To measure or not to measure? What and when is the question?

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Measuring limbs and noting patients’ reports tells us about the effects of a disrupted lymphatic system not about changes to lymphatic function. To know something of the latter, the only option is lymphoscintigraphy. Each measurement we make adds something to our knowledge and we must continue to measure as we think best, according to the limitations of our equipment. Our greatest gain will come not from ‘what’ we measure but what and when we measure, with our greatest aim being early detection of subtle changes prior to any clinically discernable phase.

Good understanding of a patient’s lymphoedema or their risk of it is based on accurate and appropriate assessment of their medical, surgical and familial history, as well as taking baseline measures which can provide an indication of structural and functional changes. If we want the holistic picture, we should also examine the impact that lymphoedema has on the patient’s quality of life and activities of daily living.

Such information can inform the targeting, sequencing and type of treatment and management options.

Once in a programme, both the healthcare professional and the patient will benefit from monitoring the treatment or management option in order to see how effective it is. It is important to know if the outcomes are as good as would normally be expected according to previous clinical trials, personal experience or anecdotal information.

One of the great frustrations from the perspective of the healthcare professional (and very often also the patient) is the inability to achieve and show outcomes which are as good as those published in clinical trials. Good measurement may not help reduce these frustrations, but at least it will let you know what is happening and where, and allow you to know and explain why the outcomes are different.

If there is an indication of poor outcomes, the measurements taken might provide an indication of changes to your strategies. Perceived interest from the healthcare professional on the part of the patient may encourage a more enthusiastic and rigorous approach to their self-management.

In deciding what measurement to undertake we have to weigh up many factors, including:

- The time
- The cost of the measure
- The possible inconvenience
- The measure’s sensitivity and specificity.

One of the major issues is that many of the measurements we make are concerned with the effect of a disrupted or damaged lymphatic system, i.e. we record changes to tissue fibre with tonometry, changes to fluids using bioimpedance, and limb circumference and volume changes using perometry. If we wanted, we could go one step further and use fractal analysis of ultrasound or magnetic resonance imaging (MRI). Some healthcare professionals might have access to functional magnetic resonance imaging (FMRI) which can give an indication of how things change with action or activity.

Thus, while we can see what has happened, a softening of the tissues, a reduction in fluids or in the size of the limb and improvements in feeling or movement, we know little of what has happened at the tissue and cellular level to bring about these changes.

Are our measurements wrong?

All of us at some time have observed a patient outcome in which there has been significant reductions in limb size but no change in the patient’s perception of how the limb feels or their movement and use of the limb (or vice versa). There does not necessarily have to be a connection between the objective and subjective measures — but when there is little or none, it begs the question as to why? On other occasions, you might have spent a great deal of time and effort on a particular patient, giving a full intensive complex physical therapy
(CPT) programme, and yet there were no positive outcomes for all your work and the patient’s enthusiasm when you came to measure the limb and ask the patient their perception of its progress.

This prompts the question of whether our measurements are wrong? Are we measuring the wrong parameters, are they appropriate or so inaccurate that they do not reflect what is happening to the lymphatic system?

This will be discussed later in this article since measurements can contribute to a perception of a poor outcome if they are not undertaken correctly. However; as said before, we must acknowledge the key issue that none of the measurements described above measure the functional changes that are occurring in the lymphatic system.

We have no idea about the initial problem of the lymphatic or vascular systems; we are only reading the signs of it.

Ideally, we should gain an understanding of the changes in the functioning of the lymphatic system and look at what is abnormal within it and then find strategies to address this. This is not to say that all of our other measurements are of no value, they are, but the fact that they do not often match each other or come up to our (or our patients’) expectations of a good match each other or come up to our baseline or, at very least, normative values.

The message is then, ‘let’s get functional’ for each new patient (particularly those who have a complex case history) and encourage the use of lymphoscintigraphy to determine better any functional changes to the lymphatic system — the very system we are trying to help and yet often do not bother to collect the information about. In addition, Laser Doppler studies should be used to see what is happening to the vascular system and whether it is a possible contributing factor.

Early detection
If there have been significant functional changes, they will manifest as changes in structure such as fibrotic induration, the composition and volume of extracellular fluids, or in how the limb feels.

What, then, is important if we cannot have access to functional assessment tools such as lymphoscintigraphy? Ideally, we need to be able to detect the changes that result from functional impairment: whether they are quantitative or qualitative, and as early as possible.

To do this well we need a firm baseline or, at very least, normative values.

There can be confusion from the therapist’s perspective as to which measurement will give them the information they need.

