Tissue Dielectric Constant Measures in Women With and Without Clinical Trunk Lymphedema Following Breast Cancer Surgery: A 78-Week Longitudinal Study

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AUTHOR BYLINE: Linda Ann Koehler, Harvey N. Mayrovitz

AUTHOR INFORMATION:

L.A. Koehler, PT, PhD, Department of Rehabilitation Medicine, Division of Physical Therapy, Division of Rehabilitation Science, University of Minnesota, Mayo Mail Code 388, 420 Delaware St, SE, Minneapolis, MN 55455 (USA) and Masonic Cancer Center, University of Minnesota. Address all correspondence to Dr Koehler at: Koeh0139@umn.edu.

H.N. Mayrovitz, PhD, College of Medical Sciences, Nova Southeastern University, Ft Lauderdale, Florida.

Objective. Following breast cancer surgery with lymph node removal, women are at risk of developing lymphedema in the upper extremity or trunk. Currently, trunk lymphedema diagnosis relies on a clinical assessment because no quantifiable standard method exists. Tissue dielectric constant (TDC) values are quantifiable measures of localized skin tissue water and may be able to detect trunk lymphedema. The goal of this study was to (1) compare parameters derived from TDC measurements with those derived from clinically accepted criteria for trunk lymphedema in women following breast cancer surgery and (2) explore the potential utility of TDC to detect trunk lymphedema early in its progression.

Methods. This prospective longitudinal study, a secondary analysis from a larger study, observed women with and without clinically determined truncal lymphedema following breast cancer surgery. TDC was measured on the lateral trunk wall at post-surgery weeks 2, 4, 12, and 78 in women who had surgical breast cancer treatment with lymph

node removal. Clinical assessment for trunk lymphedema was determined at 78 weeks by a lymphedema expert. Comparison of TDC measurements in women with and without clinical trunk lymphedema was analyzed.

Results. Clinical assessment identified trunk lymphedema in 15 out of 32 women at 78 weeks. These women had TDC ratios statistically higher than women without truncal lymphedema.

Conclusion. The overall findings indicate that TDC has the ability to quantify trunk lymphedema and might be valuable in early detection.

Impact. TDC may be a beneficial tool in the early detection of breast cancer related trunk lymphedema which could trigger intervention.

Lay summary: A new device may help recognize trunk lymphedema in patients with breast cancer so they could receive appropriate treatment.

Breast cancer related lymphedema (BCRL) is a negative sequela of breast cancer treatment. Reported incidence rates of BCRL vary from 6 to 94%.[1,2] While lymphedema incidence has been reported less frequently in women who undergo sentinel lymph node biopsy (SLNB) compared to axillary lymph node dissection (ALND), lymphedema continues to have a negative impact on quality of life and functional following treatment.[3] The true incidence of lymphedema is difficult to determine because of varying methods used to quantify it and the absence of an agreed upon diagnostic criteria to define it. Most research on BCRL focuses on upper extremity lymphedema, disregarding the ipsilateral upper quadrant (trunk and breast) which is also at risk of developing

lymphedema.[4] Trunk or breast lymphedema is rarely documented in the literature to date, largely because there have not been adequate measuring devices or a 'gold standard' for recording the measurement of lymphedema at these anatomical locations. Clinically, assessment for upper quadrant lymphedema relies on observational and palpation by a skilled therapist to identify the presence of trunk or breast lymphedema.[4]

Recent literature has identified a potential measurement device that might reliably quantify breast and trunk lymphedema using tissue dielectric constant (TDC).[5–7] The TDC device provides a measure of localized tissue water content. This device has a probe which emits a low power electromagnetic wave that, when in contact with the skin, reflects back to a processor that determines the dielectric constant of the tissue under the probe. The TDC value is strongly dependent on the local water content of the tissue below the probe. Because of this property, TDC may be useful in detecting, identifying and quantifying trunk lymphedema. A recent study demonstrated that TDC values were highly sensitive in detecting the early onset of upper extremity lymphedema in women following breast cancer treatment.[8] This is clinically important for lymphedema therapists since research shows that the early detection and intervention for upper extremity lymphedema has been able to effectively treat and prevent the progression of BCRL.[9]

The goals of this study were to: 1) compare parameters derived from TDC measurements with those derived from clinically accepted criteria for trunk lymphedema in women following breast cancer surgery, and 2) explore the potential utility of TDC to detect trunk lymphedema early in its progression. We hypothesized that inter-side TDC ratios would be significantly higher in women with clinically determined trunk lymphedema compared to woman without trunk lymphedema. We further hypothesized that TDC values measured on the trunk would be higher

at earlier visits in those women subsequently identified with trunk lymphedema at 78 weeks post-surgery. Such a finding would support the view for the potential utility of TDC for the early detection of truncal lymphedema.

