

CLINIMETRICS OF VOLUME MEASUREMENT IN UPPER LIMB LE

Michael Ng, Alexander Munnoch

Upper limb lymphoedema is a devastating sequel of breast cancer treatment. Upper limb volumes need to be measured in order to gauge the efficacy of the treatment of upper limb lymphoedema. If upper limb volume discrepancies are detected in early lymphoedema, treatment may be instituted quickly, perhaps leading to a lesser impact on patient quality of life and body image. Accurate, valid, reliable, specific, sensitive and practical tools are required to measure upper limb volumes. This review article discusses the clinimetrics of upper limb volume measurements currently used in clinical practice.

Key words

Clinimetrics
Volume measurement
Bioimpedance
Intraclass correlation coefficient

The concept of clinimetrics was put forth by Feinstein in 1983 (Feinstein, 1983), who argued for improved measurement in quantitative methods. He reasoned that data needed to be consistent, objectively observed and recorded, reproducible and accurate. Accuracy requires a standard to be measured against, but when one does not exist, a standard could be developed by a panel of experts to measure a tool's validity in the appropriate study population (Feinstein, 1983; Greenhalgh, 1997). Although clinimetrics is currently in the domain of clinical research, in the age of evidence-based practice, practitioners should be able to design and evaluate studies that utilise appropriate instruments and measurements. A tool should be able to measure what it was intended to (validity); its results should be consistent, reliable and have agreement

(reproducibility); and detect changes over time (responsiveness) (de Vet et al, 2003).

There are many instruments available at present to measure outcomes. This leads to difficulties in choosing the appropriate instrument and redundancies. The lack of standardisation also hampers the effort of comparative studies. This paper aims to evaluate critically the clinimetrics of volumetric assessment of upper limb lymphoedema secondary to breast cancer.

Lymphoedema: a brief background

To determine the validity of an instrument, the subject that requires measuring has to be identified and understood. Lymphoedema develops as a consequence of lymphatic fluid collecting in the extracellular space. Lymphatic fluid is protein-rich. When lymphatic fluid is chronically present, the fluid incites an inflammatory response, leading to lipogenesis, fat deposition and overgrowth of connective tissue (Brorson et al, 2006; Warren et al, 2007a; Brorson et al, 2009). This explains the firm and non-pitting swelling with thickened skin in severe, late lymphoedema and the pitting oedema of milder, earlier lymphoedema. Lymphoedema occurs due to a myriad of factors, including malformation of the lymphatic channels and disruption of lymphatic drainage as a result of malignancy and surgery (Warren et al, 2007a). The effect of lymphoedema can be devastating, especially for those who

have undergone treatment for cancer and then develop a chronic swelling of a limb. Patients who develop lymphoedema have significantly lower body image scores and a lower quality of life (Jäger et al, 2006). This population report higher physical disability, unemployment, and financial problems. Lymphoedema causes social anxiety (Pyszel et al, 2006), which can lead to self-imposed social isolation as a way to cope (Rumsey et al, 2002).

The incidence of upper limb lymphoedema has been reported as being between 6 and 83% following treatment for breast cancer (Clark et al, 2005). Clark et al (2005) found that approximately 20% of patients developed lymphoedema after three years of treatment, and 80% of these patients had lymphoedema by the first year. Epidemiological data on lymphoedema is inaccurate due to a lack of diagnostic criteria. When there is a good history suggestive of lymphoedema coupled with obvious limb swelling and skin changes that are pathognomonic, the diagnosis is a clinical one. Limbs naturally vary in volume and size in an individual due to arm dominance and fluctuations in weight over time (Hayes et al, 2008).

At which point does the volume discrepancy change from normal to lymphoedema? It is important to be able to identify lymphoedema early, before its clinical manifestation, as treatment of subclinical lymphoedema may prevent

Michael Ng is Specialty Registrar Plastic Surgery; Alexander Munnoch is Consultant Plastic Surgeon, both at Ninewells Hospital, Dundee, Scotland

its eventual development (Stout Gergich et al, 2008). There is a need to monitor the effectiveness of treatment modalities and compare the results objectively. This can be achieved by valid, reliable, cost-effective, easy to use tools to measure lymphoedema in a research and clinical setting (Piller, 2009).

