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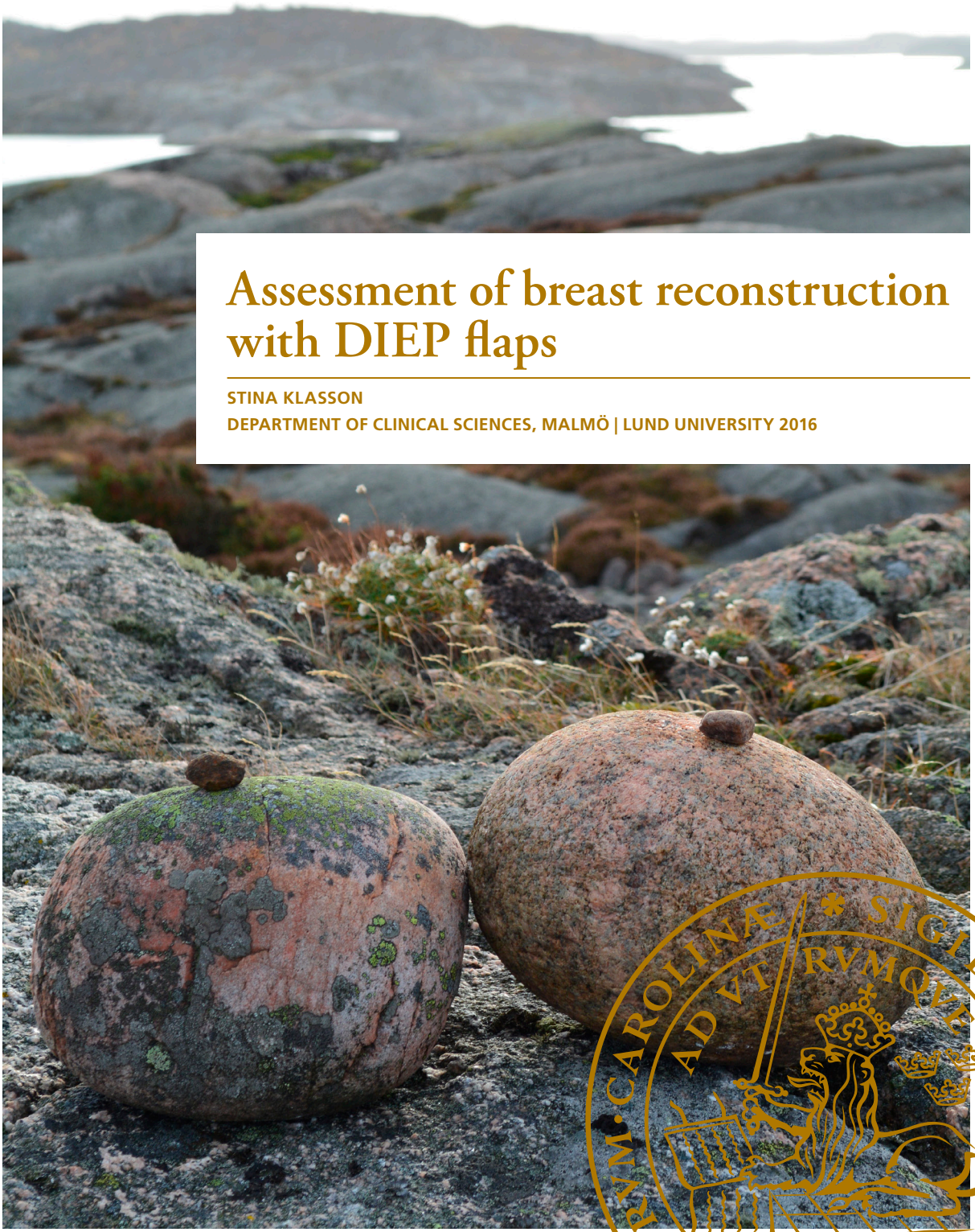

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STINA KLASSON
DEPARTMENT OF CLINICAL SCIENCES, MALMÖ | LUND UNIVERSITY 2016

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Stina Klasson

LUND
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Faculty opponent
Docent Lars Kölby, Sahlgrenska Universitetssjukhuset, Göteborg

LUND UNIVERSITY
Department of Plastic and Reconstructive Surgery
Skåne University Hospital
SE-20502 Malmö, Sweden

Author: Stina Klasson, MD

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Abstract

Reconstruction with a Deep Inferior Epigastric Perforator (DIEP) flap is considered to be the first choice for autologous breast reconstruction. Skin and fat are transplanted from the lower abdomen to the chest were the blood vessels are reconnected through microsurgery. A total of 309 patients with unilateral DIEP flap and 23 patients with expander prosthesis (EP) reconstructions were included in the present studies aimed at illustrating and optimizing breast reconstruction with the DIEP flap technique.

We evaluated blood flow before and after indirect heating, as well as sensitivity to touch, cold and warmth in ten women with reconstructed DIEP flaps. Indirect heating caused a significant increase of blood flow in both DIEP flaps and control breasts, and all patients regained some sensation of touch, cold and warmth.

Surgery time and complication rates were studied in 64 patients randomized to preoperative mapping of perforators with computer tomography angiography (CTA) or hand-held Doppler ultrasound (US) prior to DIEP surgery. Surgery time and complication rates were nearly the same in the two groups.

We studied 301 charts of patients with DIEP flap reconstructions to elucidate the impact of smoking habits and Body mass index (BMI) on complication rates. We discovered a significantly increased rate of donor site complications in former smokers but differences in BMI did not make a significant difference in complications.

Fifty patients were studied to assess early differences in health care consumption and complication rates following delayed breast reconstruction in non-irradiated women with DIEP flap or EP. DIEP reconstruction was a more complex and more health care consuming operation compared to EP surgery, which was often an easier solution from the start. In summary, a DIEP flap reconstruction has its advantages and these might be even more obvious in the long run when aspects of patient satisfaction and quality of life can be observed.

Key wordsPlastic surgery,breast reconstruction, DIEP flap

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Stina Klasson

LUND
UNIVERSITY

Supervisor: Professor Henry Svensson, MD, PhD

Co-supervisors: Karl Malm, MD, PhD, Patrik Velander, MD, PhD

Lund University, Faculty of Medicine, Department of Plastic and Reconstructive Surgery, Skåne University Hospital and Department of Clinical Sciences in Malmö, Sweden

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Lund University, Faculty of Medicine, Department of Plastic and Reconstructive Surgery, Skåne University Hospital and Department of Clinical Sciences in Malmö, Sweden

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Jag vet ingenting om tur,
bara att ju mer jag tränar desto mer tur har jag

Ingemar Stenmark

Content

List of Papers

This thesis is based on the following papers, which will be referred to in the text by their Roman numerals.

Study I: Blood flow dynamics and sensitivity in breasts after reconstruction with DIEP-flap. S. Klasson, K. Svensson, P. Wollmer, P. Velander, H. Svensson

Journal of Plastic Surgery and Hand Surgery Volume 48, Issue 6, Mai 2014, Pages 407-711.

Study II: Preoperative CT angiography versus Doppler ultrasound mapping of abdominal perforator in DIEP breast reconstructions: A randomized prospective study S. Klasson, H. Svensson, K. Malm, J. Wassélius, P. Velander

Journal of Plastic, Reconstructive & Aesthetic Surgery Volume 68, Issue 6, June 2015, Pages 782–786

Study III: Smoking increases the donor site complications in breast reconstruction with DIEP flap. S. Klasson, J. Nyman, H Svensson, P Velander

Journal of Plastic Surgery and Hand Surgery, accepted for publication 160303.

Study IV: DIEP versus expander prosthesis in breast reconstruction – a prospective randomized study. A preliminary report on health care consumption and early complications S. Klasson, P.Velander

In manuscript

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Background to the present investigation

Breast cancer is the most common malignancy among women in Sweden. In 2014, 9730 women received a breast cancer diagnosis. This is 30% of the total amount of all reported cancer in women in Sweden. Today, 80% of women diagnosed with breast cancer survive more than 10 years. Mean age when diagnosed is 60 years and less than 5% are younger than 40 years. One out of nine women in Sweden will receive a breast cancer diagnosis before the age of 75 years (1). The surgical treatment is breast conserving therapy (BCT) or mastectomy. In Sweden, about 55% of the women diagnosed with breast cancer are treated with BCT (2). Around 80 women/year in Sweden are estimated to have bilateral prophylactic mastectomy due to a genetic predisposition (BRCA1 and BRCA2) and a strong wish to reduce the risk of breast cancer. In our catchment area of about 1.7 million inhabitants, about 50% of the mastectomized women under 65 years of age whish for a reconstruction.

Breast reconstruction

The indication of breast reconstruction is the patient´s own wish for a new breast. The main reasons for wanting a new breast are practical problems with an external prosthesis, asymmetry and problems with personal and sexual relationships. Reasons for not going through a breast reconstruction can be that the woman frankly does not wish to have a new breast, comorbidity, high age, fear of disguising a recurrence of breast cancer and lack of information on the possibilities of reconstruction may be contributing factors.

Breast reconstruction aims to restore the shape, size and symmetry of the breasts and give a feeling of a natural breast. This can be a challenging task, and the expectations of the patients are sometimes difficult to achieve.

A breast can be reconstructed at the same time as the cancer surgery. This is named an immediate breast reconstruction. If this is done, it is preferable that no post mastectomy radiation therapy (PMRT) is planned. A secondary, or delayed, reconstruction is carried out after all cancer therapy is completed, including surgery, PMRT and chemotherapy. In Sweden, breast reconstruction is often delayed for two or three years in more advanced cases in order to avoid concealing a recurrence of the breast cancer disease. A breast reconstruction can be unilateral or bilateral. As we learn more about genetic risk factors for breast cancer, and the ability to detect gene mutations increases, the demand of prophylactic bilateral reconstructions will rise.

Breast reconstruction today includes many different methods that make it possible to individualize the treatment for each patient. There are three main ways to reconstruct a breast after mastectomy; lost tissue is replaced by an implant, by autologous material or by a combination of the two. The use of an implant is the most common method of breast reconstruction. In Sweden an autologous breast reconstruction is reserved for patients who have had PMRT (3) and is considered when a reconstruction with a prosthesis will probably be associated with complications (4, 5). After PMRT the tissue loses its elasticity and an implant will have a higher risk for capsular contracture, infection and other problems. In a case like this, an autologous reconstruction will be a better alternative. In most cases, an autologous reconstruction involves the transfer of both tissue and its blood supply, which means that microvascular surgery techniques are required. Microvascular surgery refers to surgery

that is performed on very small blood vessels using an operating room microscope, small instruments and tiny threads and needles.