[H1]METHODS

[H2]Design

This was a prospective longitudinal observational study which followed women for 78 weeks post breast cancer surgery. The women were assessed at 2, 4, 12, and 78 weeks. This study was approved by the University of Minnesota Internal Review Board and all women provided written consent to the study prior to participation. This study was a secondary analysis to another study where the sample size was established through estimation methods on which the study was powered.[10,11]

[H2]Participants

Women were recruited from the University of Minnesota Health Breast Center in Minneapolis, Minnesota. Women were included in the study if they had a tissue histological diagnosis of non-invasive or invasive breast cancer and underwent surgical breast cancer treatment (lumpectomy or mastectomy) with one or more axillary lymph nodes removed. Women undergoing prophylactic mastectomy on the contralateral side were also eligible to participate. Exclusion criteria included a previous history of shoulder surgery, shoulder dysfunction, a prior surgical treatment for breast cancer or current coexisting bilateral breast cancer, or upper extremity deep vein thrombosis or upper extremity lymphedema.

Participant characteristics were gathered through self-report and verified through a review of the electronic medical records.

The flow chart is presented in Figure 1 displaying recruitment and retention in the study. Fifty women who met the inclusion criteria were approached for recruitment with 14 declining participation, because they received follow-up treatment at an outside facility. The remaining 36 women provided consent and all participated in the first 3 visits. At 78 weeks, 32 women completed the study. Four women were not seen after 12 weeks; one died, two moved out of state, and one participant could not be contacted.

[H2]Device for the Measurement of Tissue Dielectric Constant

TDC was measured with the MoistureMeter D (Delfin Technologies, Kuopio, Finland). A measurement is achieved by placing a cylindrical probe on the surface of the skin for 7-10 seconds. The probe is attached to a coaxial cable which is connected to a control unit with a display window. A 300 MHz electromagnetic wave is emitted from the probe into the tissue. The probe used (M25, 23 mm diameter) has an effective measurement depth of 2.5 mm and was chosen based on its prior extensive use in women with BCRL.[12–17] A portion of the electromagnetic wave is transmitted into the tissue and a portion reflects back to a processor that calculates the TDC. The TDC value that is calculated includes contributions of both free and bound water in the tissue. The TDC is unitless because it is the ratio of permittivity of the measured tissue to that of a vacuum, with higher TDC values indicating higher water content. The displayed TDC ranges from 1 to 80 with pure water having a value of about 76 at 32°C. Concurrent validity has been demonstrated in patients undergoing hemodialysis treatment showing a high correlation ($r= -0.96$, $p<.05$) between decrease in skin water content and the amount of fluid removed during the hemodialysis treatment.[18]

[H2]Clinical Assessment for Trunk Lymphedema

Women are at risk of developing lymphedema on the ipsilateral anterior, posterior, and lateral thorax and breast following breast cancer surgery with lymph node removal. Subjective assessment for signs of swelling in the upper quadrant by a trained lymphedema therapist is the current clinically accepted means for assessment of trunk lymphedema.[4] Clinical assessment consists of comparing the ipsilateral side to the contralateral side using observational and palpation skills assessing for signs of asymmetry, differences in skin folds, bra strap and seam indentations, orange peel phenomenon, changes in skin color, and differences in tissue texture. Trunk lymphedema is evident if visual and/or palpable signs of swelling are present.

[H2]Outcome Measurement Procedures

All outcome measures were performed by a single, non-blinded physical therapist who is a certified lymphedema therapist through the Lymphology of North America with over 15 years of clinical experience specializing in lymphedema treatment (LK). The same examiner measured TDC values at 2, 4, 12, and 78 weeks and subjectively assessed for trunk lymphedema at 78 weeks. The trunk edema clinically identified at 78 weeks through subjective assessment was assumed to be related to fluid changes due to lymphedema development and not post-surgical edema. The side that underwent lymph node removal was considered the at-risk side for BCRL and the contralateral side was delineated the unaffected side.

