those patients who had completed all four visits ($n = 32$). Spatial variability in TDC and girth values among arm sites were initially assessed also using a GLM

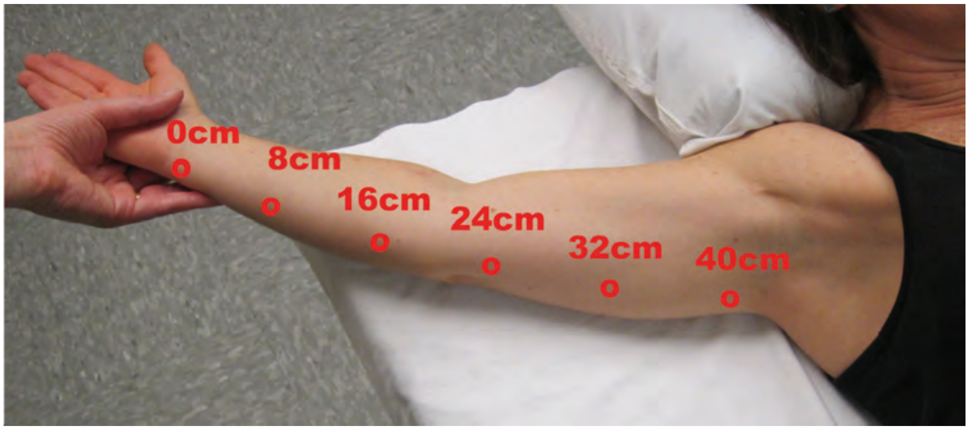

FIG. 1. Location of TDC measures. TDC, tissue dielectric constant.

for repeated measures for these same 32 patients but with site location as the repeated measure. This analysis was done for each arm at each of the four evaluation visits. An overall difference among visits or among sites was considered significant for a p-value of 0.05. Correlations between measured TDC values and girth were initially evaluated at each visit using Pearson correlation analysis by considering all TDC–girth pairs at each visit for at-risk and control arms separately. For this paired analysis, all patients were included ($N = 36$).

Results

Temporal variations of TDC values and girth at each measured arm location

At each arm site, the TDC values remained relatively uniform from visit-to-visit for both at-risk and contralateral control arms (Fig. 2A, B) with no overall statistically significant difference in TDC values among visits 1 through 4. At each arm site, the girth values remained relatively uniform