The method of reconstruction is chosen according to the patient´s health, anatomy, previous surgery and PMRT. Ideally, the chosen method should also be determined by taking account of the wishes and expectations of the patient. It is important to inform the patient about issues related to technique, advantages and disadvantages, possible complications, waiting time and what can be expected from the reconstruction. In a resolution from 2003, the European Parliament states that a woman should have the opportunity to have an autologous reconstruction after breast cancer and mastectomy, or to decide for herself if she wants an implant after having been informed about the possible health risks of such a procedure (6).

Deep Inferior Epigastric Perforator (DIEP) flap breast reconstruction

History

A French surgeon, Peyrilhe, is said to have carried out the first radical mastectomy due to breast cancer in the 1870s. In 1889, Halsted performed the first radical mastectomy in the United States. Halsted claimed that an attempt at breast reconstruction was a "violation of the local control of the disease" and therefore lectured surgeons not to perform reconstructive operations after mastectomy (7). In Heidelberg, Czerny published in 1895 a case of mastectomy that was "reconstructed" by transplantation of a fist-sized lipoma from the patient's flank and this report is said to be the first breast reconstruction with autologous tissue ever (8). Since the beginning of the 20th century, the surgical treatment of breast cancer and the use of different breast reconstructive methods have developed immensely as new facts have emerged (9).

The knowledge about DIEP and other perforator flaps started to develop when Milton in 1970 and 1971 showed that flaps of a much greater length to width ratio could be elevated safely when based on a known underlying vascular anatomy (10, 11). This gave rise to the axial pattern pedicle flap, which was described in MacGregor´s and Jackson's report of a groin flap in 1972 (12). In 1973 Taylor and Daniel invented the "free flap" which enabled the transfer of a flap by microvascular anastomosis (13, 14). In 1975, they additionally published anatomical descriptions of many of the free flap donor sites in use today (15).

The DIEP flap is an evolution from the transverse rectus abdominal myocutaneous (TRAM) flap. The superiorly pedicled TRAM flap is a flap which is based on one entire rectus abdominal muscle and an overlaying skin island. Drawbacks with this method are motor weakness, bulge formation and hernia of the abdomen due to the muscle harvest. The free TRAM flap, which involves sacrifice only of a small piece of rectus abdominal muscle, was described for breast reconstruction in 1979 (16). It was made popular by Hartrampf in the United States in the early 1980s (17). In Japan, Koshima described the preparation of skin and subcutaneous tissue based only on blood vessels that perforate the rectus abdominal muscle (18). He transferred this

tissue, a DIEP flap, in one case to the groin and in a second case to the floor of the mouth, utilizing microsurgery and consequently without sacrifice of the rectus muscle. In 1994, the DIEP flap was described by Allen and Treece from the United States for breast reconstruction (19). Blondeel et al. in Belgium further popularized this technique in the 1990s (20). Arnljots, Söderström and Liss in Malmö performed the first DIEP flap reconstruction in Sweden in 1998. Today, the DIEP flap technique is the first choice for free flap breast reconstruction for experienced reconstructive surgeons. In Sweden, 150-200 DIEP flaps procedures/year are performed. In 2014, 182 unilateral DIEP and 13 bilateral DIEP flap procedures for breast reconstruction were carried out (Table I).

Table I.
Number of DIEP breast reconstructions in Sweden in 2014 according to personal reports from the various centers.

Place	Unilateral DIEP	Bilateral DIEP
Umeå	10	0
Uppsala	40	3
Stockholm	32	2
Linköping	20	0
Göteborg	25	2
Malmö	47	6
Karlshamn	6	0
Akademikliniken Stockholm	2	0

Anatomy of the DIEP flap

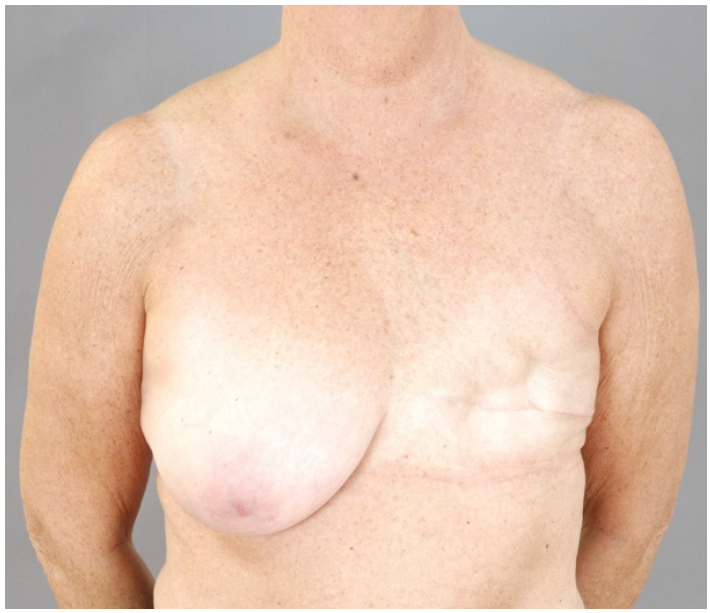
A perforator flap is a free flap consisting of skin and subcutaneous fat. The vessels supplying the tissue are perforators. These vessels pass from their source vessels in or between the deep tissues. The perforators can be muscular, musculocutaneous, septal or septocutaneous, depending on the route through the tissue.

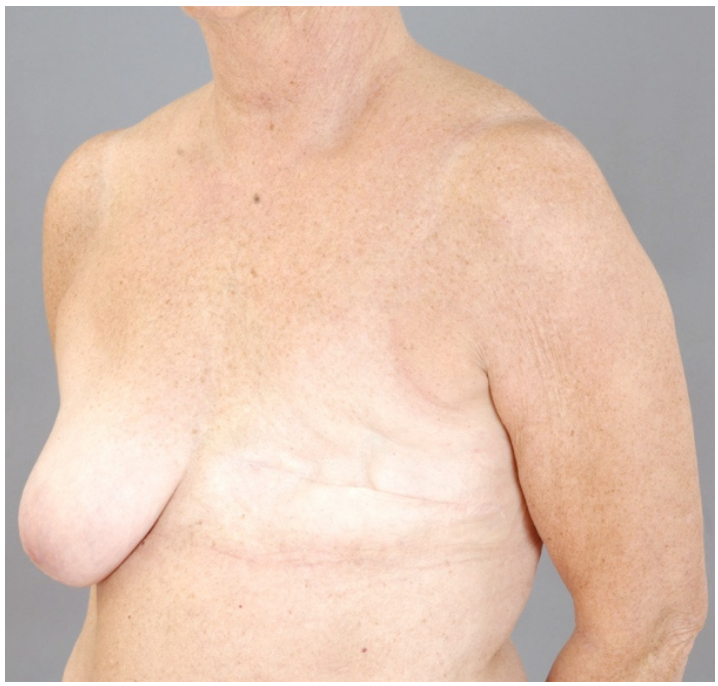
The name of the DIEP flap describes the vessel that supplies the flap with blood. The deep inferior epigastric artery branches off the external iliac artery together with two comitant veins just above the inguinal ligament. It passes lateral to the abdominal rectus muscle and ascends between the deep fascia and the muscle. It divides into a lateral and a medial branch or runs centrally, sending off perforators to the muscle, subcutaneous tissue and skin. Two to eight perforators are 0.5 mm in diameter when going through the fascia. Most of them are muscolocutaneous and located near the umbilicus (21). The length of the pedicle can vary from 8 to 16 cm. The diameter of the artery is, where bisected at the lateral border of the rectus muscle, about 2.5 mm, and the veins are about 2.9 mm (22).

DIEP flap surgery

An overwiew of the current technique was published by Granzow et al. in 2006 (23). Briefly, two experienced DIEP surgeons normally perform the surgery. Incisions are made according to the preoperative markings. One surgeon starts at the donor site by detaching the umbilicus from the surrounding tissue. The skin and subcutaneous tissue is raised from the umbilicus to the xifoid process. One or more superficial epigastric veins in the caudal part of the flap is identified and freed for at least 4 cm and then bisected for possible use. The flap is carefully raised from lateral to medial aspect above the external fascia. The largest perforator of the skin is located. One to four other perforators are saved and temporarily clamped. The chosen perforator is followed carefully through the fascia and the rectus muscle where it connects to the deep epigastric vessels. Care is taken to preserve intersecting motor nerves to the muscle. The vessels are followed close to the external iliac vessels above the inguinal ligament. The perfusion of the flap is checked and, if satisfactory, the vessels are divided. The other perforators are also cut and the flap is weighed and transferred to the chest. During this dissection, high power loupe magnification and careful microsurgical techniques are necessary.

Meanwhile, the other surgeon has prepared the recipient site by excising the mastectomy scar. 2-3 cm of the third rib cartilage is removed and the internal mammary vessels are exposed. The flap is rotated 180 degrees, placing the superficial epigastric veins cranially. Under an operating microscope the internal mammary vein is connected to the largest of the deep epigastric veins by a venous coupling device (Coupler GEM, Synovia 1.5-4.0 mm) and the internal mammary artery is sutured end-to-end to the deep epigastric artery with 9-0 Ethilon (Ethicon, Johnsson & Johnsson). It is possible to use the thoracodorsal vessels as recipient vessels, but this is seldom done because of their smaller size and due to the relative difficulty of flap insetting when using them. After revascularization, the flap is checked for bleeding and capillary refill. The skin between the former mastectomy scar and the inframammary fold is removed and the flap is attached to the inframammary fold. The poorest perfused parts are removed and the rest of the flap is molded into a breast shape. The cranial part of the flap is deepithelized and put under the skin above the mastectomy scar. The discarded parts of the flap are weighed and the weight of the reconstructed breast can be calculated (final flap weight). In the case of venous congestion, the cephalic vein is used to improve the outflow of the flap by connecting it with the preserved superficial epigastric vein. The donor site is closed using the same technique as a conventional abdominoplasty, leaving a scar that is easy to hide. The surgery takes approximately four hours and the hospital stay is five to seven days.





