Assessing Localized Skin-to-Fat Water in Arms of Women with Breast Cancer Via Tissue Dielectric Constant Measurements in Pre- and Post-surgery Patients

Article *in* Annals of Surgical Oncology · November 2014

DOI: 10.1245/s10434-014-4185-5 · Source: PubMed

3 authors, including:

Harvey N Mayrovitz
Nova Southeastern University
201 PUBLICATIONS **3,350** CITATIONS

SEE PROFILE

Assessing Localized Skin-to-Fat Water in Arms of Women with Breast Cancer Via Tissue Dielectric Constant Measurements in Pre- and Post-surgery Patients

Harvey N. Mayrovitz, Daniel N. Weingrad & Lidice Lopez

Annals of Surgical Oncology

ISSN 1068-9265
Volume 22
Number 5

Ann Surg Oncol (2015) 22:1483-1489
DOI 10.1245/s10434-014-4185-5

Springer

Ann Surg Oncol (2015) 22:1483–1489
DOI 10.1245/s10434-014-4185-5

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE – BREAST ONCOLOGY

Assessing Localized Skin-to-Fat Water in Arms of Women with Breast Cancer Via Tissue Dielectric Constant Measurements in Pre- and Post-surgery Patients

Harvey N. Mayrovitz, PhD[1], Daniel N. Weingrad, MD[2], and Lidice Lopez, PA[2]

[1]College of Medical Sciences, Nova Southeastern University, Davie, FL; [2]Cancer HealthCare Associates, Aventura, FL

ABSTRACT

Background. Skin-to-fat tissue dielectric constant (TDC) values at 300 MHz largely depend on tissue water and provide a rapid way to assess skin water by touching skin with a probe for approximately 10 s. This method has been used to investigate lymphedema features accompanying breast cancer (BC), but relationships between TDC and nodes removed or symptoms is unclear. Our goals were: (1) to compare TDC values in BC patients prior to surgery (group A) and in patients who had BC-related surgery (group B) to determine if TDC of group B were related to nodes removed and reported symptoms and (2) to develop tentative lymphedema-detection thresholds.

Methods. Arm volumes and TDC values of at-risk and contralateral forearms and biceps were determined in 103 women awaiting surgery for BC and 104 women who had BC-related surgery 26.3 ± 17.5 months prior to evaluation. Inter-arm ratios (at-risk/contralateral) were determined and patients answered questions about lymphedema-related symptoms.

Results. Inter-arm TDC ratios for group A forearm and biceps were respectively 1.003 ± 0.096 and 1.012 ± 0.143. Group B forearm ratios were significantly greater, and among group B patients who reported at least one symptom there was a significant correlation between TDC ratios and symptom burden and nodes removed.

Conclusions. Inter-arm TDC ratios are significantly related to symptoms and nodes removed. Ratios increase with increasing symptom score and might be used to detect preclinical unilateral lymphedema using TDC ratio thresholds of 1.30 for forearm and 1.45 for biceps. Threshold confirmation awaits targeted prospective studies but can serve as guideposts to provide quantitative and easily done tracking assessments during follow-up visits.

First Received: 24 August 2014;
Published Online: 12 November 2014

H. N. Mayrovitz, PhD
e-mail: mayrovit@nova.edu

Skin-to-fat tissue dielectric constant (TDC) values, measured at 300 MHz, largely depend on tissue water.[1–3] The method is a convenient, rapid, noninvasive way to assess tissue water in any skin location. One measurement takes approximately 10 s and is achieved by touching skin with a probe.[2] It has been used to study variations in local water among body sites and used in several conditions in which local skin-to-fat tissue water and its change were of interest.[4–6] These include diabetes, menstruation, lower extremity edema, and head and neck lymphedema.[7–11] It also has been used to investigate overt lymphedema and changes in localized arm tissue water accompanying therapies for breast cancer treatment-related lymphedema (BCRL).[12] These include changes subsequent to manual lymphatic drainage, low level laser treatment, and intermittent pneumatic compression.[13–15] It also has been used to characterize arm water features of women with and without breast cancer.[16,17] Despite this build up of information, the extent that TDC values correlate with patient treatment parameters and perceived symptoms is unclear. Thus, our goals were twofold: (1) to compare TDC values measured in breast cancer patients prior to surgery (group A) with those in patients who had surgery (group B) and to determine if TDC values measured in group B were related to patient treatment parameters and reported symptoms and (2) to develop tentative TDC-related lymphedema-detection thresholds based on pre-surgery TDC measurements.

