

EARLY DETECTION — A STRATEGY TO REDUCE RISK AND SEVERITY?

Despite changes in surgical techniques, radiotherapy targeting and the apparent earlier detection of cancers, secondary lymphoedema is still a significant problem for about 20–30% of those who receive treatment for cancer, although the incidence and prevalence does seem to be falling. The figures above generally relate to detection of an enlarged limb or other area, but it seems that about 60% of all patients also suffer other problems with how the limb feels, what can or cannot be done with it and a range of social or psychological issues. Often these 'subjective' changes occur before the objective ones, such as a change in arm volume or circumference.

For most of those treated for cancer lymphoedema does not develop immediately, and, while about 60–70% develop it in the first few years, some do not develop lymphoedema for up to 15 or 20 years. Those who will develop clinically manifest lymphoedema in the future are, for some time, in a latent or hidden phase of lymphoedema.

There also seems to be some risk factors which are indicators for a higher likelihood of lymphoedema post treatment, including oedema at the surgical site, arm dominance, age, skin conditions, and body mass index (BMI).

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Sometimes a person presents who appears to have a swelling on the operated side, but when the right questions are asked it is discovered that that is their dominant (or stronger) arm in the first place (and thus naturally has more muscle and a greater circumference and volume even without anything having been done). Sometimes patients are sent along an unnecessary treatment pathway with unnecessary anxiety due to an incorrect diagnosis of lymphoedema.

Irrespective of this, some person's arms are different in size, volume and ability long before any cancer has been detected. 'Arm dominance' is often misunderstood and listed as the hand with which a person writes. However, it is their strength or muscular dominance that is of interest. A similar situation can apply for the legs in terms of dominance.

NP

What are likely to be the best measurement options to detect pre-clinical lymphoedema, or the risk of it developing at some later stage?

VK: At present the two best measurement options seem to be limb volume and bioimpedance.

Limb volume can be calculated from circumferential tape measurements but its reliability has been questioned, with particular respect to inter-observer variation. While this may not be too important when this technique is used clinically to monitor the response to treatment of a significantly swollen limb, it may not be sensitive enough to detect small changes which may indicate early lymphoedema in a minimally swollen limb. In addition, when using the 'unaffected' limb as a control, there are difficulties in defining what constitutes 'established' lymphoedema, e.g. >10%

excess volume (Hayes, 2008), and this is further complicated when the impact of limb dominance is considered (as described in the introduction). Nevertheless, taking measurements pre-operatively and comparing these with subsequent recordings may facilitate the early detection of changes.

Indeed, in the ALMANAC trial using this method (Mansel, 2006), the identification of early arm swelling (4–5%) predicted that 53% of such cases would subsequently develop lymphoedema (defined by an arm swelling of ≥ 2 cm circumference) by 18 months, whereas 6% arm swelling at three or six months predicted 60% of lymphoedema cases at 18 months of follow-up.

The use of an optoelectronic volume measuring device (e.g. the perometer) may improve the accuracy and reliability of limb volume measurements and, therefore, may be more predictive, but these devices are not readily available in most hospitals in the UK and may not represent a practical proposition.

There is evidence that changes in bioelectrical impedance may be more sensitive in the early diagnosis of lymphoedema following surgery for breast cancer (Cornish et al, 2000). Again, comparing pre- and post-operative measures seems to be the best approach to this. Furthermore, one company has developed a bioimpedance index (L-DexTM, Impedimed Inc). The normal range of this index is based on a study of a population of healthy women and an abnormal result is defined as 3 standard deviations from the means (L-Dex >10). At present, devices to measure bioimpedance are not routinely available but could represent a useful way forward.

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- VK:** At present the two best measurement options seem to be limb volume and bioimpedance.
- TR:** I interpret best as being what is most available at village level, where the effective tools used in well-equipped centres are unaffordable.
- SH:** ... bioimpedance spectroscopy is developing a track record that demonstrates it meets the necessary research and clinical criteria...
- SR:** The greatest hope for predicting lymphoedema may reside in as yet undiscovered biomarkers or genetic polymorphisms...

effective tools used in well-equipped centres are unaffordable. There is no better tool than carefully questioned, listened to and recorded history-taking. If the listener is told that the cancer, the surgeon or the radiotherapist focused on lymph nodes, it is reasonable to suspect secondary lymphoedema will be a consequence. If one is told that there is immobility, lack of elevation or movement, symptoms of heart failure, a history of deep vein thrombosis or limb trauma, or if there is a story of recurrent cellulitis, then it is likely that there is lymphoedema secondary to overload.