Trunk TDC measures were taken at all four visits in the study (2, 4, 12, and 78 weeks) with the patient supine. The examination procedure began by placing a mark bilaterally on the lateral chest wall 8 cm below the axillary fold.[5] The women were lying supine for approximately 10 minutes prior to taking the lateral chest wall measure during which other outcome measures for

the primary study were taken.[10,11] The at-risk affected side was measured first, followed by the contralateral unaffected side. The measurement probe was placed on the skin over the mark on the lateral chest wall and a TDC value was recorded for the at-risk affected side and the contralateral unaffected side. A TDC ratio was calculated by dividing the ipsilateral at risk side TDC value by the contralateral control side TDC value ($TDC_{At\text{-}Risk}/TDC_{Contralateral}$ =TDC ratio).

At the 78 week visit only, the women were assessed for clinical lymphedema by the same examiner. The women were positioned upright in the sitting position. The examiner clinically assessed for trunk lymphedema through visual inspection and palpation to determine if lymphedema was present or not present on the ipsilateral side. Women were grouped into the trunk lymphedema group (Trunk Lymph) or the no trunk lymphedema group (No Trunk Lymph) based on the clinical assessment by the lymphedema expert at 78 weeks.

[H2]Data Analysis

The data from the 32 women that completed all four visits in the study was used for analysis. Group differences in the demographic and other important characteristics associated with breast cancer treatment were analyzed using chi square for categorical variables and Student's two sample t-test for continuous variables. With a sample size of 32, a difference in TDC ratio between the Trunk Lymph and No Trunk Lymph group of 0.2 could be detected with 93% power at the 2-sided 0.05 level of significance. Statistics were calculated using NCSS 11 Statistical Software (Kaysville, Utah).

The primary analysis compared the TDC ratios between groups (Trunk Lymph vs. No Trunk Lymph) across time (2, 4, 12, and 78 week) using a repeated measures analysis of variance design. A secondary analysis compared the absolute TDC values on each side (affected side vs.

unaffected side), between groups (Trunk Lymph vs. No Trunk Lymph), across time (2, 4, 12, and 78 week). The Mauchly test statistic was used to check for homogeneity of variance. If the Mauchly criterion was violated, the P-value was corrected using the Geisser Greenhouse correction.[19] If an interaction effect was present, Tukey-Kramer multiple comparison test was used to analyze all pairwise comparisons.

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[H1]RESULTS

Trunk lymphedema was identified in 15 of the 32 women that completed all 4 visits of the study demonstrating a prevalence of 47%. Table 1 depicts the patient characteristics of the women identified with and without lateral trunk lymphedema at 78 weeks.

[H2]*TDC ratios*

Group comparison of TDC ratios across time are given in Figure 2. There was no group x time interaction effect (p=0.75, F=0.33). There was a group effect collapsed across time demonstrating TDC ratios on the lateral chest wall in the Trunk Lymph group (Mean=1.33, %

CI=1.26, 1.40) were statistically higher (p<0.001, F=16.35) than those in the No Trunk Lymph group (Mean=1.12, 95% CI=1.05, 1.19). The average TDC ratios of both groups (collapsed across group) decreased over time (p=0.02, F=3.53).

[H2]*Absolute TDC values*

There was no interaction effect between time, side, and group (F=0.46, p=0.71). There was interaction between group and side (F=14.73, p<0.001) and time and side (F=3.92, p=0.01) but no interaction between group and visit (F=0.47, p=0.71). The post hoc analysis results for the group x side interaction effect and the time x side interaction effect are displayed in Table 2. The affected side was statistically higher than the unaffected side collapsed across time and group (F=75.04, p<0.001) with data displayed in Table 2.

[H1]Discussion

This study compared trunk TDC measures with clinical assessment for trunk lymphedema to determine the potential utility of TDC as a diagnostic tool to detect and quantify trunk lymphedema following breast cancer surgery. Trunk lymphedema was clinically identified in 47% of the women at 78 weeks. The TDC ratios were higher in the women with trunk lymphedema demonstrating the possible clinical utility of the TDC method to quantify trunk lymphedema.