PATIENTS AND METHODS

All group A patients had breast cancer (BC) and group B patients had been treated for BC. All patients were current

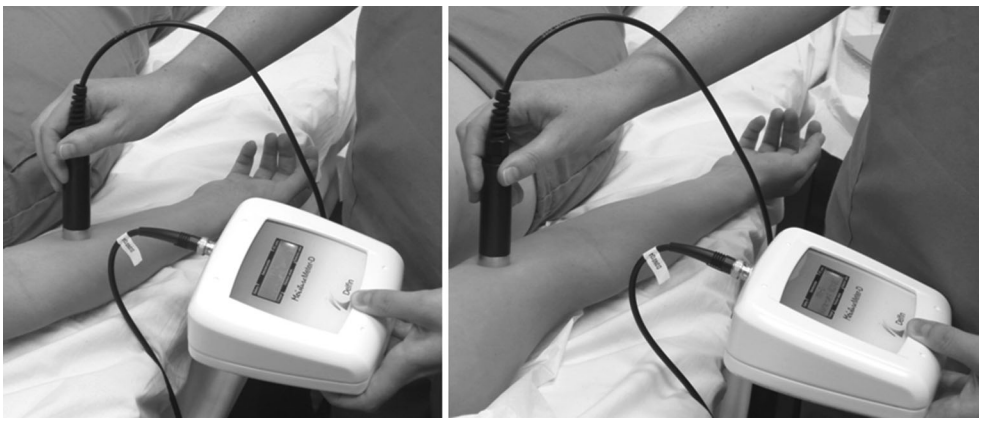

FIG. 1 TDC probes in contact with forearm and biceps measurement sites. Measurements were done first on the anterior forearm (6 cm distal to the antecubital fossa) and then on the anterior biceps (8 cm proximal to the antecubital fossa). All TDC measurements were done with the subject supine with measurements started after they had been resting in this position on a padded examination table for approximately 10 mins. Measurement data acquisition is initiated when probe comes in contact with the skin and a single measurement takes approximately 10 s

patients of one author (DW). Before research-related evaluations, the research study purposes were explained to all potential participants and all signed a university institutional approved informed consent. Measurements (described below) were made in 207 patients: 103 pre-surgery (group A) and 104 patients at various times post-surgery (group B). Group A versus group B (mean ± SD) did not differ significantly with respect to age (60.6 ± 13.2 versus 60.6 ± 12.1 years, $P = 0.991$) or body mass index (28.3 ± 6.7 versus 28.4 ± 7.1 Kg/m^2, $P = 0.980$. Of the 104 group B patients, lumpectomy with sentinel lymph node biopsy (SLNB) was the surgical procedure in 55.4% of patients, axillary node dissection was done in 26.7% of patients, and 17.8% of patients had a mastectomy. Subsequent radiation was received by 77.9% of patients with 65.4% receiving brachytherapy, 9.6% receiving whole breast radiation, 2.9% receiving external beam, and 22.1% receiving no radiation therapy. The number of nodes removed was 8.5 ± 8.9 (range 1–30, median 3.0). Group A patients were evaluated within 2 weeks of their pending surgery and group B patients were evaluated on average 26.3 ± 17.5 months post-surgery (range 7.3–131.2 months, median = 24.1 months).

Tissue Dielectric Constant Measurements

Bilateral tissue dielectric constant (TDC) values were measured in triplicate at forearm and biceps using the MoistureMeterD (Delfin Ltd. Kuopio, Finland) to an effective measurement depth of 2.5 mm (Fig. 1). The device displays and stores dielectric constant values, also called relative permittivity. TDC values are ratios of tissue permittivity to free space permittivity and thus are dimensionless. For reference, the dielectric constant of distilled water is approximately 76 at 32 °C.