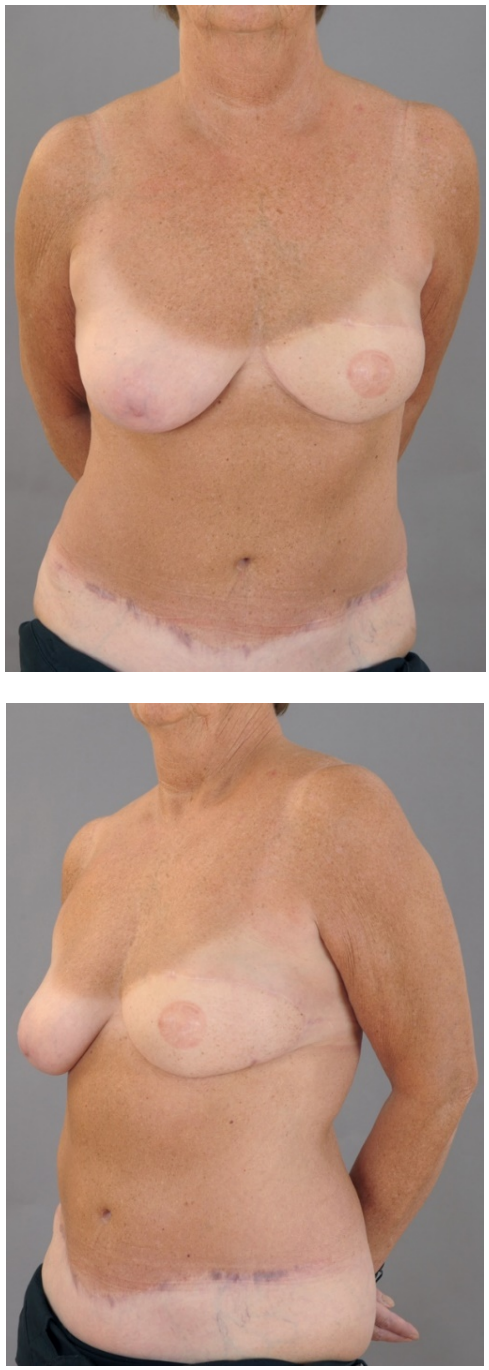


Figure 1.
Preoperative and one year postoperative photos of a sixty-one year old woman reconstructed with a DIEP flap

Implant-based breast reconstruction

History of Expander prosthesis (EP)

Cronin and Gerow introduced a silicon implant for breasts in 1963 (24), and Radovan introduced a tissue expander for breast reconstruction in 1982 (25). In 1984, Becker described a two-chambered tissue expander that had a silicone gel outer lumen with an inflatable saline lumen, which made it possible to achieve a single-stage breast reconstruction (26). Nowadays, different plastic surgery units use different methods as a routine for implant-based breast reconstruction. In our clinic, we have for many years used the one-stage EP procedure for both immediate and delayed breast reconstruction.

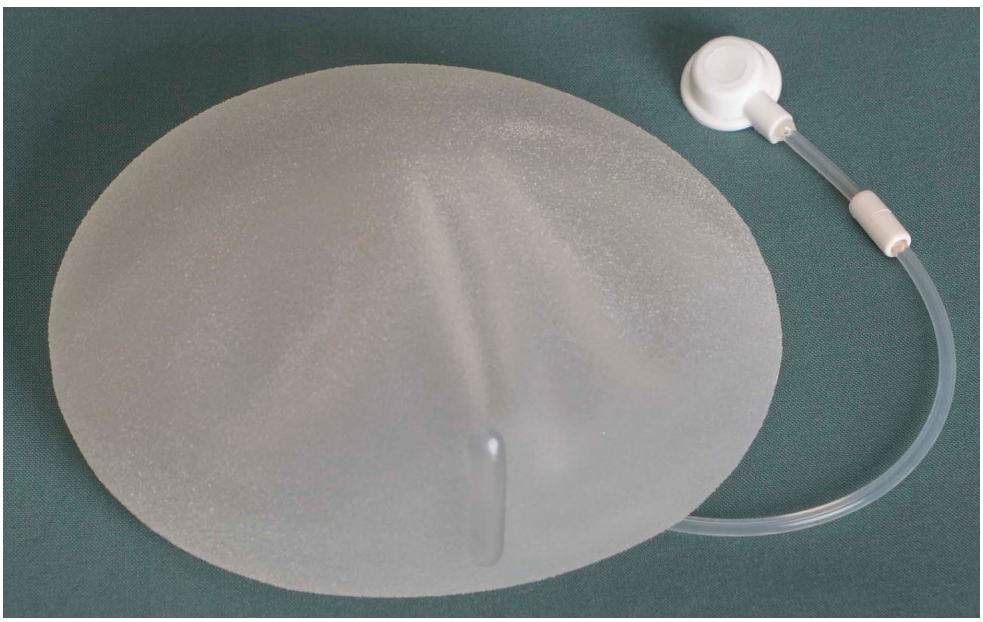


Figure 2.
Expander prosthesis with an injection port connected to the implant via a fill tube.

Expander prosthesis surgery

An incision is made in the mastectomy scar and the EP is placed under the major pectoral muscle. We use an EP with a gel-filled outer lumen and an adjustable saline-fillable inner lumen (MENTOR® Contour Profile Becker-35). An injection port is connected to the implant via a fill tube and placed subcutaneously towards the axilla. EP surgery takes less than one hour and can be done in outpatient surgery in suitable cases. Two to four weeks after surgery the patient comes once a week to the outpatient unit to have the implant gradually filled with saline until the breast has reached the desired size. Sometimes we overfill the EP and let it stay over-expanded for three months where after some of the saline is drained via the port. In this way a softer final result might be achieved. The injection port can normally be left in place. It can be removed under local anaesthesia if the patient feels discomfort or if there is a leakage problem.

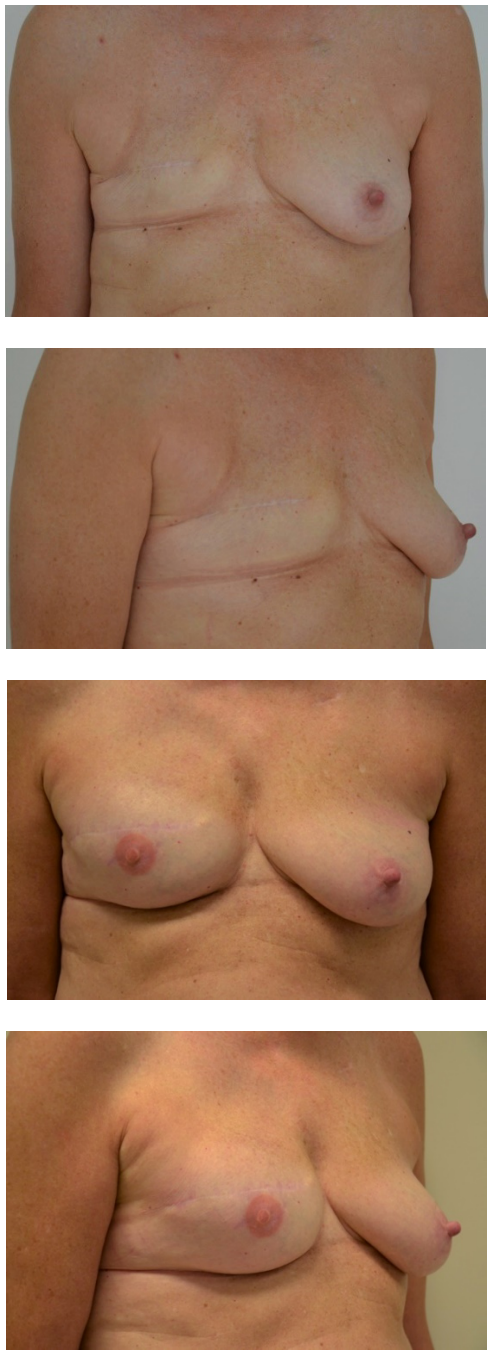


Figure 3.
Preoperative and 18 months postoperative photos of a fifty-eight year old woman reconstructed with an EP.

Flap perfusion, skin blood flow and complications

The TRAM/DIEP flap is classically divided into four zones called the Hartrampf perfusion zones (17, 27). The best perfused zone is where the pedicle is situated and is number I. The second best, zone II, is situated on the other side of the midline while zone III is the ipsilateral neighbouring tissue. More recent studies by Holm et al. have suggested swiching the names of zones II and III as the perfusion is generally better on the ipsilateral side. The most distal part of the flap on the contralateral side, zone IV, is the poorest perfused part and is almost always discarded (28). This is the general rule, but a meta-analysis of perfusion studies by Lee et al. from 2016 indicates that flap perfusion varies widely individually (29).

To identify the best perforators, preoperative mapping can be done with hand-held unidirectional Doppler ultrasound (US), colour duplex imaging (21) or computer tomography angiography, CTA (30). CTA has become the gold standard for preoperative mapping as it is said to reduce surgery time and complication rates (31).

DIEP flap complications are mainly related to impaired perfusion. Thrombosis of the anastomosed artery, or venous congestion, lead to an imminent flap loss and an acute reoperation is necessary to restore circulation of the flap. Often the major concern about vascularisation postoperatively is not arterial inflow but venous outflow. In our experience, DIEP flaps have either a dominating deep venous drainage or a dominant superficial drainage system. If the flap shows signs of congestion, it is in our opinion also necessary to anastomose the superficial vein, regardless of the size of the anastomosed deep vein. Also bleeding of the DIEP flap in the early postoperative course is usually a sign of insufficient venous drainage and necessitates the same manoeuvre. 1-2% of all DIEP surgery leads to total flap loss. When the circulatory problem is partial it may lead to a limited tissue loss or a fat necrosis. To avoid partial or total flap loss, the flap should be carefully monitored once an hour during the first two days. We use US for the arterial inflow and visual inspection for the venous outflow. Instrumental techniques for this purpose have also been suggested such as Laser Doppler perfusion monitoring (32), microdialysis (CMA Microdialysis, Stockholm, Sweden) and implantable Doppler probe, applied directly to the

anastomosed vessels with the Cook-Swartz probe (Cook Medical, Cook Ireland Ltd, Limerick, Ireland) (33).

Bleeding and hematoma at the donor site also need immediate intervention. The wound at the donor site is often under tension and sometimes wound dehiscence and delayed healing occur. Seroma at the donor site might occur and may necessitate needle aspiration. Bulging and abdominal weakness are rare late complications.

Blood flow to the skin is also important in EP surgery. To avoid compromise and ensuing skin necrosis the surgeon always has to take existing scars into account. The EP should initially be filled with caution so that the circulation of the skin will be well preserved. Skin necrosis might lead to infection and exposure of the implant, which has to be removed in such a case.

Early complications in implant surgery are bleeding, infection and seroma. It is important to evacuate a hematoma as it increases the risk for later capsular contracture (34). If antibiotics do not cure an infection the implant has to be removed. In the long-term, infection, implant malposition or rotation, saline leakage, capsular contracture, and extrusion of the implant may occur. This may lead to reoperation with implant change, capsular cleavage, and/or removal of the implant or a change in the reconstructive method.

Risk factors for complication in all kinds of breast reconstructive surgery are smoking and hypertension, and some studies have furthermore shown that a high BMI and an age >65 years also increase the risk for complications (35, 36). In a retrospective study, Thorarinsson et al. studied complication rates of five different breast reconstruction methods. They found an overall high complication rate especially related to DIEP flap surgery (37).

