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COMPARATIVE STUDY BETWEEN MOBILE INFRARED OPTOELECTRONIC VOLUMETRY WITH A PEROMETER® AND TWO COMMONLY USED METHODS FOR THE EVALUATION OF ARM VOLUME IN PATIENTS WITH BREAST CANCER RELATED LYMPHEDEMA OF THE ARM

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ABSTRACT

There is no consensus on the definition of Breast Cancer Related Lymphedema of the arm (BCRL) because there are no agreed standards in measurement methods and diagnostic criteria. The main objective of this study is to compare mobile infrared optoelectronic volumetry with a Perometer® with two commonly used methods for the evaluation of arm volume in patients with different degrees of BCRL. Bilateral arm volumes of eighty participants, with and without clinical BCRL, were calculated with a mobile Perometer®, by water displacement, and with circumferential measurements, integrated in the frustrum, single frustrum, and disc model method. The ICC of the Perometer® was between 0.997 and 0.999. The frustrum and disc model method produced the largest volume measurements and water displacement the smallest, while Perometer® measures were in between. On average, volume of the dominant arm was found to be 2.2% higher than the non-dominant arm in the healthy control group, cautioning for intra- patient differences between both arms when comparing ipsilateral to contralateral arm for the diagnosis of BCRL with a threshold value. Future research would likely benefit from the use of the Perometer® compared to the other arm volume evaluation tools for BCRL, and further, the single frustrum method should not be used for volume estimations of edematous arms.

Keywords: breast cancer related arm lymphedema, infrared optoelectronic volumetry, mobile Perometer®, arm volume measurement, hand dominance, diagnostic criteria

The incidence of Breast Cancer Related Lymphedema of the arm (BCRL) varies substantially because of a variety of different definitions, diagnostic criteria, and evaluative measurement methods that are used interchangeably within clinical practice and scientific research. The most commonly used methods to measure upper limb volume can be divided into manual direct measurements, like water displacement, and indirect manual measurements, like volume estimations from circumferential measurements, calculated by the frustum sign and the disc model method. In the literature, both techniques have been described as highly reliable and correlated, but not interchangeable, and there are noted disadvantages in using either technique (1-13).

In the mid 1980's (3), the Perometer®, an infrared optoelectronic limb volumeter, was developed and validated with geometric objects (14,15). It was then used for different body segments, like arms, legs (16-18), and knees (14) in different pathologic settings, including limb swelling due to lymphatic and blood vascular disease (19), trauma, skin wounds or burns, or elective surgery. There are even applications in clinical physiology, dermatology, and functional imaging, for example, during venous occlusion plethysmography (20).

Two studies have compared the three methods above, but not in the upper limb (18) or with different methods and materials (16). Neither of the studies examined hand dominance, which influences upper limb volume symmetry at baseline, to describe the degree of BCRL following breast cancer treatment. Therefore, intra-patient differences between the ipsilateral and the contralateral arm need to be included when setting the diagnosis of BCRL with a threshold value for arm volume differences. Other studies have compared Perometer® measurements with bioelectrical impedance spectroscopy (21-24) or circumferential measurements (2,25-27), presenting favorable results with the use of the Perometer®. It can detect minimal limb volume change, which has a significant impact on breast cancer survivors (28). Use of the mobile Perometer® for edematous arm volume measurements has not been reported before.

The main objective of this study is to compare mobile infrared optoelectronic volumetry with a Perometer® with two commonly used methods for the evaluation of arm volume in patients with and without BCRL.

MATERIALS AND METHODS

Patient Recruitment

109 female breast cancer patients, who visited the Breast Clinic of the Universitair Ziekenhuis Brussel (UZB) in the last four years for BCRL complaints, were contacted telephonically to ask if they were interested to participate in the study. Forty patients agreed and made an appointment between 06/07/2010 and 27/07/2010 for undertaking the measurements at the UZB. Two of them did not show up at the appointment. Three other patients who contacted the Breast Clinic during this period with a new BCRL case have also been included in the trial.

During the same measurement interval, eleven employees, fifteen physical therapy interns of the UZB, and five sympathizers volunteered in the study. Eight breast cancer patients without BCRL diagnosis who had a follow-up meeting during the measurement interval at the physical therapy department of the Breast Clinic also participated in the trial.