The method's principle has been well described.[1,2,18–20] Briefly, the probe acts as a coaxial transmission line through which a 300-MHz signal is transmitted. Reflections depend on the tissue's complex permittivity, which depends on signal frequency and tissue dielectric constant (the real part of the complex permittivity). At 300-MHz, the contribution of conductivity to permittivity is small, so TDC is mainly determined by water molecules (free and bound). Thus, the device includes and analyzes only the dielectric constant that is proportional to tissue water.

Intra-rater reliability was assessed via bilateral forearm TDC measurements to 2.5-mm depth on six subjects using intraclass correlation coefficients (ICC) that express the percentage of variability attributable to true subject variance as opposed to measurement related variability (between subject variation/total variation). Results showed excellent single measure ICC value of 0.996 (95% confidence interval of 0.965–1.000). Similar ICC values have been reported.[10]

Arm Girths and Volumes Measurements

Arm volumes were calculated from girths measured at 4-cm interval starting at the wrist with a spring tension tape measure and calculating volume from the sum of segmental volumes with a validated frustum model.[21–27]

Symptom Questionnaire

All patients completed a questionnaire to determine if any of 12 sensations were present or were experienced since the last clinic visit. Queried sensations were fullness, heaviness, tightness, numbness, tingling, tenderness, aching, pain, warmth, cold, swelling, and stiffness in arm, hand, fingers, axilla, or chest. An answer of yes was scored

as a value of 1, and a symptom score was the sum of scores with a maximum symptom score value of 12. The questions and their scoring were modeled after a subset of those contained in the validated lymphedema and breast cancer questionnaire (LBCQ).[28]

Theoretical TDC Lymphedema Thresholds

Following previous approaches, inter-arm lymphedema threshold ratios were determined by adding a multiple of the pre-surgery standard deviation (SD) to the pre-surgery group mean.[29,30] Ratios were used to investigate the number of postsurgical patients that exceed the threshold.

Analysis

Inter-arm TDC and volume ratios (at-risk arm/contralateral arm) were determined group A and group B patients. Shapiro-Wilk tests indicated ratios were normally distributed. Differences in ratios between groups were evaluated with independent *t* tests. TDC differences between sites (forearm versus biceps) were done using paired *t* tests. Dependence of postsurgical ratios on treatment parameters or symptoms was first investigated by dividing group B patients into subsets above and below the median value for the following parameters: (1) months post-surgery at study evaluation, (2) number of nodes removed, and (3) symptom score. Follow-up used regression analyses to determine significance of relationships between inter-arm ratios and number of nodes removed and symptom score.

RESULTS

Pre- and Post-surgery Inter-arm Differentials

Pre-surgery at-risk and control arm volumes did not significantly differ (2288 ± 726 ml versus 2300 ± 727 ml, $P = 0.367$) with an inter-arm volume difference (at-risk arm–contralateral arm) of −12 ± 122ml (range −348 to +317 ml). Postsurgical at-risk volumes were significantly greater than contralateral arms (2277 ±710 versus 2218 ± 610 ml, $P = 0.002$). The overall postsurgical inter-arm volume difference was 59 ±189 ml, but comparing patients who reported at least one symptom with those reporting no symptoms showed a significant inter-arm difference (170 ± 251 ml versus 4.6 ± 119 ml, $P < 0.01$) with at-risk arms having greater volume.

Pre-surgery at-risk and control arm TDC values did not significantly differ at forearm or biceps with arm differentials of −0.090 ± 2.444 and 0.004 ± 3.290, respectively. Post-surgical at-risk and control arm TDC values were significantly different with the inter-arm TDC difference being 1.32 ± 4.75 at forearm and 0.89 ± 5.98 at biceps. Comparing patients who reported at least one symptom with those reporting no symptoms showed a highly significant inter-arm difference at forearm (2.87 ±6.56 versus 0.56 ± 3.36, $P < 0.01$) and at biceps (2.94 ± 9.18 versus 0.10 ± 3.14, $P < 0.01$) with the at-risk arm having the greater TDC value.

