Assessing Arm Volume in People During and After Treatment for Breast Cancer: Reliability and Convergent Validity of the LymphaTech System

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Background. There are challenges related to the accurate and efficient measurement of lymphedema in people with breast cancer. The LymphaTech 3D Imaging System (LymphaTech, Atlanta, GA, USA) is a mobile, noninvasive platform that provides limb geometry measurements.

Objective. The objective of this study was to estimate the reliability and validity of the LymphaTech for measuring arm volume in the context of women seeking care in a specialty breast cancer rehabilitation clinic.

Design. This was a cross-sectional reliability and convergent validity study.

Methods. People who had stage I to IV breast cancer with lymphedema or were at risk for it were included. Arm volume was measured in 66 participants using the LymphaTech and perometer methods. Test-retest reliability for a single measure, limb volume difference, and agreement between methods was analyzed for 30 participants. A method-comparison analysis was also used to assess convergent validity between methods.

Results. Both LymphaTech and perometer methods displayed intraclass correlation coefficients (ICCs) of ≥0.99. The standard errors of measurement for the LymphaTech and length-matched perometer measurements were nearly identical. Similar intraclass correlation coefficients (0.97) and standard errors of measurement (38.0–40.7 mL) were obtained for the between-limb volume difference for both methods. The convergent validity analyses demonstrated no systematic difference between methods.

Limitations. The sample size was not based on a formal sample size calculation. LymphaTech measurements included interrater variance, and perometer measurements contained intrarater variance.

Conclusions. The LymphaTech had excellent test-retest reliability, and convergent validity was supported. This technology is efficient and portable and has a potential role in prospective surveillance and management of lymphedema in clinical, research, and home settings.

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Breast cancer is the leading cancer diagnosis among women in the United States and was expected to account for 30% of all new cancers in women and over 217,000 new diagnoses in 2017.[1] Breast cancer survivors are at risk for breast cancer-related lymphedema (BCRL) for an average of 3 years following treatment for breast cancer.[2] The reported incidence of BCRL ranges from 5% to >40%, with higher risk for women undergoing axillary radiotherapy, with obesity, who developed seroma, underwent chemotherapy infusion in the affected limb, and with advanced disease.[3,4] Differences in defining and measuring lymphedema, time since diagnosis, and accurate risk stratification contribute to the wide variation in estimates of lifetime incidence of BCRL. There is, however, broad consensus that the lifetime incidence of lymphedema in patients with breast cancer is approximately 20%.[2,5–7] BCRL is one of the most feared side effects of breast cancer treatment and can lead to reduced health-related quality of life, activity and participation restrictions, cosmetic concerns, and economic hardship.[2,8–11] Early detection and management of lymphedema through prospective surveillance appears to reduce the progression of BCRL, reducing both the impact to the patient as well as cost to the health care system.[11–13]

There are challenges related to the accurate and efficient identification and measurement of upper extremity lymphedema in patients with breast cancer. Although clinical examination is important in the diagnosis of lymphedema,[14] a common approach to the identification and quantification of BCRL is the calculation of limb volume. There is no gold standard for limb volume calculation. Methods of calculating limb volume include water displacement methods, limb circumferences converted mathematically to volume, and infrared 3-dimensional sensor imaging devices.[14] Each of these methods demonstrates clinically sufficient reliability and validity.[14–18] Water displacement, often considered a reference standard, lacks feasibility in a clinical setting.[14] Serial circumference measures converted to volume are cost-efficient but can be somewhat time-consuming in a clinical setting. The perometer is the most commonly used infrared imaging device to quantify limb volume and has been shown to be efficient to use, reliable, and valid compared with water displacement.[14,16] A systematic review reported intrarater reliability, standard error of measurement (SEM), and minimal detectable difference for the perometer for the upper extremity for pooled data from 2 studies: $R = .99$, 95% confidence interval (CI) = 0.97–1.00, SEM = 2.1% (±2.6%), and minimal detectable difference = 5.6% (±4.2%).[19] The perometer is expensive, large, and not easily available for purchase or to service in the United States.[14] Other experimental scanning devices have been proposed but have not been clinically adopted because of either difficulty in clinical implementation or insufficient accuracy.[20–24] There is a need for a reliable, valid, portable, and clinically efficient method for measuring arm volume in patients with BCRL.