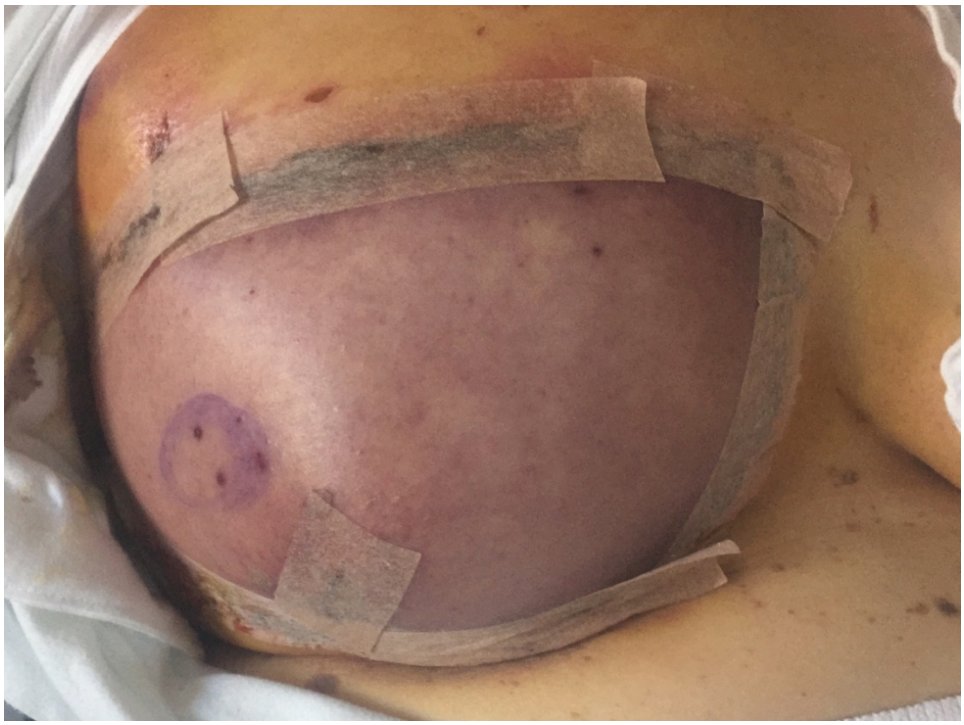


Figure 4.
Venous congestion of a DIEP flap four days postoperatively.

Cutaneous nerves and regeneration

Another dimension of a good reconstruction is the possibility of a sensate breast. Sensory perception avoids traumas to the skin caused by mechanical forces and heat or cold. In a normal breast, skin is innervated medially from the anterior cutaneous branches of the first to sixth intercostal nerves and laterally from the lateral cutaneous branches of the second to seventh intercostal nerves. The nipple-areola complex is innervated by the anterior and lateral cutaneous branches of the fourth intercostal nerve, with additional innervation by cutaneous branches of the third and fifth intercostal nerves (38). When a mastectomy is done all the nerves are divided. After healing, skin sensation regenerates to some extent. Capacity for regeneration relates to age, mechanism of injury and in particular to the proximity of the injury to the nerve cell body (39). When an autologous breast reconstruction is done, previous work has shown that the flap becomes sensate to some extent over time as a result of spontaneous reinnervation (40-43). It is also possible to make a sensory nerve repair to a DIEP flap using the sensory nerve innervating the flap and connecting it to the fourth intercostal nerve or with the best available nerve from the axillary area (40-42). Studies describing sensory nerve repair show improved sensory recovery (40, 41). Despite these findings, most DIEP flaps are performed without sensory nerve repair because of the extra time required during surgery, technical difficulty and its relatively uncertain effect.

Other methods of breast reconstruction

The TRAM flap, pedicled or free, has already been mentioned. This flap uses the same skin and subcutaneous tissue from the lower abdomen as the DIEP flap but also includes the rectus muscle. A TRAM flap is easier to harvest than a DIEP flap but drawbacks are weakness, bulging and hernia of the abdomen. A superficial inferior epigastric artery flap (SIEA) also uses the lower abdomen as donor site, but by using the superficial vessels the muscle and its fascia remain intact. The reason this flap is rarely used is that the blood vessels that nourish the flap are variable. Usually only half of the abdomen is perfused by the SIEA, the pedicle is short, and the artery small in caliber (15, 44).

In slim patients, the soft tissues of the abdomen are not bulky enough to constitute a new breast. Previous abdominal surgery may have damaged the vascular pedicles, making it impossible to use the abdomen as a donor site. Alternative free flaps to consider for breast reconstruction are then the transverse upper gracilis (TUG) flap, which uses tissue from the inner upper thigh (45), superior gluteal artery perforator flap (S-GAP), and inferior gluteal artery perforator flap (I-GAP) from the gluteal area (46, 47).

The latissimus dorsi (LD) pedicled flap is a myocutaneous flap consisting of the LD muscle with an overlying skin paddle (48). This can be raised and rotated on its vascular pedicle of the axilla and used for breast reconstruction with or without an implant (49). This procedure takes approximately three hours and the patient needs a hospital stay for three to four days. In our clinic, this procedure is nowadays only chosen when a DIEP flap is lost. Different types of implant reconstruction methods can be employed; a lateral thoracodorsal flap with an implant (LTDF) (50) is a local tissue flap that can be used together with a silicone implant. A two-stage surgery with a tissue expander and with a secondary silicone implant (51, 52) can be used as well as a one-stage direct reconstruction with a silicone implant when a small breast is wanted. In recent years the fat transplantation technique, lipofilling, has been developed and has gained increasing popularity. With serial fat grafting a whole breast can actually be reconstructed (53). In our unit, however, we do not use fat transplantation to a breast, which previously was diagnosed with cancer. The issue of breast cancer recurrence after lipofilling is namely still controversial (54).

Secondary procedures

Regardless of the method of reconstruction, the patient is offered a contralateral breast reduction or mastopexi. Even though this procedure needs general surgery it is preferably done as a second stage procedure, most commonly three months or more after the breast reconstruction procedure. Performing a contralateral reduction at the same time as a DIEP flap reconstruction is considered to add an additional risk to already extensive surgery. Also, it is easier to accomplish symmetry with the DIEP flap when this has settled for a couple of months. At the same time, or while under local anaesthesia on another occasion, the patient may have a nipple reconstruction using a local flap or a nipple sharing procedure. Finally the areola is tattooed.

In many patients with a reconstructed DIEP flap, a later correction procedure is carried out (55). Improvement of breast shape or reduction of dog-ears at the donor site is sometimes needed. Liposuction of the DIEP flap can be done if it is too big. Lipofilling is often used as an adjuvant for flap or implant breast reconstruction to improve shape and to smooth out irregularities. The lipofilling increases the aesthetic result and has a high satisfaction rate among patients. However, the issue of possible cancer recurrence still remains.

Patient related outcome

The surgeon´s opinion of a breast reconstruction may not be the same as the patient´s opinion. In current clinical research more focus than in previous days has been on patient satisfaction and important aspects of health-related quality of life (56-58). The indication for a breast reconstruction is the patient´s own wish to have a new breast, and if she is not satisfied with the result the reconstruction is a failure.

Aims of the study

The main objective of these studies is to illustrate and optimize breast reconstruction using the DIEP flap technique.

The specific aims were:

Study I:

To quantify both blood flow dynamics and sensitivity in order to get a general picture of the re-innervation of blood vessels and skin in the breast reconstructed using the DIEP flap technique.

Study II:

To investigate whether examination with CTA preoperatively results in faster and safer DIEP flap surgery.

Study III:

To elucidate the impact of smoking habits and BMI on complication rates in DIEP flap reconstructions.

Study IV:

To assess early differences in health care consumption and complication rates in non-irradiated women who have undergone delayed breast reconstruction with either a DIEP flap or an EP.

Materials and methods

Subjects

Study I:

10 women who underwent unilateral DIEP reconstruction from June 2010 to February 2011 entered the study aimed at illustrating blood flow and sensitivity of the flaps. Nine of these women were treated with PMRT. The contralateral breast of each patient was used as a control. Three patients had had a breast reduction to their control breast and one wore an implant in her control breast. All tests were carried out 12-20 months after DIEP reconstruction.

Study II:

Sixty-three women were randomized from February 2012 to June 2013 to either preoperative CTA (n=32) or US (n=31) mapping of abdominal perforators before unilateral DIEP breast reconstruction.

Study III:

The medical records of 301 consecutive patients reconstructed with a unilateral delayed DIEP flap 2006-2014 were reviewed, with particular attention to smoking habits and BMI.

Study IV:

Sixty consecutive patients who had undergone unilateral mastectomy, but no treatment with PMRT, were referred to our clinic from April 2012 to March 2016 for secondary breast reconstruction. They were randomized to breast reconstruction with one-stage operation with DIEP flap or EP. The study included 50 patients who had undergone reconstruction so far, 27 with DIEP and 23 with EP.

All patients included in studies I and II were also subjects in study III. Fourteen of the DIEP patients in study IV were subjects in study III.

Two patients in study II were also subjects in study IV.

Methods

Study I:

Laser Doppler Perfusion Imaging (LDPI)

The skin blood flow of the DIEP flaps and their microcirculatory responses to indirect heating were monitored by the PeriScan PIM II System (Lisca Development AM Linköping, Sweden). PeriScan uses LDPI technique to measure microcirculation of the skin (59). An area of 20x20 mm was examined in each breast quadrant. The LDPI delivers base line values from which changes can be monitored. A near infrared 670 nm laser beam makes a perpendicular scan over the skin surface. Moving blood cells cause a Doppler shift of scattered light, which is photo-detected and processed, leaving a colour image and a numerical value related to the superficial skin blood flow.

Semmes-Weinstein Monofilament Test (SWMT)

Tactile perception thresholds were assessed with SWMT (60). The most suitable for our purpose was the Touch-test hand-kit (North Coast Medical Inc., Morgan Hill, CA) consisting of five different monofilaments representing normal sensitivity, diminished light touch, diminished protective sensitivity, loss of protective sensitivity, and deep pressure sensation only. The filaments were applied to the skin of DIEP breasts and control breasts, not closer than 3 cm to a visible scar, to register the threshold of tactile perception.

Thermotest

The Marstock method was used to estimate thermal perception and pain thresholds (61) by using a SENSELab MSA Thermotest (Somedic AB, Hörby, Sweden) with a 9x9 mm thermode.

Temperature

Body temperature was measured in the left auditory canal by a Thermoscan Type 6022 (Braun, Kronberg, Germany). In each breast quadrant the skin temperature was measured using a precision thermometer (DM 852, Ellab, Copenhagen, Denmark. The room temperature was measured by WSE Mini-port (Artec, Germany). All temperatures were measured in °C.

Body heating

The lower extremity of the patients was heated with an electric heating blanket (OBH Nordica, type 4080, Spånga, Sweden) with an extra hospital duvet for isolation in order to raise the body temperature.