Symptom Scores

Of the 104 postsurgical patients, 34 (32.7%) reported at least one symptom with a distribution as summarized in Table 1. The most frequently reported was numbness (20.2%) followed by fullness and ache each reported by 14.4% of all patients. For those 34 patients who reported at least one symptom, the above percentages increase to 61.8% for numbness and 44.1% for fullness and ache. The overall average symptom score was 1.34 ± 2.6 (range 0–12). Among the 34 patients who reported at least one symptom, the symptom score was 4.1 ± 3.1 (range 1–12, median = 3.0). No pre-surgical patient reported lymphedema-related symptoms.

Overall Inter-arm Ratios

Comparisons of inter-arm ratios for TDC values and arm volumes (Table 2) show that postsurgical patients (group B) as a whole had significantly ($P < 0.05$) greater forearm TDC ratios and greater whole arm volume ratios ($P < 0.01$) compared with pre-surgery patients (group A). When group B patients alone were considered, divided according to having at least one symptom (Bs, $N = 34$) or having no symptoms (Bns = 70), the TDC ratios of the Bs subset were significantly greater than for the Bns subset at forearm and biceps ($P < 0.05$). Comparisons of TDC ratios between sites (forearms versus biceps) showed no significant differences within either patient group.

Impact of Number of Nodes Removed

Postsurgical patients (group B) were divided into two subsets: one set (set B−) was populated with patients in whom the number of nodes removed was less than or equal to the median number of nodes removed in the full group B. The other subset (set B+) included patients in whom the number of nodes removed was less than the median number of nodes removed. Patients in set B− and set B+ did not differ with respect to body mass index (BMI) (27.8 ± 7.6 versus 28.9 ± 6.5 Kg/m^2, $P = 0.422$) or with respect to months post-surgery (24.9 ± 13.8 versus 27.7 ± 20.7, $P = 0.426$). Comparing TDC values obtained

TABLE 1 Distribution of reported symptom sensations for the 104 post-surgery patients

	Reported symptom sensations											
	Numb	Full	Ache	Tingle	Tight	Tender	Pain	Stiff	Swell	Heavy	Warm	Cold
% of all patients	20.2	14.4	14.4	12.5	11.5	11.5	11.5	9.6	9.6	8.7	5.8	3.8
% of patients with at least one symptom	61.8	44.1	44.1	38.2	35.3	35.3	35.3	29.4	29.4	26.5	17.6	11.8

The most widely reported symptom was numbness that constituted 61.8% of the reported symptoms of patients with at least one symptom

TABLE 2 At-risk to contralateral side ratios for pre- and post-surgery groups

Inter-arm ratios (at-risk/contralateral)	Group A ($n = 103$) versus group B ($n = 104$)			Group B patients only		
	Group A pre-surgery	Group B post-surgery	P value	Symptoms (Bs, $n = 34$)	No symptoms (Bns, $n = 70$)	P value
Forearm TDC	1.003 ± 0.096	1.050 ± 0.172*	0.017	1.100 ± 0.231†	1.026 ± 0.129	0.038
Biceps TDC	1.012 ± 0.143	1.037 ± 0.219	0.318	1.113 ± 0.335†	1.001 ± 0.119	0.014
Arm volume	0.994 ± 0.051	1.021 ± 0.070*	0.004	1.065 ± 0.087§	1.000 ± 0.048	0.001
Nodes removed				11.4 ± 9.5†	7.1 ± 8.4	0.022

Groups A and B are pre- and post-surgery groups respectively. Bs and Bns are post-surgery subgroups with and without symptoms respectively

* $P < 0.05$ compared with group A

† $P < 0.05$ versus subgroup Bns

§ $P < 0.01$ versus subgroup Bns

TABLE 3 At-risk to contralateral arm ratios for postsurgical patients

	Forearm TDC ratio (A/C)			Biceps TDC ratio (A/C)			Arm volume ratio (A/C)		
Parameter	Set B−	Set B+	P value	Set B−	Set B+	P value	Set B−	Set B+	P value
Nodes removed	1.013 ± 0.096	1.091 ± 0.221*	0.022	0.986 ± 0.106	1.094 ± 0.288*	0.012	1.011 ± 0.064	1.033 ± 0.075	0.105
Symptom score	1.025 ± 0.129	1.100 ± 0.231*	0.038	1.001 ± 0.118	1.113 ± 0.335*	0.014	1.000 ± 0.048	1.065 ± 0.087**	<0.001
Months post-surgery	1.072 ± 0.203	1.028 ± 0.132	0.190	1.038 ± 0.201	1.037 ± 0.238	0.985	1.012 ± 0.071	1.031 ± 0.068	0.170