The LymphaTech 3D Imaging System (LymphaTech, Atlanta, GA, USA) was developed to improve the measurement challenges associated with lymphedema. The goal is to develop a mobile-based platform to provide limb geometry measurements in a relatively low-cost, high-accuracy system particularly suited for home use and clinical environments without trained lymphedema therapists. This is the first technology available, to our knowledge, that is capable of providing clinically meaningful limb volume information in a fast, accurate, and reliable manner while using easily obtainable off-the-shelf hardware. The current prototype consists of a commercially available depth camera (Structure Sensor; Occipital, Inc, Boulder, CO, USA) interfaced with a smartphone or tablet computer. At this time, any iOS device is compatible, and Android or Windows devices will be compatible in the future. The ability to power the depth sensor using a ubiquitous mobile device is critical for enabling wide use of the application in clinic, home, and field settings. To support the implementation of this hardware, 2 pieces of software have been developed. The first provides an application and visual cues to capture the raw spatial data, and the second carries out image processing and analysis to quantify and track patient metrics.

LymphaTech incorporates a custom software application that uses a software development kit to capture 3-dimensional depth data on a mobile device. The application acquires depth information and fuses a 3-dimensional point cloud in real-time by using 3-dimensional feature registration techniques and acceleration data from the built-in accelerometer of the mobile device. The output of the scan is a complete 3-dimensional rendering of the patient's body or body region of interest, captured as a point cloud with hundreds of thousands of unique depth points.

The software features a dynamic selection box allowing the user to isolate an object of interest and filter out the rest of the room. This feature, combined with custom joint and skeleton tracking algorithms, enables acquisition in variable environments with variable lighting conditions. The process requires clothing to be removed from the area being scanned and can be performed at a distance of 0.5 to 1.5 m. The user interface shows the patient's body position on the display screen in real-time using the built-in camera of the mobile device, and once the user begins the scan, the screen displays the progress of the 3-dimensional scan as a white overlay on top of the color image (Fig. 1). To complete the scan for the upper extremity, the user first positions the patient in 90 degrees of abduction with the hand resting on a support platform. There is no strict limitation on the arm angle required for the software. The algorithm will rotate the arm to be 90 degrees regardless of the true position of the limb. However, if the angle is low enough, it will inhibit the visibility of the axilla so the measurable length of the arm

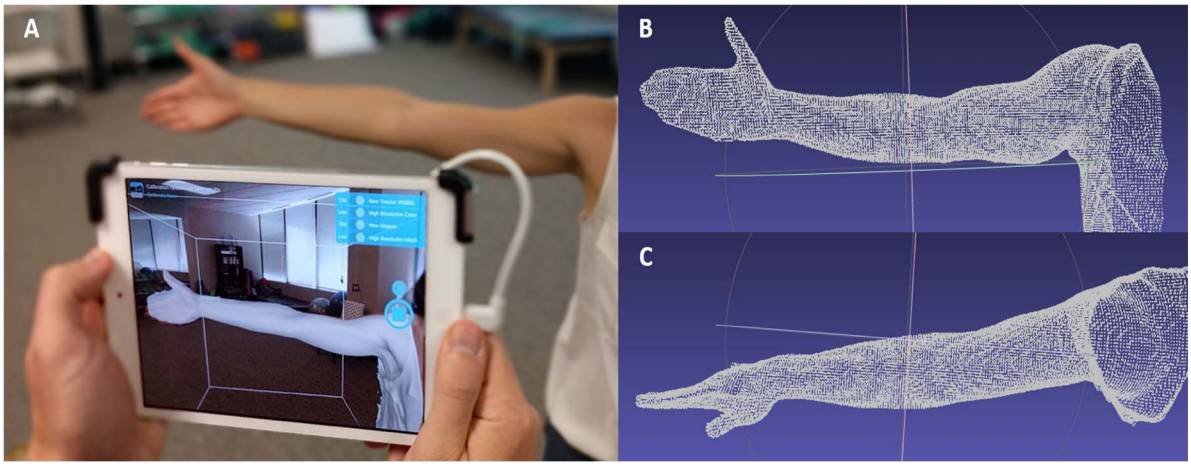

Figure 1.
Scan acquisition interface and examples of scans. (A) Screenshot of the user interface for the scan acquisition software on an iPad tablet. The 3-dimensional camera attaches to the mobile device via a custom bracket and integrates with the built-in camera of the device via a custom bracket to overlay depth and color imaging. (B) Example of point cloud viewed from the front. (C) Example of point cloud viewed from the top, highlighting the 3-dimensional acquisition.

