BMJ Open

Study protocol for a 10-year prospective observational study, examining lymphoedema and patient-reported outcome after breast reconstruction

Cecilie Mullerup Laustsen-Kiel ,[1] Elisabeth Lauritzen,[1] Linnea Langhans,[1] Tine Engberg Damsgaard[1,2]

To cite: Laustsen-Kiel CM, Lauritzen E, Langhans L, *et al*. Study protocol for a 10-year prospective observational study, examining lymphoedema and patient-reported outcome after breast reconstruction. *BMJ Open* 2021;**11**:e052676. doi:10.1136/bmjopen-2021-052676

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2021-052676).

Received 21 April 2021
Accepted 01 November 2021

[1]Department of Plastic Surgery and Burns Treatment, Rigshospitalet, Copenhagen, Denmark
[2]Institute of Clinical Medicine, University of Copenhagen Faculty of Health and Medical Sciences, Copenhagen, Denmark

Correspondence to
Cecilie Mullerup Laustsen-Kiel; cecilie.m.kiel@gmail.com

ABSTRACT

Introduction Over the last decades, treatment of breast cancer has become increasingly more effective. Consequently, an increasing number of women are living with late effects of breast cancer treatment, including disfiguring scars, deformity or asymmetry of the breast, secondary lymphoedema and other physical and psychosocial late effects. Data from this study will provide knowledge on how to guide breast reconstruction in the future towards outcomes with fewer complications, higher long-term quality of life (QoL) and satisfaction with the aesthetic outcome. The development of secondary lymphoedema, for which the effect of breast reconstruction has yet to be established, will be thoroughly examined.

Methods and analysis Women receiving breast reconstruction (autologous and implant based) at the Department of Plastic Surgery and Burns Treatment, Rigshospitalet, will be invited to participate. The patients will be followed for 10 years postoperatively. Demographic, health-related, oncological characteristics and treatment data will be registered. Validated assessment tools, such as the BREAST-Q and Beck Depression Inventory, will be used to measure an extensive range of clinical outcomes, including QoL, life and aesthetic satisfaction and depression. Arm range of motion will be measured with a goniometer and lymphoedema by bioimpedance spectroscopy, compared with circular arm measurements.

Ethics and dissemination This study will be conducted according to the 5th version of the Helsinki Declaration. The regional ethical committee for Capital Region Denmark did not find the study notifiable, according to the law of the committee § 1, part 4. All data will be anonymised before its publication. This study will be conducted according to the Danish data protection regulation and is catalogued and approved by the Capital Region Head of Knowledge Centre. According to the Danish health law § 46, part 2, this study does not need the Danish Patient Safety Authority's approval. The findings of this study will be submitted to international peer-reviewed journals.

Strengths and limitations of this study

- This study is the first prospective study that aims to collect extensive data covering the entire pathway for all patients receiving breast reconstruction, including both objective and subjective measures and outcomes for the different breast reconstruction methods, which will provide us with the knowledge to guide future breast reconstruction towards outcomes with fewer complications, higher long-term quality of life and satisfaction with the aesthetic outcome.
- Using a 10-year follow-up, time-dependent changes in both objective measurements of lymphoedema and changes in patient-reported outcomes after reconstructive surgery will aid both patients and surgeons in decision-making.
- The Danish healthcare system is free with equal access for all patients, which prevents selection bias due to a low patient income.
- A focus group will help write patient information to increase recruitment, help improve retention and minimise loss to follow-up.
- We expect to initially include 200–300 breast reconstructions per year, with a quick expansion to other hospitals, and share this knowledge on breast reconstruction in the Danish Breast Cancer Cooperative Group-database.

INTRODUCTION

Background and rationale

Breast cancer is the most common cancer in women worldwide, with a lifetime risk of almost 10% and more than 17 million disability-adjusted life-years on a global scale.[1 2] Breast cancer treatment has become more effective,[3 4] improving the 5-year relative survival rate from 79% in 1999–2003 to 88% in 2014–2017.[5 6] Improvement in survival rate and risk-reducing surgery in BRCA1 or BRCA2 mutation carriers[7–12] leads to an increasing number of women suffering from late effects following surgical treatment. In the past two decades, there has been a growing awareness of these late effects, including disfiguring scarring, a missing breast, deformity or asymmetry of the breasts, lymphoedema, sensory disturbances, and other physical and

psychosocial late effects. Studies have demonstrated that aesthetic satisfaction and minimal breast asymmetry are strongly associated with improved quality of life (QoL),[13] whereas pronounced breast asymmetry has been associated with poor psychosocial functioning.[14]

Breast reconstruction

Studies have shown that women experience a better body image, improved QoL and less intrusive thoughts about cancer and death after receiving a breast reconstruction.[13] According to the Danish Breast Cancer Cooperative Group (DBCG), all patients should be informed about the possibility of a delayed reconstruction within 2 years after having mastectomy performed,[15] thereby integrating breast reconstruction as part of the treatment for breast cancer. Moreover, immediate breast reconstruction is also considered an integrated part of breast cancer treatment[16]

In Denmark, a study from 2015 showed that 40% of women treated for breast cancer with a mastectomy underwent breast reconstruction.[17] A report from the Agency for Healthcare Research and Quality found a 67% increase in the ratio of breast reconstructions to mastectomies between 2009 and 2014, confirming that the number of women receiving breast reconstruction is increasing.[18] Breast reconstruction can be performed as immediate or delayed and consists of implant based or autologous reconstruction, or a combination of these methods, where the most common type of implant-based reconstruction is a two-stage reconstruction using tissue expander/implant.[19]

Multiple options are available when it comes to autologous reconstruction, including; the pedicled latissimus dorsi flap (LD) with or without an implant, deep inferior epigastric artery perforator flap, transverse abdominal musculocutaneous flap (pedicled or as a free flap), and gluteal and upper thigh-based flaps.[20] Previous studies have found superior aesthetic outcomes and patient satisfaction for autologous reconstruction compared with implant-based techniques and,[21–24] a study by Jagsi *et al* found that satisfaction is related to the type of reconstruction and exposure to radiation.[24]

The timing of breast reconstruction has been investigated in several studies, and immediate breast reconstruction has been found favourable compared with delayed reconstruction when looking at the psychosocial impact and the economic aspect.[25–30] After breast reconstruction, complications are a significant risk factor for dissatisfaction with the aesthetic outcome. However, complication rates after breast reconstruction vary largely in the literature ranging from 5.8% to 52%,[22 31–33] and there is no consensus on whether immediate or delayed reconstruction has the highest rate of complications.[13 32] Inadequate tissue perfusion is directly related to early complications in reconstructive procedures,[34] and the incidence of skin necrosis after mastectomy has been found to be relatively high, ranging from 10% to 20%,[35] suggesting a need for a reliable method to estimate the perfusion.[35]

Studies indicate that indocyanine green angiography-angiography of the mastectomy flaps is a valuable tool in evaluating the intraoperative perfusion and predicting healing of the skin,[36 37] but it is not used routinely.