Set B− and set B+ indicate post-surgery group B patients whose parameter values (nodes removed, symptom score or months post-surgery) were equal to or less than the median value of the indicated parameter (B−) or greater than the median value of the indicated parameter value (B+). All inter-arm ratios were significantly greater for the patient subset reporting the greater symptom score

* $P < 0.05$ versus subset B−

** $P < 0.001$ versus subset B−

in the two subsets showed that forearm and biceps inter-arm ratios were significantly ($P < 0.05$) greater for patients in set B+ (Table 3). Also, patients in set B+ compared with B− had a significantly greater symptom score (2.10 ± 3.35 versus 0.64 ± 1.33, $P = 0.004$).

Impact of Symptom Score

Dividing postsurgical patients below and above the overall median symptom score showed that compared with patients below the median, patients with symptom scores above the median had significantly greater inter-arm forearm and biceps TDC ratios ($P < 0.05$) and greater arm volume ratios ($P < 0.001$; Table 3). Patients in these two subsets did not differ with respect to age (60.6 ± 12.8 versus 60.4 ± 10.3, $P = 0.934$), BMI (27.7 ± 6.2 Kg/m^2 versus 29.6 ± 8.6 Kg/m^2, $P = 0.206$), and did not differ with respect to months post-surgery (25.8 ± 17.9 versus 27.2 ± 16.4, $P = 0.688$). Patients with symptom scores above the median had a significantly greater ($P = 0.020$) number of nodes removed (11.4 ± 9.5) versus patients with symptom scores below the median (7.0 ± 8.3).

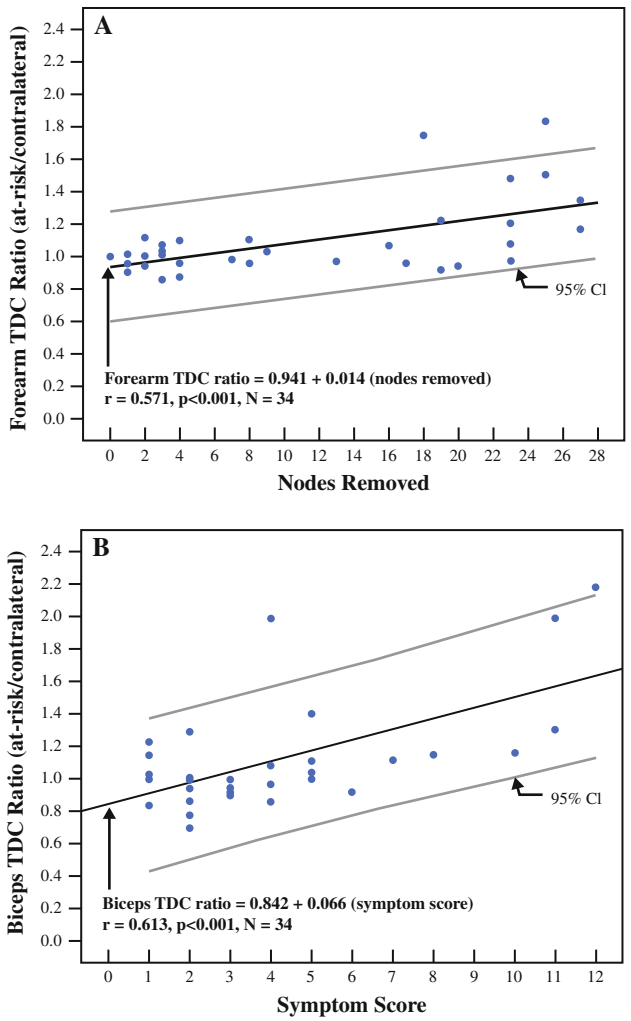

FIG. 2 Inter-arm TDC ratio relationship to nodes removed and symptom score. Data are for those postsurgical patients who expressed one or more symptoms ($N = 34$). *Solid line* is the linear regression given by the equation in the figure and the *dashed lines* indicate the 95% confidence limits. **a** shows the forearm inter-arm TDC ratio versus number of nodes removed and **b** shows the biceps inter-arm TDC ratio versus symptom score

Additionally, if the postsurgical group is divided according to those patients with at least one reported symptom ($N = 34$) versus those with no symptoms ($N = 70$), then those patients with reported symptoms also had the greater number of removed nodes (11.4 ± 9.5 versus 7.1 ± 8.4, $P < 0.05$).

