

# Palpation of Increased Skin and Subcutaneous Thickness, Tissue Dielectric Constant, and Water Displacement Method for Diagnosis of Early Mild Arm Lymphedema

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## Abstract

**Background:** Early diagnosis of mild lymphedema and treatment are important to prevent its progress. The tissue dielectric constant (TDC), measuring local tissue water in the skin and upper subcutis, has neither been related to the water displacement method (WDM) nor been used to diagnose mild arm lymphedema in patients at risk. Our aims were to evaluate TDC and WDM in combination with palpation, examine the association between TDC and WDM measurements, and compare lymphedema-related factors.

**Methods and Results:** Seventy-two women treated for breast cancer were diagnosed with mild arm lymphedema using skin palpation in combination with TDC from fixed measurement sites (threshold ratio for upper arm  $\geq 1.45$  and forearm  $\geq 1.3$ ) and/or WDM (lymphedema relative volume [LRV]:  $\geq 5\%$  to  $\leq 8\%$ ). Results revealed that 32 (45%) women were diagnosed by TDC only, 19 (26%) by WDM only, and 21 (29%) by both TDC and WDM. TDC ratios exceeding the threshold were most frequently identified on the medial site of the arm, proximal and distal to the antecubital fossa. TDC and WDM were negatively associated; LRV ( $r = -0.545$ ,  $p < 0.001$ ). The women diagnosed by TDC only were diagnosed earlier after surgery ( $p = 0.003$ ) and had a lower LRV (1.3%) than those diagnosed by WDM only (6.3%) or both TDC and WDM (6.2%;  $p < 0.001$ ).

**Conclusions:** TDC and WDM can be used together for early diagnosis of arm lymphedema, but TDC is the most valid method, determining the diagnosis earlier after surgery and at a lower arm volume than WDM.

**Keywords:** breast cancer, arm lymphedema, diagnosis, tissue dielectric constant, water displacement method

## Introduction

**B**REAST CANCER-RELATED LYMPHEDEMA (BCRL) is most commonly caused by surgery to the axillary lymph nodes and mastectomy. Other risk factors are radiotherapy, overweight, sedentary lifestyle,<sup>1</sup> and a predisposition to lymphedema.<sup>2</sup> Despite new lymph-sparing surgery using the sentinel node technique, many women still need treatment for BCRL. One reason for this might be the rising survival rates related to improved oncological treatments that further increase the prevalence of BCRL. The incidence of lymphedema varies depending on the diagnostic method used. In a cohort of 292 Swedish women with breast cancer treated with axillary dissection and radio-

therapy, the incidence of BCRL was 38.7% measured by the water displacement method (WDM).<sup>3</sup> Koelmeyer et al. recently showed a similar result in a retrospective study that screened patients with bioimpedance before and after surgery. They also reported that an early commencement of the intervention can lower the incidence of lymphedema. The incidence of arm lymphedema in the traditional referral group and early surveillance group was 39% and 14%, respectively.<sup>4</sup>

Early diagnosis of lymphedema may facilitate more effective management, resulting in reduced severity and associated disability.<sup>3,5</sup> Ramos et al. showed that a low lymphedema volume at the start of the treatment is important to prevent progression.<sup>6</sup>

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Traditionally, the diagnosis of BCRL has been based on several methods such as arm measurements of volume using WDM, circumferential arm measurements, and the use of patient surveys. The diagnosis is complicated due to a lack of consensus on appropriate measurements and a diagnostic threshold. Commonly used thresholds are >10% relative increase in volume compared with the contralateral arm or >2 cm difference in circumference between the arms.<sup>1</sup> However, there is an increased risk of missing an early mild BCRL when using these thresholds at diagnosis. Several authors recommend that patients should be screened for lymphedema at a low arm volume. Stout Gergich et al. defined a 3% volume change from a preoperative baseline as a diagnostic criterion for subclinical lymphedema.<sup>5</sup> Specht et al. suggested a threshold of >5% to <10% lymphedema relative volume (LRV) change compared with preoperative arm volume for close monitoring or intervention. This limit was significantly associated with an increased risk of LRV exceeding 10%, especially if the LRV had changed 3% to 5% within 3 months of surgery.<sup>7</sup> Moreover, an increase in LRV >5% within 1 month after surgery was associated with a 40% increased risk of lymphedema.<sup>8</sup> Johansson et al. showed that another period of increased lymphedema risk was found 3–4 months after completion of radiotherapy to the axilla, using the healthy arm as control. These results emphasize the importance of screening for lymphedema not only within 3 months of surgery but also following radiotherapy.<sup>9</sup> Along with volume measurements, clinical examination of the skin, with attention to the color and decreased visibility of subcutaneous veins, palpation of increased subcutaneous tissue, and pitting are also important diagnostic signs.<sup>10</sup> In Sweden, palpation of skin and increased thickness in subcutis together with WDM are used as standard methods in clinics for diagnosis of arm lymphedema.<sup>3</sup>