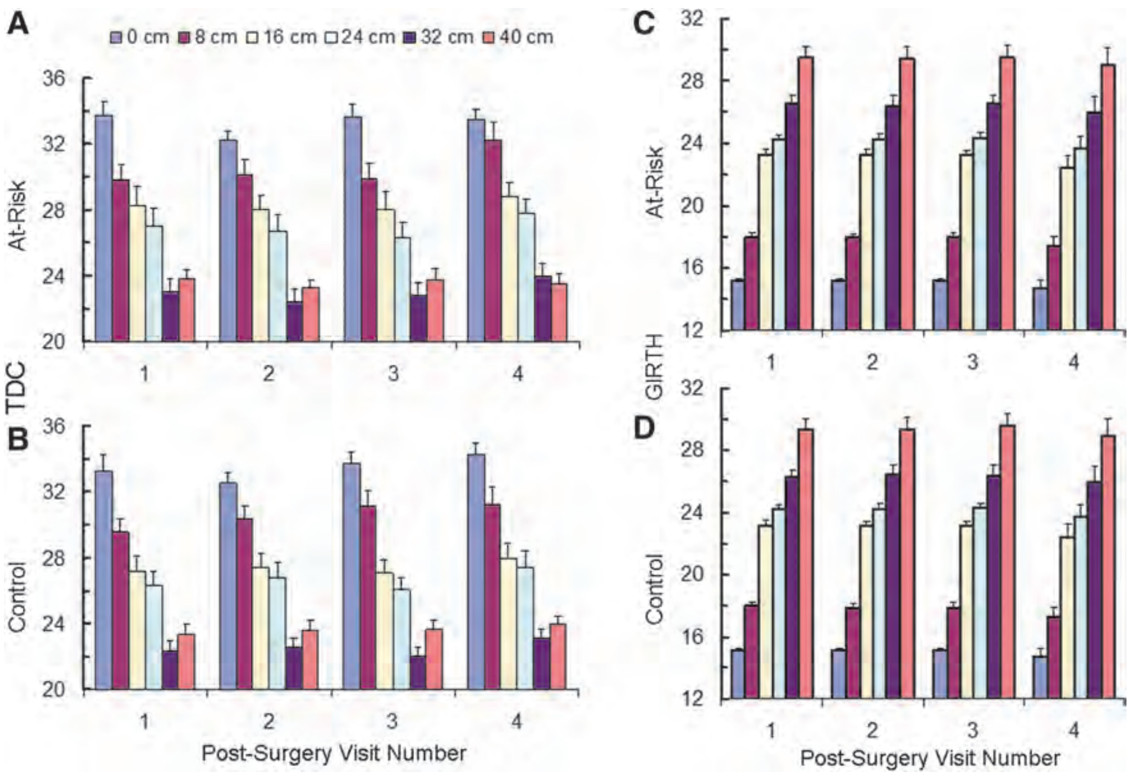

FIG. 2. Bar heights are average TDC values for at-risk **(A)** and control arms **(B)**. Arm locations are expressed in centimeters from the wrist taken as 0 cm. Postsurgery visits 1, 2, 3, and 4 correspond to 2, 4, 12, and 78 weeks postsurgery. Error bars are SEM. TDC values tend to decrease with increasing distance from the wrist at each visit but repeated measures analysis reveals no statistically significant changes in TDC values from visit-to-visit for eight either control or at-risk arms. **(C, D)** Bar heights are average girth values for at-risk **(C)** and control **(D)**. As expected, girth values increase with increasing distance from the wrist at each visit. Repeated measures analysis reveals no statistically significant changes in girth from visit-to-visit for either arm. Interarm girth differences were insignificantly different at all visits. SEM, standard error of the mean.

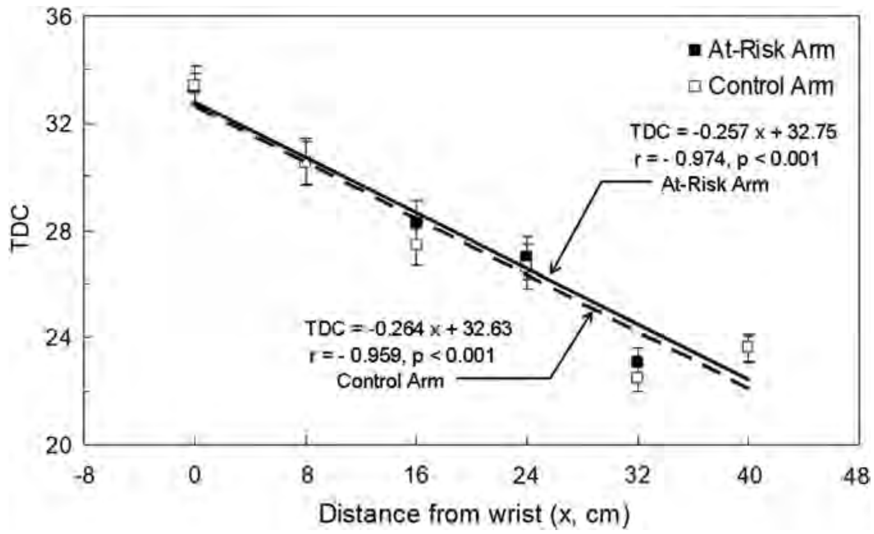

FIG. 3. Each data point is the average of TDC values measured during the four visits (2, 4, 12, and 78 weeks postsurgery). *Filled squares* are at-risk arms and *open squares* are contralateral control arms. Error bars are SEM. *Solid line* represents linear regression for at-risk arms and the *dashed line* represents control arms. Corresponding regression equations and parameters are shown in the figure. Results show a significant decrease in TDC values with increasing distance from the wrist.

from visit-to-visit for both at-risk and contralateral control arms (Fig. 2C, D) with no overall statistically significant difference in TDC values among visits 1 through 4.

On average, at-risk and control arms did not differ in girth at any of the measured sites, and both increased with increasing distance from the wrist with linear regression equations for at-risk and control arms expressed, respectively, as follows: Girth = 0.353X + 15.74, $r = 0.985$, $p < 0.001$ and Girth = 0.358X + 15.82, $r = 0.984$, $p < 0.001$, where X is distance from wrist in centimeters.

Spatial variations of TDC values along arms

TDC values for at-risk and control arms tended to decrease with increasing distance from the wrist, resulting in statistically significant ($p < 0.001$) linear regressions of TDC upon distance for both arms with regression features and equations as shown in Figure 3. TDC values used in the regressions for each site were the average of visits 1 through 4. Table 2 includes the site average TDC values for at-risk and control arms and the at-risk to control arm ratios.

