This item is the archived peer-reviewed author-version of:

Current and future perspectives on the evaluation, prevention and conservative management of breast cancer related lymphoedema : a best practice guideline

Reference:

Gebruers Nick, Verbelen Hanne, De Vrieze Tessa, Vos Lore, Devoogdt Nele, Fias Lore, Tjalma Wiebren.- Current and future perspectives on the evaluation, prevention and conservative management of breast cancer related lymphoedema : a best practice guideline
European journal of obstetrics and gynecology and reproductive biology - ISSN 0301-2115 - Amsterdam, Elsevier science bv, 216(2017), p. 245-253
Full text (Publisher's DOI): <https://doi.org/10.1016/J.EJGRB.2017.07.035>
To cite this reference: <http://hdl.handle.net/10067/1449750151162165141>

Accepted Manuscript

Title: Current and future perspectives on the evaluation,
prevention and conservative management of breast cancer
related lymphoedema: a best practice guideline

Author: Nick Gebruers

PII: S0301-2115(17)30369-X
DOI: <http://dx.doi.org/doi:10.1016/j.ejogrb.2017.07.035>
Reference: EURO 10005

To appear in: *EURO*

Author: Hanne Verbelen

PII: S0301-2115(17)30369-X
DOI: <http://dx.doi.org/doi:10.1016/j.ejogrb.2017.07.035>
Reference: EURO 10005

To appear in: *EURO*

Author: Tessa De Vrieze

PII: S0301-2115(17)30369-X
DOI: <http://dx.doi.org/doi:10.1016/j.ejogrb.2017.07.035>
Reference: EURO 10005

To appear in: *EURO*

Author: Lore Vos

PII: S0301-2115(17)30369-X
DOI: <http://dx.doi.org/doi:10.1016/j.ejogrb.2017.07.035>
Reference: EURO 10005

To appear in: *EURO*

Author: Nele Devoogdt

PII: S0301-2115(17)30369-X
DOI: <http://dx.doi.org/doi:10.1016/j.ejogrb.2017.07.035>
Reference: EURO 10005

To appear in: *EURO*

Author: Lore Fias

PII: S0301-2115(17)30369-X

DOI: <http://dx.doi.org/doi:10.1016/j.ejogrb.2017.07.035>

Reference: EURO 10005

To appear in: *EURO*

Author: Wiebren Tjalma

PII: S0301-2115(17)30369-X

DOI: <http://dx.doi.org/doi:10.1016/j.ejogrb.2017.07.035>

Reference: EURO 10005

To appear in: *EURO*

Received date: 24-2-2017

Revised date: 2-6-2017

Accepted date: 28-7-2017

Please cite this article as: Tjalma Wiebren. Current and future perspectives on the evaluation, prevention and conservative management of breast cancer related lymphoedema: a best practice guideline. *European Journal of Obstetrics and Gynecology and Reproductive Biology* <http://dx.doi.org/10.1016/j.ejogrb.2017.07.035>

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Title Page:

Current and future perspectives on the evaluation, prevention and conservative management of breast cancer related lymphoedema: a best practice guideline

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Condensation: This guideline provides the best practice approach for the management of breast cancer related lymphoedema. Practices are motivated based upon the best evidence available. Future perspectives in BCRL-management are discussed.

Abstract

Breast cancer (treatment) related lymphoedema (BCRL) puts a high burden on breast cancer survivors after breast cancer treatment. Despite a decreasing incidence of BCRL, its prevalence still increases due to the improved survival after breast cancer treatment. However, lymphoedema is a debilitating, chronic and progressive condition that affects patients' daily life and quality of life (QoL). Although an international consensus treatment is established for primary as well as secondary lymphoedema, patients are often undertreated; excluding an optimal result for many patients.

The current guideline combines the best available evidence to provide a best practice approach for the management of BCRL. This guideline is limited to the multidisciplinary, conservative treatment of chronic BCRL.