Water displacement

Volumetry provides an indirect measurement of both pitting and non-pitting lymphoedema. Volume can be measured in several ways. Water displacement is considered the gold standard by some (Sander et al, 2002; Karges et al, 2003). Figure 1 illustrates the concept of water displacement volume measurement. The volume of water displaced by an object is equal to the volume of the object. This principle was first discovered by Archimedes. Although it is simple in principle and in practice, there are many variables that need to be considered. The accuracy of the water displacement principle is dependent on the object sinking to the bottom of the water tank. Water buoyancy alters the volume displaced by a partially submerged object (Hauser, 1995). Subjects normally submerge their arm up to a level determined by the researcher and the design of the water tank. The arbitrary level poses a few problems. To compare the different methods of volume assessment, the most appropriate study design should be within-subject as this reduces variation. Each participant is measured with the various methods of volume assessment and the volumes compared, as opposed to between-subjects where each group of participants are measured with a different assessment method and the results compared. Water volume and density is influenced by temperature and the water temperature used in studies varies. A range of temperatures between 20°C (Deltombe et al, 2008) and 38°C (Damstra et al, 2006) have been used, or researchers stated that the water was 'tepid' (Sander et al, 2002). Water volume and weight have been recorded and converted using the assumption of 1 cm³ equals 1 mL, without taking into account temperature and type of water (Deltombe et al, 2008). For example, distilled water has a different density

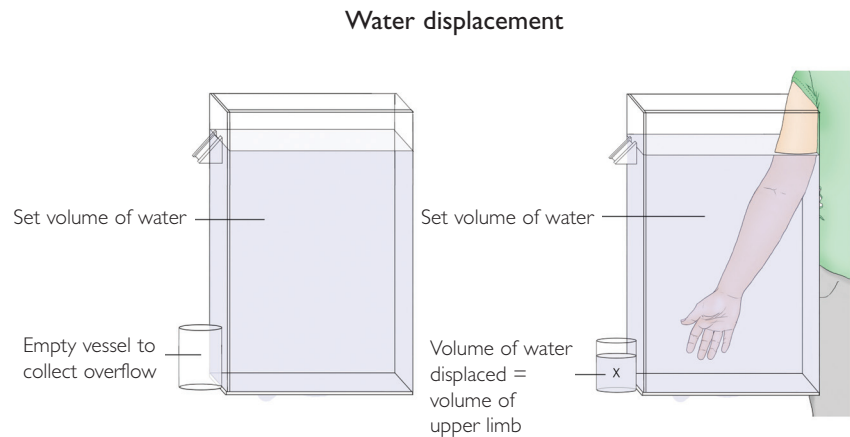


Figure 1. Schematic diagram illustrating limb volume measurement using water displacement.