SH: When deciding which method(s) are optimal, several factors must be considered, such as the accuracy, sensitivity, and specificity of the measure, whether the measure has been shown to detect 'subclinical' lymphoedema (before patients report symptoms), and whether the measure is affordable, transportable, practical for clinic use, non-invasive and time-efficient. While measurement of arm volume (particularly by measuring limb circumferences) predominates as the measure of choice in the research literature and clinical practice (Langbecker et al, 2008), bioimpedance spectroscopy is developing a track record that demonstrates it meets the necessary research and clinical criteria, particularly for diagnosing arm lymphoedema following breast cancer (Hayes et al, 2008a, b).

SR: It is possible to argue that detecting 'pre-clinical lymphoedema' and determining who is at risk of developing lymphoedema at a later stage are two different questions, with different answers that require the use of different scientific and clinical approaches. Let us start by addressing the first part of this question, about the best measurement options to detect 'pre-clinical lymphoedema', which for purpose of

this answer I will define as swelling yet unnoticed by either patient or practitioner. I would suggest that there is no 'gold standard' best method. The choice of method is dependent upon many factors, such as the anatomical segment of the body that you need to measure (e.g. limb vs head or neck) and resources available to clinicians.

Anatomical location: There may be several 'acceptable' methods for limb lymphoedema, most of which involve some variation of volume or impedance measurement (Ridner et al, 2007). Unfortunately, for areas such as the head and neck, there may not be any proven effective measurement method, and photography may be a reasonable 'measurement' option, if you are able to store or retain patient photographs in the medical record to allow for comparisons over time (Lymphoedema Framework, 2006).

Resources available to clinicians: infrared scanning devices and bioelectrical impedance devices, while excellent measurement methods, are costly. Many treatment centres may not have access to them, particularly in rural and similarly underserved areas. So, the question is, can we set as a universal standard the use of these devices? Probably not. In some cases, tape circumferential measurements may be best, if use of this low-tech approach ensures measurements can and will be done routinely. Developing and using a standardised procedure for measurement in a practice setting is key, regardless of which method the setting chooses to use.

The second part of this question concerns how to best predict the risk of developing lymphoedema at some point of time after trauma to the lymphatics has occurred. The greatest hope for predicting lymphoedema may reside in as yet undiscovered

biomarkers or genetic polymorphisms, that are common to those who develop secondary lymphoedema and uncommon in those who do not. At this time, we are unable to reliably predict this.

When is the best time to undertake these measurements?

VK: As stated above, a baseline measurement pre-operatively is ideal with subsequent measurements taken at the time of follow-up appointments, e.g. at three months, six months, one year, 18 months, etc. It is recognised that most patients who develop lymphoedema will develop it in the first few years. In the UK, routine breast cancer follow-up is often limited to three years by specialist breast cancer clinics (National Institute of Clinical Excellence [NICE], 2002), so the detection of later onset lymphoedema is likely to have to rely upon subjective reports by patients.

TR: Wound healing responses such as inflammation and scarring take a year to settle. Measurements of swelling should not be interpreted as certainly lymphatic failure until after that time.