Late effects of breast cancer surgery

Other significant late effects of breast cancer surgery include decreased range of motion (ROM) and lymphoedema. ROM after breast reconstructive surgery is previously investigated[38–40]; though, a systematic review and meta-analysis from 2018, focusing on ROM after LD flap reconstruction was inconclusive.[41] Lymphoedema is a known late effect of breast cancer, being the most common cause of secondary lymphoedema in the USA.[42] The incidence varies in different studies,[43–45] and a meta-analysis, including data from 72 studies of 29 612 women with breast cancer, found an incidence of 16.6%.[46] Thus far, the effect of breast reconstruction on lymphoedema is not evident. One study found immediate breast reconstruction to be associated with a higher risk of lymphoedema development.[47] Nevertheless, a study by Coriddi found no significant differences in the development of lymphoedema when comparing immediate and delayed breast reconstruction,[48] and a study by Chang found that delayed breast reconstruction with autologous tissue might even reduce lymphoedema already present.[49]

Objective

Assessment of breast reconstructive surgery's effect and added value on QoL, long-term risk of lymphoedema and complications are currently missing. Even though every element is valuable, previous studies often focus on a single parameter rather than the overall picture/conception. The purpose of the study is primarily to examine the impact of different types of breast reconstruction on the development of lymphoedema and shoulder function. The second aim is to gain knowledge on the impact of breast reconstruction on several patient-reported outcomes, aesthetic outcomes and treatment-related complications.

Data from this study will provide us with the knowledge to guide future breast reconstruction towards outcomes with fewer complications, higher long-term QoL and satisfaction with the aesthetic outcome.

METHODS

The study is designed as a 10-year prospective cohort study, chosen for its advantage in assessing causality. Collection of specific exposure details (eg, details on adjuvant therapy, breast reconstruction type, and baseline QoL) will be performed and the relative risk of lymphoedema due to an exposure examined.[50] Inclusion will be initiated by February 2022 to January 2032, and follow-up time will end in January 2042. The data collected will include patients' data, questionnaires regarding QoL, long-term aesthetic satisfaction, measured aesthetic outcome and lymphoedema development.

Outcomes

Primary outcomes

- Does breast reconstruction influence development of lymphoedema?
- Does the type of breast reconstruction affect development of lymphoedema and shoulder function?
- Does the timing of breast reconstruction affect the risk of lymphoedema development and shoulder function?
- When is the onset of lymphoedema in relation to breast reconstruction?

Secondary outcomes

- Does immediate breast reconstruction yield higher short and long-term satisfaction with the aesthetic outcome and QoL compared with delayed breast reconstruction, and are these measures affected by the type of breast reconstruction?
- Is there any correlation between adjuvant therapy and patient satisfaction?
- Do baseline factors such as age, smoking, body mass index (BMI) affect the choice of immediate or delayed reconstruction and the type of reconstruction?
- What is the correlation between tumour size and fear of recurrence for the patient?
- Does the type and timing of breast reconstruction effect;
  - Postoperative complications?
  - Postoperation hospitalisation time?
  - Patient and clinician assessment of the scars measured by the Patient and Observer Scar Assessment Score (POSAS) scale?
  - Development of depression?

Study population: inclusion and exclusion criteria

Inclusion will be from February 2022 to January 2032, and follow-up time will end in January 2042. Patients will initially be recruited in the outpatient clinic at the Department of Plastic Surgery and Burns Treatment, Copenhagen University Hospital, Rigshospitalet. Within a few months, inclusion will start at Odense university hospital and Vejle Regional hospital. The plan is to expand to six university hospitals and two regional hospitals in Denmark within the first 2 years, ensuring more participants.

Inclusion criteria:

- Female patients ≥18 years.
- Eligible for immediate or delayed breast reconstruction.
- Understand enough Danish to comprehend the given information, complete the study questionnaires and provide written informed consent.

Patients eligible for inclusion will receive oral and written information, from either a doctor or a nurse familiar with the study and will be asked to participate in the study. They will be offered a reflection period of at least 24 hours if needed before giving informed consent. Patient consent forms and information about the research project will be developed in collaboration with a focus group of breast cancer patients to secure understandable information on a participant level.

Withdrawal and replacement

Patients included in the study can withdraw consent to participate without affecting the present or future treatment at any time without justification. Patients withdrawing consent will be considered as 'lost to follow-up'.

Data collection

Patients will receive the relevant questionnaires via the electronic system; Research Electronic Data Capture (REDCap).[51 52] The questionnaires consist of validated patient-reported outcome measures, including QoL measures, body image, aesthetic breast satisfaction, satisfaction with life and questions on demographic and health-related characteristics. The timeline for the patient's pathway in the study is outlined in figure 1. Patients will undergo the standard preoperative, peroperative and postoperative procedures and follow-ups according to the department's standard guidelines. Also, patients will be seen at 4 weeks, 4–6 months, 1, 2, 3, 4, 5 and 10 years postoperatively by a doctor, physiotherapist, or nurse familiar with the study. Lymphoedema will be measured with circumferential measurements,[53] as well as a bioimpedance spectroscopy (BIS) system called SOZO (https://www.impedimed.com/products/sozo/)[54]; and categorised according to the International Society of Lymphology staging system,[55] where stage 0 is subclinical lymphoedema, and stage 3 is severe lymphoedema with >40% increase in limb volume.[56] Instead of measuring the arm's volume, BIS uses an electrical current (painless) to scan the upper extremities by measuring the resistance to the current. A goniometer will be used to measure the shoulder ROM of both arms in degrees on a full circle,[57] and graded into a specific scale for ROM, where a deficit from 0% to 5% from full ROM=normal; 6%–15%=mild; 16%–40%=moderate; ≤40% = severe, as previously used in literature.[58] BMI will be measured by a physiotherapist,[57] and the Breast Aesthetic Evaluation Score (BraScore) will be used to evaluate aesthetics.[13] The surgeon will perform standard breast measurements. Patient demographics, preperoperative, perperoperative and postoperative data will be obtained from the electronic patient file (online supplemental table 1), processed and analysed (data will be anonymised). All data will be entered and stored in the REDCap database.