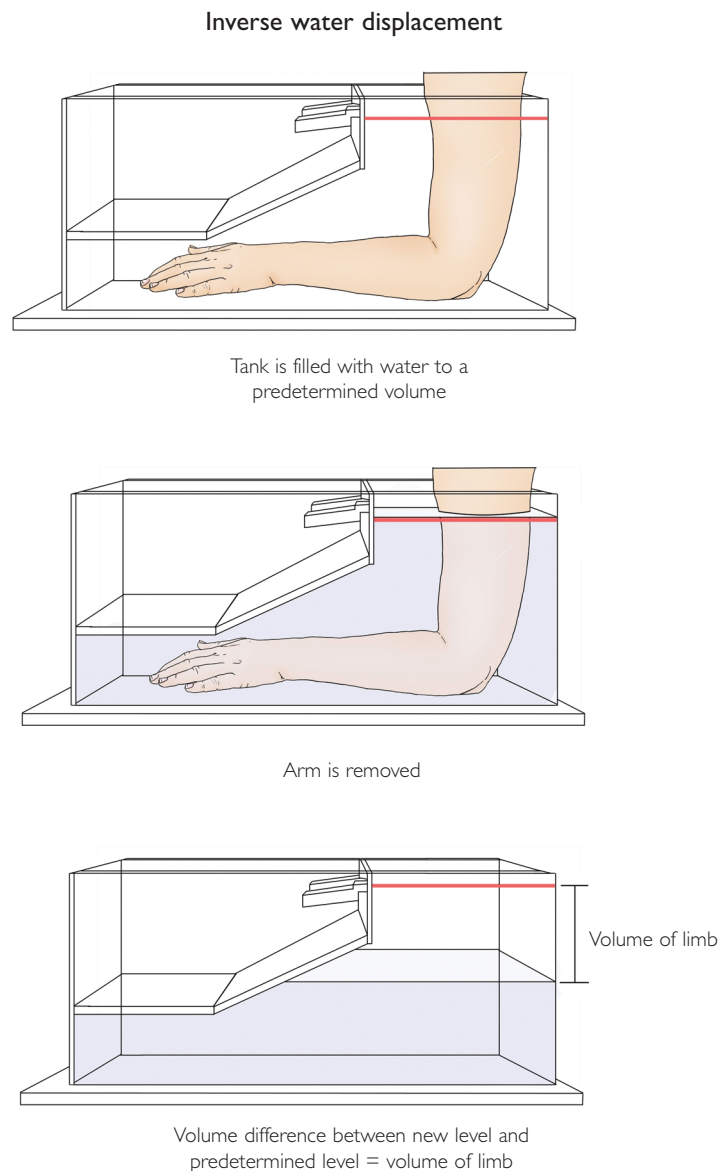


Figure 2. Schematic diagram illustrating limb volume measurement using inverse water displacement.

than tap water; and the density of tap water differs with the time of year (Buskirk, 1959). Although the differences are only three to four decimal places, effort should be made to standardise the water used in order to reduce the margin of error. King (1993) highlighted that more extreme water temperature, 5°C compared to 45°C, produced significantly different volume displacement by the hand, but the difference was not significant in temperatures between 20°C and 35°C. The water displacement method is not suitable for those with breaks in the skin because of the risk of infection. It is also difficult to clean and takes a long time to fill. Therefore, hygiene is an issue, as well as being labour intensive. On the other hand, it has excellent intra- and inter-observer reliability (intraclass correlation coefficient [ICC] for intrarater reliability was 0.99 and interrater reliability was 0.99) (Sander et al, 2002) and is able to include volume measurements for the hand.

To circumvent the problem of hygiene and the cumbersome collection of litres of water spilling out of the tank, two centres investigated the validity of inverse water displacement (Sagen et al, 2005; Damstra et al, 2006). Instead of submerging the arm in a water tank, the arm is placed in the tank and water is poured into the tank until a predetermined level is achieved. The arm is removed and the remaining water is measured. The difference between the predetermined volume and the remaining water should be the volume of arm submerged. The tank has to be emptied to obtain a reading and therefore more easily cleaned between patients. *Figure 2* is a schematic diagram illustrating inverse water displacement volume measurement.

Sagen et al (2005) recruited healthy volunteers and did not compare their method with any other assessment tool. On the other hand, Damstra et al (2006) had a cohort of 25 with unilateral lymphoedema. They claimed their method to be the new gold standard but failed to compare it to the apparent gold standard, which is water displacement. Instead, Damstra et al (2006) utilised the Herpertz method which measures four fixed point measurements and

calculates the difference between the two arms. Both studies show that the method has good intra- and inter-observer reliability (ICC range 0.98–0.99). Water displacement is attractive as a tool due to its non-invasive and direct method of obtaining arm volume, but it is by no means portable and impractical for everyday clinical use. It is also not recommended for use in limbs with broken skin due to the risk of infection.

Circumference measurement

An alternative method that is more practical and portable for clinical use is circumferential measurement. A tape measure is the essential instrument. The choice of tape measure can influence the reliability of the study. During the course of their study, Karges et al (2003) discovered that a spring-loaded tape measure was less consistent than a retractable tape measure. Readings from the spring-loaded tape yielded readings that varied compared to a retractable tape measure. Technique is as important as the instrument — errors are easily introduced if the tape is too tight, compressing the tissue, or too loose. The sum of circumferences at specific landmarks can be used. For example, Hayes et al (2008) tested the sensitivity and specificity of circumferences and self-report in identifying lymphoedema diagnosed using bioimpedance. Hayes et al (2008) utilised the sum of arm circumferences (SOAC) as a measure of lymphoedema. SOAC had a sensitivity of 42.1% and a specificity of 88.3%. Therefore, approximately three out of five cases of lymphoedema were missed, compared to two out of five cases of undetected lymphoedema in the self-report group.

