Faculty of health sciences
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Optimising breast reconstruction

A clinical study on autologous breast reconstruction

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A dissertation for the degree of Philosophiae Doctor

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Contents :

To my family

“Reconstructive surgery is innovation”

Stephen J. Mathes (1943-2007)

Plastic surgeon and former editor of

Journal of Plastic and Reconstructive Surgery

Acknowledgements

My journey into plastic surgery research started in 1997 when I was given the opportunity to work with plastic surgeons Salathiel Mzezewa and Lars Salemark in a project related to burns treatment in Harare, Zimbabwe. They, together with professor Kent Jönsson at the University of Zimbabwe, became true friends and inspirers during my time abroad, and helped me to publish my first papers. My sincerest gratitude goes to these colleagues for allowing me to take my initial steps in medical research!

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Abbreviations

BMI	Body mass index
CT	Computed tomography
CTA	Computed tomography angiography
DIEP	Deep inferior epigastric artery perforator
DIRT	Dynamic infrared thermography
ERAS	Enhanced recovery after surgery
ICG	Indocyanine green
ICG-FA	Indocyanine green fluorescence angiography
IR	Infrared
IRT	Infrared thermography
LD	Latissimus dorsi
LFM	Liberal fluid management
LICAP	Lateral intercostal artery perforator
LSGAP	Lateral superior gluteal artery perforator
LTD	Lateral thoracodorsal
MFM	Modified fluid management
mK	Millikelvin
MRA	Magnetic resonance angiography
MRI	Magnetic resonance imaging
ms-TRAM	Muscle sparing TRAM
nM	Nanometer
NIR	Near infrared radiation
PMRT	Postmastectomy radiotherapy
SGAP	Superior gluteal artery perforator

SIEA	Superficial inferior epigastric artery
SIEV	Superficial inferior epigastric vein
TDA	Thoracodorsal artery
TDAP	Thoracodorsal artery perforator
TRAM	Transverse rectus abdominis musculocutaneous
TUG	Transverse upper gracilis muscle

List of papers

Paper I

Thomas Sjöberg, Louis de Weerd

The pedicled LICAP flap combined with a free abdominal flap in autologous breast reconstructions

Plastic and Reconstructive Surgery Global Open 2018; 6(1), e1562

Paper II

Thomas Sjöberg, James B. Mercer, Sven Weum, Louis de Weerd

The value of dynamic infrared thermography in pedicled thoracodorsal artery perforator flap surgery

Plastic and Reconstructive Surgery Global Open 2020; 8(7), e2799.

Paper III

Thomas Sjöberg, Anmar Numan, Louis de Weerd

Liberal versus modified intraoperative fluid management in abdominal flap breast reconstruction. A clinical study.

Plastic and Reconstructive Surgery Global Open 2021; 9(9), e3830

Abstract

Brystrekonstruksjon etterspørres hyppig etter behandling av brystkreft eller kreftforebyggende kirurgi. Brystet gjenoppbygges enten ved bruk av syntetiske brystimplantater (brystproteser) eller ved å flytte kroppseget vev, såkalt autolog rekonstruksjon, og noen ganger ved å kombinere disse teknikkene. Etter at rekonstruktiv brystkirurgi ble introdusert ved professor Vincent Czerny i Heidelberg i 1895, har stadig mer avanserte metoder blitt utviklet for å oppnå et optimalt estetisk resultat med lavest mulig risiko for komplikasjoner. Best mulig kirurgisk teknikk og optimal anestesiologi (narkose/bedøvelse/ væskebehandling under operasjonen) er viktig for sluttresultatet.

Ved bruk av autolog brystrekonstruksjon kan man i størst mulig grad etterligne et naturlig bryst, både til fasong og konsistens. Moderne mikrokirurgiske teknikker benytter seg av forflytting av vev fra nærliggende eller fjernere donorsteder, hvilket betyr at vevet (lappen) som skal flyttes frigjøres fra sin opprinnelige plassering og enten dreies over til nytt sted (stilket lapp) eller løsnes helt fra kroppen (fri lapp). Opprinnelig ble ofte hele eller deler av underliggende muskel tatt med for å sikre tilstrekkelig blodforsyning, men nyere metoder tillater flytt av slike lapper uten muskelvev ved bruk av såkalte perforantlapper. Dette reduserer negative følgevirkninger av å bruke eget vev til brystrekonstruksjonen og bevarer normal funksjon i størst mulig grad. Uansett metode er blodforsyningen i det nye brystet avhengig av små blodkar under lappen, som må lokaliseres og løsnes fra omkringliggende vev før vevsflyttingen. Disse perforantene er oftest kun noen få millimeter store, men kan likevel forsyne et stykke vev på størrelse med et normalt bryst. En rekke metoder brukes for på finne de beste perforantene og så langt som mulig sikre en adekvat blodforsyning til det nye brystet. Noen metoder krever avansert utstyr og spesiell kompetanse, imens andre metoder er nokså enkle å håndtere for pasient og personell. Doppler ultralyd og fremstilling av blodkarene ved CT (computertomografi) er de hyppigst brukte teknikkene i forbindelse med autolog brystrekonstruksjon.

Autolog brystrekonstruksjon innebærer oftest langvarige operasjoner. Best mulig bedøvelse og optimal kontroll på viktige fysiologiske parametere, slik som blodtrykk, kroppstemperatur og erstatning av væsketap under kirurgien, bidrar i vesentlig grad til et vellykket resultat. Flere nyere studier har funnet god nytte av moderat væsketilførsel og tidlig mobilisering for at oppnå maksimal blodforsyning i lappene, ettersom man dermed reduserer unødvendig væskesamling i vevet under og etter operasjonen. Slikt gir en lavere risiko for komplikasjoner. Helt entydige retningslinjer for optimal anestesiologi i forbindelse med autolog brystrekonstruksjon er dog fremdeles ikke klarlagt.

Denne avhandlingen presenterer tre forskjellige studier med hensikt å evaluere nye metoder for å optimalisere resultatet ved brystrekonstruksjon med eget vev.

Den første studien beskrev en kirurgisk metode for å rekonstruere bryst hos pasienter med begrenset vevsoverskudd på magen. Ved å kombinere flytting av vev fra magen (DIEP lapp) med en stilket lapp fra siden av brystkassen (LICAP lapp) klarte man å oppnå et større volum og bedre fasong på det nye brystet, enn det som hadde vært mulig med DIEP lapp alene. På tross av denne kombinasjonen med to lapper var det mange pasienter som trengte ytterligere operasjoner for å oppnå symmetri med det ikke-opererte brystet.

Den andre studien evaluerte nytteverdien av å bruke et varmekamera for å lokalisere og vurdere kvaliteten på perforanter i huden i øvre laterale del av ryggen, i forbindelse med brystrekonstruksjon med stilket perforant lapp (TDAP lapp). Varmekamera ble også brukt under og etter operasjonen for å vurdere blodgjennomstrømningen i lappen etter at denne var dreid over til ny plassering. Studien viste at kombinasjonen av ultralyd (Doppler) og varmekamera (DIRT) var en utmerket måte å finne de beste perforantene i det aktuelle området. Videre fant man at varmekamera var nyttig for å påvise problemer med blodforsyningen i lappen under og etter operasjonen. Derved reduserte man risikoen for komplikasjoner tidlig i forløpet. Varmekamera-undersøkelse, til forskjell fra andre hyppig brukte metoder slik som CT, er forholdsvis enkel å bruke og medfører ingen risiko for pasienten.

Den tredje studien sammenlignet risikoen for komplikasjoner under og etter autolog brystrekonstruksjon i relasjon til to forskjellige strategier for å stabilisere blodtrykk og erstatte væsketap under operasjonene. Opprinnelige strategi, brukt under perioden 1999 – 2005, tillot mere voluminøs væsketilførsel og bruk av løsninger med større molekyler (kolloider) for å opprettholde et adekvat blodtrykk. Etter 2005 ble den anestesiologiske tilnærmingen endret, slik at tilført væskevolum under operasjonen ble redusert og trykkstøttende medikasjon (vasopressor) ble brukt for å vedlikeholde adekvat blodsirkulasjon. Studien fant en redusert risiko for kirurgiske og medisinske komplikasjoner etter at den nye protokollen ble tatt i bruk. Størst forskjell ble observert i relasjon til kirurgiske komplikasjoner, da opprinnelig anestesiprotokoll oftere førte til delvis eller totalt tap av det nye brystet som følge av utilstrekkelig blodforsyning i lappene på bakgrunn av større væskeoppsamling i vevet. Oddsraten for komplikasjoner etter operasjonen ble redusert med over 50 %.

Behandlingsmetodene som er beskrives i denne avhandlingen kan også benyttes i forbindelse med annen kirurgi. Nytteverdien ved bruk av varmekamera er verifisert i en rekke tidligere studier. Redusert tilførsel av væske i forbindelse med langvarige operasjoner av forskjellige karakter har ført til lavere risiko for komplikasjoner på lik linje med våre funn. Strikt bruk av optimal anestesi, inklusiv kort fasteperiode før operasjonen, samt tidlig mobilisering inngår i de mest moderne strategiene for avansert kirurgisk behandling. Såkalt ERAS (*enhanced recovery after surgery*) protokoll innføres nå i de fleste kirurgiske disipliner og kan bidra til kortere og enklere sykehusopphold.

Brystrekonstruksjoner vil etterspørres i overskuelig fremtid. Selv om rekonstruksjon ved syntetiske implantater for de fleste fremstår som en enklere og mindre risikabelt alternativ, kan en forvente at fremtiden bringer enda bedre metoder for å optimalisere behandlings-forløpet og redusere risikoen for komplikasjoner også ved autolog rekonstruksjon. Robotassistert kirurgi vil derfor sannsynlig bli betydelig hyppigere fremover.

Denne avhandlingen kan bidra til å vise veien videre i noen aspekter av rekonstruktiv brystkirurgi.

Introduction

Plastic surgery is a problem-solving specialty, with almost every patient presenting a unique challenge requiring a likewise unique solution. Regardless of the aetiology, location or type of problem, the reconstructive plan must acknowledge the anatomical extent of the defect and the future requirements for the reconstruction. Different from many other surgical specialties, the reconstructive surgeon frequently needs to divert from established protocols as the individual problems usually need a tailored solution or an innovative technique to succeed (Fig. 1). Once such a technique has been introduced it can often be optimized to improve the final results.

Figure 1: An illustration of the "Italian method" to reconstruct nasal defects described by Gaspare Tagliacozzi (1545-99). Skin from the upper arm was brought to the nose as a pedicled flap and the raised arm was supported by a customized dressing until the pedicle could be divided at 20 days after the initial surgery. From: Gaspare Tagliacozzi, De Curtorum Chirurgia per Insitionem. Venezia, Roberto Meietti, 1597, tab. VIII. Bologna, Putti's Donation, Rizzoli Orthopaedic Institute

Innovative reconstructive surgical techniques have been endorsed since the start of this discipline and were a prerequisite in the evolution of plastic surgery.[1] Novel procedures to correct nose or earlobe defects were described approximately 800 B.C. by the Indian physician Maharshi Sushruta.[2] Further progress in reconstructive surgery through novel thinking and thoughtful observation of anatomy has expanded the field tremendously to enable surgeons to provide service to patients of all ages and with reconstructive needs in all anatomical areas. The work presented in this thesis is an example of the on-going evolution of reconstructive breast surgery.

The challenges in autologous breast reconstruction

Studies have demonstrated the value of breast reconstruction to improve quality of life in terms of body image, vitality, sexuality and general well-being.[3-5] Today, breast reconstruction has become an integrated part of breast cancer treatment. Increased awareness of the possibilities with current reconstructive techniques sees more women asking for reconstructive breast surgery after treatment of malignancies as well as to treat benign conditions, such as defects after trauma or congenital malformations. Breast reconstruction after prophylactic removal of a healthy breast, following contralateral breast cancer or confirmed gene-mutations with increased risk of malignant disease, is also more in demand. The goal of reconstructive breast surgery is to recreate a natural looking, aesthetically pleasing breast with a natural softness. In addition, the risk for complications and other adverse outcome during and after the surgery should be kept as low as possible.

Women opting for autologous reconstruction, utilizing surplus tissue from their own body, are commonly put through rather long-lasting and complex surgical procedures. The result is expected to meet the highest possible standards in terms of aesthetic appearance and experienced “normality”.[6] Advanced reconstructive surgery comes with the highest demands for technical skills by the surgical and anaesthesiologic team. Nevertheless, complications occur in a small number of patients. Previous medical conditions, unhealthy lifestyle habits or prior surgery may contribute to an increased risk of adverse events.

This thesis presents new strategies and innovative techniques on how to optimize autologous breast reconstruction, in order to continue the pursuit for better results with less risk. The included papers describe the planning and execution of flap-based reconstructive breast surgery with an emphasis on surgical and anaesthesiologic approaches.

Background

The beginning of reconstructive breast surgery

The first reported attempt to reconstruct a breast with autologous tissue was by professor Vincent Czerny in Heidelberg in 1895.[7] Following mastectomy due to a benign disease, a large lipoma was removed from the flank to recreate the breast. One year later, he reported that the breast had maintained its shape and fullness.

Nowadays breast reconstruction is an integrated part of the treatment following breast removal due to established breast malignancies or as a prophylactic measure in case of increased risk for breast cancer as well as to correct congenital breast malformations. Papyrus writings from ancient Egypt dating back to 600 B.C. are among the earliest known descriptions of breast cancer. Initial treatment focused on only removing the affected part of the breast. This surgical approach changed radically in 1894, when the US surgeon William Stewart Halsted introduced a more aggressive technique in an attempt to control the disease by removing more of the pericancerous tissue (the Halsted radical mastectomy).[8] Moreover, he openly discouraged reconstructive breast surgery, claiming that reconstruction would hide a local recurrence of the malignancy or adversely modify the course of the disease. Despite Halsted’s opinion, in 1906 the Italian surgeon Tansini introduced the pedicled musculo-cutaneous latissimus dorsi (LD) flap to create a new breast.[9] Nevertheless, because of Halsted’s strong influence, it was not until the 1970’s that breast reconstruction using autologous tissue became more acceptable. By this time breast cancer surgery had shifted towards a more conservative strategy combined with radiation and chemotherapy. Reports of flap reconstructions by pioneers such as Obredanne, Sir Harold Gillies, Hohler and Bohmert led the way towards more efficient reconstructive techniques with fewer stages and less donor site morbidity.[10-12] In addition, two-staged breast reconstruction using permanent silicone implants was introduced in 1963 by Cronin et al.[13] This was later followed by reports on immediate breast reconstructions with tissue expansion and implants.[13-16]

Musculocutaneous flaps

The musculocutaneous LD flap was reintroduced to reconstructive breast surgery in 1976 by Olivari et al.[17] The resulting donor site scar on the back, problems with postoperative donor site seroma and frequent need for contralateral breast reduction to achieve symmetry, nonetheless stimulated reconstructive surgeons to develop other techniques, such as endoscopic harvesting and pre-expansion.[18,19] Since the LD flap often does not provide adequate volume on its own it is often combined with an implant.[20] Interest in total autologous breast reconstruction initiated the search for methodological refinements to achieve larger volume of the reconstructed breast.[21,22] Also other donor sites came into play. Based on surplus abdominal skin and subcutaneous tissue, both vertically and transversally oriented flaps were invented. [23,24] The transverse flap was especially beneficial from an aesthetic standpoint, because of the more inconspicuous donor site scar on the lower abdomen. However, both flap types comprised at least one of the vertically oriented rectus abdominis muscles as a pedicled bridge carrying the necessary flap vasculature within and under the muscular tissue. The reduced muscle stability, after removing one or both rectus muscles, increases the risk for donor site morbidity such as weakness and herniation.[25-27] The introduction of a free transverse rectus abdominis musculocutaneous (TRAM) flap by Holmström in 1979 was a major step forward.[28] Compared with the pedicled flaps, the free

TRAM flap provided improved freedom to shape its transverse adipocutaneous segment into a breast-like design of adequate volume. This was the starting point for further development of free flaps based on abdominal wall tissue, resulting in procedures where the rectus abdominis muscle is only partially severed (ms-TRAM flaps) or left intact (superficial inferior epigastric artery (SIEA) flap) in order to reduce the postoperative donor site morbidity.[27,29] Also other donor sites for musculocutaneous flaps, such as the free transverse upper gracilis (TUG) flap, are occasionally used in situations when the abdominal tissue in unsuitable for the reconstructive needs.[30] The dominating development in free flap breast reconstruction, however, is to use perforator flaps, in which no muscular tissue has to be sacrificed.