Patient questionnaires

One of the most widely used patient-reported outcomes is the BREAST-Q.[59 60] The BREAST-Q is a validated instrument specific to breast surgery and used in more than 20 000 patients undergoing breast reconstruction.[61] One of BREAST-Q's advantages is that specific modules have been developed for breast reconstruction, which consider the type of breast reconstruction performed. The preoperative modules of the BREAST-Q consist

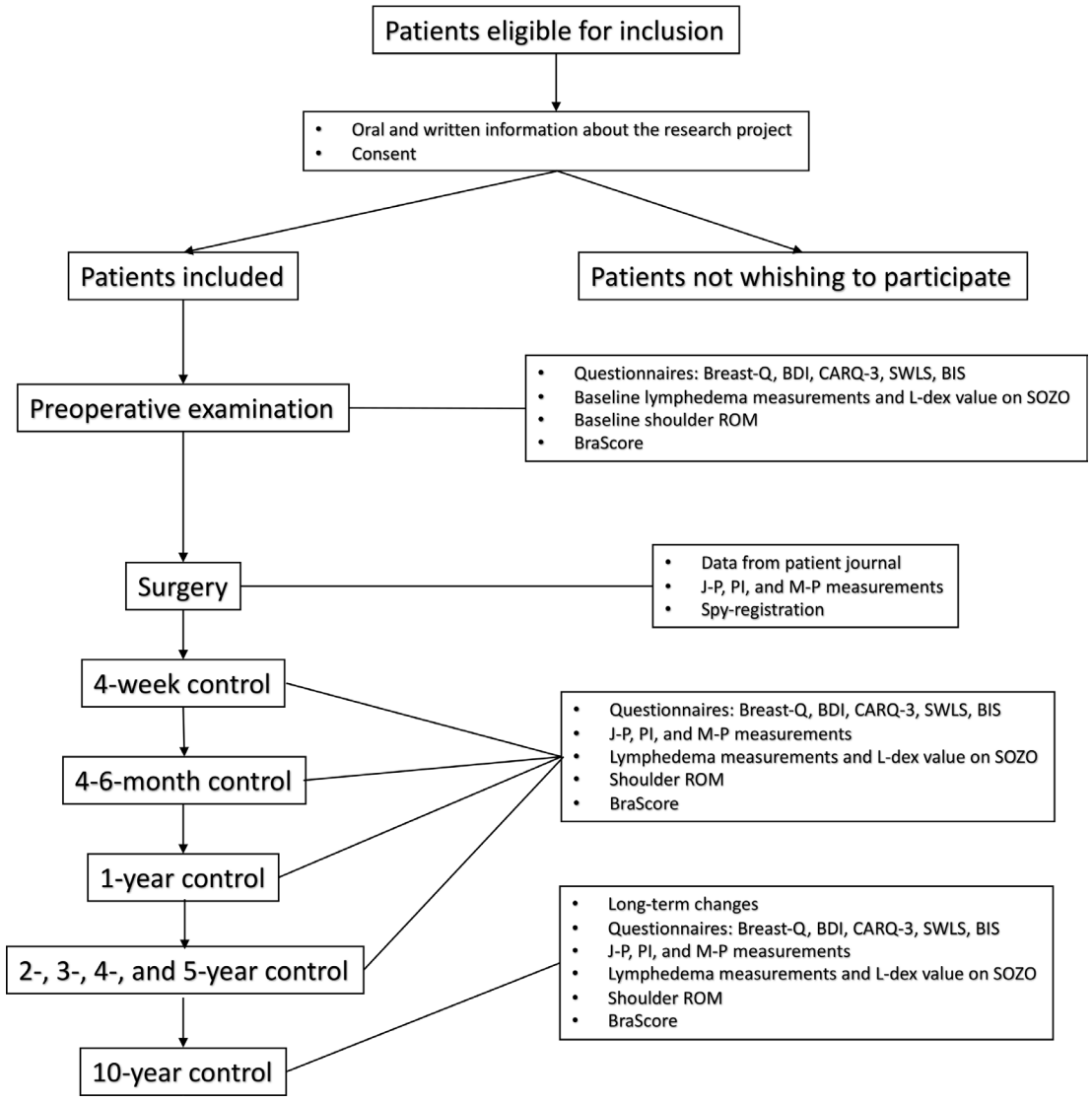

Figure 1 Flow chart of patient inclusion and study design. BDI, Beck Depression Inventory; BIS, bioimpedance spectroscopy; CARQ-3, Concerns About Recurrence Questionnaire; ROM, range of motion; SWLS, Satisfaction With Life Scale. M-P, Midtlinie - papilla distance; PI, Papilla - inframammary fold distance; J-P, Jugulum - papilla distance.

of four identical subscales: Satisfaction with Breasts, Psychosocial Well-being, Sexual Well-being and Physical Well-being. Each scale is analysed using the Q-Score data analysis programme developed by Rasch Unidimensional Measurement Models Laboratory. Each scale is transformed into a summary score ranging from 0 to 100, with higher scores indicating higher satisfaction or better QoL. The Reconstruction module that we plan to use in our study includes a Physical Well-being Abdomen for patients receiving autologous reconstruction.[60] The BREAST-Q has only one question directly related to arm lymphoedema; however, a scale regarding lymphoedema—Lymphoedema-Q—is developed, and the Danish translation is currently being validated. We are awaiting the publishing of the Danish Lymph-Q, which we will then include in a sequel of the study.

The Beck Depression Inventory (BDI) is a self-rating measurement of the behavioural manifestations of depression,[62] without the clinician's subjective bias and will, therefore, be more valid for a long follow-up period where different clinicians otherwise would be evaluating symptoms of depression. The BDI also has the advantage that it is designed to reflect the depth of depression, which means that it can monitor changes over time and provide an objective measure of improving or worsening symptoms.[63] BDI consist of 21 items of descriptive statements. Each statement's score ranges from 0 (symptom not there) to 3 (symptom present most of the time). This gives a scale of 0–63 points where ≤9: no depression, 10–18: mild depression, 19–29: moderate depression, ≥30: suicidal or severe interference with work or social life extending into the inability to work.

It has been reported that up to 70% of young women with breast cancer experience moderate to severe levels of fear of cancer recurrence.[64] We intend to evaluate fear of cancer recurrence with the Concerns About Recurrence Questionnaire (CARQ-3), which is validated and breast cancer-specific.[65] Higher scores indicate a higher

fear of cancer recurrence.[66] CARQ-3 consists of three items answered on an 11-point Likert scale ranging from 0 to 10.

The POSAS is a validated instrument designed to measure scar quality, and it consists of two scales, one completed by the patient and the other completed by the observer.[67–69] It is more comprehensive and has a higher correlation with patients' ratings than previous tools used to assess scar quality.[70]

We will evaluate aesthetic appearance using the BraScore,[13] a seven-item study-specific scale. Each item on the BraScore is scored on a seven-point Likert scale ranging from 1 (very dissatisfied) to 7 (very satisfied) and summated into a total score ranging from 7 to 49. These items include satisfaction with the breast appearance without a bra and with a bra; satisfaction with size, shape, and the breast's softness; the fulfilment of expectations, and overall result. Higher scores indicate greater satisfaction with aesthetic appearance.[13]

Hopwood's Body Image Scale (HBIS) is a 10-item breast cancer-specific scale evaluating surgical procedures' impact on the patient's body image.[71] The scale has previously been used in Danish breast cancer studies, is highly reliable, clinically validated, and sensitive to change.[71 72] Each item in the HBIS is scored on a four-point Likert scale ranging from 0 (not at all) to 3 (very much) and summated into a total score ranging from 0 to 30, with lower scores indicating better body image.[66]

QoL will be measured using the Satisfaction With Life Scale (SWLS),[73] which reflects on satisfaction with life conditions and own achievements. Individuals will value different components of 'the good life', such as health, money, or successful relationships, differently from other people with a different set of values—or different weighting of values. The SWLS items are not specific, allowing the respondent to weigh their lives' domains according to their values.[74] The scale consists of 5 statements; for each statement, there is a 7° scale from 1, 'I definitely do not agree', to 7, 'I definitely agree'. The range of scores on SWLS is from 5 to 35. The Sten scale is applied for interpretation,[75] where 1–4 Sten scores signify low satisfaction with life, 5–6; mediocre satisfaction and 7–10; high satisfaction.