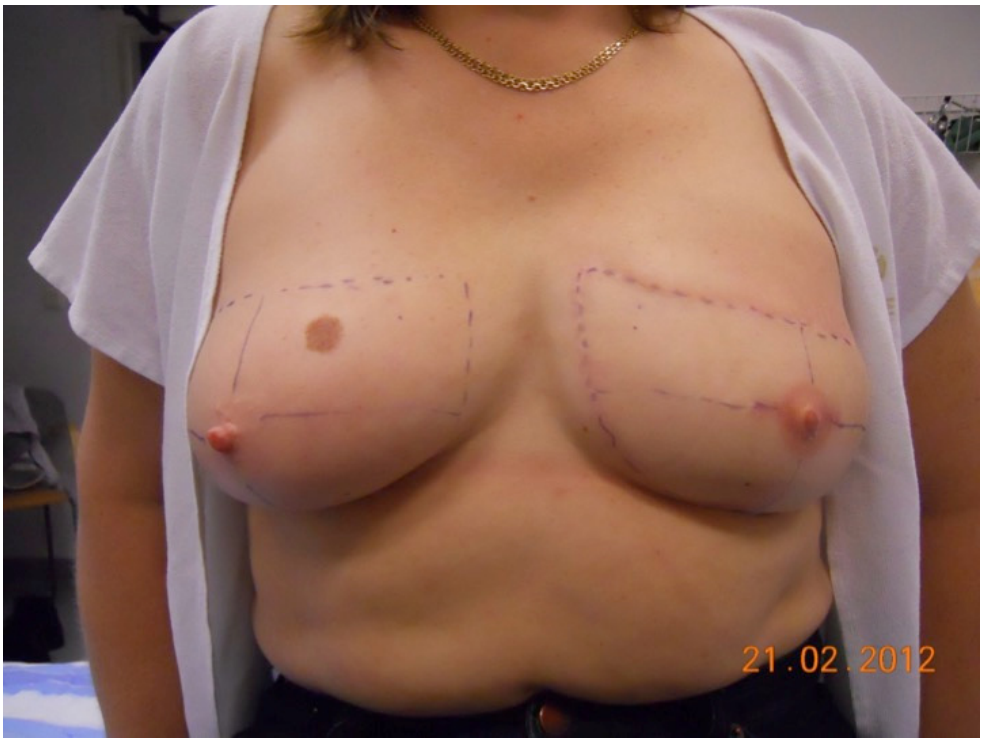


Figure 5.
Quadrants marked on the left reconstructed breast and on the right control breast.

Study II:

CTA and Image Analysis

Preoperative CTA to show the perforators of the flaps was performed on a 16- or 64-chanel multidetector CT (Somatom®, Siemens Healthcare/Medical Solutions, Erlangen, Germany). Patients were examined in the supine position. Clothes that might deform the anatomical landmarks and all metal objects were removed prior to examination. All patients were given Iohexol contrast medium (Omnipaque™ 300mg I/ml, GE Healthcare, Sweden) at 320 mg I/kg bodyweight using a peripheral venous access and a power injector (Spectris Solaris, Medrad, Pittsburgh, US). The contrast medium was injected for 15 seconds and the examination was triggered by bolus

tracing in a region of interest in the abdominal aorta at the level of the renal arteries set to 140 HU and a caudocranial direction from the groins to 5 cm above the umbilical plane was used. Reconstructed images were sent to PACS (IDS7, Sectra Medical Systems, Sweden).

Image Analysis was done in Sectra PACS in transaxial images and coronal and sagital reconstructed images. The inferior epigastric artery was described from its origin, including its branching pattern (62) and its major anterior musculocutaneous perforators supplying the abdominal wall. Each perforator was described including its origin, the length of its intramuscular passage, the location at which it exits the muscle related to the umbilicus, and its size and branching pattern in the subcutaneous tissue. All major perforators were described and ranked based on these radiological characteristics.

All image assessment was carried out by one dedicated radiologist one to two weeks ahead of surgery. Radiological imaging and the recommendations for the best perforators were studied preoperatively by the operating plastic surgeons and the coordinates of the perforators were marked on the patient's abdominal skin.

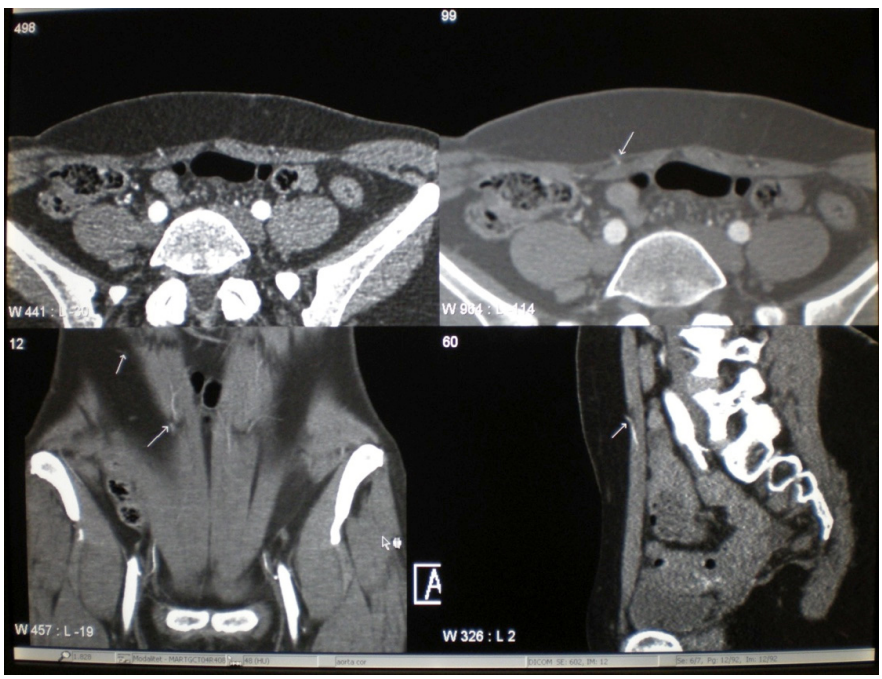


Figure 6.
Preoperative CTA. Arrows indicate perforators passing through the abdominal rectus muscle.

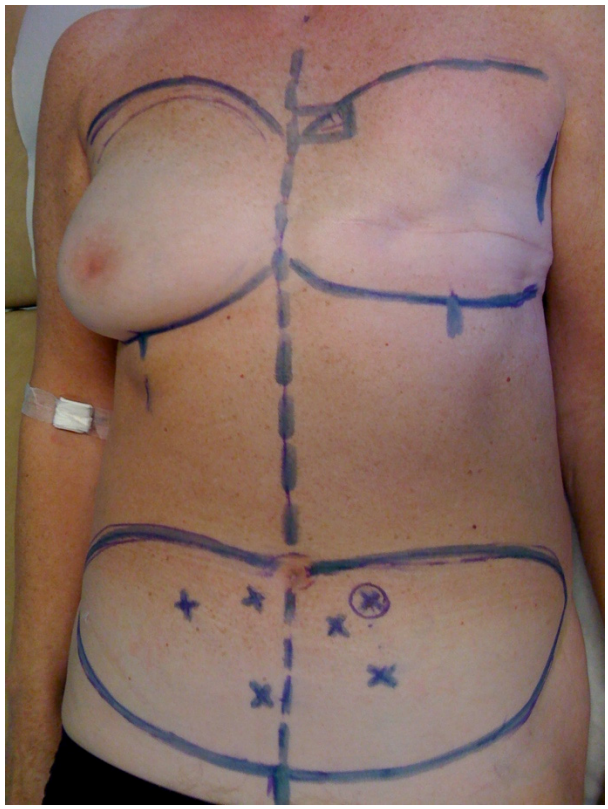


Figure 7.
Preoperative markings before DIEP flap surgery in the patient shown in Figure 1.

Ultrasound

The hand-held Doppler ultra sound was performed on the day before surgery by the surgeon. We used the conventional method of the hand-held Doppler ultrasound with an 8 MHz probe to obtain Doppler signals (dopplex® D900 Non-directional Doppler, Huntleigh). Perforators found were marked on the patient's abdominal skin.

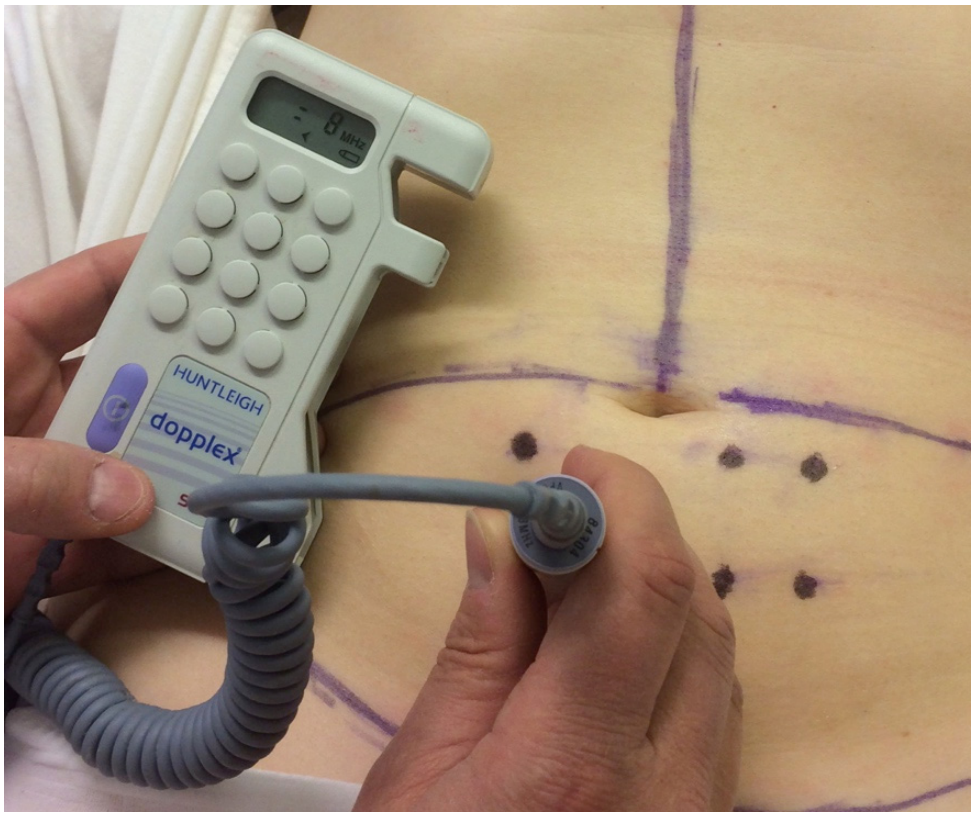


Figure 8.
Preoperative mapping of perforators using hand-held Doppler.