SH: We know from work involving women with breast cancer that the majority of lymphoedema cases (70–80%) occur within the first 12 months post-cancer diagnosis, with up to two-thirds of cases occurring by six months post-diagnosis (Clark et al, 2005; Hayes et al, 2008b). Therefore, integrating a lymphoedema assessment during routine follow-up visits would seem beneficial for tracking lymphoedema status. However, there are two important caveats: (1) if lymphoedema is assessed too early following surgery or radiation treatment, there is the risk of misclassifying normal post-treatment swelling as lymphoedema; and (2) taking baseline measurements prior to the start

- VK:** Some symptoms may be related to the cancer treatment rather than lymphoedema *per se*, e.g. heaviness, tightness, aching, stiffness and limited mobility.
- TR:** Human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) and scarification by traditional healers are significant risk factors...
- SH:** Evidence does consistently support increased risk of secondary lymphoedema with more extensive surgery, radiation therapy and other arm symptoms...
- SR:** ... unless there is a plan for post-treatment measurement, pre-treatment measurement provides no added value to patient treatment and is unlikely, in and of itself, to improve patient outcomes.

of any cancer treatment, irrespective of the measure used, significantly aids the ability to detect the development of lymphoedema post-treatment. So, it would seem that a pre-treatment measurement session, followed by assessments at regular intervals starting somewhere between two and six months depending on treatment, may be optimal, with the duration of the interval perhaps increasing after 12 months post-diagnosis.

SR: Some cancer patients at long-term risk for lymphoedema do not experience surgery as their first method of treatment, some have chemotherapy before their surgical procedures. Due to this, any measurement would ideally be performed prior to initiation of any cancer treatment, including chemotherapy. Given the normal variation in limb size and face and neck asymmetry, pre-treatment measurements, or in some cases photography, are needed for all types of at-risk cancer patients. Pre-treatment measurement allows for post-treatment measurements to be compared to the patient's own normative values. However, it is important when conducting post-treatment measurements to have a good understanding of the normal 'healing trajectory' of patients. This is necessary to avoid a 'false positive' diagnosis of lymphoedema. Such 'false positives' can occur when acute swelling/inflammation is mistakenly labelled lymphoedema. This causes the patient unnecessary psychological distress.

Integration of lymphoedema assessment as routine standard care is highly desirable. In terms of post-treatment measurements, measurements are most likely to be done if they take place at all scheduled follow-up appointments. Post-treatment measurement should always use the same method that was used pre-

treatment, although clinicians may want or need to employ additional methods under certain circumstances. The timeframe for post-treatment measurements may be driven by follow-up intervals that vary by the type of cancer and the internal procedures in the healthcare system or setting providing the care. The key point is that unless there is a plan for post-treatment measurement, pre-treatment measurement provides no added value to patient treatment and is unlikely, in and of itself, to improve patient outcomes.

What are the best predictors of outcome, i.e. the risk of developing lymphoedema — objective measures of physical parameters or subjective parameters?

VK: Although there is some evidence that subjective changes in the limb may be associated with fibrosis and other changes in the subcutaneous tissues without affecting limb volume (Tassenoy, 2008), there is other evidence that symptoms alone are not necessarily an accurate indicator of swelling (Kissin et al, 1986). Some symptoms may be related to the cancer treatment rather than lymphoedema *per se*, e.g. heaviness, tightness, aching, stiffness and limited range of movement. These may be as common in patients without lymphoedema as those with (Armer and Fu, 2005).

Physical measures of limb volume and bioimpedance, as described above, may therefore be more helpful.

TR: The risk of developing lymphoedema is detailed in the list of things to avoid which is usually given to the patient. I rate venous overload and recurrent barrier breach by infective organisms or irritants as factors that increase risk. Becoming

obese is definitely to be avoided. Human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) and scarification by traditional healers are significant risk factors in some of the clinics that I have attended in Africa.

SH: The aetiology of secondary lymphoedema seems to be multifactorial, with contributory factors including pre-existing conditions as well as acquired abnormalities (Rockson, 1998). Unfortunately, to date, the nature of the relationships between many patient, treatment and behavioural characteristics, such as age, body mass index (BMI), treatment on the dominant side, socioeconomic status, social support, and participation in physical activity, are inconsistent in the scientific literature (Hayes et al, 2008a; Hayes, 2008). Evidence does consistently support increased risk of secondary lymphoedema with more extensive surgery, radiation therapy, and the presence of other arm symptoms, such as pain, numbness, stiffness, etc (Hayes et al, 2008b; Hayes, 2008).