Perforator flaps

The development of precise surgical instruments, high-definition surgical microscopes and innovative anatomical studies facilitated microsurgical evolution towards tissue flaps supported by more delicate pedicles.[31] By meticulous dissection, small subcutaneous vessels could be freed from the surrounding muscle or other soft tissue, to provide flap perfusion without “unnecessary” tissue harvest. The knowledge of, and experience with, such perforator flaps have since expanded tremendously. A huge variety of new flaps have been described, based on the multitude of perforators that arise between or pass within muscles towards subcutaneous tissue and skin.[32] The accepted nomenclature dictates that perforator flaps are named after their source vessels, although other classifications are still occasionally used.[33] The obvious benefits compared to musculocutaneous flaps are the increased freedom of design, the possibility to combine several flaps on a single vascular source pedicle and less donor site morbidity. [34,35]

Commonly utilized perforator flaps in reconstructive breast surgery recruit surplus tissue from the lower abdomen, the buttocks or the back (Fig. 2).

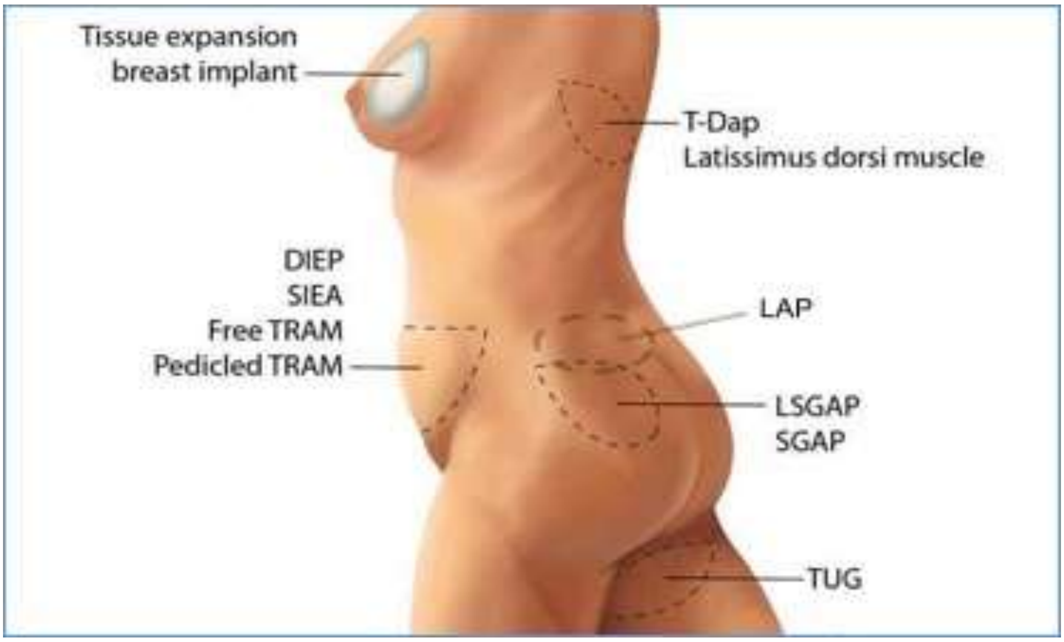


Figure 2: The illustration describes frequently used options in reconstructive breast surgery, utilizing either synthetic implants or surplus tissue from various anatomical areas of the body. Most tissue flaps are named after their perforating vessels. T-DAP: thoracodorsal artery perforator, DIEP: deep inferior epigastric perforator, SIEA: superficial inferior epigastric artery, TRAM: transverse rectus abdominis muscle, LAP: lumbar artery perforator, LSGAP: lateral superior gluteal artery perforator, SGAP: superior gluteal artery perforator, TUG: transverse upper gracilis muscle. Modified from an illustration of www.hopkinsmedicine.org.

The disadvantages of perforator flaps are related to the delicate dissection needed to free the small blood vessels from surrounding tissue, as inadvertent damage can easily occur. Thorough understanding of the local vascular anatomy and precise surgical technique is of outmost importance to promote successful results.[36] Furthermore, detailed preoperative mapping of the donor site vasculature is often necessary to facilitate selection of the most appropriate perforator. In comparison to flaps with a larger pedicle comprising several perforators, such as musculocutaneous flaps, the blood perfusion to perforator flaps depends on a single or few vessels of small calibre -, i.e. perforators. It is therefore very valuable to obtain thorough information on the perfusion pattern of the selected perforator(s) to allow for a design that ensures adequate flap viability while also providing tissue of suitable quality and character to mimic the lost integument. Perforator flaps usually comprise several vascular territories, where each territory has its own source artery to provide blood perfusion to that particular area. In addition, adjacent vascular territories are interconnected through a network of vessels at the subcutaneous and subdermal level, which allow for blood perfusion over territorial borders. Therefore, also large flaps, such as the DIEP flap, can be reliably perfused by a single perforator even though adjacent source vessels have been severed when the flap is dissected. In order to reveal possible problems related to the flap vasculature, and therewith flap perfusion, intra- and postoperative flap monitoring is essential since compression, kinking and torsion of the tiny blood vessels can easily occur during and after surgery.

All perforator flaps are composed of skin and subcutaneous tissue, that should be possible to harvest without imposing overly tense or unsightly scars at the donor site. However, in some patients this might be a challenge if neither the subcutaneous tissue volume nor the available skin at a single donor site suffice to fulfil the requirements. In addition, previous surgery can reduce the availability of donor site tissue and will increase the risk for complications in relation to both donor site and flap.[37,38] There are various surgical techniques to increase flap size and volume, such as extended flaps or stacked flaps.[39-43] Although such procedures can help to achieve acceptable outcome, some of them are complex and time demanding, which can increase the risk for complications.[44]

Other reconstructive techniques

Modern breast reconstructive surgery also includes autologous fat transplantation, either as a stand-alone procedure or in combination with other reconstructive options. Thereby, fat is harvested through cannulas connected to a suction device as in any liposuction procedure. Following removal of superfluous interstitial, the purified fat is transplanted in several layers into the recipient site tissue.[45] The fat graft is initially dependent on diffusion of oxygen and nutrients from the surrounding subcutaneous or muscular vasculature, as the free fatty transplant lacks blood vessels. Neoangiogenesis at the recipient site is crucial to enable permanent survival of the transplanted fat, although some loss of tissue (20 – 90 % of postoperative transplant volume) is expected during the first three months after surgery.[45] Since oxygen and nutrients can only diffuse over a short distance, relatively thin layers of fat will survive at each level. Thus, several successive procedures may be required to complete the reconstruction when large volumes of fat are required. Adipose-tissue derived stems cells or platelet derived growth factors can be added to the fat graft in order to enhance graft survival.[46] Such might be a way to reduce the number of procedures needed in large volume fat transplantation.

In selected cases, a combination of several reconstructive techniques can be necessary to achieve an optimal outcome.

The evolution of perioperative fluid management

Intravenous fluid replacement to compensate for fluid losses was first performed in England during the early 19th century. In 1831, William Brooke O`Shaughnessy reported on the clinical picture of cholera during the British epidemic. He had observed that blood analysis of the patients indicated a devastating fluid loss that might be compensated by intravenous infusion of water and soluble salts (Fig. 3).[47]

Figure 3: "Blue stage of the spasmodic Cholera", November 1831.
Sketch by Thomas Wakley. Printed in 19th Century. The Lancet, 1832, Wellcome Collection.

Based on this notion, in 1832 Thomas Latta was the first to describe the beneficial effects of repeated intravenous infusions of salt solutions to compensate for the diarrhoea-related fluid loss.[48]

Although the first reports described remarkable recovery in a few cases, a general acceptance of intravenous fluid therapy was hampered by the overall low success rate. This was related to the fact that intravenous resuscitation was often started too late on patients with severe dehydration that could not be corrected. Moreover, lack of proper aseptic techniques increased the risk for bacteraemia following intravenous puncture. With increased understanding of the possibilities with intravenous solutions as well as on how to prevent infections the interest in fluid management slowly gained momentum. In 1896, the Dutch physiologist Hartog Jacob Hamburger described normal saline (Hamburgers solution) and proposed that 0.9 % was the normal salt concentration in blood.[48] This composition soon became universally regarded as the standard in intravenous fluid replacement although later studies have pointed to several drawbacks in large volume infusion, including hyperchloremia and high fluid retention.[49] More balanced crystalloid infusions were developed during the late 19th and early 20th centuries among which Ringer's solution, composed of a physiological mixture of salts and eventually modified with the addition of lactate, was invented during the

1930's.[50] The newer infusions had compositions that were far better tolerated and were therefore commonly preferred in large volume fluid resuscitation.

There has been considerable controversy regarding the most appropriate fluid management. Historically, a widely accepted strategy in trauma surgery was to use early and aggressive fluid replacement in order to achieve normal blood pressure levels before surgery.[51] Others argued against superfluous resuscitation as such could increase the risk for intraoperative bleeding.[52]

Early studies on fluid replacement in other surgery described loss of extracellular fluid volume into an ill-defined "third space". [53] Assuming that this loss had to be compensated, liberal fluid replacement was widely implemented in elective surgical procedures. Holliday and Segar in 1957 presented a protocol advising a rather simple approach, according to which the hourly infusion rate was calculated based on the patients' weight.[54] This later evolved into the 4:2:1 rule, according to which 4 ml/h was given up to 10 kg of body weight, another 2 ml/h was added up to 20 kg and 1 ml/h was added for patients weighing more than 20 kgs. Such estimates did not consider the medical status of the patient or other pathologic conditions. Fluid loss (urinary output and insensible losses) was assumed to be directly related to age and body surface area. The introduction of colloid resuscitation during the Second World War started a debate on the merits of colloids vs. crystalloids in trauma resuscitation. The theoretical advantage of colloids is that their osmotic properties should allow for more efficient plasma expansion, promoting adequate blood pressure and sustained cardiac stroke volume with less infusion volumes as compared to crystalloids alone. However, this mechanism has been contradicted in several studies, where also potential harm related to colloid use (nephrotoxicity, impaired blood coagulation) have been observed.[55] To avoid postoperative oedema, Twigley and Hillman in 1985, among others, advocated a restricted crystalloid infusion strategy in minor and moderate surgical procedures.[56] Although the debates is still on-going, much recent evidence support the use of crystalloids as these seem to be as effective as colloids to maintain an adequate plasma volume at a lower cost and lower risk of complications. A goal-directed fluid therapy, aiming to achieve a zero balance of fluid volumes at the end of surgery, is nowadays commonly regarded as the most beneficial intraoperative practice.[57,58]

Anatomical considerations

Vascular anatomy of the skin

Based on cadaver studies, Manchot in 1889 and Salmon in 1936 published the first ground-breaking reports on the microvascular system of the skin and subcutaneous tissue.[59,60] Their work was further expanded by Taylor and Palmer, who described the three-dimensional microvascular network that is the keystone of all perforator flap surgery.[61] According to Taylor and Palmer, the human skin and underlying tissue can be divided into vascular territories of different size, named angiosomes. The perfusion of each angiosome is dependent on a single source artery and its accompanying vein(s). Moreover, each angiosome is interconnected with adjacent angiosomes either by true anastomoses between arteries and veins, respectively, or by vessels of reduced calibre that run in all anatomical layers, the so-called choke vessels. Within each angiosome the source vessel is divided into a varying number of smaller perforators that perfuse the skin and subcutaneous tissue (Fig 4).

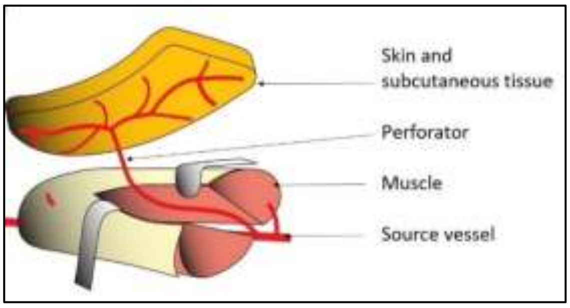


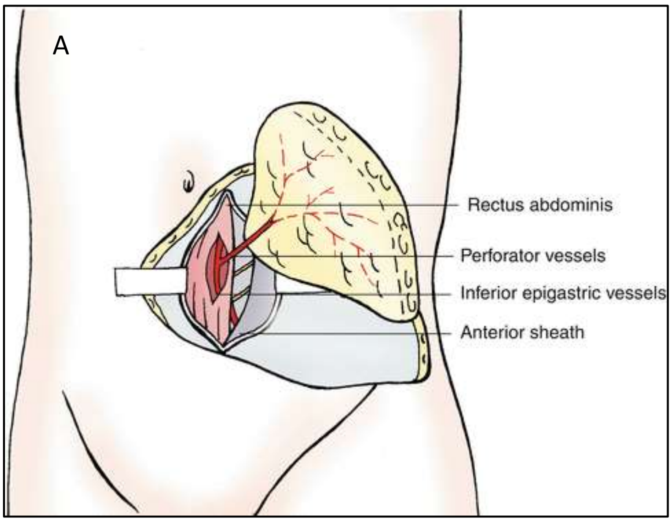
Figure 4: Illustration of the anatomical layout of a perforator with an intramuscular course. Printed with permission from Weum S., UNN and UiT, The Arctic University of Norway.

In line with Taylor and Palmers' angiosome theory, St Cyr et al in 2009 introduced the perforasome theory according to which each perforator has its own unique vascular arterial territory, named perforasome.[62] Adjacent perforasomes are interconnected through direct or indirect linking vessels located around the periphery of such a vascular territory. Importantly, each perforasome can be the basis for a unique perforator flap. Several adjacent perforasomes can be perfused through a single perforator via linking vessels given adequate perfusion pressure in the flap.[32,63]

Deep inferior epigastric artery perforator (DIEP) flap

The DIEP flap was first described in 1989 by Koshima and Soeda.[31,64] Since 1996, when Allen and Treece initially described the DIEP flap in reconstructive breast surgery, this flap has become the most frequently used free flap in autologous breast reconstruction.[65] The DIEP flap is composed of the lower abdominal skin and subcutaneous tissue, which closely resembles the consistency of a normal breast. An additional advantage of harvesting a lower abdominal flap is the resulting improved abdominal contour and an inconspicuous scar similar to the outcome of a cosmetic abdominoplasty.

The DIEP flap usually comprises one or two perforators originating from the deep inferior epigastric artery. The vascular pedicle of the DIEP flap approaches the rectus abdominis muscle from below, runs vertically underneath the muscle and gives rise to perforators providing the main blood supply to the overlying skin and subcutaneous tissue around and below the umbilicus (Fig. 5). [66]



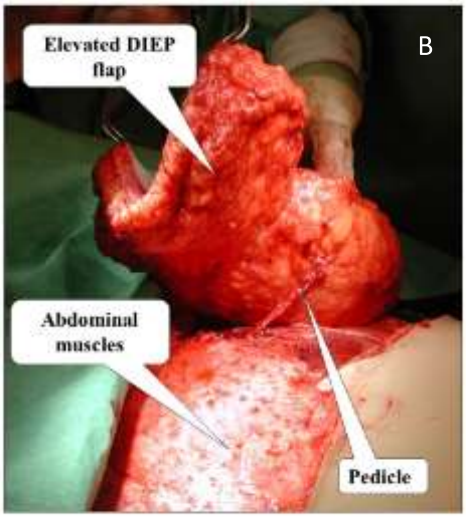


Figure 5, A: Illustration of the raised DIEP flap after dissection of its transmuscular perforators originating from the deep inferior epigastric artery (DIEA). Reprinted with permission from Springer Nature, Springer eBook. Surgical Atlas of Perforator Flaps by Hou C., Chang S., Lin J., Song D. (2015)

B: digital photograph of a raised DIEP flap showing the flap and its pedicle still attached to the abdominal wall. Dept. of Plastic and Reconstructive surgery, UNN.