New diagnostic methods have improved sensitivity over traditional methods. Optoelectronic perometry measuring limb volume using infrared light,<sup>11</sup> dual-energy X-ray absorptiometry measuring tissue composition,<sup>12</sup> and non-contrast magnetic resonance lymphography are used to diagnose and classify primary lymphedema.<sup>13</sup> Indocyanine green near-infrared lymphangiography has been used to visualize the edema fluid and to evaluate lymphedema treatment,<sup>14</sup> and bioimpedance spectroscopy (BIS) measures extracellular fluid by calculating the impedance ratio between the arms or the change from the preoperative baseline.<sup>15,16</sup> However, some of these methods are not useful in the clinic because they cannot detect local lymph changes, they require specialized equipment or skills, and are time-consuming or expensive.

The tissue dielectric constant (TDC) can be used to identify local tissue water. Lahtinen et al. compared TDC with BIS in a total of 100 women with breast cancer treated with axillary dissection and radiotherapy. Using only one measurement site in the forearm and in the upper arm, 38 patients were clinically diagnosed with lymphedema. Of these, 18.4% were detected only by TDC and 2.6% only by BIS.<sup>17</sup> They concluded that discrepancies between TDC and BIS techniques were related to different techniques and the assessed anatomical regions. The results supported the role of TDC as a method for early diagnosis of lymphedema.<sup>17</sup>

In the early phase of BCRL, accumulation of fluid in the subcutaneous tissue may not uniformly affect the whole arm

volume. New, more sensitive diagnostic methods are needed for use in the clinic to detect and diagnose mild lymphedema in the early phase in tissues where lymphedema may manifest initially. To our knowledge, the TDC measure of local tissue water in skin and upper subcutis has not been evaluated in relation to WDM to diagnose mild arm lymphedema. It is also important to examine the association between arm volume and superficial local lymph changes to increase our knowledge of the relationship between these conditions.

The aims of this study were to (1) evaluate the TDC and WDM in combination with palpation for early diagnosis of mild arm lymphedema, (2) examine the association between TDC and WDM measurements, and (3) compare lymphedema-related factors between groups diagnosed by these methods.

## Materials and Methods

### Participants

Inclusion criteria for participating in the study were women treated for unilateral breast cancer, with axillary node dissection, and diagnosed with mild arm lymphedema at the Lymphedema Unit, Department of Oncology, Skåne University Hospital, and at the Physiotherapy Cancer Unit, Department of Occupational Therapy and Physiotherapy, Karolinska University Hospital. Exclusion criteria were recurrent cancer, concurrent diseases that might interfere with the measurement of lymphedema, cognitive disability, and language unfamiliarity that makes participating in the study difficult.

### Ethical approval

The study was approved by the Regional Ethics Board, Lund University, D number: 2014/399. All participants provided informed consent and data were collected from September 2014 to November 2018.