List of Abbreviations

BCRL Breast cancer (treatment) related lymphoedema

SLN(B) Sentinel lymph node (biopsy)

ALND Axillary lymph nodes dissection

QoL Quality of Life

CPT Complex physical therapy

CDT Complex decongestive therapy

MLD Manual lymphatic drainage

Key-words:

Breast Neoplasms; Lymphoedema; Guideline; Review; Management; Treatment

Introduction

Breast cancer is the most common malignancy in women worldwide, with increasing incidence almost every year.^{1,2} One out of 8 women in industrialized Western countries will be diagnosed with breast cancer at some stage of their life.³ Despite efforts limiting complications after breast cancer treatment, many patients still develop complications, such as axillary web syndrome, numbness, loss of range of motion, pain, scapular winging, fatigue and lymphoedema.⁴⁻⁸ Although breast cancer (treatment) related lymphoedema (BCRL) incidence has considerably decreased, it still remains the most feared complication (see figure 1) because of its chronicity. To limit the burden of BCRL, several efforts have been made to reduce the invasiveness of breast cancer surgery and adjuvant therapies leading to a vast decrease of BCRL. The pooled incidence of BCRL of the upper limb is 16.6% and ranges from 11.8 – 53.5% or 0 - 15.8% for ALND- and SLN- procedures, respectively.^{9,10} Unfortunately, BCRL is not limited to the arm but can also extend to the trunk and breast. The latter is known as breast oedema, which is gaining relevance due to the recent increase in patients receiving breast conservative surgery. Breast oedema is difficult to diagnose, mainly because it is ill-defined, and therefore the reported range is broad (0-94%).⁵ Despite its decreasing incidence, the prevalence of BCRL patients still increases due to the steady increase in survival after breast cancer treatment to a 5-year survival of 85% or more at present.¹¹

Given the facts that 1) BCRL cannot be prevented entirely by means of a post-surgery exercise or physical therapy protocols¹²⁻¹⁴, 2) BCRL will deteriorate when untreated¹⁵ and 3) will affect patients' quality of life (QoL)^{16,17}; an effective treatment needs to be provided for these patients. Commonly this treatment is conservative in nature.¹⁸ Surgical treatments (see Smile et al., 2016, Table 3, p8-10) are also reported but are NOT part of the present guideline.¹⁹ The conservative treatment (see figure 1) is called the Complex Physical Therapy (CPT) or Complex Decongestive Therapy (CDT) and is commonly accepted as the consensus treatment.¹⁸ CDT combines different therapeutic modalities such as 1) Manual lymphatic drainage (MLD), 2) compression (bandages or compression garments), 3) exercises and 4) skin care. In CDT two treatment phases are distinguished. First, the intensive

phase aims at maximally reducing the oedema volume. Second, the maintenance phase aims at conserving the oedema reduction.¹⁸

For the current best practices guideline, we will focus on chronic BCRL only. Chronic BCRL is defined as an oedema that is present at least for 3 months after treatment.

To provide a clinical guideline, different systematic literature searches were performed based on the methodology described by Meeus & Gebruers.²⁰ Different searches, using the PICO(S) system^{21,22} and evidence based approaches²³⁻²⁵ were performed in (bibliographic) databases (Pubmed/Medline, Web of Science, Cochrane database). The reported levels of evidence are based upon the guidelines provided by <http://www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009>.

Management of BCRL

Early detection, diagnosis and definition

In general practice, extensive anamnesis and physical examination guide the diagnosis of BCRL, which are, if necessary, complemented by lymphoscintigraphy, CT, MRI or a lymphofluoroscopy (also known as Near Infrared Imaging).^{26,27}