There are two patient groups that we need to consider. Firstly, those identified as being at high-risk of developing lymphoedema and, secondly, those with clinically manifest lymphoedema (within its early stages).

In both cases, information about the functional status of the lymphatic system is beneficial; however, the question is what else? This question should be couched from the perspective that time is precious and that it is better to spend it treating rather than making a range of measurements, some of which may only convey limited relevant information and, at worse, may not make a difference to the practitioner’s treatment or the patient’s management plans.

Ridner et al (2007) suggest that the lack of a gold standard of measurement for measuring or detecting lymphoedema is an issue. There are many claims supporting a range of methods but there is not the space to go through these issues in detail in this article, and some of the measurements that a clinician might make will often be decided by the resources available and the time needed to undertake them, rather than what might represent a gold standard.

We tend to focus measurement issues on the measurement of fluid or circumference, or volume or hardness and forget about what the patient can offer us. Armer et al (2003) suggested a case for considering the benefits of ‘measuring’ subjective self-reported symptoms. However; while patients can be the first to observe and report changes, it is often not until the swelling is significant (Ridner, 2005) so, in some respects, even this is an issue requiring better patient education and awareness.

So, what is a good measure that you can take that is simple, easy and will correlate well with those such as perometry and bioimpedance.
Relationships between the measurements

Ridner et al (2007) compared the relationships between four commonly used measurement techniques in healthy volunteers (i.e. those who have had treatment for cancer but have not developed clinically discernable lymphoedema) and those with lymphoedema, namely:

- Self-reported arm symptoms
- Circumference tape measurements
- Opto-electronic perometry
- Bioimpedance (single and multifrequency).

As would be expected due to the similarity of frequency use and of the modelling behind the use of bioimpedance, all such measurements show a strong correlation, suggesting it may not matter whether single or multifrequency techniques are used. Perometry and circumference and calculated volume also correlated well. Cross-correlation between all four techniques showed a relationship but it was not as strong. A similar relationship was shown between perometry and bioimpedance by Moseley and Piller (2005), but while these two methods do measure different aspects of the limb, fluids for bioimpedance and total limb volume for perometry, maybe just one is enough — but which?

It would save a great deal of time for therapists if one could run through a symptom list of newly-arrived patients and use their answers to check whether they have latent lymphoedema (at risk of it) or have it in a mild form. But how reliable would this be; what is its sensitivity and specificity? No one is sure. Those with lymphoedema in the Ridner study (2007) reported more symptoms than the healthy volunteers with no lymphoedema. However, some symptoms such as tenderness, stiffness, and aching were reported by both groups. Thus, we have a problem as obviously some of the symptoms are related to the surgery and/or radiotherapy, not to the presence of lymphoedema (or perhaps the immediate risk of it). Two symptoms did though stand out as being related to circumference measurements and bioimpedance, namely firmness and tightness. Interestingly, heaviness did not feature as has been previously reported (Armer et al, 2003).

Basically, the measurement methods correlated well with each other and with self-reported arm swelling (in the prior year). However, only circumference and bioimpedance correlated with the symptom of arm firmness.

It is hard to say which measurement method is best. There are a couple of important points to consider which may help us decide on this. In part, this will depend on what we need to progress the patient through the treatment programme, and what the patient has indicated they need in terms of feedback. If we are considering publishing the outcomes from our treatment, either as a case study or as part of a clinical trial, that too may influence which measurement might be “best”.

From the point of being able to detect subtle changes in the progression of the limb we are looking at two options:

- Measuring the changes in fluid levels using bioimpedance
- Measuring the impact of these (and other) changes on how the limb’s firmness and tightness is perceived (as an example).

Why bioimpedance over circumference measurements?

Bioimpedance seems to have a greater sensitivity and specificity in detecting changes in the limb (Ward, 2006) than the more traditional circumference measurements, although at the moment bioimpedance is unable to show exactly where the fluid accumulation is in the limb, whereas the 4cm and 10cm measurement intervals (as indicated by many lymphoedema groups and garment manufacturers), can indicate this. Opto-electronic perometry can also do this at intervals of about 4mm, so it is potentially even more accurate in indicating where limb volume (fluid) changes have occurred.

To get the whole picture it seems that we still need the two, bioimpedance and circumference/volume measures in some form.
early interventions, it is likely that more patients will seek methods that address these issues.