These perforators either pass through the rectus muscle (musculocutaneous perforators) or beside the muscle. Although the extramuscular perforators are more easily freed from surrounding tissue, and therefore preferred if found suitable, the musculocutaneous perforators are more frequent. Between two and eight sizable perforators, with a diameter exceeding 0.5 mm, are commonly found on each side of the abdominal midline. Anatomical symmetry between abdominal halves is, however, rarely observed and the vascular pattern differs greatly between patients.[67,68] Frequently only one half of the abdominal flap is used, from either side of the midline. The pre- and intraoperative assessment of the local vasculature will guide the surgeon to determine which half has the most appropriate perfusion in relation to the planned flap design. In unilateral reconstructions where the patient desires a large breast the flap may be extended to include tissue also from the contralateral side. In such flaps, however, the area most distal from the vascular pedicle may suffer from reduced perfusion.[69] Although efforts are made to preserve the abdominal wall integrity, postoperative donor site morbidity such as abdominal bulging, reduced aesthetic appearance and, seldomly, herniation may follow breast reconstructions with a DIEP flap.[70] Nevertheless, the DIEP flap is considered a very desirable reconstructive technique due to the aesthetical results that can be achieved using this abdominal donor site.

In situations when only small-calibre perforators (ø < 0.5 mm) are found, an alternative to using single or a few perforators is to include several of them within a muscular cuff that is detached from the rectus abdominis muscle. Such muscle-sparing TRAM flaps (ms-TRAM) are safer than single small-calibre perforator flaps with regards to flap perfusion but can increase the risk of post-operative muscle weakness and asymmetries following intraoperative muscle injury. Even so, in clinical studies the postoperative morbidity associated with ms-TRAM flap procedures seems to be similar to that of DIEP flap surgery.[27]

Superficial inferior epigastric artery (SIEA) flap

The SIEA flap utilizes the same lower abdominal surplus tissue as the DIEP flap, however, with a different source vessel.[71] The SIEA courses more superficially in the subcutaneous tissue and does not penetrate the abdominal muscles or its aponeurosis. Hence, the abdominal wall musculature is left intact and patients commonly experience much less donor site morbidity, reduced postoperative pain and shorter hospital stay compared to other abdominal flap alternatives.[72] According to initial reports, the main drawbacks with the SIEA flap were the rather small vessel calibre and the variability in vascular anatomy, with up to 35 % of patients lacking a SIEA on surgical exploration.[34,73] However, more recent studies have shown that the SIEA is more frequently present and of a larger diameter than previously thought.[74,75] The perfusion of the transverse abdominal tissue by the SIEA has been explored with varying results. Some reports state that unilateral SIEA can only support up to half of the entire transverse abdominal flap, whereas others present successful use of the total flap based on a single SIEA[73,76-78]. Complications, such as fat necrosis and arterial insufficiency, are more common in the SIEA flap compared to the other abdominal flaps. Such might be related to the more superficial vascular network in the subcutaneous layer in the SIEA flap.[79] As a result, despite its promising characteristics, the SIEA flap has not gained the same popularity as the other flap alternatives in reconstructive breast surgery.

Lateral intercostal artery perforator (LICAP) flap

The LICAP flap comprises skin and subcutaneous tissue located on the lateral chest wall. The flap was first described by Holmström and Lossing in 1986 as the lateral thoracodorsal (LTD) flap.[80] The feeding vessels are perforators from the intercostal arteries, usually located in the lower lateral corner of the breast. In accordance with present nomenclature standards, the flap should therefore more correctly be named the lateral intercostal artery perforator (LICAP) flap.[81]

Following breast removal, many women present with an excess of lateral tissue, which can be made use of as a pedicled adipocutaneous or fasciocutaneous LICAP flap. No microvascular anastomosis is required. The LICAP flap is mainly used in breast conservative surgery, as an optimal reconstructive procedure to correct partial breast defects.[82,83]

Thoracodorsal artery perforator (TDAP) flap

The TDAP flap is modification of the LD flap that allows recruitment of surplus skin and subcutaneous tissue from the upper back without sacrificing the muscle.[84] Although the extent of functional loss after latissimus dorsi muscle harvest has been debated, most studies have found that leaving the muscle intact results in less postoperative donor site seroma and less reduction in muscular function for people with high physical demands.[85-88] The vascular basis of the TDAP flap are perforators from the thoracodorsal artery (TDA). Several patterns of vascular branching of the TDA have been described, giving rise to a large variety in the locations of perforators between patients. Nevertheless, the TDAP flap is most frequently based on perforators from a branch located at or close to the lateral border of the LD in order to facilitate the transposition of the pedicled flap to the front.[89,90] Several flap designs have been proposed, partly dependent on the planned use of the flap and partly based on aesthetic considerations.[91,92] The flap can be extended by including a large skin paddle covering several angiosomes or by incorporating more subcutaneous tissue as a broader flap base.[93,94] A small muscle cuff around the perforator(s) can be included in order to protect small or fragile perforators.[95] The TDAP flap can be used either as a pedicled flap to cover regional defects or as a free flap.[96,97] In reconstructive breast surgery the flap is usually combined with an implant, since the volume of the skin and subcutaneous tissue of the flap on its own often is insufficient to achieve a acceptable breast volume[98] Recent modifications of the flap have incorporated extended flap tissue, stacked flaps or a combination with fat transplantation to achieve larger breast reconstructions without foreign material.[22,39,93,99]

Imaging techniques to support reconstructive surgery

The success of all reconstructive flap surgery relies on an adequate blood perfusion to ensure flap survival and proper wound healing. Preoperative mapping and assessment of the hemodynamic properties of perforators is therefore an essential part in designing the final flap. The most basic measure to check tissue perfusion is clinical appraisal of the colour, temperature, and turgor of the flap. However, clinical judgement alone is not reliable to foresee circulatory anomalies in flap surgery.[100] Therefore, several other methods have been developed to improve preoperative planning and intra- and postoperative evaluation of flap tissue perfusion (Fig. 6).

		Preoperative	Intraoperative	Postoperative
Non-invasive techniques	Clinical judgement	✓	✓	✓
	Unidirectional Doppler ultrasound	✓	✓	✓
	Colour Doppler	✓	✓	✓
	Infrared thermography	✓	✓	✓
Invasive techniques	Conventional angiography	✓		
	CT Angiography	✓		
	MR Angiography	✓	✓	
	ICG Angiography	✓	✓	✓

Figure 6: Commonly used imaging techniques in the pre-, intra- and postoperative phases of reconstructive surgery. Non-invasive techniques that do not require contrast enhancement are marked in blue. Imaging techniques that commonly utilize intravenous contrast media to visualize flap vasculature are marked in red.

CT: computed tomography, MR: magnetic resonance, ICG: indocyanine green

Doppler ultrasound

Besides clinical examination, unidirectional Doppler ultrasound is the most frequently used technique to assess superficial tissue perfusion. The ease of use and the non-invasiveness of the technique makes it an attractive modality for assessment of skin perfusion during all phases of reconstructive surgery. In 1842, Christian Johann Doppler discovered how the frequency of sound waves that are reflected from moving objects varies depending on whether the object moves toward or away from the observer.[101] This phenomenon is utilized in plastic and vascular surgery as well as radiology to locate and assess the perfusion of subcutaneous blood vessels.[102,103] By using an ultrasound transducer to generate soundwaves of a certain wavelength and register the echoes bouncing of moving red blood cells, the pulsatile flow in arteries can be easily distinguished from the steadier flow in veins. However, as no information on flow volume or vessel diameter can be obtained, the reliability of unidirectional Doppler ultrasound in perforator mapping has been criticized.[102] Too small perforators or axial source vessels running superficially in the subcutaneous tissue may be falsely interpreted as suitable perforators. The accuracy of unidirectional Doppler is therefore regarded inferior to many of the other more complex imaging techniques.[104]

More detailed information may be obtained by colour Doppler imaging, allowing assessment of both flow velocity and anatomical course of the vessels (Fig. 7). In comparison with computed tomography angiography (CTA) or magnetic resonance angiography (MRA) imaging techniques, the advantage of colour Doppler ultrasound is especially evident in anatomical areas with thinner subcutaneous tissue with slender and short perforators.[105,106] Prior publications have demonstrated the value of preoperative colour Doppler mapping to facilitate determining the most appropriate perforator and flap design.[107] Moreover, the dynamic information obtained by this technique also enables differentiation between the artery and the vein in the perforator complex, which can help to avoid misinterpretation of the size of the artery on CTA images.[108] The major drawback with colour Doppler is that the imaging is time-consuming and requires considerable experience of the operator.

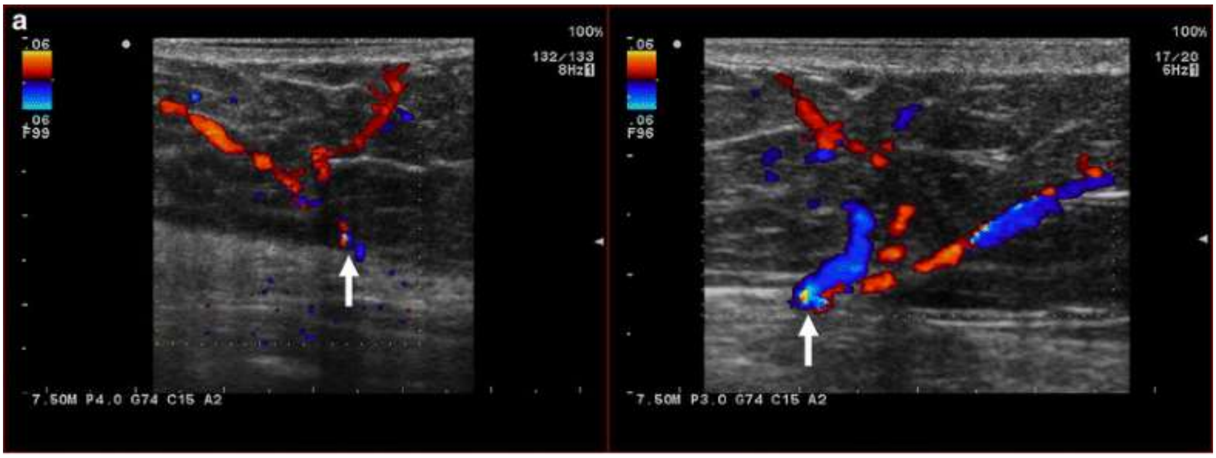


Figure 7: Colour Doppler image of the subcutaneous vessels in preoperative mapping of abdominal flap perforators. The colours represent blood flow in two different directions within an artery (red) and commitant veins(blue), respectively. Colour Doppler imaging can thus provide information on both the anatomical location and the function of subcutaneous vessels. Reprinted with permission from Aubry S et al. Preoperative imaging in the planning of deep inferior epigastric artery flap surgery. Springer Nature. Skeletal Radiology. 2012.

Infrared thermography (IRT)

IRT is an imaging technique that registers infrared (IR) radiation from the surfaces of objects.[109] For medical purposes, the focus of IRT is skin temperature, which can provide indirect information on the function of the human sensory and sympathetic nervous system, vascular system or local inflammatory processes.[110] Since 1956, when Lawson discovered the relationship between increased heat radiation and breast cancer, thermography has been used as a diagnostic tool in a variety of different medical fields.[110] In plastic surgery, thermography is most frequently used in flap-based reconstructive surgery, burn wound assessment and treatment of vascular anomalies.[111] This non-invasive technique is harmless to the patient and allows for continuous registration of high-quality thermal images without requiring physical contact.

Its value in flap surgery is based on the principle that the skin is heated by thermal conduction from subcutaneous blood vessels. A thermographic image of normal skin perfusion shows specific areas of elevated temperatures surrounded by areas of cooler skin surface (Fig.8).

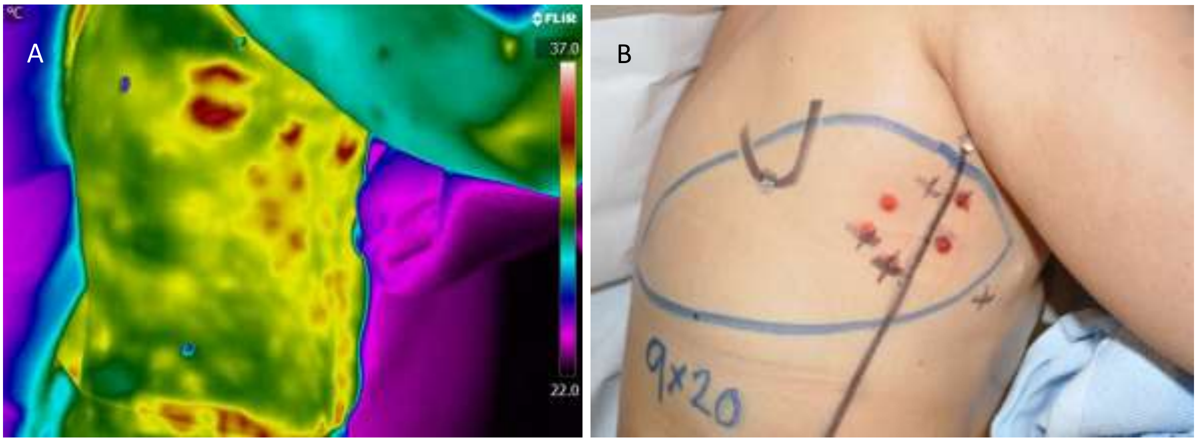


Figure 8, A: Thermographic image of the right lateral thorax of a patient scheduled for TDAP flap breast reconstruction. Temperature differences correspond to the colours presented in the scale (right). Pieces of aluminium foil (blue dots) mark anatomical landmarks (tip of scapula, crista iliaca, lateral edge of LD muscle). Areas with intense heat radiation (hotspots) correspond to the location of perforators.

B: Digital photograph showing the planned flap design marked in blue. Red dots point to the location of hotspots. Black crosses mark the location of pulsatile signals found by unidirectional Doppler ultrasound. Figure reprinted from Sjøberg et al. The value of dynamic infrared thermography in pedicled thoracodorsal artery perforator flap surgery. Plastic and Reconstructive Surgery Global Open 2020; 8(7), e2799.

The variation in heat radiation, with noticeable so-called hotspots, relates to the network of subcutaneous arteries transporting blood from deeper tissue to the skin surface. The combination of a thermographic hotspot and arterial pulsations on Doppler ultrasound investigations, has been shown to be strongly correlated to the location of perforators.[112]

IRT can be used to record both static and dynamic thermal images. In static thermography, IR radiation from the skin is registered at a single point in time, whereas dynamic infrared thermography (DIRT) images are continually recorded at a selected frequency over a given time period. Changes in the temperature of the skin area of interest provide indirect information on the underlying skin blood perfusion. With modern IR cameras the frequency at which images may be recorded can vary from very high speed (30 per second) to a very slow frequency of 1 image/hour. For medical purposes, as in study II, a frequency of 1 Hz was used. The dynamic aspects of skin perfusion can be visualized by combining the registration of infrared radiation with a local thermal challenge, for example water immersion or a mild convective cooling by blowing air at room temperature with a fan over the area of interest.[112] By comparing changes in the thermal pattern of the skin surface temperature before, during and in the recovery period after the thermal challenge, DIRT provides more information on not only the location of vessels but also the function of the local perforators, as compared to static IRT.[112] Special attention is given to the rate of rewarming at the hotspots, since rapid rewarming of a large area is indicative of a perforator that provides more blood to the skin surface compared to a perforator with slow rewarming in a small surface area. DIRT has been found useful in a variety of reconstructive surgical procedures, including autologous breast reconstructions.[111,113,114]

The indirect information on the superficial subcutaneous vascular network as obtained by DIRT corresponds well with the direct visualisation provided by indocyanine green fluorescence angiography (ICG-FA) (see below).[115-118] Although both techniques can be used pre- and intraoperatively, an advantage of DIRT is the possibility of continuous registration without intravenous contrast media. Furthermore, the latest development of IR cameras has produced smaller format IR imagers that can be fitted to ordinary smartphones making this technology more affordable and convenient albeit with reduced resolution.[119-121]

X-ray and conventional angiography

Visualization of blood vessels by angiography has been available to clinicians and researchers since the development of intravenous contrast media in the late 1920's.[122] During the following decades, a rapid increase in vascular research eventually contributed to the description of the angiosomes of the human skin by Taylor and Palmer in 1987.[61] To understand the structure of cutaneous vascularity was very important in the development of modern flap surgery. Although many other imaging techniques have since been introduced, conventional angiography is still used in preoperative planning of flap surgery, especially on suspicion of vascular damage due to trauma or congenital malformations. Its main significance lies in the information that can be obtained on source vessels, since most perforators are too small to be properly visualized by conventional angiography.