### Clinical examinations

**Increased subcutaneous thickness.** Palpation of the skin and subcutaneous tissue was performed with the subject seated.<sup>18</sup> The tissues were pinched between fingers and thumbs at the medial, frontal, and lateral sites of the whole arms simultaneously. An increased skin and subcutaneous thickness on the operated side compared with the nonoperated side indicated edema. Palpation combined with WDM has been shown to be reliable with a negative predictive value of 95%<sup>3</sup> and has previously been used to diagnose early arm lymphedema.<sup>3,10,17</sup>

**Local tissue water.** Local lymphedema was evaluated using TDC of MoistureMeterD (Delfin Technologies Ltd., Finland). The device transmits a high-frequency electromagnetic wave at 300 MHz into the coaxial probe in contact with the skin. Based on properties of the reflected electromagnetic wave, the TDC value having equal access to both components of interstitial fluid, bound and free water in the tissue, was calculated. TDC values are thus directly proportional to the tissue water content. The device allows measurement to the effective depth of 2.5 mm. This measurement has been validated to circumferential measurements of the forearm by hemodialysis treatment, showing a high correlation ( $r = -0.97$ ,  $p < 0.05$ ) of reduction of edema and fluid

removal during treatment ( $r = -0.99$ ,  $p < 0.01$ .) For repeatability, the coefficient of variation was shown to be 3%.<sup>19</sup> In the present study, 41 women were measured with TDC in the supine position and 34 women in sitting position. Both methods are used in the literature.<sup>20,21</sup> Each site was measured once according to Mayrovitz et al.,<sup>20</sup> at six points: 5 cm proximal and 5 cm distal to the antecubital fossa (medial, frontal, and lateral). If lymphedema was palpated more proximally or distally in the arm, complementary measurements were made 15 cm proximal or distal to the elbow. The TDC threshold ratio of the upper arm was set to 1.45 and of the forearm to 1.3.<sup>22</sup>

**Lymphedema volume.** Arm volume was measured using WDM. The arm volume measurements were performed with the elbow extended and fists resting with the proximal phalanges on the bottom of a container filled with water; the contralateral arm was used as a control. Water displacement was measured in grams and converted into milliliters and hand volumes were included in the total volume. The LRV in percent and lymphedema absolute volume (LAV) in milliliters were obtained by calculating the difference in volume between the affected arm and the contralateral arm. Using WDM, measurements of the LRV were adjusted by  $-1.5\%$  if operated in the dominant arm and  $+1.5\%$  if operated in the nondominant arm.<sup>23</sup> Kettle et al. found a standard deviation (SD) of 1.5% from the mean volume.<sup>24</sup> A validity test of WDM with a computerized, limb volume measurement system showed a high correlation coefficient ( $r = 0.992$ ).<sup>25</sup>

**Hand edema.** The women were asked to self-rate the presence and degree of hand edema using a scale ranging from 0 (none) to 3 (very noticeable).<sup>26</sup> The ratings were only used as descriptive data.

**Body-mass index.** Body weight and height were measured to calculate body-mass index (BMI).

#### *Lymphedema-related factors*

**Subjective experiences.** The women's self-rated experiences of heaviness, tightness, and pain in the affected arm were rated on a 100-mm horizontal visual analog scale.<sup>27,28</sup>

**Questionnaires.** One study-specific questionnaire included questions about age, education, and marital status. Another questionnaire included questions about heavy lifting at work, physical activity level/exercise, and housework before surgery.<sup>29</sup>

**Medical data.** Medical data, including surgical methods and adjuvant treatments, were collected from patients' medical records.

#### *Definition of mild arm lymphedema*

Mild arm lymphedema was defined as increased skin and subcutaneous tissue compared with the healthy side in addition to either a TDC threshold ratio ( $\geq 1.45$  in the upper arm;  $\geq 1.3$  in the forearm)<sup>22</sup> or LRV  $\geq 5\%$  to  $\leq 8\%$ .

#### *Procedures*

The women were called for routine, clinical follow-up visits 4 to 6 weeks after surgery and 3 to 4 months after completing radiotherapy. They were also informed to seek help if they noticed edema between the follow-up visits. The examinations were conducted by two of the authors (K.J. and K.K.) and two other experienced lymphedema therapists. Palpation of increased thickness in the skin and subcutaneous tissue in the operated side was noted as yes or no, and all women who demonstrated an increase were measured using both TDC and WDM. When mild arm lymphedema was diagnosed, the women were included in the study and received information about the study. Those who agreed gave both oral and written consent. The women were measured for height and weight, self-rated experiences, and presence of hand edema. Any previous erysipelas was noted as yes/no. Data on cancer treatments were collected.

