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Estimates for Assessment of Lymphedema: Reliability and Validity of Extremity Measurements

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Abstract

Background: Measuring lymphedema with high accuracy is important for several reasons. The aim of this study was to assess the reliability and validity of three routinely used methods to estimate limb volumes.
Methods and Results: Inverse water displacement, girth measurements, and Perometer measurements were executed. Although standard techniques were used, extra precautions were taken to maximize accuracy within and between observers. Water displacement, and girth and Perometer measurements resulted in standard deviations of 0.7%–0.8%, 0.5%, and 0.4%–1.0%, respectively.
Conclusion: Measuring limb volumes using routine methods is not easy. Even under optimal conditions, the measurements are quite dependent on the observer. For practical situations, an easy, objective, and reliable method is lacking.

Keywords: lymphedema, volume measurements, method

Introduction

Lymphedema is swelling of a body part due to excess accumulation of protein-rich interstitial fluid in body tissue. In most cases, lymphedema is the result of lymphatic vessel damage caused by filariasis, surgery, trauma, or infection, and is then called secondary. When arising from an intrinsic abnormality of the lymphatic system, it is referred to as primary.[1] Identification of lymphedema with high accuracy is difficult. Historical data estimate that worldwide 180–250 million people suffer from lymphedema.[2] It is, therefore, important to have an easy, objective, and reliable method to measure lymphedema in practical situations.[3,4]

There are two main goals to measure lymphedema with a high accuracy: (1) early diagnosis that may prevent clinically significant lymphedema to develop by early treatment and (2) evaluate changes in volume (lymphedema) as measure of treatment effects.[2,3,5,6]

To date, hospitals and edema clinics use (either of) three different methods to estimate limb volumes. First, volume measurement by water displacement is often considered as the golden standard for measuring arm edema.[3,7] The displaced water equals the volume of the limb; although this technique is simple, there are many variables that need to be considered. Second, indirect volumetry is possible by circumference measurements with a girth or optically with the Perometer. Volumes are subsequently calculated using mathematical models.

More recently, three-dimensional scanning technology has been developed to a high and applicable level. A mobile camera/scanner is interfaced with a smartphone or laptop, using a virtual platform or an *ad hoc* developed application.[8,9] Finally, the Peracutus Aqua Meth[10] and the BFVal-Gadro[11] are two innovative tools to improve the measurement challenges associated with lymphedema. Both water-based volumetric apparatuses make use of the water level, but differ principally from water displacement devices.

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In this study, the reliability and validity of using water displacement, circumference measurement, and the Perometer were assessed.

Materials and Methods

Water displacement

Inverse water volumetry was applied with the Bravometer (Varitex, Haarlem, The Netherlands) to assess the integral volume of the arm of a test subject.

The measurements with the Bravometer were carried out according to the supplier's manual, giving special attention to some items. The water tank was filled and the water that had run into the overflow tube was pumped out. The device was then calibrated (weight) to zero. The right arm of the test subject was placed gently into the apparatus. To carry out this process as smoothly as possible, the palm of the hand was put against the inner wall of the tank. The arm was slid down until the elbow reached the bottom of the tank; the elbow now made an angle of 90°. During movement of the arm, water flowed into the overflow tube. As the device was slightly out of (horizontal) plane, the last water flowing out of the tank appeared as a water trickle on one side wall of the tank. After ~30 seconds, the water had stopped flowing and the trickle was interrupted. The system was now regarded as being at equilibrium. The arm was then taken out again starting by moving the elbow upward. During the whole process, special attention was paid that no "extra water" flowed into the overflow tube. After emptying the overflow tube, the device was weighed again. It was empirically determined that water drops stuck to the hand and arm. During all measurements, water was shaken of, resulting in ~10 g (mL) of water that was returned to the system.

The right arm of one test subject was measured in 2 sets of 30 using water of 38°C and 16°C, respectively, by one observer. One complete measurement took ~2:30 minutes. The difference in water density at both temperatures is 0.6%[12] and was corrected for.

Girth measurements

Girth measurements were obtained by multiple circumference measurements of the right leg of a volunteer using a spring-loaded tape measure (Varodem, Horn, The Netherlands). The subject was sitting on a bed with the right leg placed on a horizontal board with a foothold at an angle of 90°. Markings were applied at 4-cm intervals starting at the ankle up toward the groin. No anatomic landmarks were used. During measurement, special attention was paid that the spool (~25 g) hung free to create the same tension on the tape and on the skin throughout the series of measurements, to maximize accuracy within and between observers. Circumferences were measured 10 times at every marking by one observer followed by the same measurement by the second observer. These accurate and precise measurements took ~90 minutes for each observer.