To our knowledge, this is the first longitudinal study to determine the temporal pattern of trunk TDC measures to the clinical assessment of trunk lymphedema by a lymphedema expert. One of the primary findings is that the women with trunk lymphedema had elevated TDC ratios above 1.2 as early as two weeks which remained elevated through 78 weeks. The women without trunk lymphedema had elevated TDC ratios above 1.2 at 2 weeks followed by a subsequent drop in

TDC measures. The difference in temporal patterns between groups may be explained by the physiological tissue changes that occurred due to the breast cancer treatment received (ie, surgery and radiation) and the development of lymphedema. The high TDC ratios at 2 weeks in both groups likely reflected localized edema due to post-surgical swelling. The persistent elevated TDC ratios in the women with trunk lymphedema could potentially be detecting the early onset of trunk lymphedema, which was not seen in the group without trunk lymphedema. Acute inflammation and erythema from radiation may have also influenced the localized water content in the target area but the extent of this impact is unknown. These results provide support for the potential utility of TDC ratios if TDC is detecting changes in post-surgical edema and/or early lymphedema development. Further studies are needed to substantiate these findings.

The 47% prevalence of trunk lymphedema discovered in this study is comparable to the very few studies that have focused on trunk lymphedema.[20–22] Ronka et al reported a range of 23-48% one year after surgery with a higher incidence in women that underwent axillary clearance with a positive lymph node status. Clinical examination by a surgeon or surgical resident was used to assess for lymphedema which was similar to our study.[20] Bosompra et al reported up to a 22% incidence 3-4 years after cancer treatment using self-report.[21] Self-report is speculated to be less sensitive than objective assessment therefore likely underestimating the incidence. Back et al reported in incidence of 21% in women immediately following breast radiation.[22] The current study demonstrated 24% of those who underwent a SLNB developed trunk lymphedema compared 86% that underwent ALND. Although the incidence was less in women with SLNB, the number was still high. The high incidence might be explained by the fact that the SLNB procedure removes the lymph node/s that drains the tumor site located in the trunk, therefore possibly increasing the development of lymphedema in the target area. Although not statistically

different, there was a high prevalence of truncal lymphedema in women that developed a seroma and had higher number of lymph nodes removed. These factors might also help explain the high prevalence of trunk lymphedema since they are both known to increase the risk for upper extremity lymphedema.[23,24]

Our results demonstrated TDC ratios statistically higher in women clinically identified with trunk lymphedema. These results differed from previous studies which compared TDC values in women with and without self-reported subjective trunk lymphedema symptoms. Mayrovitz et al found no difference in TDC ratios in a small group of patients (n=5) who experienced trunk symptoms among a larger cohort women with no self-reported lymphedema symptoms.[6] Czerniec et al found no statistical significance between TDC measures on the affected side of the trunk compared to the unaffected side in five women reporting trunk lymphedema. Cziernec and Mayrovitz used subjective trunk lymphedema symptoms for diagnosis. Our study identified trunk lymphedema through clinical assessment by a lymphedema expert which gives strength to the study since this is the current clinically accepted assessment for trunk lymphedema.[4] Czerniec's study had a very small sample size and included women at different stages of lymphedema limiting the results of the study. Our study clinically assessed for trunk lymphedema at specified sequential intervals which provides strength to the study. Our study did not assess for self-reported lymphedema symptoms therefore the impact of trunk lymphedema on subjective self-reported symptoms is unknown.

The measurement of TDC may help with the early detection of insipient lymphedema and post-surgical edema on the trunk following breast cancer but clinicians should use these results with caution until further research is performed. Physical therapists with lymphedema training should continue to rely on their experience and expertise in making lymphedema assessments and

treatment decisions. A better understanding of the association trunk TDC values have on lymphedema development, time of development, lymphedema symptoms, quality of life, function, and physiological skin changes is warranted. Further studies should focus on whether TDC measurements are predictive of lymphedema development using the results from this study as a guide for future studies. Current literature demonstrates promising diagnostic benefits of TDC but less utility in the change in TDC in response to treatment.[25-27] Further research investigating the change in TDC measures on the trunk following intervention would be clinically beneficial.