Prior to measurement, all participants confirmed they did not have restricted shoulder mobility, open wounds at the upper limb and were able to stand without any support; otherwise they were excluded from the trial. An informed consent was obtained from all patients and the protocol was approved by the Ethical Committee of the UZB. The trial is in accordance with the Helsinki Declaration of 1975, as revised in 2000.

Main Outcome Measures and Measurement Instruments

Three different measurement instruments were used to measure and calculate bilateral upper limb volume.

The first volume measurement was obtained by *water displacement*. A plexiglass water tank of 9.0 cm by 7.5 cm by 75.0 cm was filled with water until it reached the bottom of the tank's overflow. The participant was seated next to the tank and the distal point of the ulnar styloid and 40 cm proximal to this point had been marked as a blue perpendicular line with a dermatological pencil on both arms of the participant. The hand was put against the inner wall of the

tank, with the fingertip of the longest finger touching the water. The participant was asked to slide down until the water surface touched the first marked line and then hold still until the overflow stopped. The water that overflowed was collected in a measuring cup and weighed on a balance, with an accuracy of 0.1 g. This weight was transformed into a volume and noted as equal to the absolute volume of the hand. The participant had to slide further down until the water surface reached the second marker and hold still again until the overflow stopped. The weight of the collected water equaled the absolute arm volume. The arm was removed from the tank, dried and the same method was used to measure the other arm after the tank had been refilled.

The second volume calculation was obtained by circumferential measurements. 4 cm intervals were marked as a thin blue perpendicular line with a dermatological pencil between the distal point of the ulnar styloid (0 cm) and 40 cm proximal to this point. Measurements were made with a narrow circular tape measure (13), with 1 mm accuracy. The participant was seated, with the arms stretched and the hands resting on a desk.

Absolute arm volume was calculated from these eleven measurements on each arm, using three different geometrical formulae:

- $V = \sum [h (c^2 + cC + C^2)/12\pi]$
  The truncated cone method (= frustrum = Casley-Smith = Sitzia), where h is 4 cm, c is the lower circumference (cm) and C is the higher circumference (cm) of the 10 truncated cones.

- $V = h (c^2 + cC + C^2)/12\pi$
  The single truncated cone method, where h is 40 cm, c is the lower circumference (cm), at the wrist (the most distal point of the ulnar styloid) and C is the higher circumference (cm), at 40 cm proximal to the lower circumference.

- $V = \sum [(c + C)/2]^2 \times h/4\pi]$
  The disc model method, where h is 4 cm, c is the lower circumference (cm) and C is the higher circumference (cm) of the 10 discs.

The third volume measurement was obtained by measurements with a *mobile infrared optoelectronic volumeter* (Perometer® 1000M, Pero-System GmbH, Wupertal, Germany; Peroplus Software TM). The Perometer® uses infrared light transmitters, spaced every 2.54 mm, located inside the bottom and the left side of the Perometer® frame, that project light towards photo sensors, spaced every 1.27 mm, at the opposite sides of the frame. The arm is placed inside the Perometer® frame, and by blocking the transmission of light, it creates an electronic image of the arm. As the frame is moved along the arm, images are recorded every 0.47 cm, creating a highly accurate measurement of the arm circumferences and volume (*Fig. 1*).

The limb length was defined between the distal point of the ulnar styloid and 40 cm proximal to that point. The arm volume is determined by the sum of all volumes of the adjacent discs (modified disc model method), with a height of 4.7 mm and two calculated elliptical cross sectional surface areas ($\pi \times r_a \times r_b$), measured by the frame. The maximal size of a segment that can be measured with the Perometer® is 90 x 41.6 x 31 cm. Measurements were repeated three times on each side. The mean of the three measures was used as absolute volume of the arm.

Based on the absolute volumes, relative arm volumes, comparing both arms, were calculated with the following formula in healthy participants: *[volume of the dominant arm - volume of the non-dominant arm)/ volume of the non-dominant arm] * 100* and in patients: *[volume of the edematous arm - volume of the non-edematous arm)/ volume of the non-edematous arm] * 100* (29,30).