will decrease. The operator then moves the mobile device around the patient's body or body region of interest in such a manner as to allow the sensor to view all angles of the target object. The screen identifies areas that have not been scanned as uncolored holes so the user can identify areas that have been missed. This real-time visualization of scan progress is a unique feature of the system, which facilitates easy and consistent scanning, especially for nonexpert individuals (Fig. 1). LymphaTech measures can be performed in all levels of lighting, with the exception of direct sunlight, and it must be performed away from mirrors.

Once the point clouds are generated, a second custom anthropometric measurement program is used to conduct the analysis. A parametric model is used to translate and rotate the point clouds such that they are positioned in an alignment that is uniform across all scans for all patients. This element of the algorithm generates an aligned point cloud despite the fact that patients with lymphedema commonly have variable ranges of motion, thus making the system more functional for the target population.

After the point cloud is repositioned, the arms are isolated from the rest of the body by using anthropometric identification algorithms to truncate the arm at the wrist and the axilla (Fig. 2). The software includes functionality to compare the isolated segment of the left and right arms such that the lengths and the location of the segments are identical between the 2 sides. The software also performs the same segment comparison for all future scans of the same patient such that the same segment of each arm is analyzed over time.

After final segmentation is complete, total volume of the arm segment is computed (visualized in Fig. 2B) and circumference measurements are taken at intervals along the length of the arm segments (visualized in Fig. 2C). An example cross-sectional slice can be visualized in Figure 2D.

Early prototype versions of the LymphaTech system used a 3-dimensional infrared depth sensor integrated with a tablet and custom software showed promising results when measuring filarial leg lymphedema[25] and arm volume in patients with breast cancer.[26] These studies demonstrated high correlations between volumes calculated by the LymphaTech, water displacement, and tape measure methods and between the LymphaTech and perometer in upper extremities.[25,26]

The purpose of this study was to estimate the reliability and convergent validity of the LymphaTech, a new method of measuring arm volume, in the context of women seeking care in a nonprofit specialty breast cancer rehabilitation clinic. The following reliability questions were asked: To what extent does the LymphaTech measurement system display test-retest reliability, as measured with an ICC(2,1), within the declared study context? To what extent do repeated measurements vary within a patient using the LymphaTech measurement system? The following validity questions were asked: To what extent do values measured with the LymphaTech correlate, as quantified with an ICC, with values measured with a perometer within the declared study context? To what extent do measurements vary within patients between values

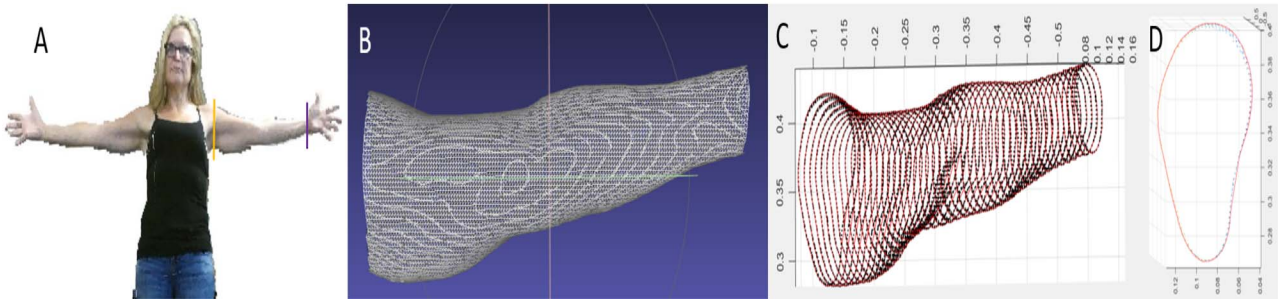

Figure 2.
Arm segmentation and measurement. (A) Screenshot of an example of a scan from the front perspective with truncation locations for wrist and shoulder. (B) Point cloud of the left arm after segmentation. (C) View of the left arm showing the depth in the *z* direction and visualization of 1-cm slices. (D) Example of visualization of the cross-sectional geometry of a single slice. The red line indicates the perimeter of the cross section.

measured with the LymphaTech and those measured with the perometer?