Within the physical examination, measurement of the excess volume of the oedematous arm is crucial in the BCRL diagnosis. Many definitions for the excess arm volume are used in scientific studies as well as in clinical practice. The most common are a 5%, 10%, 20%, 200ml or 2cm difference measured between the oedematous and the non-oedematous arm. Obviously, the use of different definitions in different studies greatly influence the reported BCRL incidence rates.²⁸ Additionally, many patients report lymphoedema symptoms without an obvious arm volume excess (referred to as subjective oedema). Therefore, we suggest the following adaptations to the current practice. **First**, when comparing arm volumes, the hand dominance of the patient should be taken into account (see

table 1). The volume of the non-dominant hand/arm is on average 3.3% smaller than the dominant hand/arm.²⁹⁻³¹ **Second**, preoperative measurements should be included. Assessing the volumes of the hand, forearm and upper arm separately will provide additional information on volume differences and volume distributions. Fortunately, when preoperative measurement are lacking, prediction formulas can be used to calculate the normal volume of the oedematous hand/arm (see table 1).^{28,29} **Third**, clear and internationally accepted definitions of arm volume excess should be used. Taking into account the hand dominance correction, the following definitions should be used: 1) < 5% difference means no or limited oedema, 2) 5-10% difference is mild oedema, and 3) > 10% difference is obvious BCRL.³² Therefore, in clinical practice a volume difference of 5-10% between both arms should be closely monitored and treatment should be started. Additionally, a 3% change in comparison to baseline measurements³³ of the same arm within 3 months after surgery is an important indication for closely monitoring the patient, since it is a significant risk factor for progression to a >10% volume change.³⁴ **Fourth**, when a patient reports common BCRL related symptoms but objective oedema based on the above definitions cannot be established, additional clinical tests are warranted and should be performed to exclude any lymphatic aetiology (by lymphoscintigraphy and/or lymphofluoroscopy)^{26,35}, or other pathology such as shoulder related problems (by clinical examination of the shoulder).³⁶

Currently, water displacement protocols are still the gold standard for obtaining objective volume measurement of the arms.^{29,37} Although circumference measurements correlates well with water displacement, this correlation is not absolute because of the large margin of error for circumference measurement (which relies on geometric formulas) which can result in a consistent over- or underestimation of the volume.³⁷⁻⁴⁰ As such, the methods are not interchangeable. Therefore, during patient follow up the therapist should rely on one of both methods for monitoring arm volume changes. Early detection of BCRL is important as with early start of treatment, its duration can be limited. Merely comparing the arm volume with pre-operative measurements is insufficient to detect

lymphoedema since changes in body weight can influence arm volumes significantly. Therefore, additionally comparing volumes of both arms is mandatory.

Water displacement tests and circumference measures can detect an objective change in volume, but do not provide information on the perceived severity of the BCRL nor on the impact of BCRL on patients' life. Therefore additionally, questionnaires should be used that assess the oedema within the ICF framework. The LYMPH-ICF is a well-established lymphoedema specific questionnaire and is recommended.⁴¹ In addition, more generic QoL questionnaires like SF-36, McGill-QoL, among others can be used.^{16,42}

The pooled incidence of BCRL is 16.6%, and the peak incidence of BCRL is at 18 and 24 months after surgery for ALND or SLNB respectively. As such, it is important to monitor patients for an extensive follow-up period.^{9,10,43} During follow up it is recommended to pay special attention to patients with a higher risk for developing BCRL. Risk factors (table 2) are divided into treatment-related risk factors, patient-related risk factors and disease-related risk factors. **Treatment-related** risk factors with level 1a evidence are ALND (compared to SNLB)^{9,44}, mastectomy (compared to breast conserving therapy or lumpectomy)^{9,45-47} and a higher number of lymph nodes dissected.^{9,48,49} Risk factors with level 1b-2b of evidence are chemotherapy and radiotherapy.^{46,47,50-52} Mainly taxane-based chemotherapy including docetaxel increases the risk of developing lymphoedema.^{47,53-55} Radiotherapy of the supraclavicular area and the use of a posterior axillary boost increases the risk of developing BCRL.^{47,51-53} The AMAROS-trial has demonstrated that lymphoedema occurs more often after surgery compared to radiation therapy.⁵⁶ ALND combined with axillary radiotherapy is also associated with more lymphoedema compared with patients who were treated with ALND or axillary radiation therapy alone.⁵⁶ **Patient-related** risk factors are a high body mass index with a BMI $\geq$ 30 (level 1b), not participating in regular physical activity (moderate level of evidence) and large post-operative weight fluctuations (level 3a).^{9,48-50,57} A **disease-related** risk factor with level 2a of evidence is the presence of metastatic lymph nodes.⁹ Several studies have shown a higher incidence rate of lymphoedema for