Study III:

Medical records of 301 consecutive patients who had undergone unilateral delayed breast reconstruction with a DIEP flap between 2006 and 2014 were retrieved. Data regarding tobacco smoking, BMI, age at surgery, total and final flap weight, abdominal scars, parity, number of perforators, chemotherapy, PMRT, and CTA or US were collected. We also looked for other medical issues that could impair normal wound healing.

Study IV:

In patients undergoing either DIEP or EP reconstruction, health care consumption in terms of surgery time and anaesthesia time was extracted from the electronic operating room charts. Data of hospital stay and outpatient visits postoperatively was

taken from the electronic patients charts. Furthermore, complications within 30 days were recorded in both groups until healing and tissue expansion was completed.

BREAST-Q

The BREAST-Q is a patient-reported outcome instrument designed to evaluate outcomes among women undergoing different types of breast surgery (56-58). This instrument includes quality of life domains such as psychosocial, sexual and physical well-being, and satisfaction domains, namely satisfaction with breasts, nipples, abdomen, outcome and care. In this study we used the reconstruction preoperative module.

Statistical analysis

The statistical studies were performed using the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) version 18.0 (paper I) and version 22.0 (paper II-IV) for data analyses. Wilcoxon´s signed-rank test was used in study I to analyse changes in blood flow and temperature. In study II the CTA and US groups showed approximately normal distribution. Measures were reported as means ± standard deviations and a T-test was adopted to assess significant differences.

In study III, odds ratios (OR), corresponding confidence intervals (CI) and probability values (p-value) were calculated using logistic regression to assess the influence of smoking and BMI.

In study IV, a Mann-Whitney U test was used to calculate p-values of the non-parametric data of short time complications in the DIEP and EP groups.

A p-value of < 0.05 was considered to indicate a statistically significant difference in all studies.

Ethics

The Regional Ethical Review Board in Lund, Sweden approved all studies.

Study I: Dnr 2011/716

Study II: Dnr 2011/664

Study III: Dnr 2014/703

Study IV: Dnr 2012/187

Summary of the results

Study I:

Indirect heating caused a statistically significant increase in blood flow in both DIEP flaps and control breasts.

All ten patients regained sensation for deep pressure in all four flap quadrants. A higher degree of sensitivity was even noted in some instances.

Seven patients perceived cold stimuli in their flaps and five perceived warmth.

Study II:

Mean surgery time was 249 minutes in the CTA group, and 255 minutes in the US group. The difference of six minutes in surgery time was not significant. Moreover there was no difference in complication rate between the two groups.

Study III:

In total, there were 102 (34%) complications in 94 patients (31%) with DIEP flaps. Sixty patients (20%) had flap complications and 42 (14%) had donor site complications. Eight patients (2%) had complications in both the flap and donor sites. Seventy-one (24%) patients needed a complementary surgery. Four flaps were lost (1.3%). Twenty-seven of 301 patients (9%) had venous congestions in the DIEP flap. There was no correlation between the size of the flap or the calibre of the anastomosed veins with occurrence of venous congestion. Complications unrelated to flap or abdomen included deep venous thrombosis (n=1), pulmonary embolism (n=2), and myocardial infarction (n=2).

In the former smoker group, the complication rate was significantly higher for donor site complications (p-value 0.025). The BMI of the study group ranged from 18-34 (mean 25.5). There was no statistical difference in complication rate depending on the patient´s BMI, age at surgery, total and final flap weight, abdominal scars, parity, number of perforators, chemotherapy, PMRT, and CTA or US.

Study IV:

The DIEP reconstruction procedure was significantly more demanding compared with EP with longer surgery time and hospital stay. However, the EP procedure required significantly more outpatient visits due to the step-by-step expansion.

Within the first 30 postoperative days, ten complications in nine patients were noted in the DIEP group while three complications occured in three patients in the EP group. We experienced neither flap loss nor early prosthesis infection.

General Discussion

Considerations regarding patients

Study I:

Eleven of 21 patients operated upon during the chosen study period did not participate. Two patients were excluded from the study, one because of flap loss and one because of newly diagnosed breast cancer in the contralateral breast. Nine patients did not want to participate for various practical reasons. We assume that the participating patients are representative for the total population reconstructed with DIEP flaps.

Study II:

Fourteen of 79 women who did not want to participate in study II had preoperative CTA according to departmental routines. One patient, randomized for a pre-operative CTA, withdrew from the study as she no longer wanted reconstruction. Due to the sudden illness of one surgeon during surgery, the operating time was considerably longer in that particular case of the US group. The patient involved in this case was considered an outlier and excluded from further analysis.

We consider these 63 patients to be representative of the total population reconstructed with DIEP flaps. Due to the prospective randomized design of the study, interpretation of results should be reliable.

Study III:

Medical charts from all 301 unilateral DIEP flap reconstructions in the period 2006-2014 were studied. The results should therefore be representative of the procedure.

Study IV:

One hundred and six consecutive patients who had undergone unilateral mastectomy, but no treatment with PMRT, were referred to our clinic for secondary breast reconstruction from spring 2012 to March 2016. Twenty-seven of these patients wanted an EP reconstruction and chose not to participate in the study. Ten patients were not suitable for inclusion; five patients were too skinny for DIEP reconstruction;

one patient had had earlier abdominal liposuction, and one had a previous abdominoplasty. Two patients were not appropriate for EP, one due to the scar situation on the chest, and the other one because of shoulder disability. One patient was excluded because of her comorbidity.

After informed consent was obtained, the remaining 69 patients were randomized to breast reconstruction either with DIEP flap (n=36) or EP (n=33). Two patients randomized for DIEP changed their minds and were reconstructed with EP outside the study. One patient withdrew from the study, as she no longer wanted reconstruction. Hence the DIEP group consists of 33 patients.

Two patients randomised to EP withdrew their participation from the study due to their wish for a DIEP flap. One patient chose to be reconstructed in her local hospital. One patient experienced a recurrence of breast cancer and was excluded. One patient who was asked to lose weight did not do so and consequently did not proceed to surgery. A surgeon who was not a member of the study team operated one patient, and this patient was therefore excluded. Hence the EP group consists of 27 patients.

In March 2016, 27 patients have undergone a DIEP flap reconstruction and 23 patients have undergone an EP reconstruction. Another ten patients await their operations. At present the cohort is not numerically complete but observed differences so far are pregnant.

Considerations regarding methods

Techniques for measuring blood flow

LDPI is a non-invasive method for estimating skin blood flow. However, it is not possible to quantify blood flow in absolute values. The LDPI delivers base line values from which blood flow changes can be monitored. Heating of the body is supposed to release vasoconstrictor tone with a following vasodilatation. This method is therefore suitable for studying a response to a stimulus such as a presumed blood flow increase due to vasodilatation following indirect heating (63). This capacity was utilized in study I where both normal and reconstructed breasts were monitored showing significantly increased LDPI values in all quadrants.

Techniques for measuring sensitivity

SWMT is an established method for measuring tactile sensitivity. It is easy to use, has acceptable reliability (64), and has been used before to assess sensitivity in reconstructed breasts (65).

The thermotest is also a well-established method (66). This test provides a quantitative measure of thermal perception in terms of thresholds.

BREAST-Q

BREAST-Q is best used to measure an effect of an intervention, for example a breast reconstruction. The frame of this study restricted us to using only the preoperative module. However, the use of BREAST-Q preoperativly enabled us to compare the two groups, and patient satisfaction and quality of life were nearly the same. Compared with a study by Sugrue (57), our patients in study IV had similar BREAST-Q scores in physical well-being chest and abdomen, but scored much lower in satisfaction with breasts, psychosocial and sexual well-being. This difference can be explained by the fact that the patients in Sugrue´s study went through a mastectomy with an immediate reconstruction and therefore did not experience life with one breast only.

Patient-reported outcome has become an increasingly important measure of different medical and surgical procedures. To score possible improvement in patient satisfaction and quality of life, our patients will be subjected to BREAST-Q reconstruction module postoperative, at the earliest 12 months after breast reconstruction and all secondary procedures are completed. The fact that many of the patients in the EP group actually wanted a DIEP may be seen in the BREAST-Q postoperatively as a lower score compared with the DIEP group. As a result of this we will ask patients who declined to participate in the study, for the reason that they wanted an EP reconstruction, to fill in the BREAST-Q postoperative form. In that way we can make a more precise comparison with the DIEP group as all patients will have received their desired reconstruction, which should be important for the perception of satisfaction.

Considerations regarding ethics

In study I, heating of the lower body was carried out within physiological ranges.

In study II, two well-established methods for preoperative mapping of perforators were compared. The gold standard CTA is invasive in terms of intravenously administered contrast medium and radiation, whereas US is completely non-invasive.

Study III is a retrospective study of medical charts. A patient could potentially experience invasion of her privacy if she knew that her medical chart had been studied. Questions may also arise in regard to handling of sensitive personal data.

In study IV we compare two well-known methods, DIEP flap versus EP reconstruction. Both methods are used in clinical routines. The DIEP flap is a more

complex procedure with an initially higher risk of complications. The patients were well informed about this but many of them actually had a preference for the DIEP procedure. Patients that preferred an EP reconstruction were able to decline participation in the study.

Taken together, we identified quite a large number of ethical issues, but the risks were judged as low in relation to the new knowledge achieved that would be of value for future patients.

Considerations concerning DIEP flap

A great advantage of a DIEP flap breast reconstruction is the fact that the flap is made of autologous material. Study I showed that a DIEP flap integrates very well with the chest with normal blood flow dynamics and capacity of regeneration of sensitivity. The skin and fat of the lower abdomen have properties that resemble breast tissue, and many women have unwanted laxity and excess skin that can be harvested to create a new breast. No muscle is sacrificed. Through clinical experience we know that a DIEP flap provides a soft, natural looking breast that gets even more natural and breast-like over time. A DIEP flap breast once completed lasts a lifetime.

In study II we found that the preoperative evaluation with CTA can be questioned. The findings rather point to the fact that the non-invasive technique of US is as good as "the gold standard" CTA. The small difference of six minutes in surgery time, in favor of CTA, is not great enough to continue to perform CTA preoperatively as a routine. In our department we have therefore ended the CTA assessment on a regular basis. Nowadays, invasive CTA is carried out on patients with abdominal scars before a unilateral breast DIEP reconstruction.

In study III we showed that a DIEP flap is successful in almost all cases. Only 1 % (297/301) of the DIEP flaps results in complete failure. However, every silver lining has its cloud. Safe surgery requires long experience and the learning curve is long. In Malmö, DIEP flap surgery was introduced in 1998 but we chose to include surgery only from 2006 onwards. We found that complications occurred related to both the donor site and the flap itself and the complication and the success rates were compatible with findings from other centers (37, 67). Even in the absence of complications the patient will have a long scar on the lower abdomen after DIEP surgery. Preliminary findings in study IV show that a DIEP reconstruction is a large-scale operation and initially health care demanding, although the surgery time for a unilateral DIEP has in Malmö been shortened from 7-8 hours in 2005 to 3-4 hours in 2014.