Computed tomography angiography (CTA)

Three-dimensional (3D) visualization of tissue was first introduced by Hounsfield in 1973.[123] With a short lasting exposure to ionizing radiation, the improved imaging of the vascular network using contrast media provided detailed information on the course and size of blood vessels. Compared to conventional angiography, modern CT scanners provide information in a much shorter period of time. CTA is by many regarded as the gold standard for preoperative mapping of perforators in reconstructive breast surgery.[124] Precise visualization of the location of perforators in relation to anatomically stable landmarks (skeleton) and surrounding soft tissue (muscle, nerves, other blood vessels) has resulted in shortened operation time and less complications.[124,125] Clinical research on vascular anatomy based on CTA has improved our understanding of the branching patterns of vessels and the vascular territories of individual perforators.[62] The major advantages of CTA are its wide availability, high reproducibility and operator independence combined with the possibility to make easily comprehendible 3D reconstructions of the anatomical features.[126] In addition, the accuracy of CTA in preoperative imaging of the vascular structures of abdominal flaps is higher than with any other available imaging techniques.[104] Still, some studies have noted a discrepancy between which perforators CTA findings indicate as the most appropriate and the final choice of perforators by the surgeon.[127] Such might relate to the fact that static CTA imaging cannot reliably distinguish between the artery and the accompanying vein in the perforator complex, nor provide information of the hemodynamic characteristics of perforators. The opacity of the contrast medium is almost the same in the artery and vein at the perforator complex level. The diameter of the combined artery and vein might therefore be falsely interpreted as the diameter of the artery alone. This can mislead the surgeon to falsely overestimate the size and appropriateness of the perforating artery.[108] The limitations of CT angiography mainly refer to exposure to ionizing radiation and iodine contrast medium, the necessity to use advanced technical resources and long time to produce high quality 3D reconstructions.[104,128] Another important disadvantage is that CTA is not accessible for intraoperative assessment of flap perfusion.

Magnetic resonance imaging (MRI)

Magnetic resonance imaging (MRI) relies on the registration of electromagnetic radio frequency (RF) pulses transmitted by nuclear components – protons – in hydrogen atoms. Because the magnetic properties vary between different tissue types, detailed information of the composition of the investigated anatomical area can be obtained without exposing the patient to harmful ionizing radiation.[129] Magnetic resonance angiography (MRA) can be used to demonstrate the vascular anatomy with almost the same accuracy as CTA. However, this is only possible with high field strength magnets and the use of intravenous contrast media.[130,131] The high price level of such MRI scanners together with the longer time needed to obtain high quality images, as compared to CTA, has hitherto favoured the use of CTA in perforator mapping.

Indocyanine green fluorescence angiography (ICG-FA)

Fluorescence dyes have been used for medical purposes since the 1950's, starting with assessment of cardiovascular and liver function.[132] At present, the most frequently used fluorescence dye is indocyanine green (ICG). After intravenous injection, ICG binds firmly to plasma proteins and is thereby carried through the vasculature. On exposure to near infrared (NIR) light, the dye molecules absorb and emit NIR, which can be registered with a video camera equipped with an appropriate optical filter (Fig. 9).

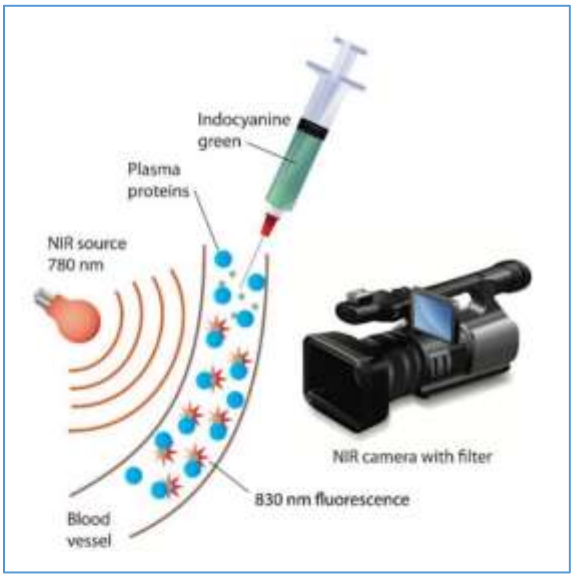


Figure 9: Illustration of the basic principles behind ICG-FA.

ICG dye is injected intravenously and carried with proteins in the blood stream. Upon exposure to near infrared (NIR) light, the dye absorbs and emits this energy as NIR light with a slightly different wavelength. A properly equipped video camera can register this emitted energy and provide information on the subcutaneous vascular structure. Reprinted with permission from Weum S. Imaging in plastic surgery. A clinical and experimental study with notes on the history of medical imaging. Department of Clinical Biology, UiT The Arctic University of Tromsø, April 2013. ISBN 978-82-7589-392-3.

The investigation conveys direct information on the vasculature, resembling the information gained from conventional angiography but omitting the ionizing radiation.[133] However, the penetrance of the NIR light to 1.5 – 2 cm below the skin surface limits the available information on subcutaneous vasculature to that of superficial vessels. In reconstructive surgery, ICG-FA has been described for preoperative mapping of perforators as well as for intraoperative and postoperative evaluation of flap and skin perfusion.[134-136] Comparative studies on imaging in breast surgery have shown that ICG-FA is inferior to CTA and MRI in preoperative perforator mapping, especially in areas with a thick pannus such as the abdomen.[137] Recent publications show that more deeply located vasculature can be visualized by using ICG fluorescence imaging with NIR light of a longer wavelength (1000 – 1800 nm) as this energy can penetrate further into the human tissue.[138] Future development in ICG imaging will show if this technique can be made available in clinical practice.

Intraoperative ICG-FA has proved to be useful to ensure patency of vessel anastomoses and to monitor flap perfusion with significantly more accuracy than clinical evaluation.[133-135] Limitations in ICG imaging are related to potential allergic reactions to the intravenous dye. Repeated assessment is possible, although somewhat limited by the time needed to wash out the fluorescent dye between investigations. Another important limitation is that the laser beam that is used to evoke fluorescence is not perpendicular all over curved surfaces, such as the abdomen, which reduces the reliability of the information obtained at the periphery of the area of interest.

As previously mentioned, studies comparing DIRT to ICG imaging have shown a close correspondence between the two techniques for obtaining information on flap perfusion.[116,118] Both techniques can reliably visualize perfusion of the superficial layers of subcutaneous tissue and skin and thus provide valuable information on flap perfusion during and after reconstructive breast surgery.

Perioperative care in flap surgery

Compared to simpler reconstructive options, the complex and often time-consuming surgical procedures used in reconstructive microsurgery are associated with an increased risk for complications. Such unforeseen events will burden the patient with increased morbidity, possibly more surgery and prolonged hospital stay in addition to the psychological strain following unmatched expectations.[139,140] Naturally, the most devastating complications of complex surgical procedures are death or significantly reduced general health. Such, however, is rare. The reported average mortality rate in elderly patients and patients with preoperative co-morbidities is less than 2 %.[141,142] In contrast, patients undergoing microsurgical breast reconstructions are generally healthy and rather young, which significantly reduces the risk for serious complications. Adverse outcome related to the flap is somewhat more common and usually observed as partial of total flap failure. The reported incidence of total flap failure is in the range of 5-10 %.[143-145] Numerous papers have been published about the impact of various medical conditions as well as that of perioperative care of patients undergoing free flap reconstructions.[146] All efforts are made to optimize the pre-, intra- and postoperative phases in order to minimize complications and maximize patient outcomes. The duration of the surgery itself is an important factor, as longer surgery often increases the risk for thromboembolic events, healing problems and postoperative wound infections.[44] Prior radiotherapy or medical conditions such as diabetes mellitus, cardiovascular diseases, hypercoagulability and poor nutritional status all affect the patients' response to surgery and their ability to recover.[147-150] The use of nicotine products and obesity are commonly described risk factors in reconstructive procedures, although their definite role in relation to flap failure has been debated.[151-153]

The perioperative surgical and anaesthesiologic management can have a significant impact on the success rate of reconstructive procedures. Unnecessary preoperative fasting and liberal intravenous fluid management will increase the risk for intra- and postoperative adverse events.[149,154,155] Intraoperative factors such as the choice of anaesthesia, use of vasoactive agents, a strict control of patients´ body temperature as well as fluid balance need to be thoroughly considered.[156,157] Careful postoperative surveillance of the patient and flap perfusion is paramount to enable adequate and swift correction to optimize the final result. Strict fluid management and blood pressure control with vasoactive agents are measures that have been associated with reduced complication rates in recent studies.[144,158] The increasing use of enhanced recovery protocols seems to be a promising development also in the perioperative management of reconstructive microsurgery.[159]

Aim of the thesis

Reconstructive breast surgery utilizing autologous tissue as free or pedicled flaps has become routine in modern medicine. The main technical and intellectual obstacles have been overcome. As the availability of reconstructive surgery has increased, so have also the expectations from patients and society. An optimal aesthetic result with minimized risk of complications is still the ultimate goal of reconstructive surgery.

The aim of this thesis was to add to the knowledge on how to optimize some aspects of autologous breast reconstruction by describing new diagnostic and surgical techniques including novel intraoperative anaesthesiologic strategies.

The specific aims of the three studies in the thesis were as follows:

- To assess the combination of a free abdominal flap with a pedicled LICAP flap for breast reconstructions in patients where the surplus abdominal tissue alone was regarded insufficient to meet the preoperative demands (Study I)
- To assess the usefulness of DIRT in pedicled TDAP flap surgery for preoperative perforator mapping as well as for intra- and postoperative monitoring of flap perfusion (Study II)
- To assess the impact of a modified intraoperative fluid management protocol on the clinical course and short-term complication rate in abdominal flap breast reconstructions (Study III)

Material and methods

Studies I and II were prospective clinical studies, whereas study III was a retrospective analysis of data from patient charts collected during a period of 20 years. All patients underwent reconstructive breast surgery, except for two patients in study II. Studies I and II were approved by the Regional Committee for Medical Research Ethics, North Norway. All patients in studies I and II gave written informed consent prior to inclusion.

Statistical analyses were performed using SPSS Statistical software (IBM Corp. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY, USA). Statistical significance was defined as $p < 0.05$.

Study I

This study assessed a combination of a free abdominal flap and a pedicled LICAP flap in reconstructive breast surgery. The rationale to combine two different flaps was to optimize breast size and appearance in secondary autologous breast reconstructions in women with insufficient abdominal surplus tissue. Other flap combinations have been proposed in the published literature but many of these include multiple free flaps and other complex procedures. The LICAP flap is a rather simple flap to raise located in close proximity to the recipient site in reconstructive breast surgery. Such would make it a logical choice when additional tissue is needed in autologous breast reconstructions. The effort and risk in raising the flap might be lower than with the more complex surgical techniques.

During a period of more than five years (2010 – early 2016) 109 patients were included in the study. A total of 121 abdominal flap procedures were performed. The combination of a free abdominal flap and a LICAP flap was used in 82 breast reconstructions (76 patients). Our DIEP flap harvesting technique did not differ significantly from other prior reports[65]. However, more often than in many other microsurgical centres we used DIRT in preoperative mapping of abdominal flap perforators, as a supplement to CTA and handheld unidirectional Doppler ultrasound (see below). DIRT was also utilized to monitor DIEP flap perfusion during and after the surgery, in addition to Doppler ultrasound and the observation of clinical signs of flap perfusion. The value of DIRT in DIEP flap breast reconstructions has been demonstrated previously.[112,117,160]

In the majority of cases the LICAP flap was raised at the subfascial plane. The maximum length of the LICAP flaps was limited to 15 cm, since previous reports have shown an increased risk of distal perfusion problems in flaps exceeding this length.[161] No effort was made to skeletonize the intercostal perforators. A protective cuff of adipose tissue around the perforators did not hinder flap transposition and was regraded beneficial to reduce the risk of pedicle problems (kinking, torsion etc.). Different from the original description of the LICAP flap by Holmström et al.[80], the pivot point of the flap was placed more cranially to optimize the aesthetic appearance of the lower lateral corner of the neo-mamma (Fig. 10).

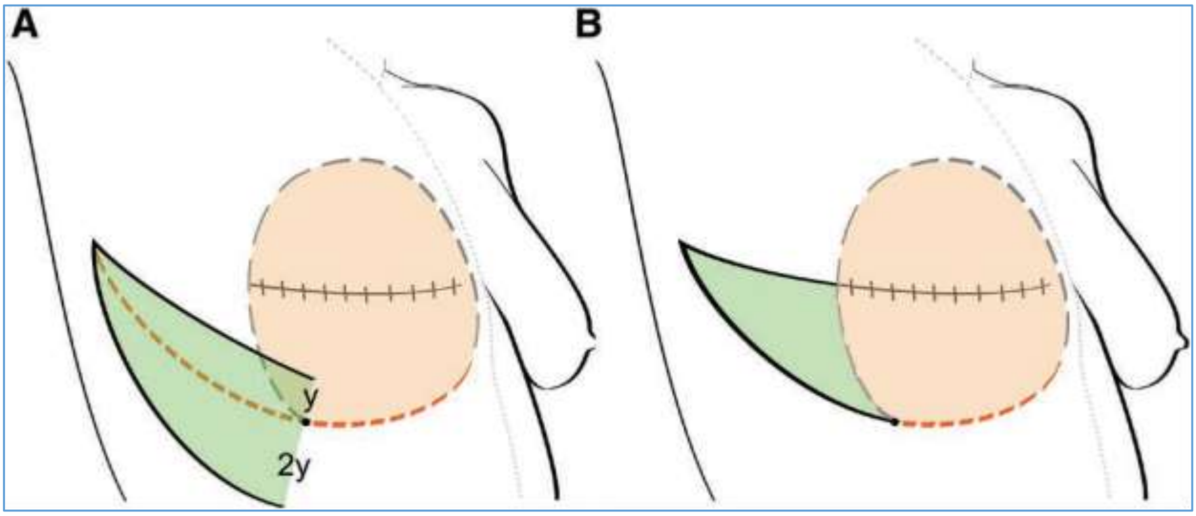


Figure 10: The illustration shows the difference between the original (A) and the modified (B) LICAP flap design. Note that the pivot point of modified flap has been raised to be at the level of the new inframammary fold. Figure reprinted from Sjøberg T, de Weerd L. The pedicled LICAP flap combined with a free abdominal flap in autologous breast reconstructions. Plastic and Reconstructive Surgery Global Open 2018; 6(1), e1562

A two-team approach allowed for simultaneous harvest of the DIEP flap (team A) and preparation of the thoracic recipient vessels and LICAP flap (team B). The flap was inset in a cranial position lateral to the abdominal flap. The donor site was closed directly resulting in a horizontal scar seen as a continuation of the inframammary fold (Fig. 11).

Figure 11: The postoperative result after breast reconstruction using the combination of a DIEP flap and a modified LICAP flap. The black line follows the periphery of the LICAP to illustrate the vertical inset lateral to the DIEP flap. The donor site scar is seen as a continuation of the inframammary fold lateral to the LICAP flap (blue line). Image: Dept, of Plastic and Reconstructive surgery, UNN.

The primary goal was to assess the applicability and possible benefits of this novel combination of a free abdominal flap and a pedicled LICAP flap in selected patients with insufficient abdominal surplus tissue. Secondly, we evaluated the impact of our modified LICAP flap design on breast projection and lateral contour. Thirdly, we compared the complication rate and type of complications between patient groups in relation to whether or not the combined flap procedure was utilized.

Statistical analyses in Study I

Independent samples t-test was used for continuous variables, such as flap weight (grams) or relative use (final breast flap weight divided by total abdominal flap weight (percent)). One-way analysis of variance (ANOVA) was performed to assess age, BMI or flap weight in relation to flap type (DIEP, ms-TRAM or SIEA). Binary logistic regression was used to determine the impact of the type of surgery (± LICAP flap) on the incidence of symmetrizing procedures that were done after the initial breast reconstruction.

Study II

In this study we evaluated DIRT imaging in reconstructive procedures using pedicled TDAP flaps. Our first aim was to determine whether DIRT could be used for preoperative perforator mapping in TDAP flap surgery by providing information on the location and quality of the subcutaneous perforators. The findings on DIRT were compared with the results of preoperative CTA and unidirectional Doppler ultrasound. Our second aim was to assess DIRT for the purpose of monitoring TDAP flap perfusion during and after the surgical procedure compared with the information obtained from Doppler ultrasound and evaluation of clinical signs of flap perfusion.