Both at-risk and control arm TDC values differed overall among sites ($p < 0.0001$) with a general trend for decreasing values with increasing distance from the wrist taken as 0 cm. Statistically significant differences ($p < 0.001$) in TDC values were found to be present between adjacent sites except for TDC values between 16 and 24 cm and between 32 and 40 cm measurement sites. Despite decrease in TDC values with increasing distance from the wrist, interarm TDC ratios remained relatively uniform with no overall significant difference among sites.

Correlations between TDC values and girth values

Considering all paired TDC–girth values from each site and for each visit ($n = 860$), there was a strong inverse correlation between arm girth and the TDC value measured with regression equations as shown in Figure 4 and expressed by the linear regression equations as TDC = −0.708 girth +43.8, $r = -0.616$, $p < 0.001$ for the at-risk arm and TDC = −0.715 girth +43.8, $r = -0.645$, $p < 0.001$ for the control arm. To determine whether this relationship is present at each measured site rather than just for the aggregate, separate regression analyses are needed for each site, making use of the range of TDC–girth pairs for each site ($n = 140$). Results of this analysis are shown in the bottom part of Table 2. Results indicate that except for the wrist all other anatomical sites demonstrate a highly significant inverse correlation ($p < 0.0001$) between TDC value and arm girth for both the at-risk and the control arm.

Interarm TDC ratios and girth measures

Figure 5 shows interarm TDC ratios (at-risk arm/control arm) for each site and visit for patients evaluated at each visit ($n = 32$). TDC ratios do not significantly vary among arm sites at any visit nor do ratios at a given site vary by visit. The overall average interarm ratio for the six measured sites ranged from 1.003 ± 0.070 at the wrist to 1.031 ± 0.054 at 16 cm proximal to the wrist. However, analysis of individual patient changes from visit-to-visit indicated that at 78 weeks postsurgery (visit 4), four patients showed interarm ratios >1.26, a value that has been reported to be indicative of lymphedema presence.[5] Table 3 displays the TDC ratios and difference in girth measures at each visit for these four patients.

Twelve individuals reported receiving treatment by a lymphedema therapist within the 18 months of this study. The type of treatment received varied between each individual, but the treatment was described as decongestive manual lymph drainage, compression therapy (garment and/or bandages), and exercise. Two of the individuals were also prescribed a compression pump. Specific details regarding the length and time of treatment were not collected as part of this study, but the treatment ranged from one visit to multiple visits. Three women reported having received treatment within the first 12 weeks after surgery.

TABLE 2. TEMPORAL AVERAGED TISSUE DIELECTRIC CONSTANT VALUES AND TISSUE DIELECTRIC CONSTANT–GIRTH CORRELATIONS

	Distance from wrist (cm)					
	0	*8*	*16*	*24*	*32*	*40*
TDC values						
At-risk arm	33.3 ± 3.3	30.5 ± 4.6**	28.2 ± 4.9**	27.0 ± 4.5	23.0 ± 3.3**	23.6 ± 2.7
Control arm	33.4 ± 4.0	30.5 ± 4.8**	27.4 ± 4.3**	26.6 ± 4.6	22.5 ± 2.9**	23.6 ± 3.0
Ratio	1.003 ± 0.070	1.005 ± 0.073	1.031 ± 0.054	1.018 ± 0.072	1.027 ± 0.092	1.005 ± 0.063
TDC–girth correlations						
At-risk arm	−0.113 (13.2–17.0)	−0.405 (15.1–22.1)	−0.468 (19.8–27.4)	−0.536 (21.2–30.1)	−0.400 (19.7–39.1)	−0.446 (21.0–43.9)
Control arm	−0.135 (13.4–16.6)	−0.432 (14.7–21.5)	−0.417 (19.1–26.7)	−0.545 (21.1–30.0)	−0.457 (19.0–37.9)	−0.419 (20.1–43.3)

TDC values are for at-risk and control arms and at-risk to control arm ratios at each measured arm site with TDC values averaged over the four visits ± SD. Both at-risk and control arm TDC values differed overall among sites ($p < 0.0001$). Statistically significant differences between the immediately adjacent distal site are denoted as * for $p < 0.001$. There was no overall statistical difference in interarm ratios among sites. Entries for TDC–GIRTH are Pearson correlation coefficients and values in brackets are the girth range in centimeters at the anatomical site for which the correlation is applicable. Except for the wrist site at 0 cm, all other correlations are highly significant ($p < 0.0001$). Each correlation is based on 140 TDC–girth pairs.
SD, standard deviation; TDC, tissue dielectric constant.