Methods

Participants

The setting for the study was TurningPoint Breast Cancer Rehabilitation, a nonprofit 501(c)3 community-based breast cancer rehabilitation organization in Atlanta, Georgia. The clinic provides evidence-based physical therapy, exercise, massage therapy, counseling, nutrition support, and survivorship education for patients with all stages of breast cancer through the continuum of medical and surgical treatments. Barriers to rehabilitation care are reduced through a financial assistance program for patients in need, clinic accessibility, and compassionate attention to the unique physical and emotional needs of patients and families going through breast cancer treatment. The study sample is representative of the sociodemographic characteristics of the patients seen at TurningPoint. Since inception in 2003, >4300 patients with breast cancer have been treated, with an average of 35 new patients per month. The study was approved by the LymphaTech Institutional Review Board. People with stage I to IV breast cancer were eligible for inclusion at any point during or after breast cancer treatment. All participants had lymphedema or were at risk for developing lymphedema, as determined by a physical therapist, on the basis of risk factors (ie, extent of lymph node removal, radiation, and body mass index).[3–5] People at risk for bilateral BCRL were not included because of the design of the analysis. Following informed consent, arm volume was measured in 66 participants using the LymphaTech and perometer methods. Data were collected over a 14-month period.

Reliability Design

Measures were taken within 30 minutes of each other on the same day using each of the LymphaTech and perometer measurement systems. This timeframe minimized the risk of true fluctuations in arm volume between measurements. To assess test-retest reliability, a convenience subsample of 30 participants was measured twice on each device. For the LymphaTech, measurements were taken by 2 raters (ie, 1 measurement per rater), and the 2 perometer measurements were performed by the same rater for each participant. Expectation bias on the part of raters was avoided because volumes were not visually available until the measurement was complete on a participant. Accordingly, the test-retest design for the LymphaTech included an interrater component, whereas the perometer measurements contained an intrarater component. This design difference was dictated by the feasibility of conducting the reliability portion of the study in a busy clinical setting.

Validity Design

Convergent validation and method comparison designs were applied to estimate the validity of the LymphaTech in the context of our participant sample and setting. These designs are appropriate when an indirect method of measurement is compared with another measurement method that is just as indirect: neither measurement method is considered to be error free. Specifically, LymphaTech-measured volumes were compared with perometer measured volumes on 66 participants who had at least 1 paired measurement on each device. This validation design is based on the premise that measures believed to be assessing the same outcome should not only correlate highly but should also display a high level of agreement.

LymphaTech Measures

Participants were asked to stand with their arm uncovered and raised to approximately 90 degrees of abduction with their hand resting on a support platform. The examiner began by standing in front of the participant at a distance of approximately 1 m. The examiner used the sensor to position the scanning area such that it included the relevant limb of the participant. Once the participant and

Table 1.
Participant Demographics[a]

Characteristic	Full Group (N = 66)	Reliability Subgroup (n = 30)
Age, y		
Mean (SD)	55 (11.2)	59 (10.7)
Minimum–maximum	30–75	39–75
Race		
White	51	24
Black	9	4
Asian	5	2
Other	1	0
Education completed		
High school	8	6
College	42	16
Advanced degree	16	4
Body mass index		
Mean (SD)	26 (5.6)	26 (6.1)
Minimum–maximum	18–44	18–38
Affected side		
Right	37	19
Left	29	2
Surgery side		
Right	20	11
Left	17	6
Bilateral	29	13
Lymphedema		
Yes	30	11
No	36	19
Type of surgery		
Lumpectomy	13	6
Unilateral mastectomy	21	9
Bilateral mastectomy	32	15
No. of nodes removed		
Minimum–maximum	1–37	1–31
Median	6	7
1st–3rd quartiles	3–13	3–12
No. of positive nodes		
Minimum–maximum	0–23	0–17
Median	0	0
1st–3rd quartiles	0–3	0–2
Reconstruction		
Yes	45	17
No	21	13
Type of reconstruction		
TRAM/DIEP flap	11	5
Latissimus with expander/implant	11	3
Expander/implant	21	9
Other	2	0
None	21	13
Radiation		
Yes	35	16
No	31	14
Chemotherapy		
Yes	34	17
No	31	13
Hormone therapy		
Yes	37	15
No	6	3
Unknown at time of study	23	12