Impact of Months Post-surgery

Dividing postsurgical patients below and above the overall median months post-surgery showed no significant differences in any inter-arm ratio (Table 3). There also was no significant difference in age (59.6 ± 12.4 versus 61.5 ± 11.7 years, $P = 0.418$, nodes removed (9.1 ± 9.5 versus 7.8 ± 8.4, $P = 0.467$), or symptom score (1.3 ± 2.5 versus 1.4 ± 2.7, $P = 0.852$) between these subsets.

Correlations Among Parameters

For postsurgical patients who had at least one symptom ($N = 34$, 33% of group B), there was a significant positive correlation between inter-arm TDC ratios and the number of nodes removed and a significant correlation between symptom score. Considering first the number of nodes removed (nodes), a linear regression analysis showed that the forearm TDC inter-arm ratio (TDC_{RF}) could be expressed as $TDC_{RF} = 0.941 + 0.014$ nodes, $r = 0.571$, $P < 0.001$ (Fig. 2a) and biceps ratio (TDC_{RB}) could be expressed as $TDC_{RF} = 0.904 + 0.018$ nodes, $r = 0.521$, $P < 0.001$. Volume ratio (VOL_R) dependence on the number of nodes removed could be expressed as $VOL_R = 1.028 + 0.003$ nodes, $r = 0.361$, $P < 0.05$. For symptom score (SS), forearm inter-arm ratios could be expressed as $TDC_{RF} = 0.931 + 0.041(SS)$, $r = 0.550$, $P < 0.001$ and biceps ratios as $TDC_{RB} = 0.842 + 0.066(SS)$, $r = 0.613$, $P < 0.001$ (Fig. 2b). Volume ratio dependence on score could be expressed as $VOL_R = 1.022 + 0.011(SS)$, $r = 0.377$, $P < 0.05$. Symptom scores significantly correlated with the number of nodes removed with the regression given by $SS = 2.04 + 0.180$ (nodes), $r = 0.552$, $P < 0.001$. Postsurgical patients who reported no symptoms ($N = 70$, 67% of group B) had no significant correlations between inter-arm ratios and either number of nodes removed or symptom score.

Percentage of Post-surgical Patients Exceeding Theoretical Lymphedema TDC Thresholds

The pre-surgery mean ± SD values for forearm and biceps inter-arm ratios are 1.003 ± 0.096 and 1.012 ± 0.143, respectively (Table 2). A theoretical lymphedema threshold may be described as an inter-arm ratio exceeds the mean + α (SD) in which the choice of α depends on the desired degree of conservativeness. Assuming a normal distribution (which applies to the current ratios) values of 2.0, 2.5, and 3.0 would have respectively 97.7, 99.4, and 99.9 % of cases less than the threshold. Choosing the most conservative criteria ($\alpha = 3.0$) produces theoretical lymphedema inter-arm thresholds of 1.293 for forearm and 1.443 for biceps. The number of patients with ratios equal to or exceeding these thresholds was seven (6.7%) for forearm and four (3.6%) for biceps. These percentages rise to 14.7 and 8.8 % when only patients with at least one symptom are evaluated. The same result was obtained for the slightly rounded up thresholds of 1.30 for forearm and 1.45 for biceps. The least conservative threshold estimate using 2SD ratios yielded thresholds of 1.200 and 1.300 for

forearm and biceps. For this criterion, ten patients (9.6 %) demonstrated an inter-arm ratio that exceeded the threshold at the forearm and six (5.8 %) for biceps. These percentages rise to 20.6 and 14.8 % when only patients with at least one symptom are evaluated.