#### *Statistical analyses*

The analyses were carried out using IBM SPSS Statistics 24. Descriptive statistics were used for baseline variables, including rates for binary variables and mean  $\pm$  SD for continuous variables. Between-group differences of lymphedema-related factors were calculated for patients diagnosed by TDC (TDC group), WDM (WDM group), and both TDC and WDM (TDC/WDM group) using one-way ANOVA for continuous normally distributed data, Kruskal-Wallis test for ordinal and non-normally distributed data, and Pearson chi-square test for nominal data. Associations between TDC and WDM measurements were calculated using Spearman's correlation coefficient. A significance level of  $p < 0.05$  (two-tailed) was chosen.

#### **Results**

A total of 447 women following surgery of the breast and axilla were called for follow-up visits. Of these, 96 women were diagnosed with mild arm lymphedema according to the definition, 75 agreed to take part in the study and were followed for 6 months. Three women had recurrent cancer within 6 months and dropped out. The remaining 72 were analyzed and baseline data are presented in Table 1. Types of breast surgeries were equally represented, and most women had both chemotherapy and hormone therapy. All but one woman received radiotherapy and almost all of them (94%) received radiotherapy to the breast, axilla, and supraclavicular lymph nodes. No one had erysipelas at the time of diagnosis. All were diagnosed early, with a lymphedema mean duration of 1.0 month and a low LRV, mean LRV: 4.5% (Table 1).

#### *Diagnosis of mild arm lymphedema with TDC and/or WDM*

Thirty-two women (45%) were diagnosed using TDC only (TDC group), 19 (26%) using WDM only (WDM group), and 21 (29%) using both WDM and TDC (WDM/TDC group). Totally, 53/72 women (74%) were diagnosed with mild arm lymphedema by the TDC technique and 40/72 (55%) by the WDM.

TABLE 1. BACKGROUND DATA FOR WOMEN WITH MILD ARM LYMPHEDEMA AT DIAGNOSIS ( $n = 72$ )

Age in years at diagnosis, mean (SD)	56.8 (12.9)
Marital status, single/partner, $n$	23/49
Education <sup>a</sup>	
Elementary school, $n$	8
Upper secondary school, $n$	29
University/college, $n$	34
BMI kg/m <sup>2</sup> , mean (SD)	26.6 (5.0)
Operated site, right/left, $n$	39/33
Operated side, dominant/nondominant, $n$	34/38
Subjective symptoms in the arm (VAS), $n$ (%)	
Pain	19 (26)
Tightness	28 (39)
Heaviness	15 (21)
Hand edema, self-rated (0–3), $n$ (%)	
0 none	57 (79)
1 yes, very slight	7 (10)
2 noticeable	7 (10)
3 very noticeable	1 (1)
Surgery, mastectomy, and ALND, $n$ (%)	34 (47)
Surgery, lumpectomy, and ALND, $n$ (%)	38 (53)
Surgery, reconstruction, $n$ (%)	5 (7)
Lymph nodes removed, mean (SD)	16 (5.8)
Lymph nodes with metastasis, mean (SD)	2.4 (2.6)
Chemotherapy, $n$ (%)	62 (86)
Radiotherapy to breast, axilla, and supraclavicular lymph nodes, $n$ (%)	68 (94)
Hormone therapy, $n$ (%)	53 (74)
Duration of lymphedema, months, mean (SD)	1.0 (1.3)
Time from surgery to onset, months, mean (SD)	6.6 (5.4)
Total lymphedema volume, mL, mean (SD)	2484 (472)
LAV, mL, mean (SD)	103 (82.1)
LRV, %, mean (SD)	4.5 (2.7)

<sup>a</sup>Missing value: 1.

ALND, axillary node dissection; BMI, body-mass index; LAV, lymphedema absolute volume; LRV, lymphedema relative volume; SD, standard deviation; VAS, visual analog scale.

**Local tissue water/TDC.** The highest TDC ratio of each woman ( $n = 72$ ) was on average (SD): 1.5 (0.26), range (1.05–2.15), for the whole arm; 1.4 (0.28), range (0.92–2.15), for the upper arm; and 1.3 (0.26), range (0.93–2.12), for the forearm.

