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Lymph node transfer for breast cancer related lymphoedema

Submission date	Recruitment status	[ ] Prospectively registered
13/12/2017	Recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
12/02/2018	Ongoing	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
12/12/2024	Circulatory System	[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Lymphedema is a collection of fluid that causes swelling in the arms and legs. Lymphedema of the arm is often due to removal of the lymph glands in the armpit (axillary clearance) during breast cancer treatment. Every year in Sweden more than 8000 women are diagnosed with breast cancer of which more than half undergo surgery of their lymph glands in addition to their breast surgery. Today, about 5000-6000 people in Sweden suffer from lymphedema of the arm due to breast cancer treatment, with around 800 new cases diagnosed annually. Lymphedema of the arm can lead to disabilities like limited range of motion, a feeling of heaviness or pressure, pain, increased infection risks, difficulty wearing clothes, poor cosmetic appearance and psychological effects. Lymphedema can be treated in different ways. Conservative treatment entails different forms of compression and manual therapy. In addition to this, general recommendations include weight loss and range of motion (physiotherapy) training. Surgical options have changed from offering the patient resection surgery (where large portions of the swelling is removed) to offering either liposuction or microsurgical methods. The goal for these microsurgical methods is to reduce the lymphedema by improving the function of the lymphatic system. Two principal methods are used today: autologous lymph node transplantation (ALNT) and lymphatic-venous anastomoses (LVA). In both of these methods superficial veins and lymph nodes are anastomosed (connected) with the aid of a microscope which is why they are called microsurgical. The aim of this study is to assess the effect of lymph node transfer in patients with lymphedema of the arm after breast cancer treatment.

Who can participate?
Women eligible for breast reconstruction who have lymphedema of the arm on the same side as the breast reconstruction

What does the study involve?
Participants are randomly allocated to undergo breast reconstruction and tissue transfer to the armpit either with or without lymph nodes. Arm volume, patient satisfaction and lymph flow are assessed before and 3, 6, 12 and 24 months after surgery.

What are the possible benefits and risks of participating?
The outcome of the different treatments is uncertain. The transferred lymph nodes are taken

from the groin and in order to prevent donor-site problems a lymphscintigraphy scan is performed before the operation.

Where is the study run from?
1. Uppsala University Hospital (Sweden)
2. Maastricht University (Netherlands)

When is the study starting and how long is it expected to run for?
May 2017 to May 2027

Who is funding the study?
1. Uppsala-Örebro Regionen (Sweden)
2. Uppsala University Hospital (Sweden)

Who is the main contact?
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
LN001

Study information

Scientific Title
Randomised trial on lymph node transfer for treatment of breast cancer related lymphoedema

Acronym
LyNT

Study objectives
Hypothesis:
Microsurgical techniques can contribute to reducing lymphedema and effect patient symptoms in a positive manner. Lymph therapeutic treatment can improve the effect of surgical treatment and should be seen as an adjunct treatment in a standardized protocol.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Regional Ethical Board, Uppsala Sweden, 08/02/2017, ref: Dnr 2016/470

Study design
Prospective single-blinded randomised controlled study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Lymphedema of the arm secondary to breast cancer treatment

Interventions
Lymphnodetransfer as a complement to scar release and free flap (DIEP) reconstruction of the breast

Patients with lymphedema referred to the clinic are informed of the present study. If they give their consent to participate they are included and follow the usual treatment plan for microsurgical reconstructive surgery with either lymphatic-venous anastomoses (LVA) or autologous lymph node transplantation (ALNT) according to the method that is the most optimal for each individual according to the pre-operative investigations. If they are candidates for breast reconstruction with ALNT they will be randomized into 1 of 2 groups:
1. Breast reconstruction with tissue from their abdomen combined with fibrotic tissue release in the armpit and tissue transfer to the armpit
2. Breast reconstruction with tissue from the abdomen and combined lymph node transfer

Pre-operative investigations are performed according to routine clinical practice and postoperative follow up follows the study protocol (appendix 12). Study protocol is filled out during clinical visits and supplementary information is obtained from patient journals and the quality registry when needed (appendix 13). Data is gathered and processed without patient identification and follows routine guidelines for data and registry handling.

Investigations include history, clinical examination and photo documentation, volume measurement using measuring tape, water displacement test, microwave analysis (measure water content in tissue and describes the inner tissue composition) and 3D measurement. Lymph flow is measured using magnetic resonant imaging, lymphoscintigraphy and Photodynamic Eye (see below) (Ogata et al 2007, Mihara et al). Participants will also answer several questionnaires (appendix 5 a-x). Assessment will be done pre-operatively and 1, 6, 12, 24 and 36 months post-operatively.

Surgery is performed according to methods described below:
1. Lymph node transfer means lymph nodes are transferred with their nourishing vessels to the area affected by lymphedema. The vessels are anastomosed using so called microsurgical technique. The lymph nodes can be part of the tissue/flap that is moved from the abdomen during breast reconstruction with a DIEP flap or as its own flap (Becker et al 2006). A perioperative lymphosctinigraphi combined with Photodynamic Eye (PDE) is performed in order to ensure that the lymph nodes that are transferred aren't the lymph nodes draining the inferior limb and cause iatrogenic lymphedema (Ogata et al 2007, Mihara et al). Lymphoscintigraphy is performed for the leg and flourescens marking from the abdomen. The lymph nodes that signal in the scintigrapghy detector are not included in the flap (Dayan et al 2015). In order to distinguish the effects of the lymph node transfer from the fibrotic tissue release the lymph node transfer group is randomized to only fibrotic tissue release and flap or fibrotic tissue release and flap + lymph node transfer.
2. Lymphaticovenous anastomosis (LVA) is performed by identifying superficial lymph channels and vessels on the affected extremity. These anastomoses are done under a microscope. With the aid of pre-operative markings and peri-operative investigations with PDE etc the vessels to be anastomosed are identified. Usually 2-5 anastomoses are done in one extremity (Koshima et al 2000)

Intervention Type

Procedure/Surgery

Primary outcome measure
Measured at baseline (preoperatively), 3, 6 and 12 months:
1. Volume of the extremity, measured using water displacement test, 3D camera, tape measurement
2. Patient satisfaction, measured using LyQli and ICL- lymph questionnaire
There will also be a long term follow-up at 24 months (not included in the study endpoint)

Secondary outcome measures
Lymph flow, measured using magnetic resonant imaging and scintigraphy at baseline (preoperatively), 3, 6 and 12 months
There will also be a long term follow-up at 24 months (not included in the study endpoint)

Overall study start date
01/05/2017

Completion date
01/05/2027

Eligibility

Key inclusion criteria
Patients eligible to breast reconstruction with a DIEP and concomitant lymphedema of the arm

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants
25 each group

Key exclusion criteria
Same criteria as for the DIEP reconstruction

Date of first enrolment
05/05/2017

Date of final enrolment
31/12/2026

Locations

Countries of recruitment
Netherlands

Sweden

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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/01apvbh93

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Uppsala-Örebro Regionen

Funder Name
Akademiska Sjukhuset

Alternative Name(s)
Uppsala University Hospital

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
Sweden

Results and Publications

Publication and dissemination plan
Planned publication in international peer reviewed journals.

Intention to publish date
01/05/2028

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date