Between 2014 and October 2018 we enrolled 21 patients (21 flaps). 19 patients were scheduled for reconstructive breast surgery, whereas two patients underwent reconstructive surgery because of previous burn injuries and hidradenitis suppurativa, respectively.

DIRT imaging setup

Two types of high-sensitive IR cameras were used: FLIR ThermaCAM S65 HS or FLIR T 420 (FLIR Systems, Boston, MA, USA). Thermal emissivity was set to 0.98. The anatomical location and rate of rewarming of the hotspots were analysed using appropriate software (FLIR Research IR, ver. 3.0.11; FLIR Systems).

The preoperative investigations were carried out in a designated laboratory with room temperature at 22-24 °C. The unclothed upper body of the patient was acclimatized to the room temperature for 10 minutes. Thereafter the patient was placed in a lateral decubitus position with the ipsilateral arm supported on a padded post in almost 90 degrees of shoulder abduction like during surgery. The skin area of interest (posterolateral thorax) was subjected to a mild convective cold challenge during which a desktop fan was used to blow air at room temperature for two minutes over the exposed body surface. Heat radiation was continuously registered using a FLIR ThermaCAM S56 HS, which was mounted to a custom-made support stand to firmly position the camera above the patient. The distance between the patient and the camera was set at approximately one meter.

For intraoperative DIRT imaging the camera was positioned above the patient using the same support stand and distance as for preoperative examinations. The cold challenge was carried out by evenly washing the skin surface of the donor site and of the raised flap with gauze soaked in saline at room temperature for 30 seconds. The skin surface was thereafter dried with gauze. The rate and pattern of the following rewarming was continuously registered for three minutes. During flap dissection we isolated all suitable perforators (ø > 0.5 mm and visible pulsations) that were found in the vicinity of the lateral margin of the latissimus dorsi muscle and within the anticipated flap design. Perforators located under the central or medial parts of the TDAP flap were not included. Using such perforators was expected to increase the risk of undue tension on the vascular pedicle after flap transposition because of the longer distance from the pedicle to the recipient site. To determine the perfusing capacity of each perforator the perforator under investigation was left open while the others were temporarily clamped. A DIRT registration including the previously described cold challenge was performed to visualize the rate and pattern of rewarming of the flap surface when perfused by only the selected perforator. Each registration cycle was continued until 3 minutes after cold challenge was ended. The flap surface temperature was allowed to normalize between each investigation to avoid registration bias (Fig. 12).

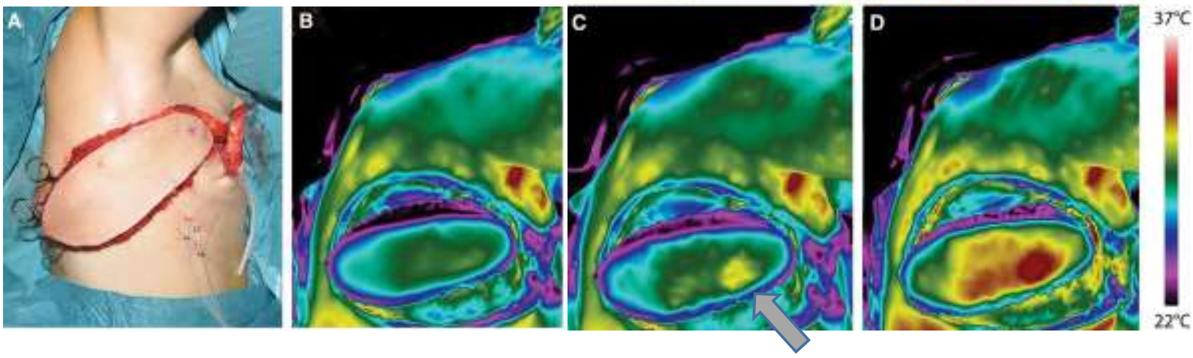


Figure 12: Intraoperative images of a TDAP flap raised and isolated on one perforator, illustrating the information obtained from the cold challenge. A, Digital photograph of the isolated flap. B, Thermal image immediately after the cold challenge showing reduced heat radiation and no hotspots. C, Thermal image 3 minutes after the cold challenge revealing increased heat radiation and a bright hotspot at the proximal end of the flap (arrow). D, Thermal image after further rewarming of the flap. Note reduced heat radiation at the distal end of the flap. The temperature corresponds to different colours as presented on the scale (right). Figure reprinted with modifications from Sjøberg et al. The value of dynamic infrared thermography in pedicled thoracodorsal artery perforator flap surgery. Plastic and Reconstructive Surgery Global Open 2020; 8(7), e2799.

Consecutive DIRT registrations were done following the same routine until all possible perforators had been assesses. The perforator with the largest area of skin perfusion and with rapid reappearance of heat radiation after the cold challenge was selected as the most appropriate for flap perfusion. All other perforators were ligated and flap transposition was completed. Further assessment of flap perfusion during inset was accomplished using the same routine with consecutive cold challenges and IR registrations.

For postoperative monitoring of flap perfusion, the more portable FLIR T 420 IR camera was used. DIRT examinations were mostly done at the plastic surgery ward on postoperative days 1, 2, 3 and 6. The mild cold challenge was accomplished using saline soaked gauze like the intraoperative procedure, although the camera was handheld instead of fixed to a support stand. As the flap was now on the anterior side of the thorax, the patient was examined in the supine position.

CTA protocol

The local protocol for the CT angiography investigations did not differ significantly from what has been reported by others.[124,127] A 128-detector row CT scanner (Siemens SOMATOM Definition Flash; Siemens Medical Solutions, Erlangen, Germany) and intravenous iodine contrast medium (Ultravist 350; Schering AG, Berlin, Germany) was used to visualize blood vessels in the body segment between the clavicle and a level just below the rib cage. The patients were positioned supine with the arms stretched above the head. Thus, because of spatial restrictions of the CT scanner, the position of the patients differed from what was used during preoperative DIRT investigations and surgery,

Doppler ultrasound investigations

Doppler ultrasound investigations were accomplished using a handheld unidirectional 8 mHz Doppler probe (8 Mhz, Multi Dopplex II; Huntleigh Healthcare, Cardiff, UK). The probe was held perpendicular to the skin surface and in direct contact with the skin through ultrasound gel. The locations of arterial Doppler sounds were marked on the skin (Fig. 8B). All investigations were done by surgeons possessing a high level of expertise in the use of unidirectional Doppler ultrasound. During surgery the probe was wrapped in a sterile glove with the probe tip covered by an appropriate layer of gel.

Postoperative monitoring of flap perfusion by Doppler was accomplished every two hours during the first 24 hours after surgery and thereafter six-hourly until 72 hours after surgery. Clinical signs of flap perfusion were observed following the same time schedule.

Study III

This retrospective study evaluated the impact of a two consecutive fluid management protocols that were used in connection with autologous breast reconstructions. Patients that had received secondary, unilateral breast reconstruction with abdominal flaps during a period of twenty years (1999 – 2018) were included. The liberal fluid management (LFM) protocol, which was used until 2005, did not limit the use of intraoperative intravenous crystalloids and colloids to maintain blood pressure and compensate for insensible loss. During this time, we occasionally observed postoperative flap failures, the reason for which we suspected was correlated to excessive tissue oedema in the flap (Fig. 13).

Figure 13: Postoperative transcutaneous leakage of clear fluid in a DIEP flap, possibly due to excessive interstitial fluid entrapment resulting from intraoperative high-volume fluid infusion. Image: Dept. of Plastic and Reconstructive surgery, UNN.

Although at that time not mentioned in literature related to microvascular flap surgery, we postulated postulated that liberal intravenous infusion of crystalloids and, perhaps more importantly, colloids could have a negative impact on the success rate of the reconstructive surgery. At this time, the first reports by Kehlet et al. on the use of strict perioperative fluid management in gastrointestinal surgery had just been published and presented lower complication rates after surgery.[162] Inspired by these results we introduced a modified fluid management (MFM) protocol. The aim was to reduce the risk for complications after autologous breast reconstructions with stricter control on intraoperative fluid volumes and to support adequate flap perfusion by other means. Information on intraoperative anaesthesiologic procedures and patients' clinical parameters were obtained from electronic or paper-based charts at the end of the study. Detailed data regarding the surgical procedure and any registered adverse events during and after the surgery was also available from the patients' journals. Complications occurring within the first two weeks after hospitalization were registered as part of the study outcome.

The study comprised 214 patients (214 flaps). The LFM protocol was used during the surgery of 42 patients whereas the MFM protocol was followed for 172 patients. A complete anaesthesia record was mandatory for inclusion.

The liberal fluid management protocol (LFM)

The LFM protocol comprised isoflurane or sevoflurane inhalation anaesthesia at the discretion of the anaesthesiologic team. Crystalloids were used to maintain normotension, aiming for a mean arterial pressure (MAP) above 65 mmHg. Intravenous colloids were added on demand, to support normotension and adequate urine output. Vasopressors were occasionally utilized to correct hypotension, unless manageable with increased volumes of intravenous crystalloids and colloids.

The modified fluid management protocol (MFM)

The modified fluid management protocol comprised sevoflurane as the predominant inhalation anaesthetic. A combination of crystalloids and vasoactive agents were used to maintain an adequate MAP (> 65 mmHg). Colloids were used very restrictively and only to correct hypotension irresponsive to boluses of norepinephrine and crystalloids. Inhalation anaesthesia was used until completion of the microvascular anastomosis and was thereafter replaced by propofol. Propofol was added to the MFM protocol to induce vasodilation and to reduce ischaemia-reperfusion injury to the flap.

Methodological aspects of surgery and clinical care

All surgery was performed by experienced microsurgeons in a two-team approach. One team raised the flap and the other team prepared the recipient vessels, which mostly were the internal mammary vessels. Preoperative perforator mapping was accomplished by CTA (Somatom Definition Flash, Siemens Healthcare, Erlangen, Germany), handheld unidirectional Doppler ultrasound (Multi Dopplex II, Huntleigh Healthcare, Cardiff, UK) and DIRT (FLIR ThermaCAM S65 HS or FLIR T 420, FLIR Systems, Boston, MA, USA), according to the standard in-house protocol.[117] Intra- and postoperative monitoring was done by DIRT imaging and Doppler ultrasound. Routine preoperative blood tests including haemoglobin and haematocrit levels were obtained prior to surgery. Postoperative levels of haemoglobin and haematocrit were measured one and two hours after transfer to the postoperative recovery unit. Postoperative monitoring of flap perfusion was based on clinical signs supplemented by unidirectional Doppler ultrasound. Flaps were checked hourly for the first 24 hours, thereafter every three hours until postoperative day 3 and followed by a 6-hourly check until discharge. Postoperative normotension was maintained by intravenous crystalloids, occasionally supplemented by norepinephrine. Complications were classified as per Table 1.

Table 1: Assessed complications by category		
Intraoperative complications	Postoperative surgical complications	Postoperative medical complications
Bleeding > 500 ml Inadequate flow in recipient artery on surgical exploration Arterial anastomotic thrombosis Venous congestion	Bleeding > 500 ml Wound infection Wound rupture Partial flap loss Total flap loss Hernia at abdominal donor site	Cardiac arrythmia Congestive heart failure Myocardial infarction Pulmonary embolism Deep vein thrombosis Acute renal failure Respiratory distress Urinary tract infection

Table 1: The categories of intra- and postoperative complications registered in study III. Table reprinted from Sjöberg T et al. Liberal versus modified intraoperative fluid management in abdominal flap breast reconstruction. A clinical study. Plastic and Reconstructive Surgery Global Open 2021; 9(9), e3830.

Statistical analyses in Study III

Patients were divided into two cohorts depending on which fluid management protocol was used during their surgeries. Differences between patient cohorts in binominal categorical variables were determined using Chi-Square or Fisher's exact tests (FET), whereas independent sample *t*-test for was used for normally distributed ordinal continuous variables. Single variables that were significantly different between cohorts were analysed by univariate logistic regression to determine their association with outcome. Variables with significant association were included in a multivariate logistic regression model. All regression models were constructed using a hierarchical entry method with stepwise inclusion of selected variables.

Summary of results

Study I

The mean size of the free abdominal flaps did not differ significantly between the 76 patients treated with the flap combination of a free abdominal flap and a LICAP flap, and the remaining 33 patients treated without the LICAP flap supplement. The addition of a LICAP flap to the abdominal flap breast reconstruction resulted in additional volume and improved projection of the neo-mamma. Harvesting a LICAP flap did not increase the total procedure time.

Four abdominal flaps failed (2 DIEP flaps, 2 ms-TRAM flaps). Although no LICAP flap exceeded the recommended maximum length of 15 cm, partial tip necrosis and distal epidermolysis resulted in minor revisions in 21 LICAP flaps (26%). The majority of patients with LICAP flap complications had a history of previous radiotherapy as part of their prior oncologic treatment. Despite the increased volume provided by the LICAP flaps, insufficient breast volume compared to the contralateral side was noted in 47 out of 79 reconstructions (57%). Contralateral breast reduction was used in most patients to achieve symmetry. In patients treated with only the abdominal flap transfer-i.e., no LICAP flap, 18 of 38 reconstructions (49%) were followed by additional symmetrising procedures. Contralateral free fat transplantation was the most frequent additional surgery in this patient group, since the reconstructed breast was larger.

The modified LICAP flap design resulted in increased projection and a more natural lateral contour of the breast, as compared to the outcome after a LICAP flap procedure of the original design (Fig. 14).

Figure 14: Digital photographs showing the postoperative results of two patients after breast reconstruction with the combination of a DIEP flap and a LICAP flap. The postoperative difference in lateral contour achieved by the original LICAP flap design (left) compared to the modified design (right) is clearly shown. A square box form is prevented due to the shift in pivot point of the flap. Figure reprinted from Sjøberg T, de Weerd L. The pedicled LICAP flap combined with a free abdominal flap in autologous breast reconstructions. Plastic and Reconstructive Surgery Global Open 2018; 6(1), e1562

Shifting the pivot point did not compromise flap perfusion. The intercostal perforators were left protected by a subcutaneous pedicle of fatty tissue. The skin incisions could be placed more cranially without endangering flap perfusion to optimize the aesthetical appearance of the lateral contour of the breast. This study showed that the combination of an abdominal flap and a modified LICAP flap is a simple solution that can contribute to improving the outcome of autologous breast reconstructions in patients with insufficient abdominal flap tissue.

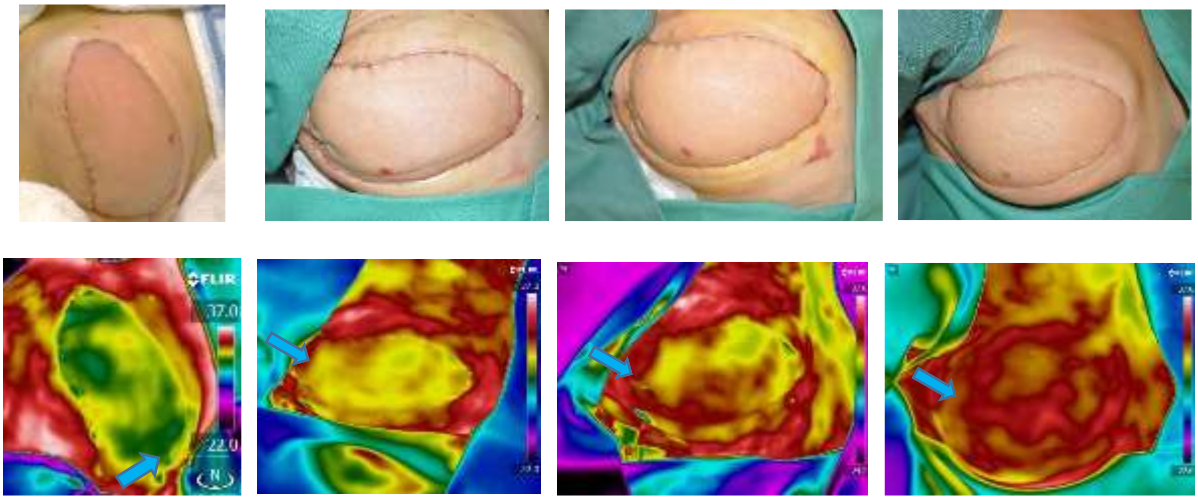
Study II

Bright and rapidly emerging hotspots on preoperative perforator mapping by DIRT were always associated with arterial Doppler sounds. Hotspots with intense heat radiation indicated perforators with more voluminous flow and larger size than hotspots that were less distinct. The pattern of emerging hotspots and the progression of heat radiation from the skin surface as registered during the first minutes after the cold challenge helped to determine the most appropriate TDAP flap design with respect to the preferred perforator. Preoperative CTA visualized the branching patterns of the thoracodorsal vessels but, unlike DIRT imaging, did not provide useful information for preoperative perforator selection.