DISCUSSION

Evaluation of 103 breast cancer patients who were awaiting breast surgery allowed the characterization of inter-arm volume and TDC features of a patient group not yet subjected to the potential lymphedema-causing procedures associated with breast cancer treatment. Evaluation of the separate group of 104 patients allowed a comparison of inter-arm volume and TDC features as present approximately 2 years after breast cancer surgery. These groups did not differ with respect to age, weight, or body mass index. The pre-surgery group showed no significant differences in inter-arm TDC values or in arm volumes. This similarity among at-risk and contralateral arms allowed the determination of at-risk to contralateral arm TDC ratios potentially useful as reference ratios in relation to post-surgery patients.

A main finding of this study was the demonstration that inter-arm TDC ratios show a significant direct relationship to patient perceived symptoms and to the number of nodes that were removed during the patients breast cancer related surgery. The fact that the at-risk to contralateral arm TDC ratios increase with increasing symptom score may indicate that even at a low perceived symptom burden such TDC ratios may herald the onset of pre-clinical incipient lymphedema development. Although at this stage such a hope is premature the present study offers a first step in formulating theoretical TDC lymphedema thresholds based on the TDC ratio variance in breast cancer patients prior to their surgery. Based on the patient populations evaluated we would recommend a conservative threshold corresponding to ratios equal to the mean value prior to surgery to which is added 3 SD. For the present series, this would place the threshold for unilateral lymphedema if the TDC ratio was $\geq$1.30 for the forearm and 1.45 for the biceps. A less conservative estimate using 2.0 SD or 2.5 SD may result in greater sensitivity but likely a decreased specificity. Because in the present study post-surgery patients were not followed sequentially and no systematic clinical assessments were made, confirmations of the suitability of these thresholds and their predictive values must await the outcomes of such targeted prospective studies. However, we believe that the suggested threshold levels may serve as usable guideposts for the present. Such thresholds would provide for useful quantitative and easily done tracking assessments of patients previously treated for breast cancer during routine follow-up visits.

CONFLICT OF INTEREST No author has any commercial interest in the subject of this study

REFERENCES

1. Alanen E, Lahtinen T, Nuutinen J. Variational formulation of open-ended coaxial line in contact with layered biological medium. *IEEE Trans Biomed Eng.* 1998;45(10):1241–8.
2. Nuutinen J, Ikaheimo R, Lahtinen T. Validation of a new dielectric device to assess changes of tissue water in skin and subcutaneous fat. *Physiol Meas.* 2004;25(2):447–54.
3. Stuchly MA, Athey TW, Stuchly SS, Samaras GM, Taylor G. Dielectric properties of animal tissues in vivo at frequencies 10 MHz–1 GHz. *Bioelectromagnetics.* 1981;2(2):93–103.
4. Mayrovitz HN, Luis M: Spatial variations in forearm skin tissue dielectric constant. *Skin Res Technol.* 2010;16(4):438–43.
5. Mayrovitz HN, Bernal M, Carson S. Gender differences in facial skin dielectric constant measured at 300 MHz. *Skin Res Technol.* 2012;18:504–10.
6. Mayrovitz HN, Bernal M, Brlit F, Desfor R. Biophysical measures of skin tissue water: variations within and among anatomical sites and correlations between measures. *Skin Res Technol.* 2013;19(1):47–54.
7. Mayrovitz HN, McClymont A, Pandya N. Skin tissue water assessed via tissue dielectric constant measurements in persons with and without diabetes mellitus. *Diabetes Technol Ther.* 2013;15(1):60–5.
8. Mayrovitz HN, Brown-Cross D, Washington Z. Skin tissue water and laser Doppler blood flow during a menstrual cycle. *Clin Physiol Funct Imaging.* 2007;27(1):54–9.
9. Birkballe S, Jensen MR, Noerregaard S, Gottrup F, Karlsmark T. Can tissue dielectric constant measurement aid in differentiating lymphoedema from lipoedema in women with swollen legs? *Br J Dermatol.* 2014;170(1):96–102.
10. Jensen MR, Birkballe S, Nørregaard S, Karlsmark T. Validity and interobserver agreement of lower extremity local tissue water measurements in healthy women using tissue dielectric constant. *Clin Physiol Funct Imaging.* 2012;32(4):317–22.
11. Nixon J, Purcell A, Fleming J, McCann A, Porceddu S. Pilot study of an assessment tool for measuring head and neck lymphoedema. *Br J Community Nurs.* 2014;19(Sup4):S6–S11.
12. Mayrovitz HN. Assessing local tissue edema in postmastectomy lymphedema. *Lymphology.* 2007;40(2):87–94.
13. Mayrovitz HN, Davey S, Shapiro E. Localized tissue water changes accompanying one manual lymphatic drainage (MLD) therapy session assessed by changes in tissue dielectric constant in patients with lower extremity lymphedema. *Lymphology.* 2008;41(2):87–92.
14. Mayrovitz HN, Davey S. Changes in tissue water and indentation resistance of lymphedematous limbs accompanying low level laser therapy (LLLT) of fibrotic skin. *Lymphology.* 2011;44(4):168–77.
15. Fife CE, Davey S, Maus EA, Guilliod R, Mayrovitz HN. A randomized controlled trial comparing two types of pneumatic compression for breast cancer-related lymphedema treatment in the home. *Support Care Cancer.* 2012;20:3279–86.
16. Mayrovitz HN. Local tissue water assessed by measuring forearm skin dielectric constant: dependence on measurement depth, age and body mass index. *Skin Res Technol.* 2010;16(1):16–22.