[a]Data are reported as numbers of participants unless otherwise indicated. TRAM/DIEP = Transverse Rectus Abdominis Myocutaneous/Deep Inferior Epigastric Perforator.

the scanning area were properly positioned, the examiner performed a 360-degree rotation around the participant's arm to capture all views of the limb with the sensor. Once the measurement was complete for the first arm, the process was repeated for the second arm. Volume and circumference were then automatically calculated by the software and displayed on the screen. The software included algorithms for automatic identification of the wrist and the axilla, and the arm was segmented between these anatomic boundaries. The software further included a segmentation matching algorithm such that the same relative segment of the limb was analyzed between left and right arms and between repeated measures of each arm. The total scanning time was approximately 30 to 40 seconds per arm, or a total of 3 to 4 minutes for both arms including participant positioning.

Perometer Measures

The perometer used in the study was the Pero-System Model 1000 M (Pero-SystemGmbH, Wuppertal, Germany). The participant was positioned next to the device with the arm of interest uncovered and extended straight, resting the finger tips on a support at the end. The frame was moved forward and back into position once per scan per arm. For each set of scans (of the right and left arms), the

volume measurements were collected off of the Pero-System database. The distal start point for the measure was at the narrowest circumference that best approximated the position of the wrist, matched for both arms, on the basis of visual output from the perometer software. This allowed elimination of the hand in the volume calculation and best matched the segmentation approach of the LymphaTech. The proximal end point for the volume calculation was the shortest length captured by the perometer for both arms. This proximal point was then matched between arms and trials. The time taken for measures of both arms, including participant positioning, was less than 5 minutes.

Analysis

Participant characteristics were summarized as means and SDs for continuous measures and counts or percentages for categorical data. All parameter estimates included 95% CIs, and analyses were performed using STATA v15.1 (StataCorp, College Station, TX, USA).

Relative reliability was quantified by ICC (2,1) (participant variance/[participant variance + trial variance + error variance]), and absolute reliability was estimated by calculating the SEM (square root of error variance) obtained from a randomized block analysis of variance in which "participants" was the blocking factor at 30 levels and "trials" was the repeated factor at 2 levels (ie, test and retest).[27]

This was performed on a subsample of 30 participants for whom 2 trials were obtained for the LymphaTech and perometer. Given the study design, the trial variance component for the LymphaTech included interrater variance and for the perometer intrarater variance. In addition to estimating the reliability for affected and unaffected limbs, an estimate of reliability for the between-limb difference was also obtained.

Two validation analyses were performed to examine the agreement between LymphaTech and length-matched perometer measures. First, for 66 participants who had at least 1 paired LymphaTech and perometer measurement, a method-comparison analysis as described by Bland and Altman was applied.[28,29] Specifically, the difference between measurements taken by the 2 measurement systems—calculated as the LymphaTech value minus the perometer value—for each participant was plotted against the average volume for each participant. Also, included on the graph were the 95% limits of agreement, defined as the mean difference ± 1.96 times the SD of the differences.

The second validation analysis was performed on the same subsample of 30 participants for whom 2 trials were obtained for each device. LymphaTech and perometer measured volumes were compared and quantified by an ICC. This ICC was calculated from the participants, measurement systems, participants-by-measurement systems interaction, and error variance components obtained from a restricted maximum likelihood estimation analysis (ICC = participant variance/total variance). Participants were considered to be a random factor and measurement systems a fixed factor. An ICC is appropriate when measured values are obtained on the same metric and have similar variances. The latter requirement was evaluated and subsequently confirmed from the reliability analysis. Applied in this context, the ICC has 3 advantages over the Pearson correlation coefficient: the ICC accounts for a systematic difference between measurement systems—important when the goal is to assess agreement; the measurement system variance term comments directly on a systematic difference between the LymphaTech and the perometer; and the all-inclusive error, represented by the SD of the difference between measures from the Bland-Altman analysis, is partitioned into interaction and error terms.