**Arm volume difference/WDM.** A significantly lower LAV and LRV ( $p < 0.001$ ) was found in the TDC group (mean LAV = 24.5 ± 91.3 mL/LRV = 1.3% ± 3.1%) compared with the WDM group (mean LAV = 151.2 ± 362 mL/LRV = 6.3% ± 0.8%) and the WDM/TDC group (mean LAV = 156.2 ± 54.5 mL/LRV = 6.2% ± 1.2%).

#### TDC diagnosis site

Among the 53 women diagnosed with TDC (32 from the TDC group and 21 from the TDC/WDM group), the highest frequencies of TDC ratios exceeding thresholds were found at the medial site close to the antecubital fossa in the upper arm and forearm, followed by the distal parts of the forearm. Only a few exceeded thresholds at the lateral and frontal sites of the forearm, and none were found at the frontal or lateral site of the upper arm (Table 2).

TABLE 2. MEASUREMENT SITE OF THE TISSUE DIELECTRIC CONSTANT AND FREQUENCY OF TISSUE DIELECTRIC CONSTANT RATIO EXCEEDING THRESHOLDS FOR THE UPPER ARM ( $\geq 1.45$ ) AND FOREARM ( $\geq 1.3$ ) IN BREAST CANCER PATIENTS WITH ARM LYMPHEDEMA ( $n = 53$ )

Measurement site	$n$ (%)
Upper arm and/or forearm medial 5 cm proximal and/or distal to the antecubital fossa	45 (84.9)
Upper arm frontal or lateral 5 cm proximal to the antecubital fossa	0
Forearm ventral 5 cm distal to the antecubital fossa	2 (3.8)
Forearm lateral 5 cm distal to the antecubital fossa	1 (1.9)
Forearm medial and/or frontal and/or lateral 15 cm distal to the antecubital fossa	5 (9.4)

#### Association between TDC ratio and WDM measurements

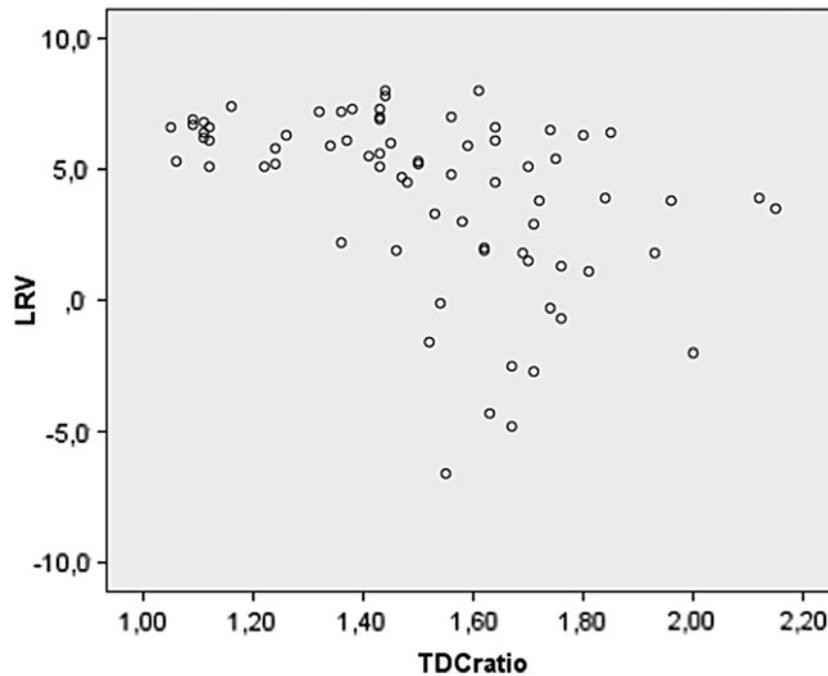
There was a significant negative association between the highest TDC ratios, among all the measured points (medial, frontal, and lateral) in the upper arm and forearm of each woman, and LRV ( $r = -0.545$ ,  $p < 0.001$ ), respectively (Fig. 1).

#### Difference in lymphedema-related factors

A significant difference in time from surgery to onset of lymphedema ( $p = 0.003$ ) was found in the TDC group (on average, 4.1 months) compared with the WDM group (on average, 9.1 months) and the WDM/TDC group (on average, 6.7 months). There were no between-group differences in age, BMI, surgical method, lymph nodes removed, lymph nodes with metastasis, chemotherapy, hormone therapy, duration of lymphedema, lymphedema in the hand, physical activity level before surgery, operation on the dominant side, education, marital status, heavy lifting at work, or symptoms of pain, heaviness, and tightness in the arm.