The volume of the arm can be calculated from circumference measurements using mathematical models. Before Sander et al (2002), the arm was assumed to be a cylinder for ease of calculation. The subjects in previous studies quoted by Sander et al (2002) did not have any swelling, which may account for the cylinder model being more accurate. Sander et al (2002) were the first to apply different geometric models to calculation of arm volume in subjects with lymphoedema. The frustum

(truncated cone) assumption yielded volumes closest to water displacement and had high intra- and inter-observer reliability. The ICC value for both intrarater and interrater reliability was 0.99. The recommendation was to use readings at 6 or 9cm intervals, while maintaining a small standard error of measurement. The cylinder model overestimated the volume. However, the limits of agreement between circumference measurement and water displacement was too large (approximately 500mL), despite a significant correlation between the two readings ($r=0.97-0.98$). Therefore, both methods were reliable but they were not interchangeable.

Taylor et al (2006) followed with a controlled study to test a simplified version of the frustum model, utilising anatomical landmarks, fixed intervals and water displacement. Measurements using anatomical landmarks were the closest to water displacement volumes and this method identified significant differences ($p<0.001$) in the volume in the lymphoedema group. Their findings confirmed that of Sander et al (2002) and Karges et al (2003), which were that circumferential measurements are valid and reliable, but are significantly different from water displacement volumes. Therefore, only one method should be used in a study and for the individual subject.

There have never been two studies which use the same method to calculate volume. The differences are apparent with regards to the limits of measurement, that is whether the hand is included, and the proximal and distal limits of measurement, the intervals used and the mathematical calculation. One argument for smaller intervals is that the arm is not uniformly swollen and therefore these irregularities are taken into consideration. However, it is more time-consuming and thus not feasible in a clinical setting. For example, Mayrovitz et al (2000) measured limb volume from the metacarpal phalangeal joints to the axilla at 4cm intervals, Deltombe et al (2007) measured from the metacarpal shaft to 20cm proximal to the lateral epicondyle at 5cm intervals, and Ridner et al (2007) started proximal to the metacarpals to the axilla at 4cm intervals.

If longitudinal studies were designed with within-participant statistical analyses, then the limits of measurement and measurement intervals would need to be replicated for each subject at reading.

Deltombe et al (2007) compared the reliability of volume measurements, including two circumferential measurement models. One was assuming that the arm was a single truncated cone, and another assuming a series of truncated cones. Both had fair intra- and inter-observer reliability (ICC range 0.93–0.99). However, there was no comparison of the volumes obtained from the two models. Furthermore, the limits of the arm for measurement were different for the water displacement method and circumferential measurement, which prevents any direct comparison between the two volumes. Therefore, the validity of this particular method of measurement could not be commented upon. *Figure 3* illustrates the concept of circumferential measurement to yield a calculated volume.

Perometry

Perometry or infrared optoelectronic volumetry utilises infrared laser on two axes and a receptor that captures the shadow cast (*Figure 4*). Although the instrument is expensive, it only takes five minutes to measure both arms, as opposed to 25 minutes for circumferential measurements. Depending on the make and model of the perometer; the limb volume measurement starts from the fingertip to 40cm from the fingertip (Deltombe et al, 2007), or from the hand to as proximal a point as feasible (Mayrovitz et al, 2000; Ridner et al, 2007). Deltombe et al (2007) found excellent intra- and inter-observer reliability (ICC 0.997), exceeding that of water displacement (ICC intra-rater 0.991, ICC inter-rater 0.987). Perometry is also significantly correlated with circumferential readings (Mayrovitz et al, 2000; Deltombe et al, 2007), thus it is a valid tool. Additionally, Mayrovitz et al (2000) found the readings from perometry to be significantly higher than circumferential calculation. Unfortunately, the two studies subsequently undertaken did not examine the readings from perometry and circumference volume (Mayrovitz