A number of simple and easy to use tools and strategies are available that not only detect early changes in the tissues before they can be seen as a change in limb size, but also indicate how a particular treatment is progressing and its effectiveness. The use of tools and techniques to detect lymphoedema before it actually becomes clinically manifest (since presence indicates a lifelong battle) remains crucial for future cohorts of patients.

Let’s now look at some tools and techniques to help us measure the range of changes in tissue structure and function associated with lymphatic system disruption or failure.

**Measurement of fibrotic tissue changes**

One of the first noticeable effects of surgery and radiotherapy is the formation of local or diffuse fibrous tissue. This is part of the tissue repair process, but can also be associated with wound infection. Fibre may significantly reduce the ability of new lymph capillaries and collectors to grow, or prevent existing ones from regenerating. Often, as lymphoedema progresses, so too does the extent and distribution of fibrotic tissue. Tonometry, which is based on measuring the resistance of the tissues to compression, is a good indicator of the extent of underlying fibrosis (Foeldi et al., 1977; Casley-Smith et al., 1993; Bates et al., 1994) (Figures 1 and 2). This method has been in use since 1976 when it was first developed by Clodius et al. It can indicate the degree of fibrosis and the impact of treatment when used over the major lymphatic territories. Tonometry measures the resistance of the tissues above the deep fascia to compression by a standard weight after a given time, and provides a measure which correlates with the extent of fibrotic induration there. With current tonometers (made by Biomedical Engineering [BME] at Flinders Medical Centre), accuracy to 1mm is possible. Variations in fibrotic tissue can be cross-confirmed with ultrasound when it is performed over the same area as tonometry. When fibrotic induration is detected, theoretically, strategies such as low level laser, frictional massage, or special manual lymphatic drainage (MLD) can be used to target it. There are more accurate ways of measuring fibre and its location (i.e. ultrasound, MRI) but they take longer, are expensive, and are out of a practitioner’s control.

There are also simple ways of measuring fibre build-up but these are not quantitative. Firstly, we can palpate the surgical or radio-therapeutic scar area and record the scarring on an arbitrary scale. Secondly, you can pick up the tissues near the middle of the various lymphatic territories and roll them between your thumb and forefinger and see if there are differences between the affected territories and the corresponding normal ones on the contra-lateral limb. You could measure the tissue thickness between your fingers (or use skin fold calipers) and record those values and note their differences. There has been a long-used test called the Stemmer’s sign, in which the skin at the base of the toes or fingers is picked up (or tried to be picked up). A positive Stemmer sign indicates distinct lymphoedema while a negative one indicates none or early stage (Figure 3). This test helps distinguish between lymphoedema and other orthostatic oedemas and is useful in that sense. Perhaps the test of picking up and rolling the tissues of the major lymphatic territories between thumb and forefingers can tell us more about the earlier stages of lymphoedema, if not the latent phase, but its validity and reliability remains to be tested.

**Measurement of fluid content**

One of the early signs of a failure of the lymphatic system is the accumulation of small amounts of extracellular fluids in the affected lymphatic territory. Normally in the early stages, this fluid accumulation is not detectable as an increase in limb volume or circumference, but can easily be detected by low-frequency bioimpedance. With current techniques, it is possible to detect differences and changes in extracellular fluids as little as 3ml, although some outputs, such as those from the ImpediMed units, provide ratios of changes in impedances. To determine a volume difference, mathematical manipulation of bioimpedance data is needed; however, in reality, this is not necessary since the recognition of relative and/or comparative change is just as valuable as absolute estimations. There are a large range of bioimpedance devices available at the moment, but few are specific for lymphoedema. ImpediMed produces the Imp’ SFB7 Bioimpedance Spectroscope’ (BIS) and the handheld Imp’ XCA’ (Figure 4) for lymphoedema assessment and monitoring. Like tonometers, these devices can provide useful information about the subtle changes in the latent phase (non-clinically manifested) of lymphoedema, and of the impact of treatment once it becomes clinically apparent. Understanding the tenets of
bioimpedance is important if we are to better understand what it might offer us (Cornish, 2006). A study by Cornish et al (2001) suggested the BIS was able to predict the onset of lymphoedema up to 10 months before it was able to be clinically diagnosed, so it has some exciting potential. Estimates of sensitivity and specificity were close to 100% (Cornish, 2001; Ward, 2006). It is worth noting that only one of the 20 patients whose lymphoedema was predicted had a clinically measurable circumference and volume difference. For further details of our most recent knowledge and thinking on the benefits of bioimpedance, see the key papers from the symposium on bioimpedance analysis in the management of lymphoedema (Rockson, 2006; Cornish, 2006; Ward, 2006).