The TDC measurement may be useful in the assessment of lymphedema in other locations, and potentially other edemas, which could assist with diagnosis and guide treatment interventions. Obtaining normative values for different body regions and in other populations may improve the evaluation and treatment of both acute and chronic conditions routinely seen in physical therapy. TDC could potentially quantify other areas of localized swelling that are difficult to measure such as in the head, neck, abdomen, foot/ankle, and hand. Growing evidence demonstrates the benefits of using TDC in measuring lymphedematous arms, legs, head, and neck but further evidence is needed.[6,17–23] TDC measures have been used to assess the induration-related water in individuals on dialysis, cardiac patients, diabetes, cerebral edema, and irradiated skin in breast cancer patients.[28–31] TDC measures could potentially be used on other locations and in other physical therapy populations that experience edema such as orthopedic issues, surgical edema, traumatic edema, venous insufficiency, kidney failure, congestive heart failure, and other edema related conditions.

Although missing data due to loss of follow up was a limitation to the study, few women were lost to follow up (1 moved, 1 death, 2 who did not return a phone call). All the measures were taken by a single lymphedema expert (LK) for all visits which reduced variability and error in the measures. Without a valid gold standard for trunk lymphedema to compare to TDC measures, we were unable to establish criterion-related validity which was a limitation to the study. By using a clinical trunk assessment by a lymphedema expert, we were able to provide support for face and construct validity under the assumption that high water content measured by TDC at 78 weeks reflected fluid changes due to the development of lymphedema and not post-surgical edema. A single non-blinded evaluator collected the TDC values and classified the presence or absence of trunk lymphedema and reliability of the physical assessment was not tested which was another limitation of the study; therefore, potential error and bias could not be eliminated. TDC measures were taken at multiple time periods from 2 weeks to 78 weeks without the tester knowing the final clinical lymphedema assessment results which reduced potential error and bias. Preoperative measurements were not taken therefore baseline status was unknown. Women with contralateral prophylactic mastectomy were included in the study which may have been a limitation if contralateral surgery affected the results. Lymph nodes were not removed on the contralateral side; therefore, the effects should have been minimal. Investigating a single location limits the generalizability as the results cannot be generalized to other areas of the body. A single academic health center was used for participant recruitment limiting the generalizability of the findings to other populations.

Currently, physical therapists do not have a method to quantify and detect the early onset of trunk lymphedema and other localized edemas thus rely on clinical subjective assessment. This study provides evidence that TDC is able to quantify trunk lymphedema following breast cancer

surgery with lymph node removal and potentially detect the early onset of lymphedema development. TDC measures may be beneficial in the early detection of trunk lymphedema but further research is needed to determine the clinical utility for diagnostic, predictive, and prescriptive use. The TDC method could be used as an adjunct diagnostic tool in clinical practice, but clinicians should continue to rely on their experience and expertise in making lymphedema assessments and treatment decisions until further research is performed to understand the full utility of the TDC method.

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Concept / idea / research design: L.A. Koehler

Writing: L.A. Koehler, H.N. Mayrovitz

Data collection: L.A. Koehler

Data analysis: L.A. Koehler, H.N. Mayrovitz

Project management: L.A. Koehler

Fund procurement: L.A. Koehler

Providing participants: L.A. Koehler

Providing facilities / equipment: L.A. Koehler

Providing institutional liaisons: L.A. Koehler

Clerical / secretarial support: L.A. Koehler

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Ethics Approval

This study was approved by the University of Minnesota Internal Review Board, and all women provided written consent to the study prior to participation.

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Disclosures

The authors completed the ICMJE Form for Disclosure of Potential Conflicts of Interest and reported no conflicts of interest.

TWITTER HANDLE: UMN Physical Therapy@UMN_PT

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Tables:

Table 1: Participant Characteristics of Women With and Without Clinical Trunk Lymphedema[a,b]

Characteristic	**Trunk Lymphedema n = 15 (47%)**	**No Trunk Lymphedema n = 17 (53%)**	**Total n = 32 (100%)**	**P[c]**
	n (%)	**n (%)**	**# (%)**	
Breast Surgery				.53
Lumpectomy	6 (19)	10 (31)	16 (50)	
Mastectomy	6 (19)	4 (12)	10 (31)	
Contralateral prophylactic mastectomy	3 (9.5)	3 (9.5)	6 (19)	
Axillary surgery				.02[d]
SNB	9 (28)	16 (50)	25 (78)	
ALND	6 (19)	1 (3)	7 (22)	
Radiation	9 (28)	11 (34)	20 (62)	.78
No	6 (19)	6 (19)	12 (38)	
Chemotherapy				
None	6 (19)	12 (37)	18 (56)	.21
Neoadjuvant	3 (9)	2 (7)	5 (16)	