patients with an advanced stage of breast cancer.⁴⁵⁻⁴⁷ Still the evidence on other risk factors such as age, race, education, hand dominance, blood pressure and comorbidities is **inconclusive**. Several of the reported risk factors are reversible and need to be taken into account in the aftercare programme of breast cancer patients for preventing lymphoedema. Patients should be well informed and aware about their BCRL risk and they should be informed about when to contact their physician/surgeon/oncologist, etc.

Current conservative treatment of BCRL and its evidence

Complex Decongestive therapy (CDT)

As mentioned above, CDT consists of four main pillars: manual lymphatic drainage (MLD), compression (bandaging and/ compression garments), exercises and skin care.^{18,27} CDT is a combination therapy and is provided to the patient in two consecutive phases: an intensive phase for maximal oedema volume reduction is followed by the maintenance phase aiming at the conservation of the lean volume.

CDT as a combination therapy is effective (level 2a) in reducing the oedema volume.^{58,59} However, as demonstrated in the systematic review of Smile et al. 2016, in most studies follow-up periods were often limited.^{19,60} Additionally, only few studies report on the maintenance phase. Overall, these studies provide evidence (level 2b) for the use of flat knit compression garments, exercise and skin care to maintain a lean volume.^{61,62} It is essential that compression garments are replaced often enough (at least every 3 to 4 months). Moreover, in more recent studies the effectiveness of MLD cannot be statistically proven and as such MLD seems not to be clinically beneficial in CDT.⁶³⁻⁶⁵ Therefore, the different pillars will be discussed separately in the following sections.

Manual Lymphatic Drainage (MLD)

MLD is a skin to skin (no oils or creams are used) massage technique that aims at improving the lymphatic transport as well as the uptake of interstitial fluid by the lymphatic system. Despite the different “Schools of MLD” (Vodder, Leduc, Casley-Smith, Földi, ..) with their own specific methodology, a traditional MLD provided to the patient starts with draining or clearing the lymph nodes at the root of the lymphatic system followed by the drainage of the oedematous area. For the upper limb the MLD starts at the neck and supraclavicular area, next the axilla and thorax are drained. Subsequently, the oedematous arm is drained proximally to distally. Although MLD is one of the oldest therapeutic modalities used for the treatment of lymphoedema, its effectiveness is still debated internationally. In 2015 the conclusions of a Cochrane review were that MLD was safe but had only an added value of 7% in the reduction of BCRL. As such, the need for more randomized trials was emphasized in the review by Ezzo *et al.*⁶⁶ Recently two new Randomized Controlled Trials (RCTs) have demonstrated the lack of an additional effect of 30 minutes of MLD in combination with compression and exercise therapy for BCRL.^{64,65} Therefore, sound evidence is present to omit MLD from the CPT/CDT. However, an important statement concerning MLD in the treatment of BCRL is that to date MLD was administered blindly (without any knowledge of the patient-specific lymphatic transport) to the patients. Nowadays, it is possible to visualize, by means of lymphofluoroscopy, the superficial lymphatic architecture of a patient.³⁵ Combining lymphofluoroscopy with MLD might still be effective, but evidence needs to be established which will be further discussed in the ‘future perspectives’ section.