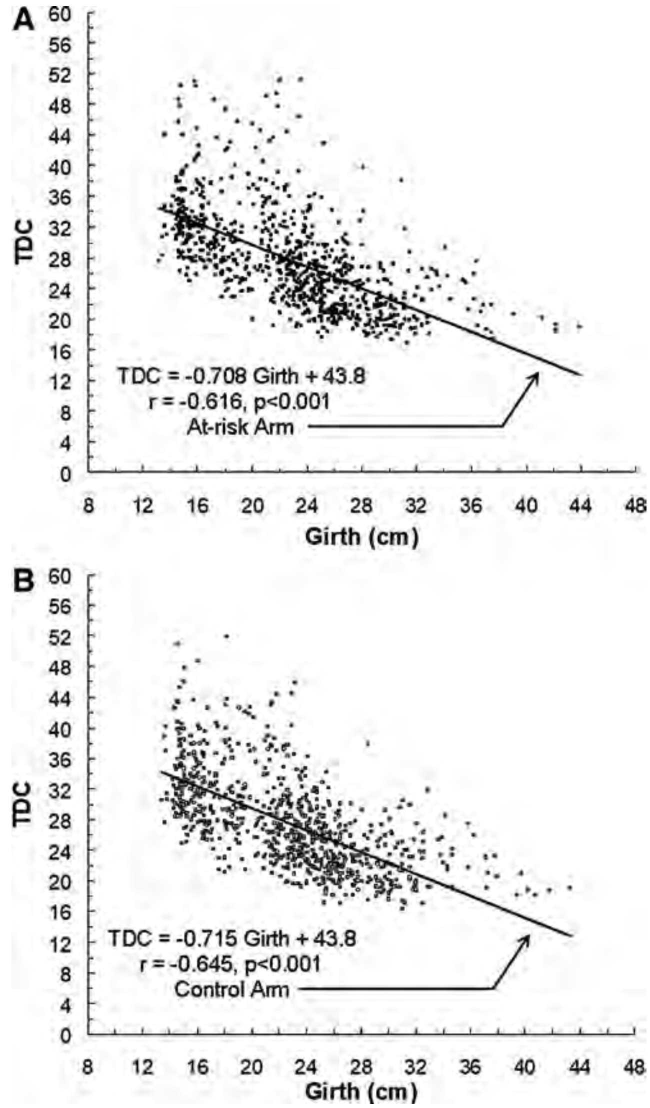

FIG. 4. Data points are paired TDC–girth values for all sites and visits ($n = 860$) and *solid line* represents linear regression with parameters as shown in the figure. **(A)** At-risk arm and **(B)** Control arm.

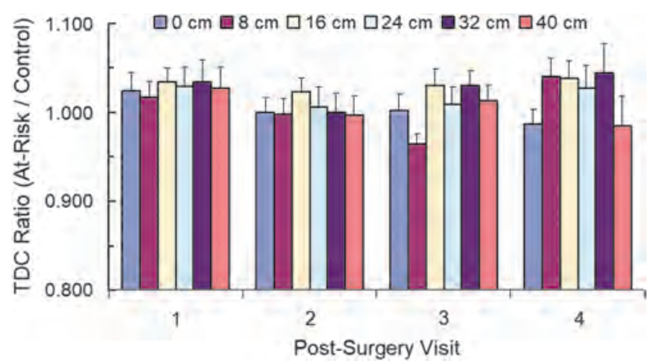

FIG. 5. Interarm TDC ratios (at-risk/control). Bar heights are mean value of interarm TDC ratios (at-risk arm/control arm) and error bars are SEM. TDC ratios do not significantly vary among arm sites at any visit nor do ratios at a given site vary by visit.