The order of measurement of the different techniques and the order of

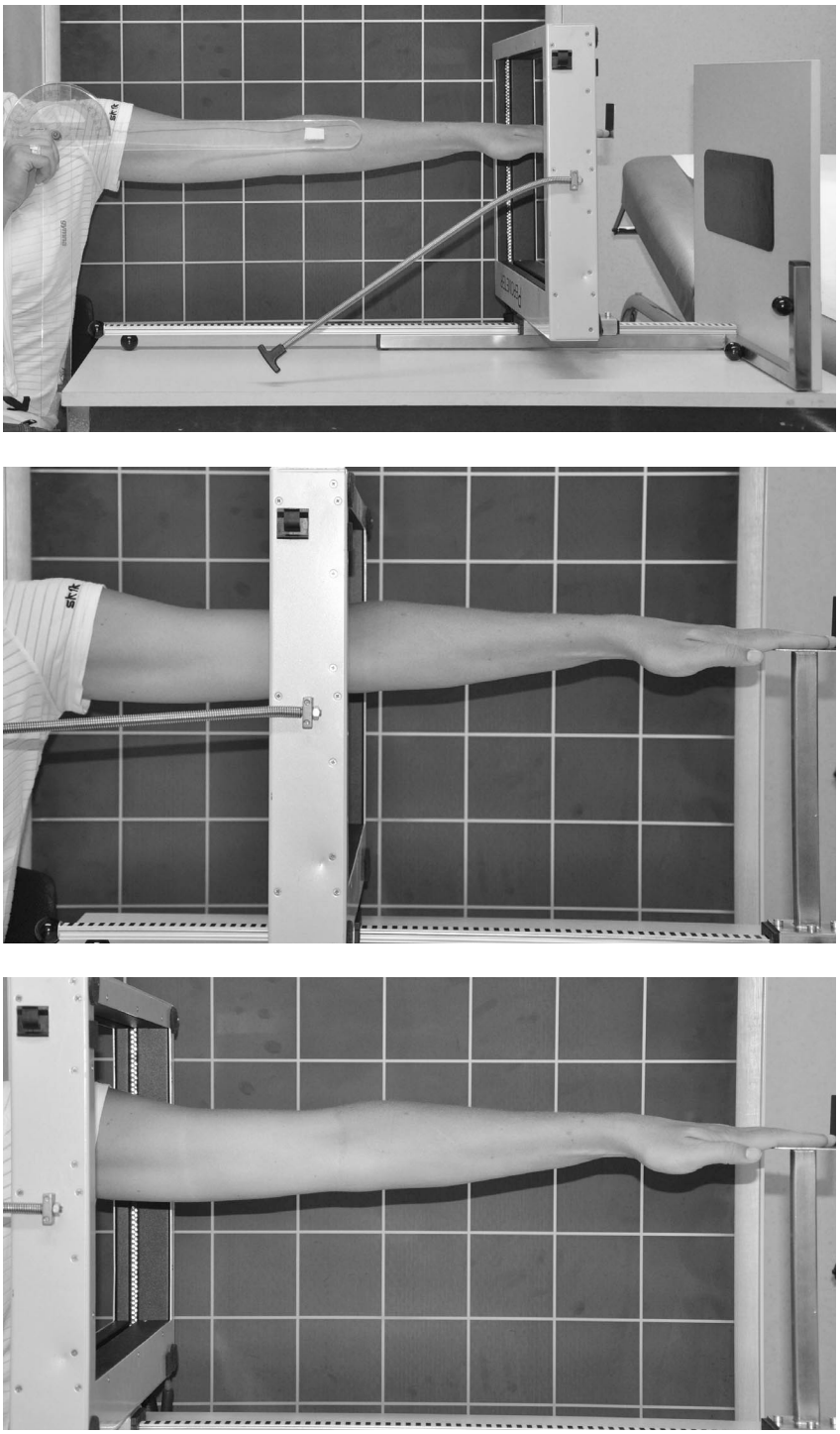

Fig. 1. Illustrative use of the mobile Perometer® to obtain measurements for the study. All subjects were seated with their arm extended perpendicular to their body and the base plate, their hands were placed level on the finger pad with thumb tucked in, and the frame was moved as close to the trunk of the body as possible.