Compression

During the intensive phase of CDT, several types of compression modalities are used. It is important that the compression modality is easy to adjust to the decreasing lymphoedema volume. This is most commonly achieved by the use of short-stretch multilayer bandages.⁶⁷ Bandages (see figure 3) should be applied with a high static stiffness, low resting pressure and high working pressure to assure the

effectiveness (level 2b)⁶⁸ and comfort of the bandages. For upper limbs initial sub-bandage pressures in supine position of 45 mmHg are effective and are reported as comfortable by the patients.⁶⁹ It is important to take into account the pressure loss over time in multilayer bandages. For the upper limb it has been demonstrated that >30% of the initial pressure is lost after 2 hours of wearing.⁷⁰ Therefore, it is recommended to reapply the bandages at regular moments during the day. Self-bandaging by the patient is a valuable tool to achieve maximum oedema volume reduction.

During the maintenance phase, bandaging can be continued. However, more often compression garments are provided to the patients. Compression garments consist of an arm sleeve provided with or without a glove and/or a compression shirt/bra (see figure 4). Compression garments for lymphoedema are flat-knit with high static stiffness indexes. Mostly, class II (mean pressure 23-32 mmHg) or III (mean pressure 34-46 mmHg) are used for BCRL. All mean pressures are determined in vitro, therefore an assessment of sub-sleeve pressures is warranted for every individual patient. To provide the most appropriate sleeve for every patient a close collaboration between the patient, therapist, surgical appliance retailer/orthopaedic worker and supplier is essential. Because of the wear and tear of a compression sleeve it is important to frequently assess its effectiveness. If an insufficient pressure (or pressure distribution) is measured, the sleeve needs to be replaced. Every sleeve should be custom made based on adequately taken measurements of the upper limb to assure proper pressure, fitting and comfort.

The aim of compression garments is to maintain a lean volume. Therefore the effectiveness of compression garments is best expressed in its ability to prevent swelling which was demonstrated in a large cohort with prospective follow-up. Patients wearing compression garments had a risk reduction (level 2b) of 61% for a volume increase of 10% when compared to patients wearing no compression garments or bandages.⁶¹

Exercise is an important pillar in the treatment of BCRL. There is sufficient level Ia evidence concerning the beneficial effects of aerobic exercise as well as resistance training for BCRL.^{14,71-76} Despite the evidence in favour of exercise therapy many BCRL patients still believe they should avoid intense physical activity. When surveyed, up to 70% of breast cancer patients reported to avoid strenuous activities. Additionally, patients vulnerable to BCRL development were even more likely to avoid strenuous activities.^{77,78} Because of this wrong general perception in breast cancer survivors and BCRL patients that strenuous activities will induce or exacerbate lymphoedema, it is very important that therapists provide their patients with correct information about exercise therapy and resistance training: it is possible to perform physical activities, even strenuous ones, and **exercise therapy is very beneficial** in the treatment of BCRL. Improving the use of muscle pumps will stimulate the lymphatic transport, and improving the overall physical endurance and strength will lead to a better physical condition and coping.^{71,72,79} However, in reluctant patients with a probable fear-avoidance belief, a graded activity approach is recommended.^{80,81} In this way, patients will experience the beneficial effects of training, be convinced of the safety of performing exercises, and are more likely to incorporate exercise therapy into their treatment.

At this stage of the therapy, guided self-management is imperative. Due to the chronicity of the condition, treatment adherence (to exercise therapy as well as the wearing of compression garments) remains a large hurdle to overcome. As demonstrated by Bourke et al., patients with a sedentary lifestyle previous to the diagnosis of cancer (mainly breast cancer studies) will not change their behaviour after treatment.⁸² As such, unsupervised exercise programs lack effectiveness (level 1b) to achieve at least 150 minutes of aerobic exercise and two sessions of resistance training per week. Therefore an individually supervised approach with independent exercises is warranted in previous sedentary patients to achieve sufficient adherence to being physically active.⁸²