Results

Demographic data for all participants and the subset of 30 participants in the reliability portion of the study are reported in Table 1. There was no appreciable difference between the full group and the subgroup, and all participants in the study were either currently undergoing treatment for breast cancer or within 3 years of initial diagnosis and treatment. The majority of participants had bilateral mastectomies and reconstruction. The average number of axillary lymph nodes removed was 8, and approximately 50% of the participants received radiation. Thirty participants had BCRL and the remaining 36 participants were at risk. Volume statistics by affected limb status for the subgroup of 30 participants who had test and retest measurements for the LymphaTech and the perometer are reported in Table 2.

Both the LymphaTech and the perometer displayed ICCs of ≥0.99. The SEMs for the LymphaTech and length-matched perometer measurements were nearly identical (Tab. 3). Similar ICCs (0.97) and SEMs (38.0–40.7 mL) were obtained for the between-limb volume difference for the LymphaTech and perometer measurements.

The mean volumes for the 66 participants' affected limbs included in the Bland-Altman analysis were 2215.9 (SD = 637.7) mL for the LymphaTech and 2223.7 (SD = 622.2) mL for the length-matched perometer measurements. Figure 3 displays the Bland-Altman plot showing the mean difference of −7.8 (SD = 96.2) mL and the 95% limits of agreement (±188 mL). For volumes of >3000 mL (n = 8), there appeared to be slightly greater variability between measurement methods. A similar result was obtained for unaffected limbs, with the mean difference being −4.8 (SD = 100.2) mL and the 95% limits of agreement being ±196 mL.

Table 2.
Summary Statistics for LymphaTech and Perometer Analyses (n = 30)

Parameter	Volume (mL) at:							
	Time 1				Time 2			
	Mean (SD)	Minimum–Maximum	Median	1st–3rd Quartiles	Mean (SD)	Minimum–Maximum	Median	1st–3rd Quartiles
LymphaTech affected	2262 (707)	1208–4050	2120	1820–2516	2253 (702)	1267–3988	2085	1742–2505
LymphaTech unaffected	2185 (601)	1302–3782	2071	1760–2357	2183 (600)	1267–4285	2067	1727–2414
Perometer affected	2276 (692)	1247–4001	2110	1816–2562	2268 (688)	1237–3911	2106	1799–2521
Perometer unaffected	2190 (583)	1255–3761	2064	1833–2450	2181 (576)	1257–3688	2032	1814–2415

Table 3.
ICCs and SEMs for the LymphaTech and the Perometer (n = 30)[a]

Test	Arm	Single Measure (Volume, mL)		Difference Between Affected and Unaffected Limbs (Volume, mL)	
		ICC (95% CI)	SEM (95% CI)	ICC (95% CI)	SEM (95% CI)
LymphaTech	Affected	0.99 (0.99–1)	31.9 (25.4–41.9)	0.97 (0.94–0.98)	38.0 (30.2–51.1)
	Unaffected	0.99 (0.99–1)	35.8 (28.5–48.2)		
Perometer	Affected	0.99 (0.99–1)	28.3 (22.5–38.0)	0.97 (0.94–0.99)	40.7 (32.4–54.7)
	Unaffected	0.99 (0.99–1)	32.8 (26.2–44.2)		

[a]SEM = standard error of measurement.

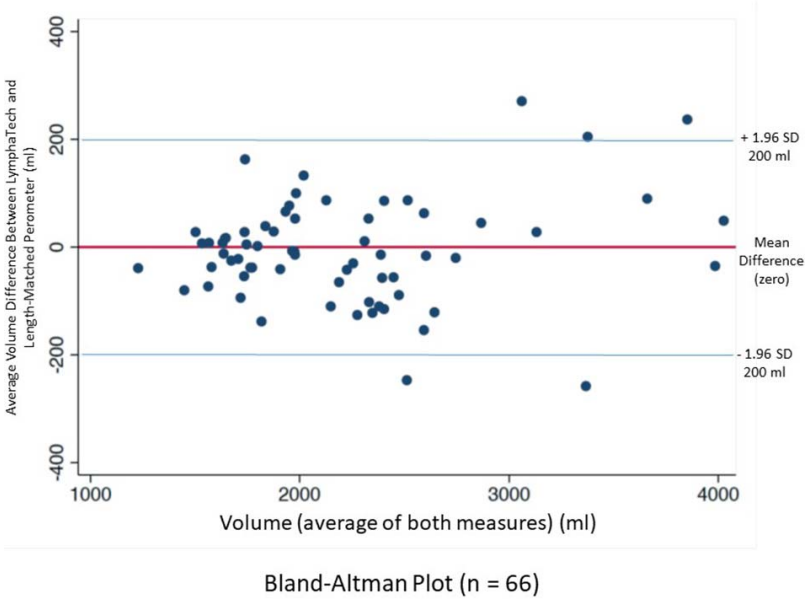

Figure 3.
Bland-Altman plot depicting the mean difference and 95% limits of agreement (n = 66).