However, even these consistently reported characteristics do not alone distinguish who will and who will not get lymphoedema, or who will have problems with upper-body function. For example, in the breast cancer setting, those who have sentinel lymph node biopsy are at lower risk of developing lymphoedema, but some of them still may get it, and the prevalence of arm symptoms is high even among women who never develop lymphoedema (ranging between 35% for tingling and 62% for numbness). Therefore, lymphoedema is most likely to be diagnosed early when pre-treatment and regular post-treatment assessment occurs, considering the individual patient's treatment and behavioural characteristics, as well as report of additional symptoms.

VK: ... there is a suggestion that a short trial of a compression garment may treat sub-clinical lymphoedema.

TR: One factor that clearly helps in the clinic in India described by Narahari et al (2007) is a supportive family.

SH: The acceptability of treatment strategies to patients may be as important as monitoring compliance or treatment efficacy to successful outcomes...

SR: The evidence base for true prevention of lymphoedema is virtually non-existent and research is greatly needed in this area.

SR: Right now, we simply do not know how to 'predict' which patients are the most likely to develop lymphoedema after cancer treatment, or for that matter, after any other traumatic injury that damages the lymphatic system. We think that, for certain cancer patients, the more extensive the treatment (e.g. more lymph nodes removed, mastectomy vs lumpectomy), the more risk patients have for developing lymphoedema (Ridner, 2002). It is also possible that comorbid conditions such as age, obesity, cardiac problems, and inflammatory disease may be associated with lymphoedema (Ridner and Dietrich, 2008), but longitudinal studies are needed to shed further light on these relationships.

Changes over time in objective physical measurements, such as volume or impedance values, may help us detect lymphoedema earlier. Regarding subjective parameters, such as patient reported symptoms, I would argue that some symptoms, such as self-reported new onset swelling, or new or different sensations in the arm may be warning signs of developing lymphoedema. Even though breast cancer patients may have odd feelings in their arms with no identifiable swelling, a change in symptoms, in any at-risk individual should never be ignored and should trigger further assessment.

Unfortunately, however, neither objective measures of physical parameters nor subjective parameters truly 'predict' lymphoedema onset or risk. They can tell us if changes have happened that may cause major problems for our patients. The value of that knowledge should not be underestimated.

What is the evidence from long-term follow-up of patients who have signs of sub-clinical lymphoedema

that its early detection and subsequent intervention (to reduce the risk through education awareness, etc) make any difference to the likelihood of clinically manifest lymphoedema developing?

VK: Much of the current risk reduction guidance is aimed at avoiding further damage to the lymphatic system in the 'at risk' limb, e.g. by avoiding trauma and minimising the risk of infection as much as possible. Unfortunately, there is little evidence to support the validity of this advice and whether it helps to prevent lymphoedema developing (Hayes, 2008).

Other, more interventionist approaches may, however, also be worth considering. One recent prospective observational study using pre- and post-operative perometer measurements looked at the effect of wearing graduated compression garments on the development of swelling (Stout Gergich et al, 2008). Lymphoedema was defined as a $\geq 3\%$ increase in limb volume compared with the pre-operative measurements (using the contralateral limb as a control). This is a much lower 'cut-off' than is usually used to define lymphoedema and may be considered 'sub-clinical' swelling. Those women meeting this criterion wore compression garments (20–30mmHg compression) for a mean duration of 4.4 (± 2.9) weeks followed by continued use of the garment during exercise or if swelling appeared. Using this approach, a mean arm volume reduction of 4.1% ($\pm 8.8\%$) was achieved (< 0.0001), and this was maintained at an average follow-up of 4.8 (± 4.1) months after the intervention. Although this was not a randomised trial, there is a suggestion that a short trial of a compression garment may treat sub-clinical lymphoedema. Further work on this would help to identify whether such an approach is truly preventative.

TR: In my opinion, more studies are needed to produce such evidence.

I agree with VK and SH but would add that the patient has to struggle to keep up a programme of management. One factor that clearly helps in the clinic in India described by Narahari et al (2007) is a supportive family. The supplement accompanying this issue emphasises the concept of patient participation.