Measurement of limb volume and circumference

We have a number of ways to measure limb volume and circumference, as reviewed by Ridner et al (2007). Perometry is suited to larger clinics, while water displacement and/or determination of segmental or whole limb volume by calculation following the use of a tape measure is often easier for smaller ones. All can be equally accurate and reliable, but are dependent on correct use. Perometry, for instance, can discriminate at 1mm for circumferences and to the nearest 10ml for volume. Similar accuracy is possible with water displacement. Both can be used to assess segmental changes in limb volumes, but water displacement needs additional circumference measurements to be made, allowing for cross-checking. We are also able to cross-check fluid volume measurements using bioimpedance with perometry, which measures whole limb volume to see what is changing in the limb, be it solely fluid or perhaps fatty tissues (Moseley et al, 2002).

When tape measurements at specified positions are used, care must be taken to minimise errors in the tension on the tape, the placement of the tape, the distance between measurement sites, and the side of measurement. Excel or other statistical software programmes can be used to calculate volume. Tape measurement is able to discriminate to 1mm but, due to the above variables, 5mm is more realistic. The Australasian Lymphology Association (ALA) has defined a protocol to ensure accuracy and repeatability in measurement using tapes (Figure 5).

Despite this apparent value of circumference measurements there are a number of issues to be considered. These include possible pre-existing differences between limbs, differences due to limb strength dominance and the often assumed error that when a person is ‘left-handed’ in terms of the limb they use for writing, that this is their dominant limb as far as muscularity and strength are determined. We may find it better in the future to ask those at risk of, or with lymphoedema, which is the hand they use to undo or unscrew a lid. This issue and its impact on our decisions to ascribe the diagnosis of lymphoedema (or not) needs further investigation if we are to improve the accuracy and diagnostic worth of limb circumference measures.

Some of these issues have been raised by Hayes et al (2005), who sought to compare objective measures and a self-report measure in terms of their ability to yield prevalence estimations of lymphoedema. It must be made clear that in all estimates of prevalence, it is the definition of what criteria are used to define the lymphoedema that will be a prime factor in point prevalence determinations. Hayes et al (2005) indicated similar point prevalence figures of about 12% with circumference and BIA measurements, but a much higher figure of more than double with self-reported symptoms.

Measurement of functional status of the lymphatic system

The most cost-effective technique to determine the functional status of the lymphatic system is lymphoscintigraphy (Keeley, 2006; Brautigam et al, 1998). It is not cheap, and it is probably best used in patients where the treatment outcome is poor. In such instances, the cost can be worthwhile in terms of the range of information it can provide, including the functional status of the lymphatic system, the location of functional and dysfunctional collectors, and relationships between the deep and superficial lymphatics and areas of dermal backflow. Importantly, the information can be used to help the healthcare professional direct flow to functional pathways (Piller et al, 1998). There are qualitative aspects to lymphoscintigraphy in the interpretation of the location of the radiotracer and its density and distribution, but also quantitative aspects in terms of the rate and time of arrival at specified regions of interest (such as the groin or axilla). Graphs of these events can help determine functional status and repeat measures can show intervention effects (Keeley, 2006). Accuracy is possible to mm/min of travel of the tracer, although most often graphs are compared for slope and tracer counts at specific times at a region of interest. Modi et al (2007) have also been able to show that lymphoscintigraphy is able to indicate lymph collector pumping pressures and contractility. Thus, as our techniques improve, we can build up a an even better functional picture of the lymphatic system.

Figure 5. Accurate measurement is essential even when using a tape measure. These measurements can be used to estimate volume changes.
The accurate and objective use of information from such tools as lymphoscintigraphy can also help to relieve the stress of those who are worried about developing lymphoedema, by indicating the impact of the surgery or radiotherapy, or of their genetics on the lymphatic transport capacity, as measured by clearance of tracer from a injection site and/or its time of arrival at a designated nodal system. If, despite the interventions or genetics, the transport capacity is normal or near normal, with reasonable care and attention the risk of developing lymphoedema will be no greater than a normal individual, thus enabling survivors to ‘get on’ with their lives.

### Measurement of the structural status of the lymphatic system and of the limb

The most effective means of measuring the structural status of the lymphatic system and of the limb itself is by ultrasound. Even if it is only done once and undertaken at established tonometry points, a cross-correlation can be made between this and tonometry to then allow only simple tonometry measurements to be taken in measuring limb fibrous changes. Ultrasound provides information about changes to the thickness of the deep and superficial fascias, and of what has happened between them in terms of fibrous tissue deposition. Again, there are qualitative and quantitative aspects to this data, with the measurement of thicknesses and depths resulting in an accuracy of 1 mm. Of course, MRI and similar techniques offer greater accuracy and certainty, but cost often precludes their use.