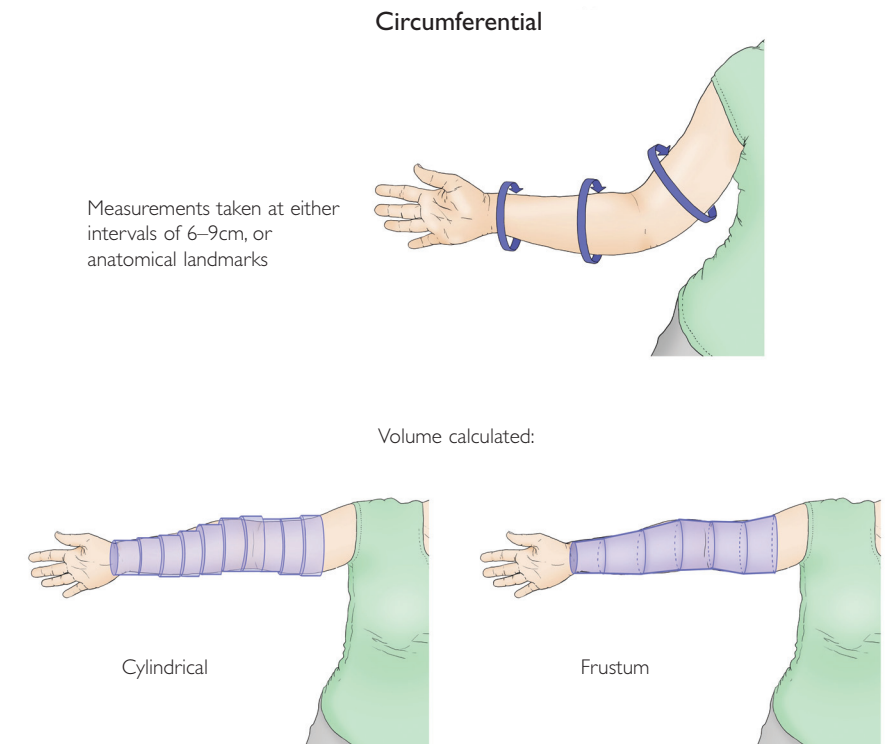


Figure 3. Schematic diagram illustrating calculation of limb volume using circumference measurements.

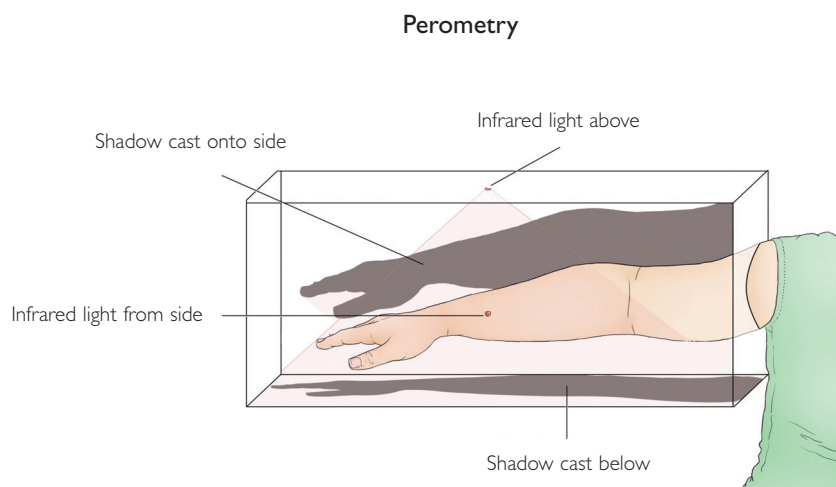


Figure 4. Schematic diagram illustrating the concept of perometry.

et al, 2000; Ridner et al, 2007), and the published data were insufficient to compare the three studies.

Detecting early lymphoedema

Ridner et al (2007) demonstrated that swelling and firmness (self-reported by subjects) in the last year correlated significantly with circumferential and bioimpedance measurements. It has been noted that some patients do report subjective swelling before any manifestation of lymphoedema.