Storing of data and data treatment

Data will be stored in REDCap, and permission is granted by the Capital Regional Data Inventory, with the journal number P-2019-751 in accordance with article 30 of the data protection regulation.

Risks, side effects and disadvantages

There are no risks or side effects for patients included in the study. Patients follow standard treatment and controls. Patients need to spend extra time filling out questionnaires and visit the hospital more frequently for extra follow-up visits, which could be a disadvantage for some. An advantage for patients included in the study could be earlier detection of lymphoedema and issues with ROM, leading to earlier treatment.

Patient insurance

Any harm or injury of the patient directly related to participation in the project is covered by the public patient insurance (Patienterstatningen). Participating patients will not be given any reimbursement.

Potential bias

There is a potential for selection bias since patients recruited in the study are mainly people living in the capital area with a different demographic distribution than other areas of the country. The plan is to expand the study to a multi-centre study minimising/preventing this type of bias. The Danish healthcare system is free with equal access for all patients, which prevents selection bias due to a low patient income. Other factors, such as socioeconomic status, level of education and language barriers, might influence the decision to choose breast reconstruction. Recruitment bias and lost to follow-up will be minimised by inviting a focus group of patients to help write the patient information for the study, as patient involvement has shown to increase recruitment and help improve retention.[76 77] We do not expect interviewer bias as patients are given self-rating questionnaires.

Sample size

Approximately 300 breast reconstructions are performed yearly at the Department of Plastic Surgery and Burns Treatment, Rigshospitalet. The patients are offered the whole plethora of reconstructive techniques, including implant-based or autologous (free or pedicled flaps) or combinations thereof. The reconstructions at Rigshospitalet are distributed as follows: Around 150–200 immediate reconstructions a year, of which 50% are with autologous tissue, 80–120 delayed breast reconstructions a year, of these, 75% are with autologous tissue, 50 oncoplastic surgeries (either volume replacement or volume displacement depending on the patient's body habitus).

Patients will be included continuously for 10 years, with a possibility for expansion. A minimum of 2000 patients is expected to be included, and we expect a maximum of 300 patients will be lost to follow-up, yielding a minimum sample of 1700 patients. The sample size is not calculated based on a statistical perspective, as the study is observational.

Statistical considerations

Analysis of data will be done both as 1-year, 2-year, 5-year and 10-year results. Baseline statistics will be analysed with descriptive statistics, where continuous variables such as BMI will be reported as mean values with SD and range, and will be compared between different reconstruction types using t-test. Categorical variables will be counted and reported as percentage and compared using Pearson's χ^2 test. Primary outcomes of lymphoedema development and shoulder function will be analysed with survival analysis, using absolute risks and HRs (cox regression).

Death will be used as competing risk. Time to event will be defined as the time from surgery to development of lymphoedema grade 1, data collection or death, whichever came first, and for ROM grade under grade 4, data collection or death, whichever came first. Patient who do not develop lymphoedema or decreased ROM will be censored in the analysis. There will be separate analysis for lymphoedema and ROM. Patients that suffer from lymphoedema will be analysed using descriptive statistics.

BREAST-Q has previously been analysed with multiple linear regression, in order to identify which variables were associated with BREAST-Q scores.[60] The authors have previously used multiple logistic regression models to test associations between patient-reported aesthetic outcome (BraScores) and perceived change in QoL.[13] Linear regression models have used to analyse the influence of different factors on SWLS.[78] Another potential way to analyse QoL, aesthetic satisfaction and depression changes over time in the BREAST-Q subscales, SWLS, BraScore and HBIS, is using a linear mixed model for each dimension of the different scales and using the baseline score as a covariate. The main advantage of this approach is that each measurement of each subject is used, regardless of time-to-drop-out. Missing items and death will be dealt with in two different ways. Death before 10-year follow-up will be dealt with by competing risk and censuring.

Missing items that are not due to death will be dealt with in the following way: Variables with missing data over 60% will be dropped if the data is deemed insignificant; however, we do not expect to encounter such an issue. Therefore, missing data will be imputed for the body image scale, BraScore and SWLS using individual mean imputation. The final analysis will depend on different factors such as mortality and year of follow-up.

The statistical expertise has been provided by Statistical Advisory Services, Rigshospitalet, in preparing the protocol. Moreover, the institutional statistician will be a key player in statistical analysis of the data obtained.

DISCUSSION

Studies have shown that female patients with lymphoedema experience a significantly lower QoL, are more anxious, and prone to a depressive state of mind than cancer patients without lymphoedema.[79] Axillary lymph node dissection, radiotherapy, obesity, a history of chemotherapy infusion in the affected limb, and age above 50 are all well-known risk factors for developing secondary lymphoedema.[43–48 80–82] However, the effect of timing of breast reconstruction and type of breast reconstruction on lymphoedema has yet to be established, as only few studies have examined this relationship. A retrospective study from 2010 by Crosby *et al* compared the incidence of upper extremity lymphoedema in patients with breast cancer undergoing immediate breast reconstruction and did not find the type of reconstruction to have a significant effect on lymphoedema,[83] but the diagnosis of lymphoedema was determined by journal notes and not systematic objective measures.

There is currently no treatment that can cure lymphoedema. Surgery in lymphoedema treatment has shown promising results using different approaches such as lymphaticovenular bypass, inguinal lymph node transfer, autologous lymph vessel transplantation, lymphatic venous anastomosis and suction-assisted lipectomy,[84–90] and delayed autologous breast reconstruction was found to improve lymphoedema symptoms in a study by Siotos *et al*.[91] Treatment of subclinical lymphoedema with compression garments has shown to be effective but requires early diagnosis.[92] Further studies are needed to set a new gold standard and personalise lymphoedema treatment, and we expect our study to supply data for this, as treatment of lymphoedema also will be recorded. The hypothesis of a positive effect of delayed breast reconstruction on lymphoedema previously expressed in literature will be examined as part of our study.

A recent European study of 543 patients with cancer estimated that lymphoedema management was delayed at an average of 3.6 years from the initial onset of symptoms.[93] Lymphoscintigraphy is considered the gold standard imaging modality for diagnosing lymphoedema,[94] but many different diagnostic modalities exist: Water displacement,[95] circumference measurement,[95] perometry,[96] and recently, the use of BIS has been initiated. Multiple studies have documented its ability to detect subclinical lymphoedema up to 10 months before the appearance of clinical symptoms.[97–103] It has been shown that early detection and treatment of subclinical lymphoedema can led to a significant reduction in clinical lymphoedema.[104 105] We will investigate this further in our study, where we will use the BIS SOZO system to identify differences in lymphoedema development, dependent on the type of reconstruction. Our study will provide data for validation of the BIS SOZO system, and we hope the clinical experience of integrating it into clinical practice will set it forward as a standard diagnostic instrument for all breast cancer patients. This could help minimise delay in diagnosing lymphoedema and facilitate the potential for early treatment.