### Measurement of the status of the vascular system

It is clear that there are often significant changes to the vascular inflow and outflow patterns. Laser Doppler and other strategies such as fractal ultrasound allow these to be determined and responded to. The recent work of British and other researchers (Stanton et al., 1999) indicate that perhaps we should be paying more attention to changes in the vascular system inflow and outflow of a limb at risk, or one affected with lymphoedema. It seems that increased blood flow into the limb may contribute to swelling just as much as changes in blood capillary filtration pressure due to venous congestion, and that these add to the problems of the impaired lymph drainage system. This is an interesting but still emerging area where we may find some leverage points to help achieve better outcomes for our patients.

### Evaluation of symptoms

Lymphoedema involves more than just a swelling of the tissues (Morgan, 2005; Amer and Ramati, 2002; Ridner, 2005). Its symptoms (even in the early stages) include heaviness, tension, aches and pains, significant impact on quality of life and degree of ability to perform activities of daily living. For some patients, it is this which is important, even more so than the size of the limb or its range of movement. If we are going to help a patient cope with their problem from an holistic perspective, we must also undertake measurement of these and other subjective parameters using visual analogue and other scales. There are a range of simple and validated test instruments available. Using them allows us to evaluate the impact of the condition on a patient, their quality of life and their ability to carry out daily activities, while also offering a chance to discuss these factors with the patient and orient treatment towards improving those which are the most problematic (Ridner, 2005).

Often in lymphoedema, one of the first impacts of treatment is on how the limb feels, followed by its softening, then perhaps subtle changes in the levels of extracellular fluids, and lastly, a change in volume or circumference. Detection and response to these changes not only help the healthcare professional in determining the impact of their treatment, but can also be used to show the patient that change is occurring that the treatment from the healthcare professional is working or that what they (or their partner) is doing to manage the limb is working. Patients often suffer treatment fatigue and it is important to give them continued feedback concerning lymphoedema management and treatment strategies.

We have an obligation to collect as much objective patient information as possible from the moment they enter our sphere of influence until they are adequately treated and placed within an ongoing management programme. This information should be collected accurately and appropriately to build up the most inclusive picture of the issues affecting the patient, which can be used to assess progress and communicated to other healthcare professionals in the team, advancing research and individual knowledge.

### When our measures don’t match each other’s or the patient’s comments

Lymphoedema is a complex interplay of changes within and between the blood tissue lymph systems. Most often, unless we are part of a large multidisciplinary clinic, we cannot hope to be able to measure all of those changes and interactions. In the main (in the simplest sense), we must remember we are measuring the outcomes of a failure of the lymphatic system and not the failure itself (unless we have access to lymphoscintigraphy). Even though we might measure with the best tools and look at the signs of lymphatic failure at each of the stages of lymphoedema, it is difficult to capture the spectrum of these changes and specifically target those that might be influencing the ache in the axilla of the limb, or the tension in one of the lymphatic territories.

While subjective comment and objective measurement do show in some instances a relationship, and that some patient indicators are better than objective measures in terms of knowing about the lymphoedema, we cannot be always sure (or even often) of causality. Patients are able to finely discriminate changes (or differences) in their perception of the limb and how it feels or what they can do with it. We possibly do not as yet have the ability to be that sensitive or specific with our testing.
Another issue is that of the measurements themselves. Tonometry and ultrasound will give a surrogate measure of changes to fibre content only at the point(s) where it is measured. Circumference measures will tell us what happened at those points. Perometry can tell us about limb volume changes and circumference changes every 4 mm — but only for the parts of the limb we can measure (usually not the hand, or near the roots of the extremity, where often changes can be significant). Bio-impedance can currently measure whole limb changes (although some research-based equipment can measure local area changes). Thus, while we currently have been able to show some correlations between these different measurement techniques, they are all measuring different changes in the tissues, some from the whole limb perspective and others locally.

We should acknowledge this and work to better integrate the measurements but also continue to work towards the development of even better measures and methods which are representative of both local area and total limb change.

We do not and need not measure every parameter of the limb every time, but take measures which will inform us and the patient about the limb’s status or progress under treatment.

We need to be clear about what the measurement is able to tell us and if that relates to the function or dysfunction of the lymphatic system, or if its about the changes which have occurred as a consequence of these lymphatic system changes.

References