The truncated cone model (Kuhnke)[13] was used to calculate the volume of the leg.

Perometer

The Perometer 400T (Pero-System Messgeräte GmbH, Wuppertal, Germany) is an optoelectronic leg volume approximation system.[14,15]

The Perometer frame was lowered to the lowest possible position. A healthy volunteer then stepped his or her dominant (right) leg into the frame in a central position on the Perometer platform. The other leg was supported on a stool (~40 cm high), with the knee flexed to reduce obstruction to frame movement. The dominant leg of a volunteer was vertical to the ground in frontal and lateral planes. Once the leg was stable, the observer slid the Perometer frame upward to the upper boundary of the leg, that is, until the frame touched the other leg, and down again.

In the first series of experiments, the possible influence of the duration of the measurement, that is, the speed at which the frame is moved up and down, was assessed by moving the frame regular (14–28 seconds) and fast (3–5 seconds) up and down. In both cases, one observer measured 15 times, with ~1:30 minutes in between two successive measurements. All other measurements with the Perometer were done by moving the frame at a regular speed.

The test was then performed using the leg of a mannequin hung stable with a rope and fixed in place at the foot with a towel. One hundred measurements as one set were carried out by an observer and the results were compared with 100 measurements of a leg of a healthy volunteer.

The possible influence of the vertical alignment of the leg was assessed. First, four sets of 25 measurements each were carried out on the same day by one observer. The complete measurement took 2:30 hours. The stool was removed and the same test was performed with the dominant leg leaning in the lateral plane at an angle of ~30° with the vertical plane. Two sets of 50 measurements were carried out. Both sets took ~3 hours each; there was an intermission of 3:30 hours.

Data collection and statistics

Data collection was carried out by persons not experienced in the measurement concerned. However, before start of each series of experiments, a lymphedema nurse explained the procedure in detail. In all cases, the extremity of a healthy person or from a mannequin was used.

The number of measurements was chosen to allow profound statistical analyses of the results. Each observer is defined individually. Measurements are presented using the mean and standard deviation (SD). The significance of differences was assessed using the Student's *t*-test for paired observations, and $p = 0.05$ was considered as significant.

Research ethics and patient consent

The local medical ethics committee approved the conduct of this study (University Maastricht Medical Centre, The Netherlands; IRB waiver METC 2018-0748). All three participants in this study provided written informed consent.

Table 1. Results of 30 Consecutive Measurements of the Upper Limb of a Volunteer Using Water Temperatures of 38°C and 16°C, Respectively

Temperature	38°C	16°C
Mean volume (mL)	2598	2591
Standard deviation (mL)	18.0	20.7
Coefficient of variation %	0.7	0.8

Results

Volume measurement using the Bravometer

The results of 30 consecutive volume measurements of the upper limb of a healthy volunteer in the bravometer with water temperatures of 38°C and 16°C, respectively, are presented in Table 1. Between both temperatures, there was no statistical significant difference for the means and for the SDs. Even the coefficient of variation at both temperatures did not show a statistical significant difference.

Volume measurement using a girth

The mean of 10 girth measurements for 17 positions on the leg as measured by two independent observers is presented in Figure 1A. The SD for each position and for both observers is shown in Figure 1B. The mean SD of the girth measurement for both observers is <0.35 cm.

With each set of measurement, the volume of the leg was calculated. The mean volume measurements of the leg, the SD, and the coefficient of variation are presented in Table 2. Although each observer can determine the volume with an error <0.5%, the mean volume of both observers is statistically significantly different.

Volume measurement using the Perometer

The results of 15 consecutive regular (routine) and 15 consecutive fast measurements on a healthy volunteer are presented in Table 3. The volume, the SD, and the coefficient of variation show no difference.