17. Mayrovitz HN, Weingrad DN, Davey S. Local tissue water in at-risk and contralateral forearms of women with and without breast cancer treatment-related lymphedema. *Lymphat Res Biol.* 2009;7(3):153–8.
18. Aimoto A, Matsumoto T. Noninvasive method for measuring the electrical properties of deep tissues using an open-ended coaxial probe. *Med Eng Phys.* 1996;18(8):641–6.
19. Alanen E, Lahtinen T, Nuutinen J. Penetration of electromagnetic fields of an open-ended coaxial probe between 1 MHz and 1 GHz in dielectric skin measurements. *Phys Med Biol.* 1999;44(7): N169–76.
20. Nuutinen J, Lahtinen T, Turunen M, et al. A dielectric method for measuring early and late reactions in irradiated human skin. *Radiother Oncol.* 1998;47(3):249–54.
21. Casley-Smith JR. Measuring and representing peripheral oedema and its alterations. *Lymphology.* 1994;27(2):56–70.
22. Mayrovitz HN. Limb volume estimates based on limb elliptical vs. circular cross section models. *Lymphology.* 2003;36(3):140–3.
23. Karges JR, Mark BE, Stikeleather SJ, Worrell TW. Concurrent validity of upper-extremity volume estimates: comparison of calculated volume derived from girth measurements and water displacement volume. *Phys Ther.* 2003;83(2):134–45.
24. Mayrovitz HN, Sims N, Macdonald J. Assessment of limb volume by manual and automated methods in patients with limb edema or lymphedema. *Adv Skin Wound Care.* 2000;13(6):272–6.
25. Meijer RS, Rietman JS, Geertzen JH, Bosmans JC, Dijkstra PU. Validity and intra- and interobserver reliability of an indirect volume measurements in patients with upper extremity lymphedema. *Lymphology.* 2004;37(3):127–33.
26. Sander AP, Hajer NM, Hemenway K, Miller AC. Upper-extremity volume measurements in women with lymphedema: a comparison of measurements obtained via water displacement with geometrically determined volume. *Phys Ther.* 2002;82(12): 1201–12.
27. Sitzia J. Volume measurement in lymphoedema treatment: examination of formulae. *Eur J Cancer Care (Engl).* 1995;4(1): 11–6.
28. Armer JM, Radina ME, Porock D, Culbertson SD. Predicting breast cancer-related lymphedema using self-reported symptoms. *Nurs Res.* 2003;52(6):370–9.
29. Ward LC, Dylke E, Czerniec S, Isenring E, Kilbreath SL. Reference ranges for assessment of unilateral lymphedema in legs by bioelectrical impedance spectroscopy. *Lymphat Res Biol.* 2011;9(1):43–6.
30. Ward LC, Dylke E, Czerniec S, Isenring E, Kilbreath SL. Confirmation of the reference impedance ratios used for assessment of breast cancer-related lymphedema by bioelectrical impedance spectroscopy. *Lymphat Res Biol.* 2011;9(1):47–51.