Sites where a bright hotspot coincided with arterial Doppler sounds always corresponded to the location of an adequate perforator as revealed on subsequent surgical exploration. After a transient cold challenge, the increasing heat radiation from the flap surface depending on the perfusion of a single perforator could be clearly demonstrated, as previously described, and so comparison of the perfusion capacity of the isolated perforators was reliably done (see Fig. 12). In such, DIRT could also be used intraoperatively to guide final selection of the most suitable perforator to perfuse the TDAP flap.

After the flap had been transferred to its recipient site, DIRT imaging was also useful for flap monitoring during the surgery. Compromised flap perfusion due to arterial or venous circulatory problems in the pedicle was detected earlier and more easily by DIRT as compared to Doppler ultrasound or clinical judgement. This allowed for swift re-exploration of the flap pedicle to correct undue compression or other complications. In cases where no obvious compromise to the flap pedicle was found or when such had been corrected, while the flap perfusion still seemed to be suboptimal, repetitive transfer of the flap between the donor and recipient site seemed to augment flap perfusion. Such short-term repeated cycles of reduced and normal flap perfusion were thought to enhance flap perfusion following the same mechanisms, such as arteriolar dilation, that have been observed in studies on flap preconditioning.[163] This finding of possible preconditioning of the flap by positioning and re-positioning and the possibility to monitor the resulting alteration in flap perfusion by DIRT might be worthwhile to explore further.

During the postoperative period, consecutive DIRT registrations demonstrated the dynamic changes in flap perfusion that occur over time. We found a stepwise progression of heat radiation towards the distal end of the flap and hotspots emerging in adjacent angiosomes, especially during the first five postoperative days (Fig. 15). This clearly gives further support to the angiosome theory and perforasome concept. Such dynamic changes could not be registered by observation of clinical signs, but unidirectional Doppler examinations found arterial sounds in an increasing number of locations corresponding to the changes in heat radiation.



POD 1 POD 2 POD 5 6 weeks PO

Figure 15: The postoperative stepwise progression of flap perfusion is demonstrated in a series of thermal images obtained three minutes after cold challenge on postoperative days (POD) 1,2, 5 and 6 weeks after surgery. Note the increased heat radiation from the flap surface on the consecutive images. The angiosome containing the perforator is marked by an arrow. The corresponding digital images are shown above.

Similar to the findings on intraoperative assessment, postoperative perfusion problems in the flap were strongly associated with abnormal heat radiation from the flap surface, as visualized by DIRT. A disappearing or less visible pattern of hotspots followed by a progressively lower flap surface temperature indicated a compromised arterial inflow, whereas alterations toward a homogenous heat radiation without distinguishable hotspots pointed to venous congestion. On two occasions we observed such venous congestion related to internal compression from a breast implant that had been used in combination with the soft tissue to achieve sufficient breast volume (Fig. 16). After removal of the implant both flaps could be salvaged, although one required a minor revision to remove a small area with tissue necrosis at the distal end.

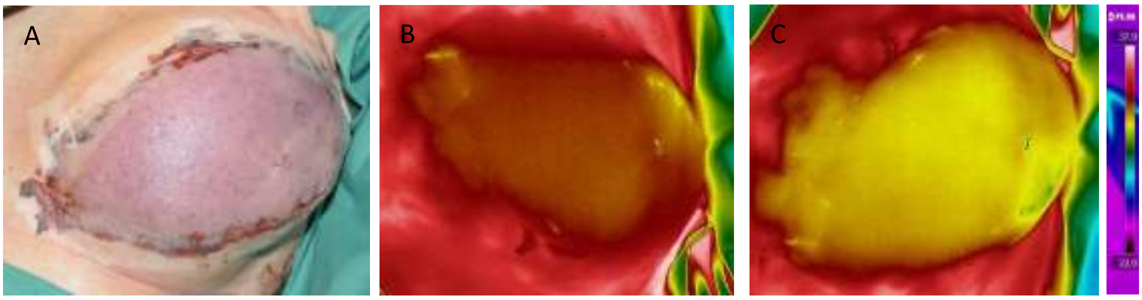


Figure 16: Series of images demonstrating the clinical and thermographic appearance of venous congestion, due to internal compression of a large implant. A. Digital photograph of left-sided breast reconstruction with TDAP flap and implant. Note bluish skin colour due to venous congestion. B. Thermographic image before cold challenge showing homogenous but weak heat radiation due to pooling of blood in the flap. C. Thermographic image 2 minutes after cold challenge showing cold flap surface without emerging hotspots.

Figure reprinted with modifications from Sjøberg et al. The value of dynamic infrared thermography in pedicled thoracodorsal artery perforator flap surgery. Plastic and Reconstructive Surgery Global Open 2020; 8(7), e2799.

Although the end-surgery thermography indicated sufficient flap perfusion, two flaps failed due to inadequate flap perfusion that resulted in progressive ischaemia during the first postoperative days. DIRT showed reduced heat radiation, primarily from the distal end of the flap but eventually from the total flap surface area. Both patients had received local radiotherapy due to prior breast cancer, which could have had a negative effect on the flap vasculature although no obvious signs of vessel anomaly were seen during surgery.

Study III

Comparison of basic data of the two patient cohorts (liberal vs. modified fluid management protocol) showed no difference regarding age or BMI but prior radiotherapy was more frequent in the MFM cohort (73.3 % of patients) compared to the LMF cohort (40.5 %) ($p < 0.05$).

The fluid management protocols differed substantially regarding intraoperative anaesthesiologic approach, which was reflected in the total volumes of intravenous fluids as well as the estimated interstitial fluid accumulation at the end of surgery. The final fluid balance was almost double as high in the LFM cohort, ending at a mean of 53.8 ± 22.0 ml/kg, compared the MFM cohort at 29.6 ± 10.6 ml/kg ($p < 0.05$). Colloids were much more frequently used in the LFM cohort (66.6 % of patients) compared to the MFM cohort (4.7 %). Furthermore, propofol was used during surgery of almost all patients in the MFM cohort, whereas only in 35.7 % of procedures in the LFM cohort. Vasoactive drugs, mostly norepinephrine, were administered during 159 procedures (92.5 %) in the MFM cohort, while only one patient received vasopressor in the LFM cohort ($p<0.05$). Sevoflurane was by far the most frequent inhalation agent in both cohorts. Procedure time or flap weight did not differ significantly between cohorts, although venous superdrainage was more common in the MFM cohort (73.8 %) compared to the LFM cohort (35.7 %) ($p < 0.05$).

The complication rates were generally higher in the LFM cohort. Intraoperative complications occurred in 12 patients (28.6 %) in the LFM cohort and in 25 patients (14.5 %) in the MFM cohort ($p < 0.05$). Intraoperative blood loss exceeding 500 ml was the most frequent complication in the LFM cohort, whereas problems related to the vascular pedicle, such as post-anastomotic thrombosis in the internal mammary artery or insufficient flow from other causes, was seen mainly in the MFM cohort.

Postoperatively, both surgical and medical complications occurred more frequently in the LFM cohort. The higher incidence of surgical complications, observed in 27 patients (42.9 %) in the LFM cohort compared to in 33 patients (21.9 %) in the MFM cohort, was by and large related to partial and total flap failures ($p < 0.05$). Other postoperative surgical complications were rather scarce, apart from postoperative hematoma in 12 patients (7 %) in the MFM cohort. Such was mainly related to the abdominal donor site. Medical complications were reported in 6 patients (14.3 %) in the LFM cohort and 4 patients (2.3 %) in the MFM cohort ($p < 0.05$). Respiratory tract problems (pneumonia, pulmonary oedema) were the most frequent medical complication in both cohorts. Mean length of stay was significantly longer for patients in the LFM cohort at 12.7 (± 6.5) days compared to 10.5 (± 2.7) days for the MFM cohort patients ($p < 0.05$).

The study shows that the stricter MFM protocol was associated with fewer complications compared to the liberal fluid management. Clinically, the difference between the two groups was related to a higher incidence of respiratory tract complications and much higher incidence of partial and total flap failures in the LFM protocol cohort. No detrimental effect of vasoactive drugs was observed.

Discussion

Autologous breast reconstruction using free flaps, in particular abdominal flaps, has become increasingly popular due to the aesthetic results that can be obtained. The lower abdomen is a very suitable donor site because the consistency and volume of this tissue approximates that of the breast. As most patients have surplus skin and fatty tissue on the lower abdomen, an additional benefit is the improved abdominal contour that can be achieved after surgery. The challenges with autologous breast reconstructions in patients with slim body configuration or limited surplus tissue for other reasons have been described in section 6.3. Many authors have advocated the use of a combination of free flaps to increase the volume of the neo-mamma.[42,43,164] Technical complexity and longer operation time are known risk factors for complications of such surgery. [44] Even so, recent reports have not observed an increased complication rate in complex reconstructive breast surgery with combined flaps.[41,165]

An alternative to autologous reconstructions based on several free flaps is to increase the volume of the reconstructed breast by using fat transplantation or synthetic implants. One such common procedure is to combine a pedicled latissimus dorsi musculocutaneous flap with a breast implant, to compensate for the limited filling volume gained from the flap tissue.[20] More recently, the addition of implants have also been advocated in combination with free perforator flaps, such as DIEP or S-GAP flaps, to achieve increased breast size.[166,167] Although such procedures are simpler and less time demanding compared to combining several free flaps, the advantage of pure autologous breast reconstructions in terms of a natural appearance and avoidance of foreign materials is thereby lost. An alternative pure autologous technique is to combine fat transfer and a free flap, but several sessions of fat transfer are often necessary to reach the expected long-lasting volume.

Study I demonstrates that the combination of an abdominal flap with a modified pedicled LICAP flap can be a simple and elegant technique to increase the volume and aesthetic outcome of breast reconstructions in case of limited abdominal soft tissue resources. Such limitations can be observed in patients with slim body configuration or when a bilateral reconstruction is needed. Even in patients with an excess of abdominal skin and subcutaneous tissue, prior abdominal surgery can substantially reduce the available tissue due to scarring and postoperative alterations in the subcutaneous vasculature. The LICAP flap is a rather uncomplicated supplement of autologous tissue to augment the volume of an abdominal flap breast reconstruction at a lower cost in terms of effort, risk and length of the procedure when compared to combining several free flaps. The original rationale for using a LICAP flap in secondary breast reconstructions was to enable the placement of a larger breast implant without having to use prior skin expansion.[80] The LICAP flap provided surplus tissue on the lateral side and contributed therewith to creating an adequate subcutaneous pocket as well as to providing additional breast volume. LICAP flaps have also previously been merged with other flaps in reconstructive breast surgery. Hudson et al. combined pedicled TRAM flaps or

LD muscle flaps with LICAP flaps in breast reconstructions.[168,169] The LICAP flap allowed for creation of a colour matching envelope, into which the pedicled flaps from the abdomen or back could be placed. In salvage procedures, a LICAP flap can suffice to correct partial flap failures after TRAM or DIEP flap breast reconstructions.[170] Nevertheless, the most common use of the LICAP flap is as a standalone option in breast conservative surgery when partial tissue loss needs to be corrected. [83,171,172] The combination of a free flap and a LICAP flap as a primary procedure, aiming to achieve larger breast volume and/or ptosis, has not been previously presented.

Our modification of the LICAP flap design is also a novelty. In the original LICAP flap description, the pivot point was below the level of the inframammary fold to include the area where the intercostal perforators emerge within the flap base.[80] As shown in figure 14, this design may result in an unnatural appearance at the lower lateral corner of the breast. The new design raised the pivot point so that it was *at* the inframammary fold (Fig. 10).

The preservation of a subcutaneous fatty pedicle around the intercostal perforators allowed this modification without endangering the flap perfusion. The novel LICAP flap design provided improved projection, increased volume and a more natural lateral contour of the new breast. Importantly, our novel flap design did not result in a significantly increased complication rate compared to other reports utilizing the original LTD flap. We observed partial flap necrosis at the flap tip in 26 % of the LICAP flaps. In the paper by Woerdeman et al. on surgical outcome and risk factors related to LTD flap breast reconstructions, partial or total flap failure was observed in 22 % of the flaps, which was similar to the outcome presented by Blomqvist et al.[161,173] Analogous to our findings, they too observed more frequent LICAP flap complications in patients with previous radiotherapy. Prior radiotherapy to a flap donor site can have a negative effect on the tissue due to subcutaneous fibrosis and damage to the local vasculature. [174,175] To our knowledge there are no studies addressing the impact of radiotherapy on flap complications in LICAP surgery. In a study on reconstructive breast surgery with pedicled TRAM flaps , however, Chun et al. did not observe an increased complication rate among patients with prior neoadjuvant radiotherapy to the chest wall, including the area of the flap pedicle.[176] Still, the microvasculature in the distal part of the LICAP flap could have been affected by radiation, thus explaining the higher complication rate in those patients in our study.

The intercostal perforators were mapped by handheld Doppler ultrasound before surgery, in order to ensure that the subcutaneous dissection would include the flap pedicle. The partial tip necrosis that has been reported, especially with flap length over 15 cm, is most likely the result of insufficient distal flap perfusion.[161] A possible solution to reduce such flap complications is supercharging the flap with an additional venous anastomosis at the distal flap perimeter, which was recently demonstrated by Kim et al.[82] Raising the flap at a suprafascial plane can also contribute to reducing postoperative morbidity. This technique was used in a few cases without negative impact on flap survival.

A supplementary benefit of the LICAP flap is the subcutaneous craniolateral fullness that can be provided by a cranially positioned, de-epithelialized LICAP flap tip to imitate the natural cranial extension of the normal glandular breast tissue (tail of Spence). Moreover, the cranial inset of the LICAP flap reduces tension on the transverse mastectomy scar, making it easier to insert the deepithelialized part of a DIEP flap underneath the mastectomy flaps (Fig. 17).

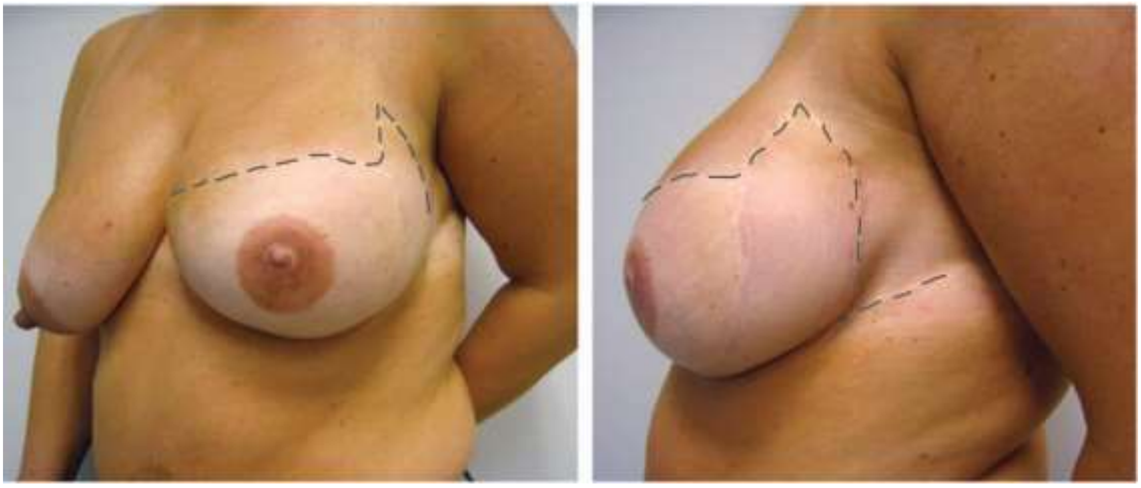


Figure 17: modified from figure 4 in paper 2: The postoperative result after breast reconstruction using the combination of a DIEP flap and a modified LICAP flap is demonstrated. The black line follows the course of the cranial scar, to illustrate how the inset LICAP flap can contribute to alleviate the tension on the suture lines, similar to a Z-plasty. Figure reprinted with modifications from Sjøberg T, de Weerd L. The pedicled LICAP flap combined with a free abdominal flap in autologous breast reconstructions. Plastic and Reconstructive Surgery Global Open 2018; 6(1), e1562

Importantly, harvesting the LICAP flap did not increase operation time, as this flap can be quickly raised by an experienced surgeon and the whole procedure could be completed within the customary time frame given a two-team approach.