Tassenoy et al (2006) found 8% difference in volume despite the absence of clinical lymphoedema. Imaging techniques, that is ultrasound and magnetic resonance imaging (MRI), and histological examination revealed early signs of lymphoedema. Therefore, subtle differences in total volume or extracellular fluid volume may indicate early lymphoedema. Volume-rendered computer tomography (CT) images have been used in a research setting to calculate volume of a limb (Brorson et

al, 2006). High resolution imaging may seem an obvious choice for accurate, early volume assessment, but it carries with it a high dose of irradiation. It would be impractical, costly and not in the best interest of the subject to be exposed to large amounts of radiation at regular intervals to measure volume.

Bioimpedance measures the resistance to electrical currents, thereby indicating the amount of extracellular fluid in the limb (Figure 5). The resistance is converted into an index score, which reflects volume measurements. Ward et al (2009) found a strong correlation ($r=0.926$) between the bioimpedance index scores and volume measurements by perometry. Warren et al (2007b) demonstrated that bioelectrical impedance detected significant differences in the extracellular fluid ratios of lymphoedema patients and the control group (0.9 vs 0.99, t-test, $p=0.01$). However, the actual range of extracellular fluid level between the two groups overlapped (lymphoedema group 0.67–1.01, control group 0.95–1.02). However, an earlier study by Cornish et al (1998) demonstrated differences in the range of impedance readings in the control and lymphoedema group, although no statistical significance was undertaken due to the small study group. The tool was unable to differentiate between lymphatic and venous oedema as both are extracellular fluid. Therefore, the validity and reliability of bioelectrical impedance is inconclusive. Its validity in non-pitting lymphoedema dominated by adipose and fibrous tissue is not known. Non-pitting lymphoedema with excess adipose and fibrous tissue will have increased volume but may have normal bioimpedance because the extracellular fluid is less than in pitting lymphoedema. Heavy lymphoedema also induces muscle hypertrophy, adding to limb volume (Brorson et al, 2009), but is not taken into account when bioimpedance is measured. Bioelectrical impedance remains a research tool, although its use as a diagnostic tool in the community is under scrutiny (Ridner et al, 2009). Ridner et al (2009) trialled the use of single frequency bioimpedance in the community and found that it could differentiate between normal and lymphoedematous limbs.

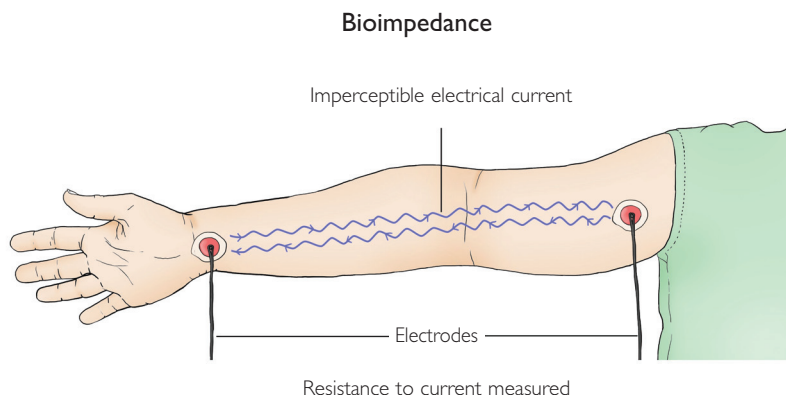


Figure 5. Schematic diagram illustrating the concept of bioimpedance.

However, to use bioimpedance in the community it would need to be portable, fast and easy to use and interpret. One significant advantage in bioimpedance is the ability to measure bilateral limb lymphoedema, for example, the bioimpedance index of bilateral upper limb lymphoedema can be compared to a non-lymphoedematous leg.

The interpretation of early lymphoedema requires close clinical correlation with the investigative findings. If lymphoedema is assessed soon after surgery or radiotherapy, the normal post-treatment swelling could be mistaken for lymphoedema (Piller, 2009). There was no indication in any of the studies quoted how soon after treatment these measurements took place. In order to monitor the development of lymphoedema or measure the response to lymphoedema treatment, pre-treatment readings should be done and followed with regular measurements. In the first few months after breast cancer treatment, swelling of the arm may occur as a result of post-treatment swelling rather than lymphoedema (Piller, 2009). Bioimpedance cannot differentiate between the different types of extracellular fluid, and thus the positive results from bioimpedance testing in the first few months after breast cancer treatment should be treated with caution.