The validity analysis performed on the 30 participants for whom 2 trials were obtained yielded an ICC of 0.99 (95% CI = 0.98–0.99) for the affected limb. Variance components were as follows: participants = 480580, measurement system = 0, participant-by-measurement system interaction = 4969, and residual error = 916. The participant variance quantifies the differences among participants, and the measurement system variance comments on a systematic difference between devices. The interpretation of the interaction term is that for some participants the LymphaTech provided larger volumes and for other participants the perometer provided larger volumes. The residual error term represents the within measurement system error. The Supplementary Figure (available at https://academic.oup.com/ptj) provides a visual summary of the within-participant–between-measurement-system agreement. Consistent with the information conveyed by the variance estimates, this figure shows that for some participants the LymphaTech provided larger volumes and for other participants the perometer displayed larger volumes (ie, interaction). A second observation is that the difference between trial values within a measurement system is similar between measurement systems (ie, residual error). A similar result was obtained for the unaffected limb, with the variance components being as follows: participants = 342,570, measurement systems = 0, participant-by-measurement system interaction = 4236, and residual error = 1163; the corresponding ICC was 0.98 (approximate 95% CI = 0.97–0.99).

Discussion

The goal of this study was to estimate the reliability and validity of the LymphaTech measurement system in the context of women with breast cancer treated at a nonprofit specialty breast cancer rehabilitation clinic. The relative reliability estimates expressed as ICCs were similar for the LymphaTech and perometer volume measurements. SEMs for the LymphaTech and perometer measurements were also similar. The validity analyses provided complementary results that revealed a high agreement coefficient and no systematic difference in measured values between measurement systems for matched length comparisons.

The interpretation of the validity analyses is that there was no systematic difference in the mean LymphaTech and length-matched perometer volumes. The data presented in the Bland-Altman plot (Fig. 3) appear to display greater between-measurement variability for volumes of >3000 mL.

Based on our findings, in participants with larger arm volumes, repeating the measure on each arm and averaging the results may be appropriate. However, given that there were few data points exceeding 3000 mL, this issue requires further investigation. Additionally, the perometer assumes an elliptical cross section when calculating arm volumes, whereas the LymphaTech device forces no such constraint on the cross-sectional geometry of the arm. It is possible that the error associated with forcing an elliptical cross sectional geometry becomes more pronounced with larger arm volumes.

For any extremity volume calculation, it is critical that the length used for the measure is standardized between arms and tests. In this study, the perometer start position was standardized as the narrowest point to approximate the wrist. Currently available measurement techniques, including the perometer, require the tester to manually standardize lengths and employ cross-sectional assumptions to compute volume. Matching the wrist and upper arm points between 2 perometer measures on different occasions can be cumbersome. The LymphaTech computes the true cross-sectional geometry and standardizes length automatically between arms and tests.

Prospective surveillance for the impairments and activity limitations related to breast cancer and its treatment has been recommended by expert panels convened by the American Society of Breast Surgeons and American Cancer Society. Research suggests that establishing baseline preoperative measurements followed by ongoing surveillance is useful in the early detection of lymphedema, but this model is not yet regularly implemented for most women at risk for lymphedema.[11,13,30–32] One of the barriers to widespread implementation of screening and management is lack of an efficient and portable measure of volume that is suited to clinic, home, and field use. LymphaTech appears to be a highly reliable and valid method of volume measurement that is easy to use, takes about 4 minutes per patient, has a small footprint, and is noninvasive.

Further validation is needed to estimate sensitivity to change and diagnostic accuracy of the LymphaTech. Further research is needed to examine the measurement properties of LymphaTech in other settings and to compare LymphaTech measures with other commonly used measures of arm volume, such as circumferential tape measures converted to volume. To our knowledge, this is the first study that has examined and reported systematic increases in error at larger limb volumes. Further clarification of this finding was limited by a relatively small number of limbs >3000 mL, and further research is needed to investigate this finding for both LymphaTech and Perometer methods.