In addition to larger breast size, the combined procedure resulted in increased projection and ptosis of the reconstructed breast. This was possible due to the lateral support provided by the LICAP flap, by which the abdominal flap could be positioned more medial than what was feasible without the combined procedure.

After breast removal many women have an extra fullness on the lateral thoracic wall that they would like to have corrected, especially if the original breast had a wide base. An aesthetic

bonus of the LICAP flap procedure is the removal of this lateral fullness. However, an obvious disadvantage of the flap combination is the additional lateral scar on the neo-mamma and thoracic wall, which might result in a non-aesthetic “patchwork” appearance.
We expected that the additional volume provided by the LICAP flap would allow us to match the size of the contralateral in the majority of cases. Nevertheless, more than half of the patients treated with the combined flaps (57 %) asked for additional surgery due to unequal size and more pronounced ptosis of the non-operated breast. The most common symmetrizing procedure was contralateral breast reduction, as most women among these preferred a contralateral smaller breast rather than to enlarge the reconstructed breast further. Still, although not discussed in detail in paper I, it was interesting that a number of patients in the population wanted to have rather voluminous breasts, the size of which could not be reached despite the added LICAP flap tissue. As a result, a relatively large number of women opted to increase the volume of the reconstructed breast by fat transfer.

Besides the lower abdomen, the dorsal thoracic wall is also a favourable donor site for breast reconstructions. Historically, the musculocutaneous LD has been the most frequently used flap from this donor site. Increased anatomical knowledge and improved surgical techniques have allowed for more delicate flap pedicle dissection, resulting in less demand for muscle transfer to support flap perfusion. This evolution towards avoiding unnecessary tissue damage and donor site morbidity follows in line with the historical progress from pedicled abdominal flaps to DIEP flaps, which has contributed to the increasing use of the perforator based flaps from the back such as the TDAP flap.[91]

The vascular pedicle of the musculocutaneous LD flap is quite robust as the muscle carries several perforators to support perfusion of the overlying skin. Comparable to all perforator flap surgery however, the perfusion of the TDAP flap relies on a single or few perforators. Selecting the most appropriate perforator(s) is therefore crucial in the planning and execution of a reconstruction with a TDAP flap. Traditionally, Doppler ultrasound and, more seldomly, CTA imaging have been used in preoperative perforator mapping of TDAP flap reconstructions.[95,177,178] Based on previous experience with DIRT in other reconstructive surgery[113,114], we wanted to evaluate the usefulness of infrared thermography also in TDAP flap surgery. To our knowledge, there is only one previous report assessing DIRT in relation to reconstructive surgery with a flap based on the thoracodorsal pedicle. In a case presentation comprising a free musculocutaneous LD flap, Romansky et al. found DIRT to be a valuable imaging technique to monitor flap perfusion during and after surgery.[179] Our findings in study II showed that DIRT imaging could provide valuable information also in relation to TDAP flap surgery. We obtained indirect information on the location and function of the perforator, which was essential in determining the flap design as well as to support the realization of the surgery itself. After the mild cold challenge, increased blood perfusion in the perforators seems to be responsible for the rewarming of the skin. In such, there is no need for a quantitative numerical analysis of the information obtained by DIRT, as it is quite easy to qualitatively assess the increased heat radiation and the extent of the perfused skin area of each individual perforator just by visually observing the changing thermal patterns on the thermographic image. Similar observations have been reported by Tenorio et al. in a comparison of thermography and Doppler ultrasound in perforator mapping of the lower abdomen and lateral leg.[180] Using static thermography, they found a close correlation of the location of perforators revealed on surgical exploration with what was expected from the findings of thermography and Doppler ultrasound. This was especially evident on the lower extremity, where the subcutaneous tissue is thinner. However, their study did not provide hemodynamic information on the perforators, as no cold challenge was used to enable such assessment. Although others have found that CTA can provide information on subcutaneous perforators from the thoracodorsal pedicle[177,181], preoperative CTA in our study was not useful for this purpose. One reason might be that the TDA perforators are often small and might therefore not be easily detectable by CTA. Furthermore, even if such perforators would have been located on preoperative CTA, comparison with the findings from the other preoperative investigations might be difficult due to the limitations of the CT scanner, which forces the patient to rest in a supine position different from the lateral decubitus position with raised ipsilateral arm that was used during preoperative perforator mapping by DIRT and Doppler ultrasound and during surgery. On the other hand, CTA could provide detailed information on vascular anatomy of the thoracodorsal artery. This is valuable information when designing the flap, as a study by Elzawawy et al. has shown that the branching patterns are not as constant as previously reported.[89] Sizeable lateral perforators that one usually relies on in TDAP flap surgery were reportedly found in approximately 60 % of their dissections, whereas the medial perforators were dominating in the other 40 %. Based on these findings one would expect that in a number of patients a medial muscle-sparing LD flap would be more reliable as compared to a TDAP flap. We did not encounter absence of lateral perforators in any of our patients. In the two cases with TDAP flap failure, however, preoperative CTA showed slender thoracodorsal vessels. In addition, both patients had received radiotherapy prior to their reconstructive surgery, which also might have affected the quality of the flap pedicle. One might speculate that the outcome in these patients might have been better if another flap had been raised, possibly relying on medial perforators instead. However, flaps based on medially located perforators are not as easily transposed to the anterior thoracic wall, since the reach of the flap pedicle is likely to be shorter.

During the dissection of perforators inadvertent vessel damage may easily occur. Flap inset and modulation of the flap can also result in compromised perfusion due to kinking, torsion, compression or stretching of the pedicle. Most flap failures are initiated on the operating table rather than postoperatively.[182] Therefore, early detection is of paramount importance to prevent partial or total flap failure.[183] We used DIRT for real-time intraoperative surveillance of the flap circulation throughout the surgical procedure. DIRT monitoring enabled us to promptly detect and correct circulatory problems in TDAP flap surgery before clinical signs appeared. By analysing the changes in the rate and pattern of rewarming, both arterial and venous perfusion problems could be detected. These findings follow in the line of other reports from abdominal free flap surgery.[111,112,114,184,185]

The thermal images provided by the IR camera were easily interpreted by surgeons and other staff. The surgeon may be more confident regarding flap perfusion with the support of DIRT, which can contribute to reduced procedure time. Moreover, thermal imaging can help surgeons with less experience or trainees to appreciate the dynamic changes in the flap perfusion as part of their microsurgical training. Nonetheless, one must keep in mind that DIRT imaging conveys indirect information of flap perfusion. Other causes of reduced heat radiation such as hypotension or hypothermia, might contribute to alter the thermographic readings. In preoperative perforator mapping, it is therefore essential to have a stable hemodynamic condition as well as steady room and body temperature. One should allow time for the bare skin to acclimatize to the surrounding before IR imaging, especially when using static IRT,

The intra- and early postoperative monitoring with DIRT showed that heat radiation from the flap surface was always more pronounced in the vicinity of the perforator. The flap tissue most distal from the pedicle produced lower heat emission indicating lower perfusion compared to tissue adjacent to the pedicle. During the first days after surgery, there was a stepwise increase of heat radiation starting from the proximal part of the flap, where the preserved perforator was located, towards the distal part of the flap that was originally perfused by medial intercostal perforators. The registration by DIRT, showing a profound rewarming at the perforator and a gradually improved perfusion of the distal part over the following days supports the notion that a TDAP flap with a horizontal design comprises two angiosomes. Hence, we believe that the use of intraoperative DIRT can contribute to our knowledge of the dynamics of TDAP flap perfusion and possibly also other flaps, given more widespread use of thermography in reconstructive flap surgery. Our findings are supported in a recent meta-analysis by Raheman et al.[114]

Adequate flap perfusion will not be possible without proper intraoperative fluid and blood pressure management. Because the flap has been denervated on dissection, the vessels in free flaps lack the normal innervation by the autonomic nervous system. Therefore, the remaining regulatory mechanisms will only be controlled by circulating mediators in the blood and tissue temperature. Raised hydrostatic pressure, for example resulting from excessive intravenous fluid infusion, will contribute to increase the physiological transport of fluid into the interstitium through the endothelium of dilated capillaries. In situations with interstitial fluid overload, small-calibre vessels in the flap may collapse, which in turn increases the risk for ischemia and flap failure.

In study III we aimed to evaluate the impact of two different fluid management protocols on the clinical course related to abdominal flap breast reconstruction. Our modified protocol based on restricted intravenous crystalloid infusion was associated with a better outcome. Our early observations showed that flap failures occurred more often when plasma expanders, such as dextran or starch, had been used during the surgery. Clinically the flaps were more oedematous, indicating excessive fluid entrapment within the flap tissue. Colloids were often administered only after large volumes of crystalloids had been given, as a measure to regain normal blood pressure if crystalloid infusion was insufficient to counteract a hypotensive event. Increased extravascular leakage of colloids might have contributed to raise the interstitial osmotic pressure and to accelerated fluid transfer out of the intravascular compartment, to explain the increased fluid entrapment in the flap tissue. Still, we could not find a significant association between flap complications and colloid use per se. Other studies on free flap surgery have also used colloids without problems.[154,186] Laszlo et al. compared the effect of crystalloid and colloid infusion to determine the impact on macro- and microcirculation in free radial forearm flaps.[187] In their study, adequate regional microcirculation was more dependent on haemodynamic stability than the type of fluid that was used to support adequate prefusion. We observed a greater variation in blood pressure in the LFM cohort compared to the MFM cohort, as determined from the number of hypotensive episodes observed during surgery. In the LFM protocol, hypotension would be counteracted by increased crystalloid infusion and possibly combined with colloids. One can argue that the interstitial fluid accumulation might have been reduced if colloids had been administered earlier. Plasma volume restoration in situations with acute intraoperative hypovolemia, due to acute blood loss or vasodilation, is more effectively done by using colloids than by crystalloids, possibly related to increased plasma osmotic pressure after colloid infusion.[188] Swift correction of hypotensive episodes by colloids might therefore have reduced the need for large volume crystalloid infusions in order to achieve haemodynamic stability. Attentive use of norepinephrine in the MFM protocol also contributed to counteract significant fluctuation in the blood pressure and tissue perfusion. Vasoactive drugs, through their effect on alpha adrenergic receptors, act to reduce vascular diameter and increase flow velocity, both of which were beneficial to support flap perfusion. Moreover, the short half-life of norepinephrine allowed for more precise blood pressure control in comparison to management by intravenous fluids. The lower end-surgery fluid accumulation in the MFM cohort was related to both less fluid infusion and increased urine output, which partially can be explained by the effect of norepinephrine on restoring perfusion pressure. Such improves organ perfusion including kidney perfusion. Hence, the use of norepinephrine contributed to limiting the end-surgery fluid accumulation, as adequate blood pressure could be upheld without the need for additional intravenous fluid.

Although early reports from animal studies stated that the use of vasopressors might be harmful in flap surgery as a consequence of vasoconstriction in the flap vasculature, several later publications on reconstructive surgery in humans have not observed any unfavourable effects and, in fact, showed that vasopressors are perfectly safe to use.[144,189,190] The safety of vasoactive drugs during microvascular surgery was confirmed in our study, as we did not observe any detrimental effects of such treatment. Although one might think that the administration of vasopressors could be most harmful early after the completion of the microvascular anastomosis when the vessels are more prone to vasospasm, intraoperative timing of vasopressor administration did not make a difference in our study. Similar findings have also been reported in other publications. [144,189]

Inhalation anaesthesia was used in both fluid management protocols. The merits of sevoflurane compared to isoflurane, which was mostly used in the beginning of our study, are that sevoflurane to a greater extent acts to reduce capillary filtration of plasma into the interstitial space and protects the endothelium of the flap vasculature from the ischaemia-reperfusion injury that might follow the temporary lack of tissue perfusion during flap transport.[158] Propofol, mainly used in MFM cohort, has been shown to inhibit platelet aggregation, to support vasodilatation and to protect against the effect of free radicals after flap re-perfusion.[191-193] The combination of sevoflurane and propofol therefore seems especially favourable in free flap surgery. Propofol could also have contributed to counteract vasospasm early after completion of the anastomoses. A synergistic effect of norepinephrine and propofol was assumed to be an important contributor to the reduced complication rate in the MFM cohort.

Postmastectomy radiotherapy (PMRT) can have a negative effect on the outcome of reconstructive breast surgery.[194,195] The impact is most evident in implant breast reconstructions, resulting in increased risk for wound healing problems and considerable scarring after surgery.[196] In autologous reconstructions the breast is reconstructed using non-irradiated tissue. Several studies show that there is less post-radiotherapy morbidity after autologous reconstruction as compared to reconstruction based on synthetic implants.[197] Even so, prior radiation can cause intravascular fibrosis and increased vulnerability of recipient vessels.[174] Such might result in circulatory problems, resulting in partial or total flap failure associated with thrombosis or vascular damage.[198,199] PMRT was more common among patients in the MFM cohort, which we therefore thought could have resulted in an increased complication rate. However, on post-hoc intra-cohort analysis in the MFM population, there was no significant difference in the incidence of recipient vessel problems intraoperatively (recipient artery thrombosis or insufficient flow in recipient vessels) between those who had received prior PMRT as compared to those who had not. We therefore assume that the impact of prior radiotherapy on recipient vessels in MFM cohort patients was rather limited.

A surgical twist was added in the modified protocol. A common cause for partial or total flap failure is venous congestion, resulting from inadequate blood drainage from the flap tissue.[200] One can increase the venous draining capacity by not only connecting the vein(s) of the flap pedicle to recipient vessels but also make use of other veins found at the periphery of the flap, such as the superficial inferior epigastric vein (SIEV) (Fig. 18).

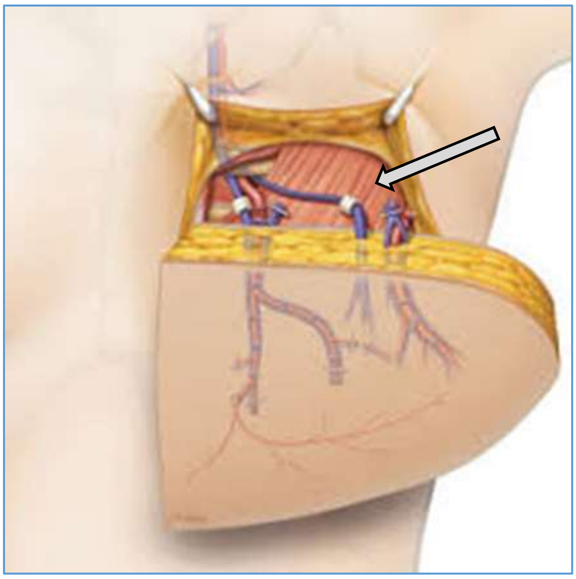


Figure 18: Illustration of additional venous coupling that can be used to enhance flap perfusion in situations with anticipated or observed venous congestion. The arrow points to a venous anastomosis (by coupler device) between one intramammary vein and SIEV. The regular pedicle anastomosis (one artery and one vein) is seen to the left.

Reprinted with permission from Bartlett et al. Algorithmic Approach for Intraoperative Salvage of Venous Congestion in DIEP Flaps. J Reconstr Microsurg. 2018.

Several reports have presented a positive association between increased number of venous anastomoses and outcome, thus favouring such venous superdrainage.[201] We did not observe an increased complication rate in the modified protocol cohort despite a higher prevalence of prior radiotherapy. Since the reconstructive procedures in these patients more often included additional venous drainage compared to procedures in the original protocol population it is possible that these two factors outweighed each other so that the impact of neither radiotherapy nor venous superdrainage was recognized.