Skin care aims at maintaining a healthy skin barrier. Due to the lymphoedema, the structure of the skin may change. As such, patients with BCRL should be instructed about wound prevention. Table 3 provides an overview of evidence based and common sense practices. Although most prevention programs and information given to the patients rely on common sense, the scientific evidence is less unequivocal. As demonstrated in the systematic review of Asdourian et al, some practices cannot be confirmed as truly detrimental, e.g. taking blood pressure or air travel do not seem to provoke lymphoedema or exacerbate the existing lymphoedema. However, infections, sauna use, and skin puncture on the ipsilateral arm were found to be risk factors for aggravating oedema.^{83,84} In a recent large cohort study, only infections, BMI ≥ 25 and ALND were related to a higher risk for exacerbating lymphoedema.⁸⁵ Therefore the overall advice should be to use common sense and be strict when necessary; namely: avoiding infections, maintain healthy BMI, be careful with extreme temperatures, and avoiding skin punctures in the affected arm as much as possible.

Self-management

In the maintenance phase, the same therapeutic modalities as provided in the intensive phase (MLD, compression, skin care, exercise) are continued, but the main responsibility of the treatment lies with the patient. During this phase, self-management of the treatment by the patient becomes key, and (self)-MLD and (self)-bandaging should be taught to the patient or a caregiver. The adherence to the compression therapy, skin care and regular physical activity remains very important in the maintenance phase.⁶²

It should be noted that the maintenance phase is lifelong and poses a serious treatment burden on the patient. Although the self-management in itself is not difficult, many patients fail to adhere. Several studies have shown adherence to self-management to be sub-optimal with only 50% of the patients reporting sufficient self-management.^{86,87} Risk factors associated with decreased adherence for self-management in BCRL are psychological issues (anxiety, depression, distress, negative self-

identity), (psycho)social factors (social isolation, perceived social abandonment), low self-efficacy and false perceptions & beliefs concerning BCRL.⁸⁸ In addition to the aforementioned risk factors, financial impact of the treatment should not be underestimated. In most countries the reimbursement for BCRL treatment is inadequate and imposes a threat for patients with an insufficient income. Nevertheless, it is important to increase patients' engagement and empowerment so that they can take an active role in their treatment and have an adequate understanding of their condition and plan of care. This requires education, clear instructions, motivating and coaching of the BCRL patients by their therapists. When the patients experience positive results from their self-care routine they will be motivated to continue to perform self-management. However, some patients are difficult to persuade to self-management; in that case different behavioural approaches can be used to achieve self-management.⁸⁹⁻⁹¹

Future perspectives

As mentioned earlier, lymphofluoroscopy or near infrared fluorescence imaging is a technique that has emerged into the field of lymphology.⁹² The use of lymphofluoroscopy might be beneficial in reducing the risk of BCRL and could change current MLD application. First, with lymphofluoroscopy an Axillary Reverse Mapping (ARM) procedure can be performed, by which the axillary lymph flow is mapped from the breast as well as from the ipsilateral arm.^{93,94} It was demonstrated that the risk for BCRL after surgery can be reduced by performing ARM during breast cancer surgery.⁹³ However, these results should be confirmed by well-designed RCTs. Second, lymphofluoroscopy might change current MLD practice. Currently, MLD is performed blind, without any insight in the patient-specific lymphatic architecture. With the introduction of lymphofluoroscopy the superficial lymphatic architecture can be visualised which can guide the therapist in providing an optimal oedema drainage (see figure 5). In addition, the current MLD manoeuvres are still evolving and subject to study. Recently, Belgrado et al. have introduced the "Fill& Flush" technique, which applies higher

pressure and a provides a more direct manipulation of the skin to improve lymph transport.²⁶

Whether the addition of lymphofluoroscopy guided MLD is beneficial in the combination therapy of CDT needs to be further established. Currently, the EforT-BCRL trial (<https://clinicaltrials.gov/ct2/show/NCT02609724>), a multi-centre RCT designed to answer this specific question, is ongoing.