SH: At this time the evidence base for prevention recommendations is limited. There is a clear need for well-designed, population-based, prospective studies to investigate the causal relationship between suggested risk factors and subsequent development of secondary lymphoedema. However, until results from such studies are available, it seems reasonable for healthcare professionals to discuss the rationale and relevance of commonly recommended preventive strategies, but importantly to encourage healthy lifestyle behaviours (Hayes, 2008).

With respect to effectiveness of treatment, evidence supporting the effectiveness of available treatment strategies is graded as poor to satisfactory (Hayes 2008). Nonetheless, treatment guidelines exist, and there is some consistency in outcomes from research. The bulk of evidence demonstrates volume reductions following secondary lymphoedema treatment, particularly when conservative treatment options are used (Hayes, 2008), with the most recent attention being given to the effectiveness of compression in the treatment of subclinical lymphoedema (Stout Gergich et al, 2008). It is also thought that lack of treatment is related to secondary lymphoedema progression, although this too requires further confirmation. However, potential adverse consequences, such as

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TR: The people who benefit most are those who can make the lifestyle adjustments to their condition that are necessary to keep a job...

SH: ...early detection of lymphoedema would clearly lead to significant physical, social, emotional, financial, psychological and functional benefits for the individual.

SR: ... patients may benefit from early detection. If they respond to treatment, infections are reduced, and disease progression is slowed.

financial, time and lifestyle burdens, have also been associated with treatment for secondary lymphoedema (Hayes, 2008) and need to be considered. Therefore, the acceptability of treatment strategies to patients may be as important as monitoring compliance or treatment efficacy to successful outcomes (as defined by reductions in swelling or associated symptoms).

SR: The evidence base for true prevention of lymphoedema is virtually non-existent and research is greatly needed in this area. To be of the greatest value, such research ideally would be experimental in design, with longitudinal follow-up over many years, as lymphoedema can occur decades after treatment. One study, the first attempt to scientifically evaluate this issue, suggests that wearing a compression garment may be helpful in reducing the risk of progression, but this was not a randomised trial and follow-up was not long-term (Stout-Gergich, 2008). Because we do not have data, we do not know if 'latent' lymphoedema progresses (clinically manifests) in all, or only a small percentage of individuals. If 'latent' lymphoedema progresses in all individuals, intervention at this early stage may be highly desirable. If it progresses in only a small percentage of individuals, we face an ethical dilemma. Do we treat everyone with 'latent' lymphoedema as if they have lymphoedema? You might argue, yes, this is the only logical response, and cite as precedent the treating of ductal carcinoma in situ (DCIS) in women. You may say, no, as labelling someone with lymphoedema, who may never become symptomatic, creates undue psychological distress and treating them with compression garments, etc. uses healthcare dollars unwisely. You may use 'watchful waiting', as done with prostate cancer in men, to support this position.

What are the likely health economic aspects of early detection and lymphoedema prevention. Who benefits and by how much?

VK: There is evidence that lymphoedema causes a significant impact on patients' quality of life with a vulnerability to recurrent cellulitis, work implications and psychological morbidity (Moffatt et al, 2003). There is also evidence that treating lymphoedema reduces the incidence of cellulitis (Ko et al, 1998). Therefore, it is likely that the early detection and prevention of lymphoedema is going to reduce this morbidity. The costs of doing this will depend on what type of measurement is employed and whether interventions such as compression garments are required.

TR: The economic benefits include income generation and participation. The people who benefit most are those who can make the lifestyle adjustments to their condition that are necessary to keep a job, or be as active in the community as they were before the onset of disability.

SH: We do know that lymphoedema is a chronic, disabling condition that potentially impacts all aspects of daily life. Based on available evidence to date, approximately 20% of survivors of breast, gynaecological and prostate cancers and melanoma will experience secondary lymphoedema (Hayes, 2008). Therefore, prevention and early detection of lymphoedema (assuming early detection leads to more effective treatment and prevention of disease progression) would clearly lead to significant physical, social, emotional, financial, psychological and functional benefits for the individual which, in turn, would lead to benefits for the family as well as the community. The exact cost:benefit ratio has yet to be calculated and will depend on a number

of assumptions for which good data are not yet available.