Table 3. Temporal Variability of Tissue Dielectric Constant Ratios and Difference in Girth Measures of Four Individuals with Tissue Dielectric Constant Ratios >1.26 at the Fourth Visit (in Bold)

		Wrist		*8 cm*		*16 cm*		*24 cm*		*32 cm*		*40 cm*	
Subject	*Visit*	*TDC ratio*	*Girth difference*	*TDC ratio*	*Girth difference*	*TDC ratio*	*Girth difference*	*TDC ratio*	*Girth difference*	*TDC ratio*	*Girth difference*	*TDC ratio*	*Girth difference*
1	1	1.05	0.40	1.06	0.30	1.03	–0.20	1.09	0.00	1.06	0.50	0.92	0.10
	2	1.03	0.00	1.06	0.90	1.09	0.50	1.23	0.10	0.96	0.60	0.91	1.80
	3	1.16	0.10	1.00	0.20	1.09	–0.10	0.94	–0.10	1.21	0.10	0.88	0.00
	4	0.94	–0.30	1.05	0.80	1.17	0.30	**1.61**	0.30	**1.93**	2.40	1.04	3.20
2	1	1.20	0.00	0.92	0.20	1.13	–0.30	1.00	0.10	1.17	–0.50	0.97	–1.40
	2	0.96	0.10	0.99	0.40	1.05	–0.10	0.81	0.00	1.14	–0.20	0.88	–0.50
	3	0.85	0.00	0.91	0.20	0.01	–0.40	0.93	0.00	1.22	–0.60	1.12	–0.50
	4	0.84	0.00	0.88	–0.50	0.99	–0.30	0.99	0.00	**1.26**	–0.20	1.09	–0.40
3	1	0.92	0.20	1.09	0.10	0.97	0.30	0.99	0.20	1.02	0.60	1.04	0.60
	2	1.06	0.10	1.01	–0.10	1.00	0.20	1.10	0.00	0.97	0.20	1.07	1.00
	3	1.04	0.30	1.08	0.10	1.07	0.30	1.05	0.30	0.97	–0.10	1.09	–0.20
	4	0.86	0.10	**1.30**	1.10	1.05	0.70	1.09	0.20	1.25	0.30	1.09	0.50
4	1	0.93	–0.10	0.98	–0.10	0.97	–0.90	0.93	–0.60	0.85	0.50	1.11	–0.30
	2	0.93	0.10	0.95	0.10	0.98	–0.30	0.93	–0.90	0.95	0.40	0.95	–0.60
	3	0.89	–0.10	0.95	–0.60	1.19	–0.30	1.22	–1.60	1.00	0.70	1.09	–0.60
	4	1.16	1.20	**1.37**	3.40	**1.35**	2.00	1.25	0.00	0.98	–0.30	1.07	–1.70

Visits: 1 = 2 weeks, 2 = 4 weeks, 3 = 12 weeks, 4 = 78 weeks.

Conclusion

This longitudinal study analyzed the spatial and temporal variability in TDC values in women treated for breast cancer at sequential times after their breast surgery and described the relationship of these TDC values with girth measures. TDC and girth measures in the at-risk and contralateral arms remained relatively constant for 18 months. In general, interarm metrics remained comparatively uniform across visits for individuals with a few interarm TDC ratios exceeding the suggested lymphedema parameters. The arm TDC and girth measures were inversely correlated, demonstrating a decrease in TDC values while girth measures increased proximal to distal.

To our knowledge, this is the first longitudinal study to assess the spatial variability of TDC measures at the arm that correspond to routine clinical girth measures. This study was strengthened by measuring TDC values on at-risk individuals for a 78-week time period following breast cancer surgery with lymph node removal. A limitation of the study was that few of the at-risk individuals went on to present with arm lymphedema. This was substantiated by both the girth and TDC arm measures, demonstrating little difference between the at-risk and contralateral arm and little change between visits in both measures.

The TDC interarm results indicated a relatively low number of women ($n = 4$) with interarm TDC ratios >1.26, suggestive of lymphedema.[5] These results are similar to previous research that observed similar temporal arm TDC patterns 18 months after breast cancer surgery.[3] Two of the four women had girth measures reaching the circumferential threshold of >2 cm difference in girth between sides, providing foundational support for validity. One woman with a high TDC ratio did not reach the 2 cm threshold but had >1 cm difference, which was high compared with the <1 cm difference on the rest of the arm. This demonstrates TDC's potential ability to detect early subclinical lymphedema in a localized area. One woman did not have measurable girth difference but had a high TDC value on the upper arm. This disagreement may be due to the possibility that TDC is detecting localized subclinical edema before skin stretching due to high volume edema accumulation. Further research is needed to better understand the relationships between girth and TDC measures.

Based on our data, TDC absolute values had an inverse relationship with girth measures, moving from distal to proximal in the at-risk and contralateral arm at each visit. Mayrovitz and Luis demonstrated a similar trend in TDC values, increasing from proximal to distal positions along the arm.[6] The observed decrease in arm TDC values distal to proximal is likely influenced by the variation in tissue components with increased girth being associated with increased subcutaneous fat that has lower water content.