Adjuvant	6 (19)	3 (9)	9 (28)	
Reconstruction	2 (7)	3 (9)	5 (16)	.74
No	13 (41)	14 (43)	27 (84)	
Re-excision of margins	1 (3)	2 (6)	3 (9)	.62
No	14 (44)	15 (47)	29 (91)	
Seroma	8 (25)	4 (12)	12 (37)	.08
No	7 (22)	13 (41)	20 (63)	
Handedness				
Ipsilateral	7 (22)	9 (28)	16 (50)	.55
Contralateral	8 (25)	7 (22)	15 (47)	
Ambidextrous	0	1 (3)	1 (3)	
Age at diagnosis (years) $\overline{X}$ (SD) Range	57 (10) 35-73	56 (10) 40-69	56 35-73	.64
BMI (kg/m^2) $\overline{X}$ (SD) Range	27.4 (5.8) 20-42	26.4 (6.5) 18-45	27 18-45	.64
No. of LN removed $\overline{X}$ (SD) Range	8 (9) 1-32	3 (4) 1-21	5 1-32	.08

[a]ALND = axillary lymph node dissection; BMI = body mass index; LN = lymph node; SD = standard deviation; SNB = sentinel node biopsy; $\overline{X}$ = mean.
[b]Values are numbers (percentages) unless otherwise indicated.
[c]Chi^2 and t-test p values
[d]Significance level: p≤0.05

Table 2: Comparison of TDC At-Risk and Contralateral Sides Between Women With and Without Clinical Trunk Lymphedema Across All Visits[a]

TDC Mean Values (95% CI)		**Time**				**Average of TDC Values[h]**
		2 Weeks	**4 Week**	**12 Week**	**78 Week**	
Group	**Side**					
Trunk Lymph	At-Risk	38.1 (34.1, 42.0)	37.2 (33.3, 41.1)	37.5 (34.1, 41.0)	35.2 (32.6, 37.8)	37.0[i,j] (34.4, 39.6)
	Contralateral	27.7 (24.8, 30.7)	28.1 (25.3, 30.8)	28.5 (26.2, 31.0)	28.6 (26.4, 30.9)	28.2[i,j,k] (26.1, 30.3)
No Trunk Lymph	At-Risk	37.9 (34.2, 41.6)	33.7 (30.1, 37.4)	35.2 (32.0, 38.4)	32.8 (30.3, 35.3)	34.9[j,k] (32.4, 37.4)
	Contralateral	31.3 (28.6, 34.1)	31.5 (29.0, 34.1)	31.1 (28.8, 33.3)	32.2 (30.1, 34.3)	31.5[i,j,k] (29.6, 33.5)
Total[b]	At-Risk	38.0[c,d] (35, 40.7)	35.5[d,e] (32.8, 38.1)	36.4[d,f] (34.0, 38.7)	34.0[c,d,g] (32.2, 35.8)	35.95[l] (34.1, 37.8)
	Contralateral	29.50[c,d,e,f,g] (27.5, 31.5)	29.79[c,e,f,g] (27.9, 31.7)	29.80[c,e,f,g] (28.2, 31.4)	30.40[c,e,f,g] (28.9, 32.0)	29.88[l] (28.5, 31.3)

[a]TDC = tissue dielectric constant.
[b]Subscripts in the row labeled Total indicates significant differences post hoc pairwise comparisons of the side x time interaction at p<0.05
[c] Difference in At Risk side at 2 wks to the Contralateral side at all time periods and the At-risk side at 78 wks.
[d] Difference in Contralateral side at 2 wks to all the At-Risk time points
[e] Difference in Contralateral side at 4 wks to all the At-Risk time points
[f] Difference in Contralateral side at 12 wks to all the At-Risk time points
[g] Difference in Contralateral side at 78 wks to all the At-Risk time points
[h] Subscripts in the Column labeled Average of TDC values indicates significant differences post hoc pairwise comparisons of the side x group interaction

[i]Difference in Trunk lymph at risk side to the Trunk lymph contralateral side and No Trunk Lymph At risk and Contralateral side
[j] Difference in Trunk contralateral side to No Trunk Lymph at risk and contralateral side
[k] Difference in No Trunk Lymph at risk side compared to Trunk Lymph and No Trunk Lymph contralateral sides
[l]Indicates a statistical difference between sides at $p<0.05$

Figure Captions:

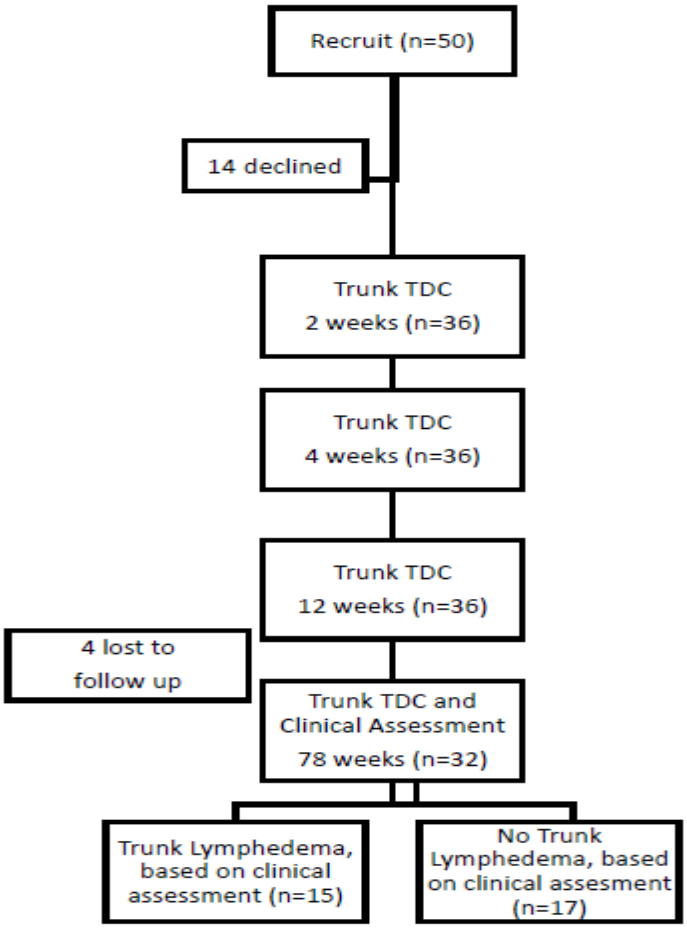

Figure 1: Flow diagram of the longitudinal study on trunk edema assessment.
TDC = tissue dielectric constant.

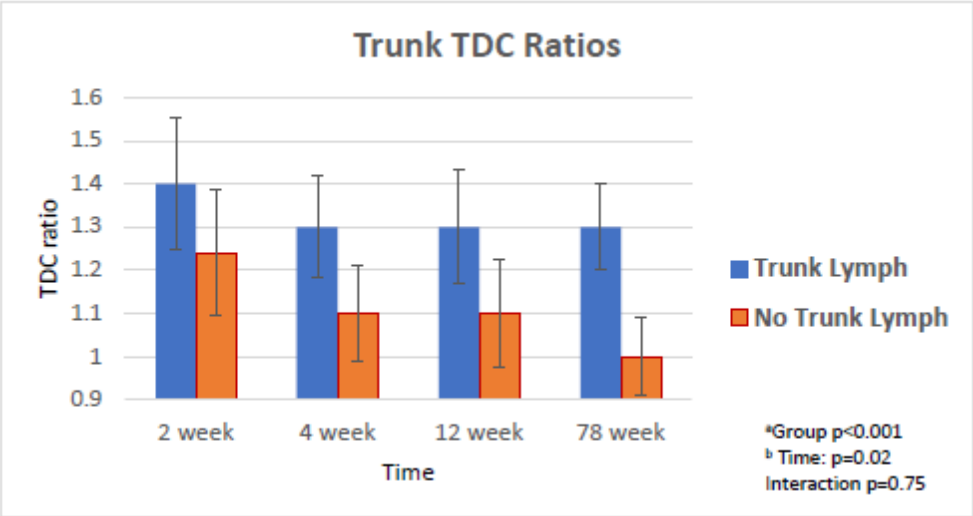

Figure 2: Comparison of trunk TDC ratios between women with and without clinically identified trunk lymphedema across 78 weeks. Lymph = lymphedema; TDC = tissue dielectric constant; TDC ratio = at-risk trunk TDC/contralateral trunk TDC. Error bars = 95% confidence intervals. [a]Significant group effect (collapsed over time) at $p<0.05$. [b] Significant time effect (collapsed between groups) $p<0.05$.