SR: We know from a recently published study (Shih et al, 2009) that in a American cohort of breast cancer patients, whose insurance claims were examined for two years after cancer treatment, patients with lymphoedema were more costly to the insurance system than were those without. The excess medical costs were from \$14,887 to \$23,167, and those with lymphoedema were also twice as likely to have lymphangitis or cellulitis than those without lymphoedema. We also know that in this same study, patients with lymphoedema lost more productive days to healthcare office visits than those without lymphoedema (73.1 vs 56.1). So we know, during the first two years after breast cancer treatment, lymphoedema is costly to both healthcare insurance companies that cover some of the expenses and to individuals with the condition. These data suggest that lymphoedema prevention not only would be a substantial cost saving to any healthcare delivery system, but also to those individuals who miss work seeking treatment for the condition. What we do not know, because data is currently unavailable, is if early detection (implying some sort of diagnostic procedure), coupled with early treatment, is less expensive in the long run, than delayed diagnosis and delayed treatment.

Logically, it would seem patients may benefit from early detection. If they respond to treatment, infections are reduced, and disease progression is slowed. They also should benefit if early detection helps reduce their symptom burden and improves quality of life.

The pre-operative measurement of patients is often at a time of turmoil for the patient — is it worth putting the patient under the further pressure of another test?

VK: ...these assessments are likely to be helpful in preventing morbidity and, therefore, it would seem reasonable to offer them to patients.

TR: I see full assessment as a benefit much desired by the patients.

SH: ...patients may feel a sense of reassurance that potential treatment sequelae are being anticipated and monitored...

SR: 'They told me... the chemotherapy could permanently damage my heart and that a risk of anaesthesia was death. Why on earth would anyone think being told about lymphoedema or having my arms measured would be more traumatic than those two things?'

VK: While it is recognised that undergoing treatment for cancer is an extremely stressful time for patients, tests such as limb volume measurements and bioimpedance are relatively quick and non-invasive and should not cause too much of a burden for the patient. The evidence described above is beginning to suggest that these assessments are likely to be helpful in preventing morbidity and, therefore, it would seem reasonable to offer them to patients.

TR: I see full assessment as a benefit much desired by the patients, who appreciate the time spent and a detailed examination of their problem.

SH: Dealt with properly, there is no reason why including a lymphoedema measure into the mix of other pre-operative measures should create more pressure for the patient. In fact, patients may feel a sense of reassurance that potential treatment sequelae are being anticipated and monitored in a manner that enables early identification and, therefore, management.

SR: A research participant with lymphoedema once discussed with me her anger that lymphoedema was not discussed with her before her treatment and her absolute inability to understand why her arms were not measured at that time (she had a full cardiac work-up pre-treatment) and on every follow-up visit. She reported that she had asked her surgeon about this and was told, 'I don't like to upset patients before surgery about this (lymphoedema), I don't want you to decide not to have surgery because of this (lymphoedema).' The woman then said, 'They told me, before I ever had any treatment, the chemotherapy could permanently damage my heart and that a risk of anaesthesia was death. Why on earth would anyone think being told about lymphoedema or having my arms

measured would be more traumatic than those two things? Or, that I would not have cancer treatment because of it? For goodness sake, I am not an idiot.' If you use the multitude of available non-invasive measurement methods, the actual time involved in this is minimal. If you properly educate the patient about the risk and need for early identification of lymphoedema, this should not be traumatic and, yes, it is worth it.

Most of the parameters we measure (whether physical [limb size] or subjective [pain, tension, etc]) are signs of a failing lymphatic system. The only way to measure the functional status is by looking at lymphatic transport using lymphoscintigram. This process has both risks and benefits. Is a pre/or post-operative/post-radiotherapy lymphoscintigram likely to be of benefit in high risk patients?

VK: While some centres advocate the use of lymphoscintigraphy pre-operatively, e.g. to determine appropriate management such as microsurgery (Campisi, 2004) this is not routine practice in most. In the UK, lymphoscintigraphy, when available, is mainly used as a diagnostic tool and as a qualitative investigation (Keeley, 2006). Sometimes qualitative lymphoscintigraphy is reported as 'normal' even in the presence of mild lymphoedema. Quantitative lymphoscintigraphy may, however, be more helpful. Pecking et al (1996) developed a 'functional index' which was abnormal in the arms in 7.5% of 428 women studied before breast cancer surgery. In those who had an abnormal functional index, 84.4% went on to develop clinical lymphoedema within 34 months of surgery and radiotherapy.