Assessment, treatment and advice for lymphoedema vary between different groups of health professionals.[106] This variation in treatment, together with physicians' limited knowledge about lymphoedema, causes distress for the patients.[107] It implies a further need for information and education of patients and healthcare professionals to improve the treatment of lymphoedema.[108] The psychosocial impact, the associated increased risk of infection, and significantly higher medical costs related to lymphoedema,[109] highlights the importance of timely and correct treatment based on the exact diagnosis. A Danish study by Gärtner *et al*, including 2293 patients, implied the need for policymakers to be aware of the need for long-term follow-up on lymphoedema.[45]

An earlier return to normal ROM is thought to maintain better shoulder girdle strength and lower the

number of patients requiring postoperative physical and occupational therapy. The recent introduction of prepectoral implants compared with postpectoral implants are thought to facilitate earlier return to normal ROM, however; as this technique is new, more data is needed to confirm the benefits.[110] Axillary lymph node dissection has been found to effect ROM,[38] however, no patients in this study had breast reconstruction, and current literature is not in agreement on whether or not the type of breast reconstruction affects ROM.[38–41 111] Our study will provide data on ROM, enabling analysis of the effect of type of breast reconstruction on ROM.

This study is the first prospective study to collect extensive data covering the entire pathway for patients with breast cancer receiving breast reconstruction. It includes both objective and subjective measures and outcomes for different types of breast reconstruction. Our study may prevent late effects of breast cancer treatment (lymphoedema, ROM, depression) in the future, as outcomes related to breast reconstruction type will be analysed, and one type will potentially be superior to others, but more likely, might be better suited for a specific type of patient. Pragmatically, knowledge accumulated in this study on risks and advantages for both physical and psychological effects, can be considered when planning breast reconstruction, both regarding timing and reconstruction type, thereby minimising the impact cancer treatment has on the patient. Eventually, the result may also reduce the total financial expense for society. The direct effect due to reduced surgical costs, such as shorter admission time to hospital and fewer complications. Indirectly, less long-term side effects such as lymphoedema or depression could also increase the rate of patients continuing work and thereby contributing to societal economy for a more extended period. With the longer life expectancy after breast cancer treatment, offering breast reconstructions that yield a high body image score and QoL score is crucial. Therefore, long-term follow-up of patients undergoing breast reconstruction on body image satisfaction and QoL is needed to evaluate established methods and improve and develop new methods for breast reconstructions. Moreover, the study may elucidate data, optimising data integration, and share this knowledge on breast reconstruction in the DBCG database.

DECLARATIONS

Ethics approval and consent to participate

This study is conducted according to the 5th version of the Declaration of Helsinki. The regional ethical committee for Capital Region Denmark has been advised about the study, and they did not find the study notifiable, according to the law of the committee § 1, part 4. All data will be anonymised before its publication. This project is conducted according to the Danish data protection regulation and is catalogued and approved by the Capital Region Head of Knowledge Centre. According to the Danish health law § 46, part 2, this study does not need the Danish Patient Safety Authority's approval since all patients in the study will give written consent to use their journal data. No adverse events are expected as a result of this study, as patients do not undergo any additional interventions. However, if any should be identified, they will be reported to the medical ethical commission.

Dissemination policy

All findings will be anonymised so that no individuals will be identifiable from the reported results. The findings of this study will be submitted to international peer-reviewed journals and presented at conferences. A focus group of breast cancer patients will also have an advisory role in disseminating findings to participants and relevant communities.

Acknowledgements AMNielsen ApS for English proofreading.

Contributors TD was responsible for the initial study design and the grant application and is responsible for supervising as project leader. TD and CML-K wrote the statistics part of the manuscript. CML-K did the background research and was responsible for the protocol's in-depth development and drafting of this manuscript, including its figures and tables. EL helped with the article search, methods section, and the grant application. LL helped supervise. TD, EL and LL contributed with thorough revisions to the manuscript. All authors read and approved the final manuscript.

Funding The planned study is supported by the Alfred Benzon Foundation, which has funded the research nurse. The coauthor of this project, EL MD, is also funded by a grant from the Alfred Benzon Foundation. The Alfred Benzon Foundation has not been part of designing the study, nor will the foundation be part of the collection, analysis or interpretation of data. The University of Copenhagen and the Department of Plastic Surgery and Burns Treatment, Copenhagen University Hospital covers TD's salary. CML-K and LL are currently not receiving a salary for this work.

Competing interests None declared.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iD

Cecilie Mullerup Laustsen-Kiel http://orcid.org/0000-0003-4393-974X

REFERENCES

1 The global cancer observatory, 2019. Available: https://gco.iarc.fr/today/data/factsheets/populations/208-denmark-fact-sheets.pdf [Accessed 3 Jan 2020].
2 Li N, Deng Y, Zhou L, *et al*. Global burden of breast cancer and attributable risk factors in 195 countries and territories, from 1990 to 2017: results from the global burden of disease study 2017. *J Hematol Oncol* 2019;12:140.