TABLE 1
Patient Characteristics and Arm Volumes, Measured with the Five Different Methods, of the Control Group (Dominant and Non-Dominant Arm, Left Column) and the Patient Group (Edematous and Non-Edematous Arm, Right Column)

	CONTROL GROUP	PATIENT GROUP
Number of participants (n)	31	49
Age (years) (±SD)	32.7 (13.4)	62.5 (9.7)
Female sex (%)	80.6	100
Right hand dominance (%)	87.1	98
	Dominant arm	**Edematous arm**
Perometer (ml) (±SD)	1771.7 (338.0)	2504.0 (701.2)
Water displacement (ml) (±SD)	1697.6 (264.9)	2409.8 (592.5)
Frustrum method (ml) (±SD)	1920.1 (380.3)	2734.9 (704.6)
Single frustrum method (ml) (±SD)	1767.4 (375.6)	2353.1 (614.6)
Disc model method (ml) (±SD)	1919.2 (380.0)	2733.9 (704.2)
	Non-dominant arm	**Non-edematous arm**
Perometer (ml) (±SD)	1731.4 (324.4)	1996.4 (426.6)
Water displacement (ml) (±SD)	1657.9 (245.2)	1930.5 (387.7)
Frustrum method (ml) (±SD)	1882.3 (377.0)	2249.6 (458.8)
Single frustrum method (ml) (±SD)	1760.7 (386.3)	2101.0(469.4)
Disc model method (ml) (±SD)	1882.5 (376.2)	2248.6 (458.6)

measurement sides (dominant/non-dominant or operated/non-operated) was arbitrary. The dominant arm was determined by asking the participant with which hand he/she writes.

Statistical Analysis

Data were analyzed using SPSS 19.0 (IBM Corporation, Somers, NY 10589, USA). Descriptive statistics (mean ± SD for continuous variables, frequencies and cross-tabulations for discrete variables) were used to summarize basic characteristics of the respondents and their different volume measurements. Independent samples t-tests were used to check for difference in the mean volume measurements between independent groups. Paired samples t-tests were used to check for significant differences between the dominant and non-dominant mean arm volume measurements in the control group. A repeated measures analyses of variance was used to compare the mean volume measurements using the different methods, separately in the patient group and the control group. An interclass correlation coefficient (ICC) for absolute agreement was used to check the intra-rater reliability of the three Perometer® measurements. The α-level was always set at 0.05.

RESULTS

Patient Characteristics

Eighty included participants were divided into two groups: a control group with healthy persons (n = 31) and a patient group (n = 49) with the breast cancer patients, with and without objective BCRL. Bilateral arm volumes were measured with five methods in both groups (*Table 1*).

In the patient group, 46.9% were operated on the dominant side, with a mean

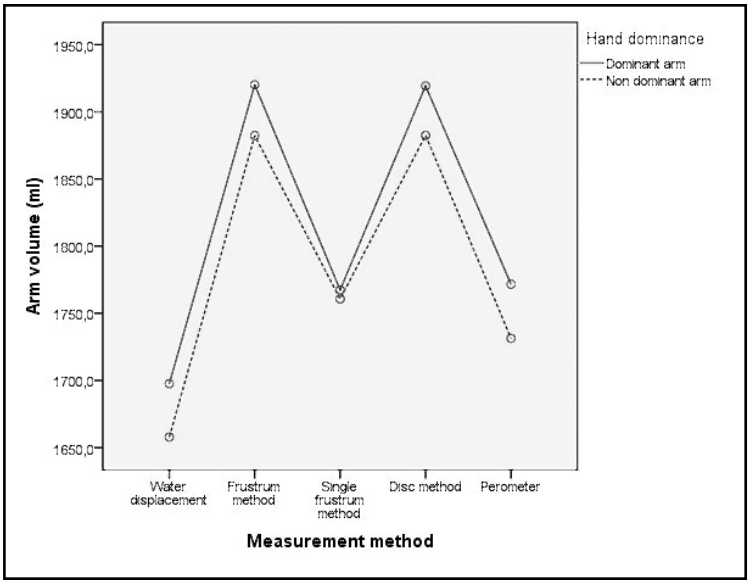

Fig. 2. Arm volume measurements of the dominant and the non-dominant arm with five different measurement methods in the control group (n = 31).