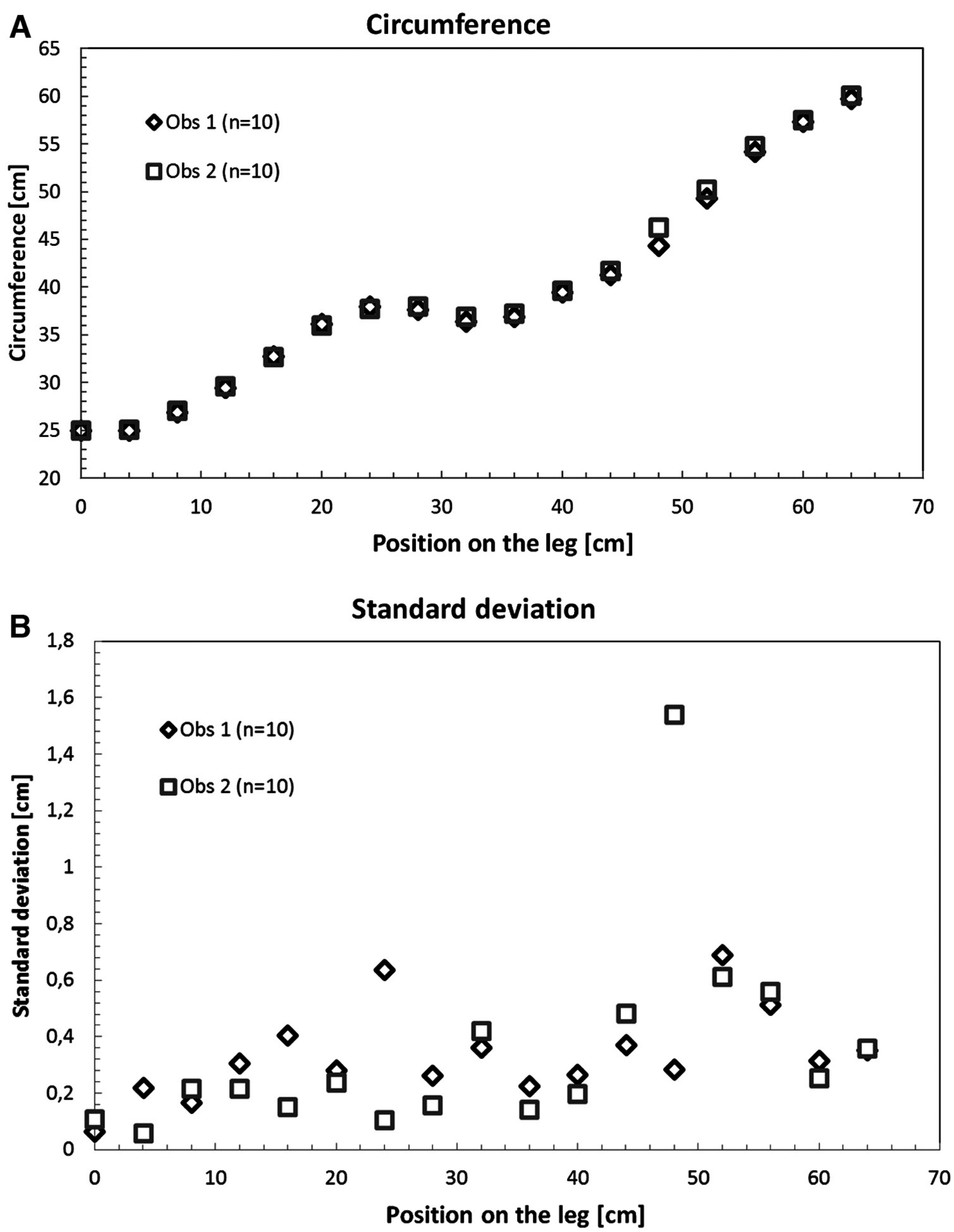

FIG. 1. **(A)** Average tailor tape measurements at different positions on the leg for two observers. **(B)** Standard deviations for the tailor tape measurement at different positions on the leg for two observers.

TABLE 2. CALCULATED VOLUMES OF A LEG BASED ON TAILOR TAPE MEASUREMENTS AT 17 POSITIONS BY TWO OBSERVERS

	Observer 1	*Observer 2*
Mean volume (mL)	8296	8453
Standard deviation (mL)	45	44
Coefficient of variation %	0.5	0.5

Then, the measurement of the volume of the leg of a mannequin was repeated 50 times consecutively. This ideal situation was compared with the leg of a healthy volunteer measured 100 times. It took 2.5 hours to perform the latter set of measurements. The results are presented in Table 4.

The coefficient of variation measuring the leg of a mannequin was the same as in the previous experiment, whereas this value was higher if the mean of the 100 consecutive measurements is compared. However, if the 100 measurements are separated in four consecutive groups of 25 measurements, the mean volume does not show a statistical significant difference.

The influence of leg alignment was studied by performing 50 measurements on the leg of a volunteer with a proper (vertical) and a misaligned position of the leg. The results are presented in Table 5. The means for the volume in both positions differ statistically significantly.

Discussion

In this study, the reliability and the validity of limb measurement with the Bravometer, a girth, and the Perometer were assessed.