Higher distal TDC values could also potentially be influenced by pooling of fluid in the distal arm due to the dependent position of the arm. Theoretically, one would expect fluid content to be higher in the distal arm and hand, especially if the arm is in a dependent position over the course of a day, but this was unlikely since the TDC measures were taken ~8–10 minutes after the individual was positioned supine allowing for redistribution of fluid.

TDC measures were taken on the medial arm where the arm abuts the body, therefore, tissue approximation could also be putting pressure on the medial portion of the upper arm, leading to a reduction in proximal measures. However, tissue approximation likely had little effect since the forearm measures also demonstrated the same pattern and were not impacted by soft tissue approximation.

Few women were lost to follow-up and all the measures were taken by a single experienced tester (L.K.) for all visits to reduce variability and error in the measures, which adds strength to the study. A limitation is that preoperative measurements were not taken, therefore, baseline status was unknown. Most of the individuals underwent sentinel lymph node biopsy (SNB), theoretically putting them at less risk of developing arm lymphedema, which is consistent with our results.

Women with contralateral prophylactic mastectomy were included in the study, which may have been a limitation if contralateral surgery affected the results. But, the women did not have lymph node removal on the contralateral side, therefore, there should have been a minimal effect. Lymphedema education was provided at 12 weeks after surgery, therefore, a treatment effect may have been present since 12 women reported receiving a minimum of one lymphedema treatment. Providing early lymphedema education may have prompted a woman to seek early intervention and/or participate in risk reduction behavior. The literature shows that patient education given in the early postoperative time period followed by physical therapy is effective in reducing the risk of BCRL.[19,20]

The results of this study are clinically important as it aids in interpreting TDC value changes and also may help our understanding of the factors that contribute to such spatial and temporal variability. The TDC measures vary depending on the body site, with values decreasing proximal to distal on the arm. This means an unaffected limb is needed for appropriate comparison. In addition, it warrants research to establish normative values at relevant sites for the assessment of lymphedema.

The relatively uniform temporal variability in the TDC and girth measure results in this study not only demonstrates agreement between the measures but also demonstrates a relevant lymphedema pattern in this cohort of women. The paucity of lymphedema represented is consistent with the cohort's characteristics and the literature. A majority of the women had a lumpectomy with few lymph nodes removed (i.e., SNB). The literature shows that women with fewer lymph nodes removed and conservative surgery are at less risk of developing lymphedema.[21] A treatment effect may have also influenced the relatively uniform variability of the temporal measures.

The literature is growing rapidly demonstrating the capability and utility of many lymphedema instruments, but at this time no single instrument has the capacity to fulfill all the clinical needs to effectively assess early and late lymphedema, identify changes in response to interventions, and be cost effective and easy to use. Clinicians need to be aware of the benefits and limitations of the available lymphedema devices, such as TDC.

Recent studies have demonstrated the utility of TDC in the early detection of BCRL.[13,22,23] One study compared TDC with bioimpedance spectroscopy (BIS) in the assessment of early arm lymphedema after breast cancer treatment, demonstrating that TDC was more sensitive than BIS in the early assessment of BCRL.[22] Whole arm BIS uses multiple frequencies to assess for BCRL by measuring extracellular fluid.

The BIS method is speculated to target fluid in the deep tissue and to a less extent the superficial tissue.[22] Early lymphedema is thought to manifest in the superficial tissue (i.e., skin), which is the target area of TDC measures.[22] Although TDC appears to be beneficial in assessing localized BCRL, it appears to be less beneficial in identifying immediate tissue changes in response to treatment according to a recent study.[24] Quantitative deep tissue magnetic resonance imaging (MRI) demonstrated significant immediate changes in the deep tissue but not in the superficial tissue after manual lymph drainage treatment.[24] Non-MRI measurements (BIS, TDC, and volumetric measures) were not sensitive to the immediate tissue changes.[24]

This study investigated the spatial and temporal variability in TDC values in women treated for breast cancer and described the relationship of these TDC values with girth measures. TDC arm values were in agreement with girth measures with both remaining relatively uniform in women after breast cancer surgery. The fact that TDC values are higher distally than proximally provides new information from which TDC measurements may be interpreted and also provides a better understanding of arm spatial variability in relation to girth measures. Although TDC values vary among anatomical sites, further research is needed to determine normative values at relevant sites for the assessment of lymphedema and other edemas.

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Author Disclosure Statement

No competing financial interests exist.

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