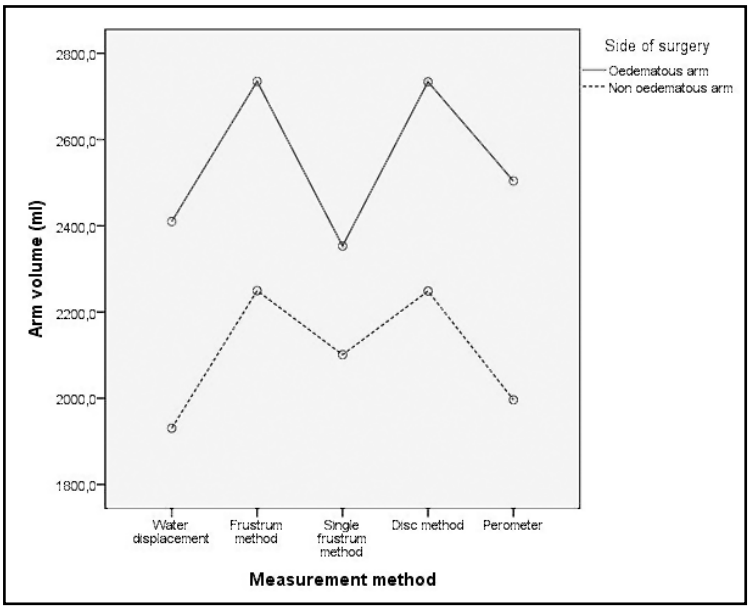

Fig. 3: Arm volume measurements of the edematous and the non-edematous arm with five different measurement methods in the patient group (n = 49).

of 84.3 months (± 69.5 months) since the operation. 52.1% had a total mastectomy with axillary lymph node dissection, 31.3% had breast conserving surgery with axillary lymph node dissection and 16.7% had breast conserving surgery with sentinel lymph node

TABLE 2
Arm Volume Difference (%) Between the Dominant and Non-Dominant Arm in the Control Group, with the Five Different Measurement Methods

	Mean (%)	± SD
Perometer	2.36	3.58
Water displacement	2.37	4.32
Frustrum method	2.14	3.29
Single frustrum method	0.60	3.90
Disc model method	2.08	3.34

dissection. All patients except one received radiation therapy, and 53.5% of the patients had concomitant chemotherapy. The location of the tumor was in the superior external quadrant (47.1%), the superior internal quadrant (14.7%), inferior external quadrant (14.7%) or inferior internal quadrant (5.9%). Other tumors were located in the central part (17.5%).

Mean volume of the *dominant* arm in the control group, measured with the Perometer® (1771.7 ml ± 338.0 ml), was higher than the *non-dominant* arm (1731.4 ml ± 324.4 ml) (*Fig. 2*) and mean volume of the *edematous* arm in the patient group, measured with the Perometer® (2504.0 ml ± 701.2 ml), was higher than the *non-edematous* arm (1996.4 ml ± 426.6 ml) (*Fig. 3*).

When comparing the volume difference between the dominant and the non-dominant arm in the control group, all measurement methods, except for the single frustrum method, resulted in a significantly higher dominant arm volume (on average 2.24%) than the non-dominant arm (*Table 2*).

Repeated Perometer® Measurements

Three repeated measurements of the *dominant* arm, with the Perometer®, in the control group, by the same physical therapist, had an intraclass correlation coefficient of 0.998. The ICC of the *non-dominant* arm is 0.997. Three repeated measurements of the *edematous* arm, with the Perometer®, in the patient group and by the same physical therapist, had an intraclass correlation coefficient of 0.999. The ICC of the *non-edematous* arm is 0.998.

Measurement Method Comparison

When comparing the five different measurement methods for the *edematous* arm in the patient group (*Fig. 3*), and the dominant arm, in the control group (*Fig. 2*), the frustrum and the disc model method gave the highest volume estimation. Water displacement and single frustum method gave the lowest volume estimation, while the Perometer® measures were in between.

When comparing the five different measurement methods for the *non-edematous* arm, in the patient group (*Fig. 3*), and the *non-dominant* arm in the control group (*Fig. 2*), the frustrum and the disc model method gave the highest volume estimation. Water displacement gave the lowest volume estimation, and the single frustum method and the Perometer® measures were in between.

In the *control* group, we found a significant effect in the measurement method ($p<0.001$) and in arm dominance ($p = 0.002$) for arm volume estimation. There was no significant interaction effect ($p>0.05$) for these factors on the arm volume estimation. In the *patient* group, there was a significant

effect of measurement method ($p<0.001$), side of surgery ($p<0.001$), and the interaction ($p<0.001$) between measurement method and side of surgery on arm volume estimation.

DISCUSSION

Patient Characteristics

Almost half of the patients had a tumor located in the upper outer quadrant. This is reported to be a risk factor for the development of breast edema following breast conserving surgery (31), however it has never been determined as a risk factor for the development of BCRL (32). Further research is necessary to study this possible correlation.