Today, we rely on a combination therapy to treat BCRL. However, recent studies have demonstrated that a comparable treatment outcome can be obtained by omitting MLD from the CDT without reducing its effectiveness.^{64,65,95} Further adjustments of the CDT should be studied in adequately designed RCT's. Additionally, monitoring patients that are at risk for developing BCRL becomes more and more important. If the onset of BCRL can be detected in a very early stage, its treatment will likely be less cumbersome for patients as well as therapists and social security. Stout-Gergich et al., demonstrated that monitoring and providing an compression sleeve when a 3% increase was established was an effective (level 2b) approach to treat BCRL.³³

Conclusion

The current guideline is based on the latest scientific evidence concerning the evaluation, prevention and conservative treatment of BCRL. It should be stressed that to improve BCRL treatment outcome, breast cancer patients need to be informed about their risk for developing BCRL and its prevention, as well as adequately monitored to ensure an early detection of BCRL.

As unstandardized definitions of BCRL hamper its treatment and follow up, in the current guideline we propose standardized diagnosis of BCRL, based on objective arm volume assessment (water displacement, circumference measures) in combination with questionnaires that assess the impact of BCRL on patients' quality of life.

Currently, the best practice towards the management of BCRL is a combination therapy (CDT), provided by a multidisciplinary team, which is organised in two phases (intensive and maintenance phase). Especially during the maintenance phase, sufficient guidance and coaching should be provided as treatment adherence is a challenge for all BCRL patients in this phase. If necessary, behavioural approaches should be used to increase adherence to self-care.

New treatment protocols for BCRL are currently studied. It has been shown that BCRL can be treated by more time-efficient protocols. New imaging techniques such as lymphofluoroscopy could result in a change in the way MLD is used. However, a radical change in the conservative approach for BCRL is not expected for the next 3 to 5 years; until the results of the ongoing RCT's can be presented.

Acknowledgements

We gratefully thank dr. Lies Durnez for proofreading and correcting this manuscript. Her expertise in academic writing has helped us significantly in the completion of this manuscript.

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Example of how to depict the pictures concerning BCRL

Figure 1: examples of breast cancer treatment related lymphoedema.

Patient 1: Oedema on the right forearm with normal hand. Patient 2: Oedema of the entire left arm including the hand. Patient 3: oedema of the right forearm and hand.

Figure 2: Consensus treatment based upon the International Society of Lymphology consensus document

Example how to depict the pictures of the short stretch bandaging

Figure 3: Compression bandage for BCRL including the fingers

A compression bandages consists of different layers. First a tubular cotton sleeve (A) is fitted to protect the skin of the patient. To protect the joints (wrist and elbow predominantly) cotton wool paddings (B) are used. Next short stretch bandages (C) are applied to fingers, hand and arm. At least two layers of short stretch bandaging are used for the hand and arm. Both layers are applied in opposite direction, this manner of bandaging secures a better fitting of bandages. Bandages are fixed by means of medical tape.

Example how to depict the picture of the compression glove

Figure 4: Example of a compression class II or III sleeve and glove provided for a patient with BCRL

The compression sleeve and glove are made by flat knit technology and based upon strict measurements made by the medical supplier. The glove is often worn on top of the sleeve. This enables fast and easy removal of the glove when necessary.

Example of how to depict the pictures of the mapping based upon lymphofluoroscopy

Figure 5: Example of a lymphatic mapping of the superficial lymphatic network in a BCRL patient

Patient A: the larger area on the forearm, elbow crest and the first part of the upper arm are oedematous. The lines with arrows provide information about the actual lymphatic drainage in this patient. As depicted in the ventral view collectors drain towards the axilla. From the axilla there is a rerouting towards the supra-clavicular area. Additional drainage is provided from the scar area towards the sternum and a dorsal route to the supra clavicular area is also present (dorsal view).

Patient B: only the upper arm and axilla were oedematous. Normal lymphatic architecture with functional lymph collectors was found in the hand and forearm. Pathological architecture was demonstrated for the upper arm, especially the medial part of the upper arm towards the shoulder. A drainage route on the frontal side of the thorax was demonstrated (not on the picture).