Clinical Implications

Clinicians play a key role in prospective surveillance for lymphedema as well as the clinical management of lymphedema. Clinical decision-making requires interpre-

tation of volume differences between arms and between test points. The SEMs associated with a single LymphaTech measure were 32 and 36 mL for the affected and unaffected arms, respectively. Because the estimation of the volume difference between arms incorporates error from both arm measures, the SEM for the difference between affected and unaffected arms was slightly greater at 38 mL.

To account for normal size differences between arms as well as bilateral change in arm size that may be related to weight change or generalized swelling, it is important to understand the error associated with the change in difference between the arms. Interpretation of the change in difference between 2 arms at a subsequent test point requires knowledge of the minimal detectable change (MDC), or degree of confidence that true change has occurred between measures taken at 2 points in time. The MDC at the 90% confidence level (MDC_{90}) indicates the upper and lower volume change limits that contain 90% of truly unchanged limb volumes. The MDC_{90} for the difference between arms was approximately 90 mL (SEM x 1.65 x $\sqrt{2}$) for the LymphaTech. The MDC_{90} for the perometer was 95 mL. The interpretation of MDC_{90}s is that 90% of truly unchanged participants will display random fluctuations equal to or less than the limits defined by the MDC_{90}. In other words, when a change of >90 mL has occurred in the difference between affected and unaffected arms, a clinician can be reasonably confident that this is a true difference. For example, in a 2000-mL arm, the MDC would translate to about 4.5%. For both devices, a change in the difference between the arms of <5% may not be a true change. When the goal is to interpret smaller changes in volume, measures can be repeated and the results for each arm averaged. In this scenario, the SEM for the difference between arms decreases to 27 mL (SEM/$\sqrt{2}$) and the MDC_{90} decreases to 63 mL.

In larger arms >3000 mL, there may be more error associated with the estimation in volume using both LymphaTech and Perometer. In this scenario, clinicians can reduce the error associated with a single measure by repeating and averaging the results.

Baseline volume measures provide clinicians with a patient's usual between-limb volume difference in the absence of lymphedema. This allows clinicians to interpret volume changes that may be due to weight change or generalized swelling, both common issues during and after breast cancer treatment. Knowledge of baseline volume, arm volume difference, and error associated with measures facilitates clinical decision-making and, therefore, the detection and management of lymphedema.

Limitations

One limitation of this parameter estimation study is that the sample size was one of convenience and not based on a formal sample size calculation. However, the confidence intervals for the ICCs were very narrow, thus supporting the estimated values and study sample size. A limitation of the test-retest component of this study is that the LymphaTech measurements included interrater variance and the perometer measurements contained intrarater variance. Given the study design, these sources of variance could not be disentangled from the trial variance. To the extent that interrater variance would be expected to be greater than intrarater variance, one would anticipate that any impact owing to the design difference would favor the obtained perometer reliability estimates.

This study was conducted in a community-based breast cancer rehabilitation clinic, and the results may not be generalizable to other settings. Although the study population is reasonably representative of people with breast cancer and survivors, further evaluation of LymphaTech in other settings is warranted.

Conclusion

Within the context of this study's sample and setting, the LymphaTech displayed high test-retest ICCs that were near identical to perometer ICCs. The LymphaTech measurement system provided similar volumes to those of length-matched perometer volumes, and differences between volumes within participants were primarily due to random fluctuation between measurement systems rather than a within-measurement system error. Collectively, these results support the reliability and validity of the LymphaTech measurement system.

Author Contributions and Acknowledgments

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Ethics Approval

This study was reviewed and approved by the LymphaTech Institutional Review Board under protocol #201701. Participants provided informed consent for enrollment and treatment.

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Disclosures

M.J. Weiler, N. Frank, and J.B. Dixon own equity in LymphaTech and may benefit financially from the technology. J.B. Dixon is affiliated with LymphaTech Inc and serves as a scientific advisor. Georgia Institute of Technology has licensed to LymphaTech technology that is related to this study and that is covered by patent applications for which J.B. Dixon is an inventor. In addition, J.B. Dixon is eligible to receive royalties under the license agreement for LymphaTech. No other competing interests were reported.

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