Previous research has shown a significant difference in arm volume between the dominant and the non-dominant arm (27,33). A 2.2% higher arm volume in the dominant arm, compared to the non-dominant arm in the control group is similar to data found in the literature, where differences vary between 1.4-1.6% (30), 2.5% (10) and 3.6% (24). A correction factor for hand dominance should always be incorporated when using arm volume differences for the evaluation of BCRL. Recently, Bourgeois et al (34) demonstrated, at least in right handed subjects, the functional asymmetry of the superficial lymphatic system of the right and left upper limbs. The consideration of lateralization and handedness should be integrated into research and clinical studies with diagnostic and therapeutic implications (34). The intra-patient volume differences between both arms, due to hand dominance, may under- or overestimate incidence of BCRL and treatment effects, when comparing ipsilateral to contralateral arm volume for setting the diagnosis of BCRL with a threshold value.

Similar to the incoherence of measurement tools, different thresholds are used interchangeably as diagnostic criteria for BCRL. Relative volume change (%) is preferred over absolute volume change (ml) (1,2,25,26) and the comparison with baseline measurements prior to operation in the ipsilateral arm are preferred over comparison with the contralateral arm (35). A cut-off diagnostic value is preferred over the use of categories to describe the degree of BCRL (6,21). When using a $\geq 10\%$ arm volume difference between arms as a diagnostic threshold for BCRL for the five different measurement methods, the single frustrum method diagnosed 63.4%, the frustrum method, disc model method, and Perometer® diagnosed 85.3%, and water displacement diagnosed 90.3% of patients with BCRL.

In the opinion of the authors, scientific research and multidisciplinary clinical approaches may benefit from the use of the Perometer®, compared to the other arm volume evaluation tools for BCRL considering its ease of use, reproducibility, and volume calculations not at the extreme of all measurement methods. Circumferential measurements with the use of the frustrum or disc model method can also be used by smaller private practices, because they diagnose the same amount of BCRL patients with the $\geq 10\%$ arm volume difference between arms.

This study did not find a significant correlation between hand dominance and degree of BCRL. This observation is similar to a recent report that did not find a significant association between relative arm volume change and hand dominance (29). However, another report demonstrated that treatment of the non-dominant side was associated with an 80% increased risk of having BCRL compared to treatment at the dominant side (7).

The volume of the non-edematous arm in the patient group is higher than the non-dominant and dominant arm in the control group. This finding could be explained by overcompensation, because the non-edematous arm is used more frequently, although dominance on the operated side is distributed equally in the patient group. By avoiding the use of the edematous arm, more muscle mass could develop in the

non-edematous arm. Another potential explanation could be a higher BMI in the patient group, since BMI is a risk factor for the development of BCRL (36). However, this possible correlation was not included in the trial because it was not one of the study aims and the data are not available. A recent study looking at the cause of swelling in the contralateral arm in breast cancer survivors has been published, but the authors concluded that further study is needed to determine the causes (37).

Standard deviation of the edematous arm in the patient group is very high, which means that the degree of BCRL varied substantially among included patients. Recognition of this variability is important in evaluating the different measurement methods, because the most appropriate technique should be able to measure little (sensitivity) as well as big differences in the evolution of BCRL (specificity) (38).

Perometer® Measurements

Intra-rater reliability has been calculated for the Perometer® measurements only, because numerous studies have discussed ICC for other measurement methods extensively in the past (3- 5,8,11-13) with only two prior studies with the full-sized Perometer® (16,18). High inter- and intra-rater reliability is concluded for circumferential arm measurements and the water displacement method, but the different measurement techniques are not interchangeable. Deltombe et al (2007) calculated inter- and intra-rater reliability for the same measurements methods as were used in this study, and the Perometer® had the highest ICC (0.997) and the lowest relative difference (1.5%) (16). Measurements with the mobile Perometer® in our study are even higher (0.997-0.999) and relative difference lower (1.4%). This high intra-rater reliability and low relative difference in both groups for both arms is important for this research, and the inter-rater reliability is necessary for multidisciplinary clinical applications of the mobile Perometer®.

In addition, upper and lower limb volumes and circumferences can be measured and analyzed with the same equipment while other options, like a specialized software program to make custom compression garments for swollen arms and legs, is also included. Previous reports suggested that although the Perometer® is the most appropriate arm volume measurement instrument for the evaluation of BCRL because of its many advantages compared with other measurement techniques, it may be too expensive for clinical use in private practices (2,3,6,12,14-16,18,24,27). With the introduction of the mobile Perometer®, the equipment has become cheaper and transportable, perhaps broadening the options. The only measurement limitation is the exclusion of part of the hand, but this is also a problem with the circumferential measurements. The Perometer® differs from the other techniques by its simplicity, time saving, accuracy, efficiency, improved ergonomics and hygiene, data collection and analysis, and multidisciplinary clinical approach.