3 Kapitel 2, Danish Breast Cancer Cooperative Group. Diagnose. I: DBCG Retningslinjer 2011, 2013. Available: https://www.dbcg.dk/PDF/Kap_2_Diagnose_24.05.2013.pdf [Accessed 27 Apr 2020].
4 Sundhedsstyrelsen. Pakkeforløb for brystkræft. For fagfolk, 2018. Available: https://www.sst.dk/-/media/Udgivelser/2019/Pakkeforloeb-kraeft-2015-2019/Brystkraeft-2018/Pakkeforl%C3%B8b-for-brystkr%C3%A6ft-2018.ashx?la=da&hash=B0ECEC63750535FC707EF4EB06EF4C8958890F5E
5 Storm HH, Engholm G, Hakulinen T, *et al*. Survival of patients diagnosed with cancer in the Nordic countries up to 1999-2003 followed to the end of 2006. A critical overview of the results. *Acta Oncol* 2010;49:532–44.
6 Cancerregisteret, Sundhedsdatastyrelsen. Available: https://www.esundhed.dk/Registre/Cancerregisteret/Kraeftoverlevelse [Accessed 20Apr 2021].
7 Meijers-Heijboer H, van Geel B, van Putten WL, *et al*. Breast cancer after prophylactic bilateral mastectomy in women with a BRCA1 or BRCA2 mutation. *N Engl J Med* 2001;345:159–64.
8 Hartmann LC, Sellers TA, Schaid DJ, *et al*. Efficacy of bilateral prophylactic mastectomy in BRCA1 and BRCA2 gene mutation carriers. *J Natl Cancer Inst* 2001;93:1633–7.
9 Rebbeck TR, Friebel T, Lynch HT, *et al*. Bilateral prophylactic mastectomy reduces breast cancer risk in BRCA1 and BRCA2 mutation carriers: the PROSE Study Group. *J Clin Oncol* 2004;22:1055–62.
10 Domchek SM, Friebel TM, Singer CF, *et al*. Association of risk-reducing surgery in BRCA1 or BRCA2 mutation carriers with cancer risk and mortality. *JAMA* 2010;304:967–75.
11 Hartmann LC, Schaid DJ, Woods JE. Efficacy of bilateral prophylactic mastectomy in women with a family history of breast cancer. *Obstet Gynecol Survey* 1999;340:381–3.
12 Geiger AM, Yu O, Herrinton LJ, *et al*. A population-based study of bilateral prophylactic mastectomy efficacy in women at elevated risk for breast cancer in community practices. *Arch Intern Med* 2005;165:516.
13 Juhl AA, Christensen S, Zachariae R, *et al*. Unilateral breast reconstruction after mastectomy - patient satisfaction, aesthetic outcome and quality of life. *Acta Oncol* 2017;56:225–31.
14 Waljee JF, Hu ES, Ubel PA, *et al*. Effect of esthetic outcome after breast-conserving surgery on psychosocial functioning and quality of life. *J Clin Oncol* 2008;26:3331–7.
15 Rekommandationer vedr. brystrekonstruktion: Danish breast cancer Cooperative group, 2010. Available: https://dbcg.dk/PDF/Retningslinier%202010%20Kap%2013%20010410.pdf [Accessed 31 Jan 2020].
16 Kirurgisk Behandling AF Brystkræft vs. 2.0 Danske Multidisciplinære cancer Grupper (DMCG) OG Regionernes Kliniske Kvalitetsudviklingsprogram (RKKP), 2019. Available: https://www.dmcg.dk/siteassets/kliniske-retningslinjer---skabeloner-og-vejledninger/kliniske-retningslinjer-opdelt-pa-dmcg/dbcg/dbcg_kirurgisk-behandling_v2.0_adm.godk_250321.pdf [Accessed 17 Sep 2021].
17 Bodilsen A, Christensen S, Christiansen P, *et al*. Socio-demographic, clinical, and health-related factors associated with breast reconstruction - A nationwide cohort study. *Breast* 2015;24:560–7.
18 Miller AM, Steiner CA, Barrett ML. *Breast Reconstruction Surgery for Mastectomy in Hospital Inpatient and Ambulatory Settings, 2009–2014: Statistical Brief #228. Healthcare Cost and Utilization Project (HCUP) Statistical Briefs*. Rockville (MD): Agency for Healthcare Research and Quality (US), 2006.
19 Surgeons. 2019 plastic surgery statistics report: ASPS national Clearinghouse of plastic surgery procedural statistics, 2019. Available: https://www.plasticsurgery.org/documents/News/Statistics/2019/plastic-surgery-statistics-full-report-2019.pdf [Accessed 21 Oct 2020].
20 Homsy A, Rüegg E, Montandon D, *et al*. Breast reconstruction: a century of controversies and progress. *Ann Plast Surg* 2018;80:457–63.
21 Christensen BO, Overgaard J, Kettner LO, *et al*. Long-Term evaluation of postmastectomy breast reconstruction. *Acta Oncol* 2011;50:1053–61.
22 Colakoglu S, Khansa I, Curtis MS, *et al*. Impact of complications on patient satisfaction in breast reconstruction. *Plast Reconstr Surg* 2011;127:1428–36.
23 Alderman AK, Kuhn LE, Lowery JC, *et al*. Does patient satisfaction with breast reconstruction change over time? two-year results of the Michigan breast reconstruction outcomes study. *J Am Coll Surg* 2007;204:7–12.
24 Jagsi R, Li Y, Morrow M, *et al*. Patient-Reported quality of life and satisfaction with cosmetic outcomes after breast conservation and mastectomy with and without reconstruction: results of a survey of breast cancer survivors. *Ann Surg* 2015;261:1198–206.
25 Al-Ghazal SK, Sully L, Fallowfield L, *et al*. The psychological impact of immediate rather than delayed breast reconstruction. *Eur J Surg Oncol* 2000;26:17–19.
26 Wellisch DK, Schain WS, Noone RB, *et al*. Psychosocial correlates of immediate versus delayed reconstruction of the breast. *Plast Reconstr Surg* 1985;76:713–8.
27 Stevens LA, McGrath MH, Druss RG, *et al*. The psychological impact of immediate breast reconstruction for women with early breast cancer. *Plast Reconstr Surg* 1984;73:619–26.
28 Elkowitz A, Colen S, Slavin S, *et al*. Various methods of breast reconstruction after mastectomy: an economic comparison. *Plast Reconstr Surg* 1993;92:77–83.
29 Al-Ghazal SK, Fallowfield L, Blamey RW. Comparison of psychological aspects and patient satisfaction following breast conserving surgery, simple mastectomy and breast reconstruction. *Eur J Cancer* 2000;36:1938–43.
30 Khoo A, Kroll SS, Reece GP, *et al*. A comparison of resource costs of immediate and delayed breast reconstruction. *Plast Reconstr Surg* 1998;101:964–8.
31 Cordeiro PG, McCarthy CM. A single surgeon's 12-year experience with tissue expander/implant breast reconstruction: part I. A prospective analysis of early complications. *Plast Reconstr Surg* 2006;118:825–31.
32 Alderman AK, Wilkins EG, Kim HM, *et al*. Complications in postmastectomy breast reconstruction: two-year results of the Michigan breast reconstruction outcome study. *Plast Reconstr Surg* 2002;109:2265–74.
33 Wilkins EG, Hamill JB, Kim HM, *et al*. Complications in postmastectomy breast reconstruction: one-year outcomes of the mastectomy reconstruction outcomes Consortium (MROC) study. *Ann Surg* 2018;267:164–70.
34 Gurtner GC, Jones GE, Neligan PC, *et al*. Intraoperative laser angiography using the Spy system: review of the literature and recommendations for use. *Ann Surg Innov Res* 2013;7:1.
35 Moyer HR, Losken A. Predicting mastectomy skin flap necrosis with indocyanine green angiography: the gray area defined. *Plast Reconstr Surg* 2012;129:1043–8.
36 Newman MI, Jack MC, Samson MC. SPY-Q analysis toolkit values potentially predict mastectomy flap necrosis. *Ann Plast Surg* 2013;70:595–8.
37 Duggal CS, Madni T, Losken A. An outcome analysis of intraoperative angiography for postmastectomy breast reconstruction. *Aesthet Surg J* 2014;34:61–5.
38 Soares EWS, Nagai HM, Bredt LC, *et al*. Morbidity after conventional dissection of axillary lymph nodes in breast cancer patients. *World J Surg Oncol* 2014;12:67.
39 Alderman AK, Kuzon WM, Wilkins EG. A two-year prospective analysis of trunk function in TraM breast reconstructions. *Plast Reconstr Surg* 2006;117:2131–8.
40 Rindom MB, Gunnarsson GL, Lautrup MD, *et al*. Shoulder-related donor site morbidity after delayed breast reconstruction with pedicled flaps from the back: an open label randomized controlled clinical trial. *J Plast Reconstr Aesthet Surg* 2019;72:1942–9.
41 Steffenssen MCW, Kristiansen A-LH, Damsgaard TE. A systematic review and meta-analysis of functional shoulder impairment after latissimus dorsi breast reconstruction. *Ann Plast Surg* 2019;82:116–27.
42 Lawenda BD, Mondry TE, Johnstone PAS. Lymphedema: a primer on the identification and management of a chronic condition in oncologic treatment. *CA Cancer J Clin* 2009;59:8–24.
43 Ugur S, Arıcı C, Yaprak M, *et al*. Risk factors of breast cancer-related lymphedema. *Lymphat Res Biol* 2013;11:72–5.
44 Shaitelman SF, Cromwell KD, Rasmussen JC, *et al*. Recent progress in the treatment and prevention of cancer-related lymphedema. *CA Cancer J Clin* 2015;65:55–81.
45 Gärtner R, Mejdahl MK, Andersen KG, *et al*. Development in self-reported arm-lymphedema in Danish women treated for early-stage breast cancer in 2005 and 2006--a nationwide follow-up study. *Breast* 2014;23:445–52.
46 DiSipio T, Rye S, Newman B, *et al*. Incidence of unilateral arm lymphoedema after breast cancer: a systematic review and meta-analysis. *Lancet Oncol* 2013;14:500–15.
47 Miller CL, Specht MC, Skolny MN, *et al*. Risk of lymphedema after mastectomy: potential benefit of applying ACOSOG Z0011 protocol to mastectomy patients. *Breast Cancer Res Treat* 2014;144:71–7.
48 Coriddi M, Khansa I, Stephens J, *et al*. Analysis of factors contributing to severity of breast cancer-related lymphedema. *Ann Plast Surg* 2015;74:22–5.