Conclusion

The current methods for upper limb lymphoedema volume assessment are valid with reasonable reliability. Circumferential and water displacement volumes had significantly higher intra-

observer reliability than inter-observer reliability (Deltombe et al, 2007). The reliability scores for these two methods were still reasonable. Due to the variations in practice, if possible and to minimise errors in the study or clinical practice, the researcher or practitioner need to choose the most appropriate method of assessment and be aware of their strengths and weaknesses in order to counter them. For example, if circumferential or water displacement volumes were utilised, it would be prudent to elect one person to obtain the readings to reduce inter-observer error.

Volumetry is the most established method of assessing upper limb lymphoedema. Volume measurements do not provide information regarding the amount of fluid in the tissues. Bioimpedance, on the other hand, determines the amount of extracellular fluid and is an indirect indicator of volume except in fibrotic non-pitting lymphoedema. There still remain many unanswered questions with regards to the clinimetrics of these tools. The sensitivity and specificity of most tools are not known. The responsiveness of these assessments has not been tested and there are no longitudinal studies on upper limb lymphoedema. There is uncertainty as to the performance of these tools in situations such as when there is bilateral lymphoedema and changes in patient body composition due to hormone fluctuations or weight gain. Due to the abundance of tools and the variations in practice, comparisons of similar studies cannot be made and firmer conclusions cannot be drawn. Part

of the problem is the lack of diagnostic criteria for lymphoedema. Without a point of reference of 'normal' or the acceptable limits of difference in volume, it is difficult to be certain of the construct validity especially in early, subclinical lymphoedema. A better diagnostic tool would be to differentiate between post treatment oedema, lymphoedema and normal variation in body composition.

In conclusion, there are valid and reliable tools to assess volume in lymphoedematous upper limbs. However, there are limitations to each method and the choice of tool depends on the subject of investigation. An agreed protocol to reduce variations in practice and standardise measurements should be developed. Specifically for patients with breast cancer, pre-treatment measurements need to be undertaken with sensitivity at a stressful time, and thus methods that are user-friendly, accurate and quick would be more appropriate. **JL**

Acknowledgements

Miss Lucy Hyde, medical illustrator. The work was undertaken as a requirement for the fulfilment of MSc in Wound Healing and Tissue Repair, Cardiff University.