Comparison Between Different Measurement Techniques

The disc model method (especially in small arms) and the frustrum method (especially in big arms) yield the most liberal estimations of absolute arm volumes in both groups for both arms. When using the disc model method, the lower circumference (c) of the disc is equaled to the higher circumference (C) (which is most commonly larger than the more distal location in the arm). This finding may be a cause of a systematic overestimation of arm volumes. These overestimations could be partially compensated by using the mean of the higher and lower circumference, which has been used in our study; however, we still found that it produced the highest arm volume estimations compared to the other measurement tools used in this study. Systematic overestimation

by indirect measurement methods has also been found in the literature (10,12,13,18,26), but there is no consensus on the most accurate method between the disc model (16,18) and frustrum method (3,8,11). Depending on size and shape of the body segment, the most precise method may vary.

On average, water displacement gives the lowest volume measurements of the arms compared to the other methods in this study. These results are similar to data in the literature in which water displacement produced the lowest and perhaps an underestimation of the volume (13). Water displacement has always been seen as the gold standard (5,9,18,30), but in the last decade, more researchers are moving away from this idea due to reports of multiple measurement errors (1-3,6,8,10,16). For example, water is unintentionally lost by spilling when the arm may move in the tank or when the arm is removed too soon from the tank before the water finishes running out of the tank.

In very large edematous arms, the single frustrum method estimates the lowest volumes compared to other methods in this study because it only uses the circumference of the wrist and 40 cm proximal to that point. The formula presumes that the arm is one big truncated cone neglecting the typical elliptical swelling of an edematous arm between those points and therefore clearly underestimating the arm volume. Because small, muscled arms look more like truncated cones, non-dominant and non-edematous arms should only be measured with this method.

The Perometer® measurements are consistently between the measurements of the other methods, especially for larger arm volumes. In non-dominant and non-edematous arms, the estimation is lower than in large arms. In the literature, investigators have reported an underestimation (14), an overestimation (15,25,26), or certainly not an overestimation (21,22) in arm volumes obtained by the Perometer® with the other methods producing values above or below the estimated arm volumes. To become a gold standard as a reference for comparing the results of the different methods, all arm volumes should be measured in ideal circumstances. Our research group has started a study on arm volume measurements prior to and following lipolymphosuction to compare the arm volume difference prior to and following surgery with the absolute volume of the tissue that has been removed. This type of study may be able to properly address the correlation between an exact volume change due to operation and the measured volume change.

There is a significant effect of the measurement method and the arm dominance/side of surgery on the arm volumes. This observation means that arm volumes of a dominant/edematous and respectively a non-dominant/non-edematous arm are significantly different when measured with the same method. The difference is more pronounced in the patient group. The different measurement methods measure significant differences in arm volumes for the same arm making the different techniques not interchangeable. Method and side of surgery together also have a significant effect on arm volume in the patient group, meaning that some techniques are more appropriate to measure edematous arms than others. The single frustrum method is not appropriate to measure edematous arms.

Based on this study, we would suggest use of the mobile Perometer® in clinical practice and scientific research to document arm volumes for the evaluation of BCRL incidence, degree, and therapy effectiveness. Our research group is preparing a formula to make the results of the arm volumes of different measurement techniques interchangeable. Normalized data for the different measurement techniques could be used to compare the results of each patient individually and possibly also studies from multiple different investigators using different methods of measurement.

CONCLUSION

Since there is currently no accepted gold standard for arm volume measurement techniques, future scientific research and multidisciplinary clinical approaches would benefit from the use of the Perometer® as an evaluative arm volume measurement tool in patients with BCRL due to its reproducibility, ease of use, and arm volume measurements which are not at the extreme high or low of multiple methods. Limb volume change of the ipsilateral arm of ≥10%, with implementation of hand dominance, could be used as a diagnostic threshold criteria for the diagnosis of BCRL. The single frustrum method should not be used for volume estimations of edematous arms. Compared to the most commonly used volume measurement techniques, we found the mobile Perometer® a reliable method for the evaluation of arm volumes in patients with BCRL, which has many advantages in performance of measurements for both patients and therapists.

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