49 Chang DW, Kim S. Breast reconstruction and lymphedema. *Plast Reconstr Surg* 2010;125:19–23.
50 Song JW, Chung KC. Observational studies: cohort and case-control studies. *Plast Reconstr Surg* 2010;126:2234–42.
51 Harris PA, Taylor R, Minor BL, *et al*. The REDCap Consortium: building an international community of software platform partners. *J Biomed Inform* 2019;95:103208.
52 Harris PA, Taylor R, Thielke R, *et al*. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 2009;42:377–81.
53 Johnson KC, Kennedy AG, Henry SM. Clinical measurements of lymphedema. *Lymphat Res Biol* 2014;12:216–21.
54 Koelmeyer LA, Ward LC, Dean C, *et al*. Body positional effects on bioimpedance spectroscopy measurements for lymphedema assessment of the arm. *Lymphat Res Biol* 2020;18:464–73.
55 The diagnosis and treatment of peripheral lymphedema: 2020 consensus document of the International Society of Lymphology. *Lymphology* 2020;53:3–19.
56 Gallagher KK, Lopez M, Iles K, *et al*. Surgical approach to lymphedema reduction. *Curr Oncol Rep* 2020;22:97.
57 Gajdosik RL, Bohannon RW. Clinical measurement of range of motion. review of goniometry emphasizing reliability and validity. *Phys Ther* 1987;67:1867–72.
58 Okunieff P, Augustine E, Hicks JE, *et al*. Pentoxifylline in the treatment of radiation-induced fibrosis. *J Clin Oncol* 2004;22:2207–13.
59 Pusic AL, Klassen AF, Scott AM, *et al*. Development of a new patient-reported outcome measure for breast surgery: the BREAST-Q. *Plast Reconstr Surg* 2009;124:345–53.
60 Mundy LR, Homa K, Klassen AF, *et al*. Breast cancer and reconstruction: normative data for interpreting the BREAST-Q. *Plast Reconstr Surg* 2017;139:1046e–55.
61 Cohen WA, Mundy LR, Ballard TNS, *et al*. The BREAST-Q in surgical research: a review of the literature 2009-2015. *J Plast Reconstr Aesthet Surg* 2016;69:149–62.
62 Beck AT, Ward CH, Mendelson M, *et al*. An inventory for measuring depression. *Arch Gen Psychiatry* 1961;4:561–71.
63 Eskelinen M, Korhonen R, Selander T, *et al*. Beck depression inventory as a predictor of long-term outcome among patients admitted to the breast cancer diagnosis unit: a 25-year cohort study in Finland. *Anticancer Res* 2017;37:819–24.
64 Butow P, Sharpe L, Thewes B, *et al*. Fear of cancer recurrence: a practical guide for clinicians. *Oncology* 2018;32:32–8.
65 Thewes B, Zachariae R, Christensen S, *et al*. The concerns about recurrence questionnaire: validation of a brief measure of fear of cancer recurrence amongst Danish and Australian breast cancer survivors. *J Cancer Surviv* 2015;9:68–79.
66 Juhl AA, Redsted S, Engberg Damsgaard T. Autologous fat grafting after breast conserving surgery: breast imaging changes and patient-reported outcome. *J Plast Reconstr Aesthet Surg* 2018;71:1570–6.
67 van de Kar AL, Corion LUM, Smeulders MJC, *et al*. Reliable and feasible evaluation of linear scars by the patient and observer scar assessment scale. *Plast Reconstr Surg* 2005;116:514–22.
68 Draaijers LJ, Tempelman FRH, Botman YAM, *et al*. The patient and observer scar assessment scale: a reliable and feasible tool for scar evaluation. *Plast Reconstr Surg* 2004;113:1960–5.
69 Weitemeyer MB, Bramsen P, Klausen TW, *et al*. Patient- and observer-reported long-term scar quality of wide local excision scars in melanoma patients. *J Plast Surg Hand Surg* 2018;52:319–24.
70 Truong PT, Lee JC, Soer B, *et al*. Reliability and validity testing of the patient and observer scar assessment scale in evaluating linear scars after breast cancer surgery. *Plast Reconstr Surg* 2007;119:487–94.
71 Hopwood P, Fletcher I, Lee A, *et al*. A body image scale for use with cancer patients. *Eur J Cancer* 2001;37:189–97.
72 Lyngholm CD, Christiansen PM, Damsgaard TE, *et al*. Long-term follow-up of late morbidity, cosmetic outcome and body image after breast conserving therapy. A study from the Danish breast cancer Cooperative Group (DBCG). *Acta Oncol* 2013;52:259–69.
73 Diener E, Emmons RA, Larsen RJ, *et al*. The satisfaction with life scale. *J Pers Assess* 1985;49:71–5.
74 Pavot W, Diener E. Review of the Satisfaction With Life Scale. In: Diener E, ed. *Assessing well-being: the collected works of Ed Diener*. Dordrecht: Springer Netherlands, 2009: 101–17.
75 Cipora E, Konieczny M, Karwat ID, *et al*. Satisfaction with life among women with breast cancer - selected demographic and social factors. *Ann Agric Environ Med* 2018;25:314–9.
76 Crocker JC, Ricci-Cabello I, Parker A, *et al*. Impact of patient and public involvement on enrolment and retention in clinical trials: systematic review and meta-analysis. *BMJ* 2018;363:k4738.
77 Sacristán JA, Aguarón A, Avendaño-Solá C, *et al*. Patient involvement in clinical research: why, when, and how. *Patient Prefer Adherence* 2016;10:631–40.
78 Johansen H, Dammann B, Andresen I-L, *et al*. Health-related quality of life for children with rare diagnoses, their parents' satisfaction with life and the association between the two. *Health Qual Life Outcomes* 2013;11:152.
79 McWayne J, Heiney SP. Psychologic and social sequelae of secondary lymphedema: a review. *Cancer* 2005;104:457–66.
80 Ribeiro Pereira ACP, Koifman RJ, Bergmann A. Incidence and risk factors of lymphedema after breast cancer treatment: 10 years of follow-up. *Breast* 2017;36:67–73.
81 Herd-Smith A, Russo A, Muraca MG, *et al*. Prognostic factors for lymphedema after primary treatment of breast carcinoma. *Cancer* 2001;92:1783–7.
82 Rebegea L, Firescu D, Dumitru M, *et al*. The incidence and risk factors for occurrence of arm lymphedema after treatment of breast cancer. *Chirurgia* 2015;110:33–7.
83 Crosby MA, Card A, Liu J, *et al*. Immediate breast reconstruction and lymphedema incidence. *Plast Reconstr Surg* 2012;129:789e–95.
84 Chang DW. Lymphaticovenular bypass for lymphedema management in breast cancer patients: a prospective study. *Plast Reconstr Surg* 2010;126:752–8.
85 Becker C, Assouad J, Riquet M, *et al*. Postmastectomy lymphedema: long-term results following microsurgical lymph node transplantation. *Ann Surg* 2006;243:313–5.
86 Lin C-H, Ali R, Chen S-C, *et al*. Vascularized groin lymph node transfer using the wrist as a recipient site for management of postmastectomy upper extremity lymphedema. *Plast Reconstr Surg* 2009;123:1265–75.
87 Weiss M, Baumeister RGH, Frick A, *et al*. Lymphedema of the upper limb: evaluation of the functional outcome by dynamic imaging of lymph kinetics after autologous lymph vessel transplantation. *Clin Nucl Med* 2015;40:e117–23.
88 Damstra RJ, Voesten HGJ, van Schelven WD, *et al*. Lymphatic venous anastomosis (LVA) for treatment of secondary arm lymphedema. A prospective study of 11 LVA procedures in 10 patients with breast cancer related lymphedema and a critical review of the literature. *Breast Cancer Res Treat* 2009;113:199–206.
89 Brorson H, Svensson H. Complete reduction of lymphoedema of the arm by liposuction after breast cancer. *Scand J Plast Reconstr Surg Hand Surg* 1997;31:137–43.
90 Damstra RJ, Voesten HGJM, Klinkert P, *et al*. Circumferential suction-assisted lipectomy for lymphoedema after surgery for breast cancer. *Br J Surg* 2009;96:859–64.
91 Siotos C, Hassanein AH, Bello RJ, *et al*. Delayed breast reconstruction on patients with upper extremity lymphedema: a systematic review of the literature and pooled analysis. *Ann Plast Surg* 2018;81:730–5.
92 Stout Gergich NL, Pfalzer LA, McGarvey C, *et al*. Preoperative assessment enables the early diagnosis and successful treatment of lymphedema. *Cancer* 2008;112:2809–19.
93 Rucigaj TP, Leskovec NK, Zunter VT. Lymphedema following cancer therapy in Slovenia: a frequently overlooked condition? *Radiol Oncol* 2010;44:244–8.
94 Pappalardo M, Cheng M-H. Lymphoscintigraphy for the diagnosis of extremity lymphedema: current controversies regarding protocol, interpretation, and clinical application. *J Surg Oncol* 2020;121:37–47.
95 Armer JM, Stewart BR. A comparison of four diagnostic criteria for lymphedema in a post-breast cancer population. *Lymphat Res Biol* 2005;3:208–17.
96 Tierney S, Aslam M, Rennie K, *et al*. Infrared optoelectronic volumetry, the ideal way to measure limb volume. *Eur J Vasc Endovasc Surg* 1996;12:412–7.
97 Hayes S, Cornish B, Newman B. Comparison of methods to diagnose lymphoedema among breast cancer survivors: 6-month follow-up. *Breast Cancer Res Treat* 2005;89:221–6.
98 Cornish BH, Chapman M, Hirst C, *et al*. Early diagnosis of lymphedema using multiple frequency bioimpedance. *Lymphology* 2001;34:2–11.
99 Vicini F, Shah C, Lyden M, *et al*. Bioelectrical impedance for detecting and monitoring patients for the development of upper limb lymphedema in the clinic. *Clin Breast Cancer* 2012;12:133–7.
100 Shah C, Vicini F, Beitsch P, *et al*. The use of bioimpedance spectroscopy to monitor therapeutic intervention in patients