Patients operated upon in day surgery in our clinic are given intravenous anaesthesia with remifentanil (Ultiva®, GlaxoSmithKline) and propofol (Diprivan®, AstraZeneca) with the target controlled infusion (TCI) technique. The short half-life of the drugs and the continuous TCI administration contribute to short recovery time with less nausea. A drawback is that these drugs are expensive in comparison to the cheaper inhalation anaesthesia with desflurane (Suprane, Baxter) or sevorane (Sevorane®, AbbVie), which is used in almost all our in-ward patients. Our findings and thoughts regarding health care consumption and thereby costs for DIEP and EP, respectively, do not fully consider these anaesthesiological circumstances over which we do not have control.

In a retrospective British study from 2011 by Atherton et al., the differences in costs between DIEP and implants were minor and could in fact be justified by increased patient satisfaction and cosmetic outcome (68). A prospective Spanish study from 2015 by Lagares-Borrego et al. concluded that DIEP flap breast reconstruction, compared to two-stage implant surgery, was more cost-effective and involved fewer serious complications that resulted in reconstruction failure or undesirable aesthetic results (69).

One possible drawback was reported by Isern et al. 2011. The retrospective study was based on a historical material from our unit. The recurrence rate of breast cancer was found to be higher in patients reconstructed with TRAM or DIEP flaps compared with patients with mastectomy without reconstruction, and the hypothesis was that major surgery might increase the risk for breast cancer recurrence although the mechanism was unclear (70). The reconstructions were performed from 1982 to 2001 during which period the women often endured very long flap surgery time. Today the situation is quite different. The observation has not been confirmed by other studies, and therefore breast reconstruction with flaps remains a worldwide clinical routine until further notice.

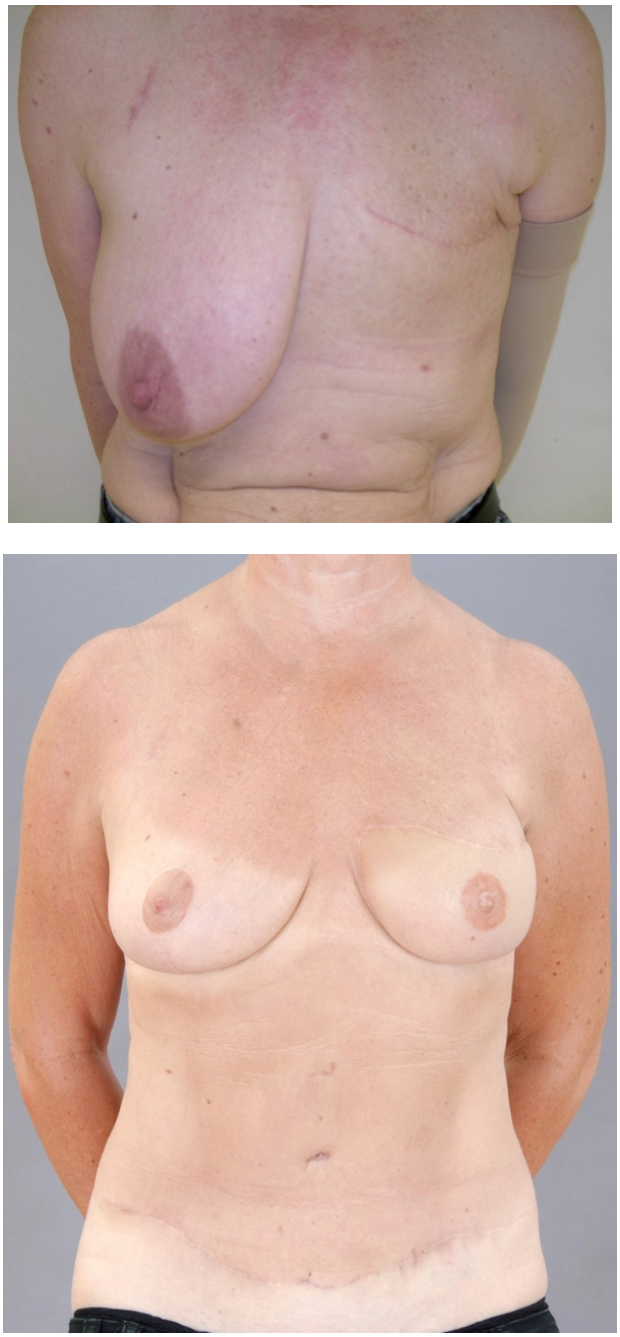


Figure 10.
Preoperative and one year postoperative photos of a fifty-two year old woman reconstructed with a DIEP flap on her left side in combination with a breast reduction on her right side.

Considerations concerning EP

A breast reconstruction with prosthesis is a safe procedure that has a good to excellent result in selected cases. A secondary EP reconstruction is a safe and fast operation that can sometimes be carried out in day surgery. The EP surgery causes no additional scars.

A soft breast with natural ptosis can hardly ever be accomplished with an EP. In patients who have had PMRT, this is particularly true due to fibrosis of the soft tissues. These difficulties with tissue expansion after radiation make the result less aesthetically appealing. A high risk for capsular contracture and other prosthesis complications are also drawbacks (5, 71).

In overweight (BMI >25) and obese (BMI>30) patients it is also harder to get an aesthetically pleasing result. The largest EP in ordinary clinical use is in the order of 700 cc. Therefore the contralateral breast has sometimes to be reduced to reach symmetry in overweight patients and in patients with large breasts.

In study IV patients reconstructed with EP needed a significant number of outpatient visits before expansion was completed. Moreover, with an implant reconstruction the risk of complications raises the more time passes. There may be a need for additional surgery with implant reposition, implant change, capsular cleavage and even change of reconstructive method to a DIEP flap. In a prospective Danish study from 2011, Hvilsom el al. studied women without PMRT undergoing breast implantations. They found a high overall 10-year risk of 68% for complication, and the risk for reoperation was 39%. Complications included severe capsular contracture and displacement/asymmetry of the implant (72). A systematic literature review by Tsoi et al. 2014 showed that tissue expander/implant reconstruction had a higher risk of reconstructive failure and surgical-site infection compared with autologous abdominal tissue reconstruction (73).

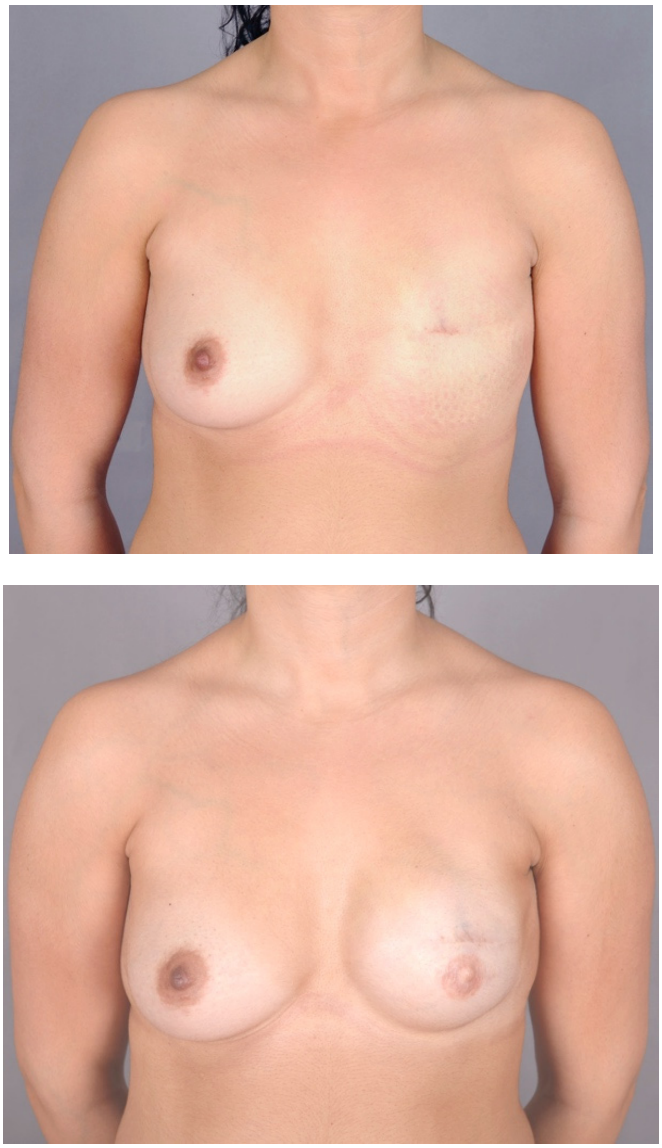


Figure 11.
Preoperative and two years postoperative representative photos of a thirty-five year old woman reconstructed with an EP.

Remarks concerning smoking and BMI

As a result of study III, we should continue to demand a smoke-free period pre- and postoperativly in order to minimize complications. In 20 years´ time, not as many women as today will have a smoking history (74) and the women who will need breast reconstructions will therefore hopefully experience fewer complications.

Obesity is getting more and more common all over the world and about 50% of Swedish women 45-64 years of age are overweight or obese (75). Today, DIEP reconstruction is seldom performed on patients from southern Sweden who have a BMI higher than 30 since there is a fear that these patients will suffer from more postoperative complications than patients with lower BMI (76, 77). This view does not gain support by our findings in study III. Moreover, our clinical impression is that the aesthetical result of a DIEP reconstruction in overweight and obese women is often better than an EP reconstruction. This indicates that we should not hesitate to reconstruct patients with a DIEP flap even if their BMI is slightly above 30.

Concerning patients with low BMI, we did not see a higher complication rate, which suggests that a DIEP reconstruction also is a suitable method for this patient group. This is in agreement with findings by Weichman et al. from 2015 who showed that microsurgical breast reconstruction is efficacious in patients with a low BMI. Furthermore BREAST-Q analysis resulted in higher satisfaction with breasts when compared with prosthetic reconstruction (78).

Conclusions

Study I:

There is a skin blood flow regulation in DIEP flaps one year after reconstruction. Blood flow dynamics are very similar to those in the normal breast. There is also some recovery of tactile and thermal sensibility.

Study II:

There are no statistical differences in surgery time or complications when US is used as an alternative to CTA.

Study III:

Smoking habits affect complication rates in DIEP surgery. Previous smokers have a risk for donor site complications that are more than doubled compared to non-smokers. Differences in BMI do not have any significant impact on complication rates.

Study IV:

Short-term follow-up shows statistically longer surgery time, anaesthesia time and hospital stay. Complications are more common in DIEP surgery within 30 days postoperativly. EP patients have a significantly higher number of outpatient visits counted from surgery to completed reconstruction.