Quantitative lymphoscintigraphy requires standardised techniques and is not widely available in the UK. In the above study, only 7.5% of patients had abnormal findings pre-operatively and, at present, it is not known whether these could have been detected by other methods such as bioimpedance. Currently, there does not seem to be sufficient evidence to warrant the routine use of lymphoscintigraphy pre-operatively.

TR: This tool, as Pecking et al (2004) stated, 'is the most advanced method for assessment of the lymphatic system'. It provides important information, so where it can be accessed it should be encouraged. However, most of the world's needy cannot access it.

SH: Sufficient evidence exists to demonstrate that less invasive measures, such as bioimpedance spectroscopy, provide accurate, sensitive and specific measures of lymphoedema status, particularly when pre-operative measures are available (Clark et al, 2005; Rockson, 1998; Ward et al, 2001). Furthermore, unlike lymphoscintigraphy, the time and cost of assessing lymphoedema by bioimpedance spectroscopy makes it feasible for integration within clinical practice. In the future, there may be benefit for conducting lymphoscintigraphy for a small subset of women, but currently we do not know how to identify the group of women for whom this might be worthwhile.

SR: It seems ironic that we are concerned about 'putting the patient under the pressure of another test' as we discuss the pros and cons of measurement, that the only functional test available is also the one most likely to cause the patient the largest amount of stress and highest possibility of risk of adverse side-effects. To determine the value of this test, it seems we should

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TR: This tool, as Pecking et al (2004) stated, 'is the most advanced method for assessment of the lymphatic system'.

SH: Sufficient evidence exists to demonstrate that less invasive measures provide accurate, sensitive and specific measures of lymphoedema status.

SR: 'What would a pre-treatment lymphoscintigram tell us about our patient that we don't already know?'

first ask, 'What would a pre-treatment lymphoscintigram tell us about our patient that we don't already know?' In most cases, it will tell us that their lymphatic system is functioning well enough to ensure that they do not have lymphoedema. I would argue that is something we should already know if we are conducting adequate pre-treatment medical histories and physical examinations on our patients. A medical history that reveals no pre-existing lymphoedema, an absence of patient reported symptoms of lymphatic failure (swelling, tightness, etc), and no signs of lymphatic malfunction during the physical exam tells us virtually the same thing as the lymphoscintigram.

A lymphoscintigram may give us an idea of baseline functioning, but right now there is no way to know for which patients a baseline may be helpful. Even under the best of circumstances, a pre-treatment lymphoscintigram is only helpful if we later compare baseline to subsequent tests. Additionally, you do not have to have a baseline for comparison to determine, via lymphoscintigraphy, if there are abnormal findings. The risk/benefit ratio currently leans more toward risk than benefit to the patient. Less stressful and less risky methods such as infrared scanning, circumferential, and bioelectrical impedance methods, when taken at baseline and repeated on follow-up visits should be considered as more reasonable and potentially helpful alternatives at this time. **JL**

References

Armer J, Fu MR (2005) Age differences in post-breast cancer lymphoedema signs and symptoms. *Cancer Nurs* 28(3): 200–7

Campisi C (2004) Italian Society of Lymphangiography Guidelines. *Eur J Lymphol Related Problems* 12(40): 2–12

Clark B, Sitzia J, Harlow W (2005) Incidence and risk of arm oedema following treatment

for breast cancer. A three-year follow-up study. *QJM* 98: 343–8

Cornish BH, Bunce IH, Ward LC, et al (1996) Bioelectrical impedance for monitoring the efficacy of lymphoedema treatment programmes. *Breast Cancer Res Treat* 38: 169–76

Cornish BH, Chapman M, Thomas BJ, et al (2000) Early diagnosis of lymphoedema in postsurgery breast cancer patients. *Ann N Y Acad Sci* 904: 571–5