Inverse water replacement was applied using the Bravometer. The right arm of a healthy volunteer was measured to be 2598 mL, with a SD of 18.0 mL (0.7%) (Table 1). Values of SDs calculated during validation of the Bravometer[3] were 78 (1.7%) and 154 (3.9%) for edema and control arms, respectively. Others using the Bravometer reported SDs of 2.8%.[16,17]

The relative small intraobserver variability in this study is the result of the extra precautions that were taken during the measurements: first, special attention was given to prevent extra water to be removed from the tank, either by overflow or by drops attached to the arm, and second, the position of the elbow was always in the utmost corner of the tank making an angle of 90°; this ensured that the arm was submerged to the same level each time.

Arm volumes determined at 38°C and 16°C were almost equal (Table 1). The results, therefore, indicate that arm volume measurement with the Bravometer is not influenced by temperature in this range. This is in agreement with water displacement measurements carried out at 20°C and 35°C. However, more extreme temperatures of 5°C and 45°C resulted in significant deviations of 1.4% from the normal temperature mean.

TABLE 3. MEAN VOLUME, STANDARD DEVIATION, AND COEFFICIENT OF VARIATION OF 15 REGULAR AND 15 FAST MEASUREMENTS WITH THE PEROMETER

	Regular	*Fast*
Mean volume (mL)	7868	7869
Standard deviation (mL)	31	30
Coefficient of variation %	0.4	0.4

TABLE 4. MEAN VOLUME, STANDARD DEVIATION OF THE VOLUME, AND COEFFICIENT OF VARIATION OF 50 CONSECUTIVE MEASUREMENTS OF A MANNEQUIN LEG AND OF 100 CONSECUTIVE LOWER LIMB MEASUREMENTS WITH THE PEROMETER

	Leg of a mannequin	*Leg of healthy volunteer*
Mean volume (mL)	3847	7805
Standard deviation (mL)	14	49
Coefficient of variation %	0.4	0.6

The Bravometer renders the total volume of the whole arm. To evaluate changes in volume as measure of treatment effects, however, local information is needed.

The girth is principally suitable for local measurements. Circumference measurements over time will vary according to the reproducibility of the reference marks. Still, even if two observers used the same reference marks, the calculated volume differed significantly: more than three times the coefficient of variance (Table 2). This shows that girth measurement is strongly person dependent. To be able to observe developments in limb volume over time, the same person should measure a patient each time. This is not easy to organize in clinical situations.

The speed of measuring with the Perometer did not influence the results (Table 3). Furthermore, the coefficient of variation measuring the leg of a mannequin was not or only slightly lower than measuring the leg of a volunteer (Tables 3–5). Again, this indicates that the person (patient) should cooperate very well to obtain high accuracy.

As the Perometer determines cross-sectional areas of horizontal segments, the alignment of the leg was expected to be of importance. Indeed, in case the leg was leaning in the lateral plane at an angle of ~30°, the calculated volume increased by 2.6% (225 mL), whereas the SD did not change (Table 5). The 2.6% is two to four times the coefficient of variation. Therefore, to be able to observe differences in volume between successive visits of a patient, the position of the leg needs special attention and a clear protocol is needed in clinical situations. Even a small inclination will result in a relevant increase in the coefficient of variance.

TABLE 5. INFLUENCE OF ALIGNMENT OF THE LEG IN THE PEROMETER

	Proper alignment	*Misalignment*
Mean volume (mL)	8558	8783
Standard deviation (mL)	89	91
Coefficient of variation %	1	1

Mean volume, standard deviation, and coefficient of variation are presented for 50 consecutive measurements in a proper alignment and in misalignment.

The right leg of the healthy volunteer was measured with the girth (Table 2) and with the Perometer (Table 3). Both methods use mathematical models to calculate the volume. However, the calculated volumes based on both methods differed considerably and results are not interchangeable.

In general, even if new proposed solutions are more reliable than the traditional approaches, the medical personnel often prefer the traditional approach. The usability feedback of the user plays a crucial role for the acceptance of the innovations.

Conclusion

Measuring limb volumes in practical situations (e.g., in a clinic) is prone to variation. The measurements in this study were carried out with great carefulness and a well-cooperating test person. In practical situations, though, it may be difficult to reach the necessary degree of standardization and differences between measurements need to be considerable to be able to distinguish true increase or decrease of limb volume.

Furthermore, also uncontrolled parameters are of importance. A method is needed that not only should be easy, objective and reliable, but fast as well. Such method could even be applicable for personal use, for example, at home, and would improve diagnostic possibilities.

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Author Disclosure Statement

F.H. is owner of Peracutus B.V. This company is developing a medical device to assess lymphedema. J.S. was co-owner of Peracutus B.V. All other authors have no competing financial interests.

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