Table 1: Prediction formulas for upper limb volumes based upon normative data with respect to gender and hand dominance.

Prediction statement	Prediction formula ($\pm$ prediction interval)
Prediction right arm volume (right handed male)	$=0.995(\text{volume left arm}) + 116.79 \text{ ml}$ ($\pm 181.25 \text{ ml}$)
Prediction left arm volume (right handed male)	$=0.964 (\text{volume right arm}) - 1.5 \text{ ml}$ $\pm 179.62 \text{ ml}$
Prediction right arm volume (right handed female)	$=0.979 (\text{volume left arm}) + 96.66 \text{ ml}$ ($\pm 148.66 \text{ ml}$)
Prediction left arm volume (right handed female)	$=0.991 (\text{volume right arm}) - 33.33 \text{ ml}$ ($\pm 148.10 \text{ ml}$)
Prediction right arm volume (left handed male or female)	$=0.949 (\text{volume left arm}) + 88.66 \text{ ml}$ (± 227.69)
Prediction left arm volume (left handed male or female)	$=1.001 (\text{volume right arm}) + 43.97 \text{ ml}$ ($\pm 234.22 \text{ ml}$)

These prediction formulas are used to determine the normal volume of an oedematous arm. Step 1 is to measure the volume of the normal control arm. Thereafter this volume is used to determine the normal volume of the “at risk” arm. By adding the prediction interval one can establish whether the ‘at risk arm’ has a larger volume than normal.

Table 2: Information for patients at risk of BCRL

1. Identify patients at risk
Treatment-related risk factors (refs 9,44-56): <ul style="list-style-type: none"> - ALND vs. SLNB - ALND vs. axillary and periclavicular RT - Mastectomy vs. BCS - Greater number of lymph nodes dissected - Crossover between ARM and SLN - Chemotherapy - Radiotherapy
Patient-related risk factors (refs 9,48,49,57): <ul style="list-style-type: none"> - BMI - Large post-operative weight fluctuations - Not participating in regular physical activity
Disease-related risk factors (refs 45-47): <ul style="list-style-type: none"> - The presence of metastatic lymph nodes - Advanced stage
2. Preventive treatment of patients at risk
Early detection of symptoms <ul style="list-style-type: none"> - Systematic monitoring of patients at risk - Recognition of symptoms <ul style="list-style-type: none"> • Heaviness of ipsilateral arm or breast

<ul style="list-style-type: none"> • Tension of ipsilateral arm or breast • Perceived swelling of ipsilateral arm or breast • Pitting possible of ipsilateral arm or breast •
Skin care recommendations and precautions
Weight control (maintaining or gaining a normal BMI)
Exercises (stimulation of the muscle pump)

Based upon the above provided risk factors patients should be instructed about their risk for BCRL. Next, all patients should be informed about the preventive actions they can perform themselves. It is important that all members of the multidisciplinary team inform the patients in a uniform way.

Table 3: Skin care practices

Skin care recommendation/precautions/practice for the lymphoedematous arm (refs 78,79, 84)	
Preventing infections (cellulitis, erysipelas)	<i>Avoid trauma</i>
	Use anti-bacteriological soap when necessary
	Use medical manicure
	<i>Avoid skin punctures, infusions and blood draws</i>
	<i>Treat wounds immediately</i>
Skin integrity	Use emollients to maintain a healthy skin
	Maintain or achieve a healthy/normal BMI
Heat	<i>Avoid sauna visits</i>
	Protect skin from sunburn
Pressure	Wear appropriate clothing and bra
	Avoid (blood) pressure cuffs
	Avoid tourniquets
Air travel	Wear your compression modality (bandage or sleeve)
Skin changes that need treatment	<i>Papillomatosis</i>
	<i>Hyperkeratosis</i>
	<i>Xerosis cutis</i>
	<i>Fungi</i>
	<i>Maceration in skin folds</i>

Recommendations *in italic* are recommendations supported by scientific evidence. All other recommendations that rely on common sense.