#### Discussion

Both TDC and WDM can be used for early diagnosis of mild arm lymphedema, but TDC determines the diagnosis earlier after surgery and at a lower arm volume than WDM. In the present study, all women were diagnosed early with a mean duration of 1.0 month. Forty-five percent of the women were diagnosed using palpation and TDC only and with a lower LRV (mean 1.3%) compared with women in the WDM group (mean 6.3%) and WDM/TDC group (mean 6.2%). These 45% with mild arm lymphedema would have been missed at an earlier stage if diagnosed with palpation and WDM only at the diagnostic threshold of LRV  $\geq 5\%$ . Diagnosing lymphedema and starting treatment at an early stage have been shown to be important for preventing its progress.<sup>3</sup> In the study by Karlsson et al., the women self-detected the lymphedema and sought help and were shown to have an average LRV of 14% at diagnosis,<sup>30</sup> which is considered to be a high level for diagnosis. In the study by Johansson and



**FIG. 1.** Association between the highest TDC ratio in each woman ( $n=72$ ) and LRV, LRV ( $r=-0.545$ ,  $p<0.001$ ). LRV, lymphedema relative volume; TDC, tissue dielectric constant.

Branje, the women were called for clinical follow-up visits and examined by palpation and WDM and were diagnosed already at LRV of 8%.<sup>3</sup> This demonstrates the importance of regular follow-up visits in detecting early mild arm lymphedema.

Stanton et al. recommend multiple criteria for diagnosing early mild lymphedema.<sup>10</sup> A strength of the present study was the examinations, where inspection and palpation were used in combination with TDC and WDM. Palpation of skin and subcutis was used as a standard method in clinics for diagnosis of arm lymphedema. The palpation was performed by experienced lymphedema therapists, which may have reduced the risk of false positive lymphedema. Palpation combined with WDM has shown good reliability with a negative predictive value of 95%<sup>3</sup> and has been applied recently by Lahtinen et al.<sup>17</sup> However, we did not determine pitting edema because in our clinical experience, pitting rarely occurs in early mild lymphedema. In the present study, we were unable to evaluate whether there was an association between palpation of increased thickness and TDC measurements as the two examinations were performed by the same person and thus not blinded. However, our clinical experience leads us to believe that TDC might in the future replace palpation in the clinic as a more objective assessment, but this has to be investigated in further studies.

In total, 74% of the women were diagnosed using either TDC alone or both TDC and WDM. This is slightly higher than the study by Lahtinen and Johansson, in which 65.8% lymphedema was diagnosed using only one measurement site in the forearm and one in the upper arm and with the same thresholds.<sup>17</sup> Mayrovitz et al. showed that the TDC threshold (also used in the present study) was high enough to avoid false positive BCRL results.<sup>22</sup> However, the threshold may be too high and therefore we could have missed detecting

some women with BCRL. Mayrovitz et al.<sup>31</sup> and Bakar et al.<sup>32</sup> suggested a TDC ratio of 1.2 as a possible threshold to detect clinical arm lymphedema. However, they only measured TDC in persons with already diagnosed lymphedema with an increased arm volume, and some of the women had chronic lymphedema for several years in comparison with the present study where the mean duration was 1 month. Perhaps it is not correct to use the same thresholds when diagnosing early mild lymphedema as when diagnosing chronic lymphedema. We recognized that the present TDC threshold and the design of this study might have limited an even higher percentage of lymphedema by TDC at an early stage. However, the present study supports prior findings that TDC has a strong potential to diagnose early mild lymphedema. Further prospective studies may show if TDC alone can diagnose mild lymphedema at an early stage or if a combination with WDM is needed.

Lymphedema is defined as swelling due to the accumulation of interstitial tissue fluid in the subcutis, often with lymphatic backflow toward the dermis. The women in the TDC group were diagnosed earlier after surgery compared with the WDM group and WDM/TDC group, indicating that the first signs of lymphedema began in the subcutis. The device used allows measurement to a depth of 2.5 mm and thus is useful in assessing lymphedema in the skin and upper subcutis. In this study, 26% of the women were diagnosed using only WDM. These women might also have been diagnosed with TDC if we had used a lower threshold or a device capable of measuring the deeper subcutis to a depth of 5 mm.