treated for breast cancer related lymphedema. *Lymphology* 2013;46:S574–92.
101 Ward LC, Dylke E, Czerniec S, *et al*. Confirmation of the reference impedance ratios used for assessment of breast cancer-related lymphedema by bioelectrical impedance spectroscopy. *Lymphat Res Biol* 2011;9:47–51.
102 Czerniec SA, Ward LC, Lee M-J, *et al*. Segmental measurement of breast cancer-related arm lymphoedema using perometry and bioimpedance spectroscopy. *Support Care Cancer* 2011;19:703–10.
103 Hayes S, Janda M, Cornish B, *et al*. Lymphedema secondary to breast cancer: how choice of measure influences diagnosis, prevalence, and identifiable risk factors. *Lymphology* 2008;41:18–28.
104 Soran A, Ozmen T, McGuire KP, *et al*. The importance of detection of subclinical lymphedema for the prevention of breast cancer-related clinical lymphedema after axillary lymph node dissection; a prospective observational study. *Lymphat Res Biol* 2014;12:289–94.
105 Yang EJ, Ahn S, Kim E-K, *et al*. Use of a prospective surveillance model to prevent breast cancer treatment-related lymphedema: a single-center experience. *Breast Cancer Res Treat* 2016;160:269–76.
106 Langbecker D, Hayes SC, Newman B, *et al*. Treatment for upper-limb and lower-limb lymphedema by professionals specializing in lymphedema care. *Eur J Cancer Care* 2008;17:557–64.
107 Carter BJ. Women's experiences of lymphedema. *Oncol Nurs Forum* 1997;24:875–82.
108 Williams AF, Moffatt CJ, Franks PJ. A phenomenological study of the lived experiences of people with lymphoedema. *Int J Palliat Nurs* 2004;10:279–86.
109 Shih Y-CT, Xu Y, Cormier JN, *et al*. Incidence, treatment costs, and complications of lymphedema after breast cancer among women of working age: a 2-year follow-up study. *J Clin Oncol* 2009;27:2007–14.
110 Glasberg SB. The economics of Prepectoral breast reconstruction. *Plast Reconstr Surg* 2017;140:49S–52.
111 Alba B, Schultz B, Qin LA, *et al*. Postoperative upper extremity function in implant and autologous breast reconstruction. *J Reconstr Microsurg* 2020;36:151–6.