Future directions

Breast reconstruction with a DIEP flap has developed continuously over the last 20 years. Today it is the first choice for autologous breast reconstruction and considered to be safe with acceptable complication rates. However, we still have difficulties to deal with.

Women with breast cancer today are very well informed, and often know before the first meeting with the reconstructive surgeon which method of reconstruction they prefer. As a consequence, the requests for autologous breast reconstruction are increasing. The demand of prophylactic bilateral DIEP reconstructions will probably also rise the more we learn about genetic risk factors for breast cancer, and the ability to detect gene mutations increases.

From these points of view, it is important to create adequate recourses to satisfy the increased number of patients wishing to have a DIEP flap. The results from study III suggest that we also have to challenge existing guidelines regarding an elevated BMI. Simultaneously, flap reconstruction techniques are getting better and better. In the future, both surgery time and hospital stay may be shortened due to further improved surgical techniques and more efficient anaesthesiological methods.

More and more focus is nowadays on patient satisfaction and quality of life. A woman that can choose the method of reconstruction is also *per se* a more contented patient. Therefore, it will be of great interest to follow the patients in study IV in the long run, both in terms of complications and in terms of patient satisfaction and quality of life. It is also of great importance to investigate the cancer recurrence rate in the two groups, as one previous study indicated an increased recurrence rate in microsurgical breast reconstruction. We therefore plan to re-evaluate the patients both five and ten years after breast reconstruction. The results can hopefully contribute to a revision of the Swedish national guidelines for breasts reconstructions with autologous tissue. Thereby, we will have better grounds for decision-making regarding the method chosen for reconstruction in each case. This would be beneficial both for surgeons and patients.

Summary in Swedish
Svensk sammanfattning

Bröstcancer är den vanligaste cancersjukdomen hos kvinnor i Sverige; en kvinna av nio kommer att få diagnosen bröstcancer före 75 års ålder. Den kirurgiska behandlingen är antingen bröstbevarande kirurgi då en del av bröstet tas bort, eller s.k. mastektomi då hela bröstet tas bort. I södra Sverige önskar hälften av alla kvinnor under 65 år, och som genomgått mastektomi, en bröstrekonstruktion. Indikationen för bröstrekonstruktion är patientens egen önskan om ett nytt bröst och målet är att återskapa form, storlek, symmetri samt känslan av ett naturligt bröst. Bröstrekonstruktion kan göras med olika metoder vilket gör det möjligt att individualisera behandlingen för varje patient. Vävnaden kan ersättas av en protes, av kroppsegen vävnad eller av en kombination av dessa metoder. Rekonstruktionsmetod väljs utifrån patientens hälsa, anatomi, tidigare genomgångna kirurgiska ingrepp samt eventuellt genomgången strålbehandling efter bröstcanceroperationen. Valet av rekonstruktionsmetod ska också sammanfalla med patientens egna önskemål och förväntningar, och många patienter vill helst ha ett nytt bröst som är gjort av kroppsegen vävnad. Bröstrekonstruktion med kroppseget material bör enligt Socialstyrelsens nuvarande nationella riktlinjer reserveras för patienter som tidigare genomgått strålbehandling eftersom en bröstprotes som opereras in i tidigare strålad vävnad har stor risk för komplikationer. Enligt riktlinjerna bör således icke-strålade kvinnor rekonstrueras med s.k. expanderprotes och det baserar sig framför allt på att bröstrekonstruktion med kroppseget material kräver mikrovaskulär teknik. Denna teknik innebär att kirurgen kopplar ihop små blodkärl med hjälp av ett operationsmikroskop och små specialinstrument, och detta är resurskrävande. Den vanligaste rekonstruktionsmetoden med kroppsegen vävnad är en s.k. DIEP-lambå. En sådan lambå som används för att göra ett nytt bröst består av hud och fett med vidhängande blodkärl från bukens nedre del. Vid operationen kopplas kärlen från bukvävnaden ihop med kärl som ligger under revbenen på bröstkorgen. Proceduren vid en DIEP-lambå liknar en bukplastikoperation och många patienter uppskattar minskningen av överskottsvävnaden på buken. Det nya bröstet återfår viss beröringskänsel, får ett naturligt häng och följer med patientens eventuella viktförändringar genom livet. Nackdelar med en DIEP-rekonstruktion är att det är en stor och resurskrävande operation med jämförelsevis lång operationstid. Vid

operationen skapas sår både på buken och på bröstkorgen och det finns en relativt hög komplikationsrisk i samband med operationen.

Avhandlingsarbetet handlar om olika aspekter på bröstrekonstruktion med DIEP-lambå efter bröstcancer.

Studie I var gjord på 10 kvinnor som genomgått DIEP-rekonstruktion ett år tidigare. Blodflöde och känsel för beröring, värme och kyla i det nya bröstet undersöktes. Sammanfattningsvis visade studien att det nya bröstets blodflöde reagerar fysiologiskt på temperaturstimulering och en viss återhämtning av känseln fanns också. Dessa regenerativa förlopp visar dock påtaglig variation mellan de olika individerna.

Studie II var prospektivt randomiserad. Före operationen undersöktes den kommande lambåns blodflöde med kärlröntgen (CTA) (n=32) respektive handhållen ultraljudsdoppler (n=31). Den primära frågeställningen var om CTA gav en säkrare bild av blodkärlens anatomi, vilket i så fall skulle innebära att operationen kunde genomföras snabbare. Den sekundära frågeställningen var om bilden av blodkärlens anatomi också ledde till färre komplikationer. Sammanfattningsvis visade studien väldigt små skillnader både vad det beträffar operationstid och komplikationer. Fyndet talar för att den enklare metoden ultraljud skulle kunna ersätta den mera komplicerade metoden CTA åtminstone i ett operationsteam med lång erfarenhet av DIEP-rekonstruktioner. Dessa resultat har medfört att vi inte längre rutinmässigt utför CTA inför en enkelsidig DIEP-rekonstruktion.

I **studie III** följde vi retrospektivt de patienter som opererats i Malmö 2006-2014 med enkelsidig DIEP-lambå. Vi studerade främst inverkan av BMI och rökning på komplikationsfrekvensen, men tittade även på faktorer som ålder vid operation, lambåvikt, ärr efter tidigare bukkirurgi, tidigare barnafödsel, antal blodkärl till lambån, tidigare cytostatika- och strålbehandling, utredning med CTA eller ultraljud inför operationen samt andra medicinska åkommor som skulle kunna vara av betydelse. Vi fann att tidigare rökare hade en signifikant ökad risk för komplikationer från tagstället, d.v.s. buken, jämfört med patienter som aldrig rökt. I vårt material hittade vi, kanske lite överraskande, inte någon ökad komplikationsrisk med högt eller lågt BMI. Övriga faktorer inverkade inte heller märkbart på komplikationsfrekvensen.

Studie IV: Våren 2012 inleddes en prospektivt randomiserad studie där vi jämförde bröstrekonstruktion med DIEP-lambå med bröstrekonstruktion med expanderprotes. Samtliga patienter som remitterades till oss för enkelsidig rekonstruktion och som inte genomgått strålning bedömdes om de var lämpliga att medverka. De patienter som avböjde att vara med i studien erbjöds en expanderprotesrekonstruktion enligt gällande riktlinjer. På kort sikt jämförde vi vårdkonsumtion i form av operationstid, narkostid, vårddygn, antal mottagningsbesök samt komplikationer inom 30 dagar efter rekonstruktionen. I studien har vi hittills inkluderat 60 patienter och fram till mars 2016 har vi opererat 27 DIEP-lambåer och 23 expanderproteser.

Av naturliga orsaker är DIEP-rekonstruktion initialt mer resurskrävande eftersom det krävs en betydligt längre operations- och vårdtid. Dessutom uppstår fler komplikationer under vårdförloppet. Antal mottagningsbesök är dock signifikant fler i expanderprotesgruppen på grund av att protesen succesivt måste fyllas med koksalt för att bröstet ska uppnå önskad volym. Resultaten pekar mot att bröstrekonstruktion med DIEP-lambå till en början är resurskrävande men ger på längre sikt ett naturligt och hållbart resultat.

Sammanfattningsvis har bröstrekonstruktion med DIEP-lambå utvecklats succesivt under de senaste 20 åren och är idag förstahandsval när det gäller kroppsegen bröstrekonstruktion. En DIEP-operation anses vara säker med ett godtagbart antal komplikationer. Vi har trots detta fortfarande många frågor att besvara. Kvinnor som genomgått bröstcancer är idag ofta välinformerade och vet redan före första besöket inför en bröstrekonstruktion vilken rekonstruktionsmetod de önskar. Efterfrågan av kroppsegen bröstrekonstruktion ökar och det är därför viktigt att skapa nödvändiga resurser för att möta denna. Teknik och logistik i samband med DIEP-rekonstruktion förbättras hela tiden. I framtiden kan kanske patienterna som ska rekonstrueras med DIEP-lambå sövas med en annan typ av narkosmedel som eventuellt kan ge en kortare vårdtid.

Med tanke på resultaten i studie II kan det finna anledning att ifrågasätta begränsningen av DIEP-rekonstruktioner till enbart patienter med BMI< 30. Alltmer fokus läggs också på patientnöjdhet och livskvalitet. En kvinna som får välja rekonstruktionsmetod är också en nöjdare patient. Därför blir det väldigt intressant att följa våra patienter i studie IV, både avseende komplikationsfrekvens, patientnöjdhet och livskvalitet. Vi följer upp patienterna när rekonstruktionen, eventuell bröstförminskning eller bröstlyft av det friska bröstet, samt vårtrekonstruktion är klar, det vill säga 1-2 år efter den initiala rekonstruktionen. Då undersöks resultatet av bröstrekonstruktionen genom mätning av volym, symmetri och mjukhet samt genom fotografering. Patienterna får också i en enkät (BREAST-Q) uppge nöjdhetsgrad samt uppskatta sin eventuellt förbättrade livskvalitet.

Av erfarenhet förväntar vi oss fler komplikationer i expanderprotesgruppen på lång sikt med till exempel s.k. kapselkontraktur, när det bildas en hård och ibland smärtsam och deformerande kapsel runt implantatet, infektion, och ett för patienten inte acceptabelt estetiskt resultat. Det kan leda till omoperationer med kapselklyvning, protesbyte, och i visa fall byte av rekonstruktionsmetod till DIEP-lambå. Av största vikt är också att undersöka möjliga canceråterfall i de båda grupperna. Vi planerar därför att följa upp patienterna i studie IV fem och tio år efter rekonstruktion. Resultaten kan komma att bidra till uppdaterade nationella riktlinjer för bröstrekonstruktion med kroppsegen vävnad. Därigenom får vi ett bättre underlag för att bestämma vilken rekonstruktionsmetod som är mest lämplig i det enskilda fallet. Detta underlättar både för kirurgen och för patienten.

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