In the present study, some of the women sought help themselves at time points other than the regular follow-up visits. It may be that these women did not notice their mild edema initially. If we had performed examinations more

frequently, we may have been able to diagnose earlier with TDC also in these women. Further studies may disclose the optimal time points to examine and diagnose with TDC.

Some individual variations are also possible in how lymphedema starts and develops. Akita et al. used indocyanine green lymphography and volume measurements to detect lymphatic disorders.<sup>33</sup> Sixty percent of respondents (21/35) were found to have a lymphatic disorder without a significant change in limb volume, and 40% (14/35) had both a lymphatic disorder and a volume change. The indocyanine green lymphography was reported to show different patterns and degrees of lymphatic disorder, and some of the patients, whose lymphatic function improved with compression, had developed collateral lymphatic routes. Suami et al. investigated the lymphatic system also using indocyanine green lymphography. They found areas of dermal backflow in mild lymphedema when the collecting vessels were still functioning, but with time, the lymphedema became more severe, the collecting vessels were damaged, and no dermal backflow could be detected.<sup>34</sup> In another study, they also found that lymphatic pathways repair themselves postoperatively in different ways and identified different types of rerouting.<sup>35</sup> Thus, these reported individual changes may explain why not all lymphedema cases in the present study could be diagnosed with TDC or WDM only.

Lymphedema diagnosed with TDC was found mostly in the medial upper arm, medial forearm, or at both sites. These results agree with clinical experience in which one can often palpate a thickness at the medial site and in accordance with findings of Lahtinen et al.<sup>17</sup> They also diagnosed a high percentage (66%) at the medial site in the upper arm and forearm, although being the only sites measured. Furthermore, in the present study, we also found that in almost all cases a positive lateral and ventral/frontal TDC ratio in the upper arm or forearm was associated with a positive medial TDC ratio, indicating that it is not necessary to measure these sites. Measuring on the frontal side also carries a risk for error from having venous vessels too close to the measuring points.

A negative association between the highest TDC ratio of each woman and LRV was found in the present study, revealing that the higher the TDC value, the lower the LRV. One explanation for the negative association in the present study may be that lymphedema in most cases began with increased TDC values, indicating an accumulation in the superficial tissue. With time, the lymphedema fluid may have moved into deeper tissue, explaining the lower TDC ratio, but higher LRV over time, in accordance with the findings of Suami et al. described above.<sup>34</sup>

In the present study, a few women diagnosed with palpation and TDC had an LRV below zero. These women may have had more muscle volume in the dominant arm due to work or sport activities. Gebruers et al. examined normal arm variation and found a mean difference of 3.2% between the right and left hands.<sup>36</sup> Dylke et al. found that an interlimb difference of 380 mL (including three SD) was required for diagnosis<sup>37</sup>; however, absolute volume differences do not take into account the individual body compositions. In the present study, we adjusted by  $\pm 1.5\%$  for arm dominance, which was the standard method used in the clinic.<sup>23</sup> This shows that there is individual variation in the arm volume and it is therefore important to have several methods to diagnose lymphedema than arm volume alone.

For practical reasons, we did not measure the women preoperatively. However, Mayrovitz et al. measured the presurgical TDC ratio and showed a very low ratio in breast cancer patients.<sup>22</sup> This may indicate that no preoperative measurements are necessary other than determination of the postoperative ratio. Future research will explore whether there is a need for preoperative TDC measurements.

## Conclusions

Both TDC and WDM can be used to diagnose early and mild arm lymphedema. However, as 45% of arm lymphedema was diagnosed by TDC only, this method may be the most valid method. The TDC method also diagnosed earlier after surgery and at a lower arm volume than the WDM. TDC ratios exceeding the threshold were most frequently on the medial site of the arm, proximal and distal to the antecubital fossa. A negative association between TDC and WDM measurements was found, indicating that the first signs of lymphedema are detected in the subcutaneous tissue and that TDC and WDM may measure different aspects of lymphedema.

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