Cornish BH, Chapman M, Hirst C, et al (2001) Early diagnosis of lymphoedema using multiple frequency bioimpedance. *Lymphology* 34: 2–11

Hayes S (2008) Review of research evidence on secondary lymphoedema: incidence, prevention, risk factors and treatment. National Breast and Ovarian Cancer Centre. Available online at: www.nbocc.org.au

Hayes SC, Cornish B, Newman B (2005) Comparison of methods to diagnose lymphoedema among breast cancer survivors: 6-month follow-up. *Breast Cancer Res Treat* 89: 221–6

Hayes SC, Janda M, Cornish B, et al (2008a) Lymphoedema secondary to breast cancer: How choice of measure influences prevalence rates and identifiable risk factors. *Lymphology* 41: 18–28

Hayes SC, Janda M, Cornish B, et al (2008b) Lymphoedema following breast cancer: incidence, risk factors and effect on upper-body function. *J Clin Oncol* 26: 3536–45

Keeley V (2006) The use of lymphoscintigraphy in the management of chronic oedema. *J Lymphoedema* 1(1): 42–57

Kissin MW, Querci della Rovere G, Easton D, et al (1986) Risk of lymphoedema following treatment of breast cancer. *Br J Surg* 73(7): 580–4

Ko DS, Lerner R, Kloser G, Cosimi AB (1998) Effective treatment of lymphoedema of the extremities. *Arch Surg* 133(4): 452–8

Mansel RE, Fallowfield L, Kissin M, et al (2006) Randomised multicentre trial of sentinel node biopsy v. standard axillary treatment in operable breast cancer: the ALMANAC trial. *J Natl Cancer Inst* 98(9): 599–609

Langbecker D, Hayes S, Newman B, Janda M (2008) Treatment for upper-limb and lower-limb lymphoedema by professionals specializing in lymphoedema care. *Eur*

J Cancer. Available online at: www3.interscience.wiley.com.ezp02.library.qut.edu.au/journal/119880063/issue

Lymphoedema Framework (2006) *Best Practice for the Management of Lymphoedema*. International consensus. London: MEP Ltd

Moffatt CJ, Franks PJ, Doherty DC, et al (2003) Lymphoedema: an underestimated health problem. *QJM* 96(10): 731–98

National Institute of Clinical Excellence (2002) *Guidance on Cancer Services: Improving outcomes in breast cancer*. NICE, London

Pecking AP, Floiras JL, Rouessé J (1996) Upper limb lymphoedemas frequency in patients treated by conservative therapy in breast cancer. *Lymphology* 29(Suppl): 293–6

Pecking AP, Desprez-Curely JP, Cluzan RV (2004) Isotope lymphography in swollen limbs: anatomical functional methods and clinical significance. *Lymphology* 37(suppl): 567–601

Ridner SH (2002) Breast cancer lymphedema: pathophysiology and risk reduction. *Oncol Nurs Forum* 29(9): 1285–93

Ridner SH, Dietrich M (2008) Self-reported comorbid conditions and medication usage in breast cancer survivors with and without lymphedema. *Oncol Nurs Forum* 35(1): 57–63

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(1): 35–46

Rockson SG (1998) Prescriptating factors in lymphoedema: myths and realities. *Cancer*, 83: 2814–6

Shih Y-CT, Xu Y, Cormier J N, Giordano S, et al (2009) Incidence, treatment costs, and complications of lymphedema after breast cancer among women of working age: a 2-year follow-up study. *J Clin Oncol* Mar 16 [Epub ahead of print]

Stout Gergich NL, Pfalzer LA, McGarvey C, et al (2008) Preoperative assessment enables the early detection and successful treatment of lymphoedema. *Cancer* 112: 2809–19

Tassenoy A, Lievens P, Lamote J (2008) Subjective oedema: does it exist? *J Lymphoedema* 3(1): 73

Ward LC, Piller N, Cornish BH (2001) Single or multiple frequency bioelectrical impedance for the assessment of lymphoedema. Proceedings XI International Conference on Bioelectrical Bio-Impedance, Oslo: 373–6