References

- Brorson H, Ohlin K, Olsson G, Nilsson M (2006) Adipose tissue dominates chronic arm lymphedema following breast cancer: an analysis using volume rendered CT images. *Lymphat Res Biol* 4(4): 199–210
- Brorson H, Ohlin K, Olsson G, Karlsson MK (2009) Breast cancer-related chronic arm lymphedema is associated with excess adipose and muscle tissue. *Lymphat Res Biol* 7: 3–10
- Buskirk ER (1959) Underwater weighing and body density: a review of procedures. In: Brożek J, Henschel A, eds. *Techniques for measuring body composition*. National Academy of Sciences. National Research Council, Washington, USA: 90–107
- Clark B, Sitzia J, Harlow W (2005) Incidence and risk of arm oedema following treatment for breast cancer: a three-year follow up study. *Q J Med* 98: 343–8
- Cornish BH, Ward LC, Thomas BJ, Bunce IH (1998) Quantification of lymphoedema using multi-frequency bioimpedance. *Appl Radiat Isot* 49: 651–2
- Damstra RJ, Glazenburg EJ, Hop WCJ (2006) Validation of the inverse water volumetry method: a new gold standard for arm volume measurements. *Breast Cancer Res Treat* 99: 267–73
- Deltombe T, Jamart J, Recloux S, et al (2007) Reliability and limits of agreement of circumferential, water displacement, and optoelectronic volumetry in the measurement of upper limb lymphedema. *Lymphology* 40: 26–34
- Feinstein AR (1983) An additional basic science for clinical medicine: IV. The development of clinimetrics. *Ann Intern Med* 99(6): 843–8
- Greenhalgh T (1997) Papers that report diagnostic or screening tests. *Br Med J* 315: 540–3
- Hauser B (1995) *Practical hydraulics handbook*. 2nd ed. CRC, Florida
- Hayes S, Janda M, Cornish B, Battistutta D, Newman B (2008) Lymphedema secondary to breast cancer: how choice of measure influences diagnosis, prevalence, and identifiable risk factors. *Lymphology* 41(1): 18–28
- Jäger G, Döller W, Roth R (2006) Quality-of-life and body image impairments in patients with lymphedema. *Lymphology* 39(4): 193–200
- Karges JR, Mark BE, Stikeleather SJ, Worrell TW (2003) Concurrent validity of upper-extremity volume estimates: comparison of calculated volume derived from girth measurements and water displacement volume. *Phys Ther* 83(2): 134–45
- King TI 2nd (1993) The effect of water temperature on hand volume during volumetric measurement using the water displacement method. *J Hand Ther* 6(3): 202–4
- Mayrovitz HN, Sims N, Macdonald J (2000) Assessment of limb volume by manual and automated methods in patients with limb edema or lymphedema. *Adv Skin Wound Care* 14: 272–6
- Piller N (2009) Early detection — a strategy to reduce risk and severity? *J Lymphoedema* 4(1): 89–95
- Pyszel A, Malyszczak K, Pyszel K, Andrzejak R, Szuba A (2006) Disability, psychological distress and quality of life in breast cancer survivors with arm lymphedema. *Lymphology* 39(4): 185–92
- Ridner SH, Montgomery LD, Hepworth JT, Stewart BR, Armer JM (2007) Comparison of upper limb volume measurement techniques and arm symptoms between healthy volunteers and individuals with known lymphedema. *Lymphology* 40: 35–46
- Ridner SH, Dietrich MS, Deng J, Bonner CM, Kidd N (2009) Bioelectrical impedance for detecting upper limb lymphoedema in nonlaboratory settings. *Lymphat Res Biol* 7(1): 11–5
- Rumsey N, Clarke A, Musa M (2002) Altered body image: the psychosocial needs of patients. *Br J Community Nurs* 7(11): 563–6
- Sagen A, Kåresen R, Risberg MA (2005) The reliability of a simplified water displacement instrument: a method for measuring arm volume. *Arch Phys Med Rehabil* 86: 86–9
- Sander AP, Hajer NM, Hemenway K, Miller AC (2002) Upper-extremity volume measurements in women with lymphedema: a comparison of measurements obtained via water displacement with geometrically determined volume. *Phys Ther* 82: 1202–12
- Stout Gergich NL, Pfaizer LA, McGarvey C, Springer B, Gerber LH, Soballe P (2008) Preoperative assessment enables the early diagnosis and successful treatment of lymphedema. *Cancer* 112: 2809–19
- Tassenoy A, Vermeiren K, van der Veen P, et al (2006) Demonstration of tissue alterations by ultrasonography, magnetic resonance imaging and spectroscopy, and histology in breast cancer patients without lymphedema after axillary node dissection. *Lymphology* 39: 118–26
- Taylor R, Jayasinghe UW, Koelmeyer L, Ung O, Boyages J (2006) Reliability and validity of arm volume measurements for assessment of lymphedema. *Phys Ther* 86(2): 205–14
- de Vet HCW, Terwee CB, Bouter LM (2003) Current challenges in clinimetrics. *J Clin Epidemiol* 56: 1137–41
- Ward LC, Czerniec S, Kilbreath SL (2009) Operational equivalence of bioimpedance indices and perometry for the assessment of unilateral arm lymphoedema. *Lymph Res Biol* 7(2): 81–5
- Warren AG, Brorson H, Borud LJ, Slavin SA (2007a) Lymphedema. A Comprehensive review. *Ann Plast Surg* 59: 464–72
- Warren AG, Janz BA, Slavin SA, Borud LJ (2007b) The use of bioimpedance analysis to evaluate lymphedema. *Ann Plast Surg* 58: 541–3

Key points

- ▶▶ Water displacement, circumference measurement and perometry are used in clinical practice and are accurate and reliable methods of volumetry.
- ▶▶ The readings obtained from different methods are not interchangeable.
- ▶▶ Bioimpedance determines extracellular fluid and provides an indication of volume.