Methodological considerations

The infrared thermography used in study II can only provide indirect information on the skin perfusion. Even so, several studies have found a significant correlation between thermographic findings and skin perfusion.[202-204] Compared to colour Doppler ultrasound or CTA investigation, no information on a detailed anatomical course of the vessel can be obtained. Precise quantitative measurement of flow velocity is also not possible. As such, this imaging technique might seem inferior to others. However, the location of hotspots in thermographic imaging corresponds well with the anatomical location of perforators.[114,117,184] Comparisons with ICGA pre- and intraoperatively has demonstrated that both techniques can convey dynamic information on flap perfusion with overlapping findings.[116,118,205] DIRT can provide valuable information on flap perfusion in all phases of surgery, with less burden than for example CTA.[119,184] The limitations known to DIRT regarding the inability to present detailed information on the course of the perforator also apply to ICG-FA. The main advantages of DIRT compared to other commonly used imaging techniques remain in its simplicity in procuring real-time information on tissue perfusion, the non-invasiveness and the easily comprehendible images produced by this technology. A major advantage is also that the patients are not subjected to ionizing radiation with its potentially hazardous long-term effects.

The two fluid management protocols compared in study III differed in several aspects. The study was not aimed at analysing the impact of single variables, such as vasoactive drugs or propofol, between otherwise similar patient populations. Therefore, the benefit of the MFM protocol over the LFM protocol can at best be defined as the result of the synergistic effect of several advantageous elements. Although the cohorts did not differ on basic parameters, potential confounding factors such as prior adjuvant therapy or experience in the surgical and anaesthesia team must be acknowledged. Adjuvant therapy was more common in the MFM cohort and could, based on current knowledge, have had a negative impact on outcome. Hence, the correlation between restricted fluid management and reduced complications might have been even stronger with less frequent adjuvant therapy in this cohort. On the other hand, less experience with the procedure concerning technical aspects of the surgery itself and how to achieve optimal anaesthesia in these long-lasting operations could have contributed to the increased complication rate in the beginning of our study. Prior reports have claimed that an improved success rate in DIEP flap reconstruction is usually observed after the first thirty cases.[206,207] As the first cohort comprised 42 patients one might assume that the outcome of a majority of these procedures was adversely affected by less expertise. However, when looking at the incidence of complications over time we observed a close correlation between improved success rate and reduced intravenous fluid resuscitation starting from 2003, when the number of included patients was less than thirty. Moreover, within a short time frame the success rate was improved more than what we think would have been the result of simply enhanced experience. The complication rate remained rather steady at a lower level after the full implementation of the modified fluid management protocol in 2005. Although the mean length of surgery did not differ between the two cohorts, which might support the assumption that the surgeons' expertise was as nearly the same in the beginning of the study period as it was later, one still needs to appreciate that improved success rate could be expected as experience grows. Moreover, the pedicled flaps were all done by a single team, which meant that the preparation of the flap and the recipient site could not be done simultaneously as was the case with the free flap procedures. Even so, the mean procedure time in the LFM cohort was no longer that that in the MFM cohort. Part of the explanation might be that dissection of a pedicled flap is more easily done than the intramuscular dissection that is needed to prepare the vascular pedicle in the free flaps.

The economical constraints put on the national health care in Norway, did not allow for a constant annual number of procedures, which therefore varied quite significantly throughout the study (Fig. 19).

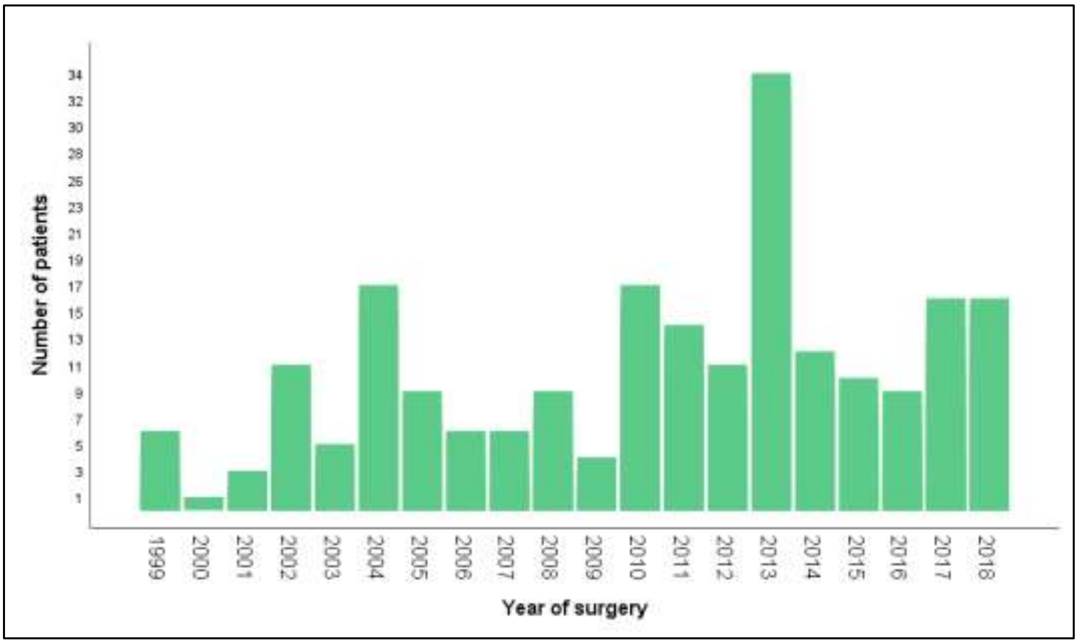


Figure 19: Number of included patients per year during the study period (Study III)

During the years of few autologous breast reconstructions, less experience and acquaintance with such procedures was gained. This might also have had an impact on the outcome from a general perspective. Still, the same principal surgeon was responsible for the main part of the procedure in all included surgeries, which would have reduced the drawback of few procedures during certain time periods. During the last five to six years of the study period the staff in the anaesthesia team has also been rather constant, contributing to the best expertise possible during periods of reduced activity. The rest of the surgical team varied somewhat over the years, since the Department of Plastic and Reconstructive surgery at UNN Tromsø is a teaching facility for residents in plastic and reconstructive surgery.

Clinical implications and future considerations

The demand for breast reconstructions is on the rise and will, no doubt, remain high in the foreseeable future.[208,209] The most natural long-term results are achieved by using autologous tissue, which is why such procedures are highly appreciated. With the development of more sophisticated surgical techniques and discovery of new flaps, the prevailing goal is to cause as little harm as possible while still creating a breast with a natural feel and design. This thesis describes some useful tools to achieve that goal.

The pedicled LICAP flap can be used in conjunction with any type of surgery on the thorax, whether there is a need to recreate a breast or cover other defects following trauma or surgery. Although this flap has been known since 1986, it is not until recently that an interest for this flap seems to be rising, as indicated by the increasing numbers of published papers. We have found the LICAP flap to be very versatile in appropriate patients and a simple alternative to more complex surgery. We therefore hope that our work will inspire others to make use of this flap in the future. The LICAP flap could also be utilized as a free flap. However, to lengthen its rather short and slender pedicle one would need to also include the intercostal vessels, which are cumbersome to prepare. It is therefore likely that a free LICAP transfer would need perforator-to-perforator anastomosis. Such procedures are reported in an increasing number of papers and will probably become more common as technical expertise and microsurgical equipment is further developed.[210] These supermicrosurgical procedures will possibly also be facilitated by the introduction of robot-assisted surgery.[211,212]

DIRT, as an imaging technique in reconstructive surgery, has been most frequently described in relation to abdominal flap-based breast reconstructions and to a lesser extent in other types of flap surgery. Although DIRT cannot provide the same detailed morphological information on subcutaneous vascularity as CTA or MRA, the most important advantage compared to other techniques is the simplicity and harmlessness of DIRT. Recent review papers on the use of DIRT in DIEP flap breast reconstructions and other free flap surgery conclude that DIRT is an ideal alternative to locate suitable perforators as well as to monitor flap perfusion during and after surgery.[114,184] This thesis provides data to support the use of DIRT in planning and execution of reconstructive surgery using pedicled TDAP flaps, thereby increasing the knowledge of DIRT in reconstructive surgery using free or pedicled flaps. New insight with regards to the dynamic alterations in flap perfusion was also gained. The technological advancements in developing more portable and cheaper IR cameras with acceptable thermal resolution will certainly enable more wide-spread use.[121,213] Postoperative monitoring of buried flaps will, naturally, not be possible by DIRT, similar to other imaging techniques relying on registration from the flap surface.

The risks related to overambitious fluid management in flap surgery have been thoroughly described, also in other publications. This thesis further contributes to the data supporting a restrictive intraoperative fluid resuscitation strategy and the safety of vasopressors to counteract inadequate flap perfusion. The increasing implementation of enhanced recovery after surgery (ERAS) protocols in reconstructive flap surgery encompasses many of the strategies with respect to fluid management proposed by us and others. We believe that future studies will further explore the possibilities to reduce complications while maintaining the best possible results in flap surgery. Our contribution merely supports this development towards safer surgery with faster recovery.

Conclusions

Study I

The LICAP flap is a versatile adjunct to abdominal free flaps to enhance the result of autologous breast reconstructions in patients with insufficient donor site tissue. The presented modifications to the original LICAP flap design can enhance the aesthetic outcome of the new breast as well as reduce the tension on cranial suture lines.

Study II

Dynamic infrared thermography (DIRT) is a non-invasive and harmless alternative to other imaging techniques in reconstructive surgery using pedicled TDAP flaps. Preoperative DIRT can increase the reliability of perforator mapping and is strongly associated with intraoperative findings of suitable perforators. DIRT is useful to assess flap perfusion during and after TDAP flap surgery. Transversally oriented TDAP flaps comprise two angiosomes. Flap perfusion increases in a stepwise progression during the initial postoperative days.

Study III

Intraoperative anaesthesiologic management favouring restricted amounts of intravenous fluids results in fewer complications. The use of vasoactive drugs contributes to maintain an adequate flap perfusion during surgery and is not associated with an increased complication rate. The addition of propofol at the end of surgery can contribute to optimizing flap perfusion and may counteract the effects of ischemia-reperfusion injury in free flap surgery.

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Paper I

OPEN
PRS GLOBAL OPEN
ORIGINAL ARTICLE
Breast

The Pedicled LICAP Flap Combined with a Free Abdominal Flap In Autologous Breast Reconstructions

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Louis de Weerd, MD, PhD*†

Background: Previous surgery or slim body configuration can limit the size of the available abdominal flap in autologous breast reconstruction. However, redundant skin and subcutaneous tissue lateral to the mastectomy site can be utilized as the pedicled lateral intercostal artery perforator (LICAP) flap. This study evaluates the combination of a free abdominal flap and a pedicled LICAP flap to achieve increased breast size and improved cosmetic outcome.

Methods: Patients undergoing secondary autologous breast reconstruction were included in a prospective study. The combination with a LICAP flap was used for women with insufficient abdominal flap tissue in relation to the desired breast size. The authors also assessed their modification of the original lateral thoracodorsal flap design to improve the aesthetic outcome.

Results: In 109 patients, 121 free abdominal flaps were performed. The combination with a pedicled LICAP flap was used in 82 free abdominal flap reconstructions (68%). The LICAP flap provided additional volume and resulted in better projection and ptosis of the neo-mamma. The overall complication rate for the LICAP flaps was 26 %; all minor complications. Despite combining flaps, the majority of patients needed additional surgery to improve breast symmetry. Breast reduction of the native breast was the most common symmetrizing procedure.

Conclusion: In selected patients with insufficient abdominal flap tissue, a combination of a free abdominal flap and a pedicled LICAP flap is a valuable option to increase breast size and cosmetic outcome. Additional symmetrizing surgery might still be necessary. *(Plast Reconstr Surg Glob Open 2018;6:e1562; doi: 10.1097/GOX.0000000000001562; Published online 12 January 2018.)*

INTRODUCTION

Free abdominal flap breast reconstruction is a well-established surgical procedure. Few other donor sites can provide the same volume and tissue quality to create a natural looking breast. Still, slim body configuration, previous surgery affecting the abdominal flap perfusion or the request for bilateral reconstructions might result in breasts with unsatisfactory volume and shape. In these patients, we therefore recognize a need to augment the abdominal flap with other tissue to fulfill patients' expectations.

Many women with previous ablative breast surgery have an excess of skin and subcutaneous tissue lateral to the original breast site, which can be utilized as a pedicled fasciocutaneous flap. This flap was originally described as the lateral thoracodorsal flap (LTD) by Holmström and Lossing[1] in secondary implant breast reconstructions. Their seminal article has been followed by several publications describing the relevance of this flap, in combination with other flaps as well as a stand-alone option in oncoplastic or salvage breast surgery.[2–6] In accordance with the recent change in flap nomenclature, the pedicled LTD

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flap should now more correctly be named the pedicled lateral intercostal artery perforator (LICAP) flap.[7,8]

At our institution, many patients wish to keep their breast size unchanged and therefore desire rather large reconstructions. The aim of our study was to assess the applicability of a novel combination of a free abdominal flap and a pedicled LICAP flap to achieve the desired breast size in selected patients. Being able to reconstruct larger breasts, we also hypothesized that there would be a reduced need for additional surgery to reach symmetry with the native breast in unilateral cases. Although the combination of a LICAP flap with other flaps already has been described in breast surgery, to the best of our knowledge there are no previous reports on the combined use of the LICAP flap and a free abdominal flap in secondary breast reconstruction.

MATERIALS AND METHODS

A retrospective study of prospectively collected data was performed in accordance with the principles outlined in the Declaration of Helsinki and in-house rules of the University Hospital. All patients consented in writing to participate in the study. Patients were nonsmokers or had stopped smoking at least 3 months before surgery. First, the maximal lower abdominal flap size was estimated based on a preoperative evaluation considering previous scars and body mass index (BMI). A pinch test was used to establish the maximal width that could be obtained. If patients asked for a breast volume larger than what could be provided by the free abdominal flap alone, the combination with an LICAP flap was discussed and a formal consent to proceed was obtained. The excess of skin and subcutaneous tissue on the ipsilateral thoracic wall was thereafter assessed, also by pinch test. The LICAP flap was initially designed as described by Holmström and Lossing[1], with 2/3 of the base of the flap positioned below the anticipated sub-mammary fold and 1/3 above (Fig. 1A). We later modified the LICAP flap design, whereby the whole base of the flap was above the anticipated sub-mammary fold, as we found this to give a more natural appearance of the neo-mamma (Fig. 1B). The inferior border of the flap was marked a few centimeters shorter than the superior border.

Surgical Technique

Using a two-team approach, one team raised the free abdominal free flap, whereas the other team prepared the recipient vessels and the LICAP flap. The abdominal flap was harvested using previously described techniques.[9,10] The superficial inferior epigastric vein was frequently included, to enable us to enhance the venous drainage in large flaps, as needed. On the thorax, the transverse postmastectomy scar was excised and the skin incision was extended in a cranial direction at the anterior axillary fold (Fig. 2). The mastectomy skin flaps were raised from the thoracic wall. The LICAP flap was harvested by incisions through skin and subcutaneous tissue along its superior and inferior borders, whereby the inferior incision was beveled in a caudal direction to recruit more tissue and protect the intercostal perforators. The flap was thereafter raised at subfascial level lateral to medial from the underlying serratus anterior musculature starting at the anterior border of the latissimus dorsi muscle. Hakakian et al.[11] have recently described a subcutaneous dissecting technique, that we used in a few cases. Once the basis of the flap was reached, no further dissection was done. Although the perforators can be skeletonized, this is not necessary for flap transposition. In fact, we recommend leaving a cuff of soft tissue for vascular pedicle protection.

The internal mammary vessels were used as recipients in all cases. Exposure and dissection was accomplished by removing a parasternal piece of the third or fourth rib. The microvascular anastomosis was done using end-to-end sutures on the arteries and a coupling device for the veins (GEM coupler; Synovis Micro Companies Alliance, Birmingham, Alabama). If the venous drainage of the flap was deemed insufficient based on clinical signs and dynamic infrared thermography, the superficial inferior epigastric vein was coupled to another local vein, most commonly the cephalic vein, to enhance the flap circulation.

The free flap was then partially deepithelialized and covered by the mastectomy flaps. The LICAP flap was transposed in a cranial direction to fill the defect created at the anterior axillary fold when raising the superior mastectomy flap. To optimize breast contour, the LICAP flap tip can be partially deepithelialized and buried. The LICAP flap donor site was closed using subcutaneous and

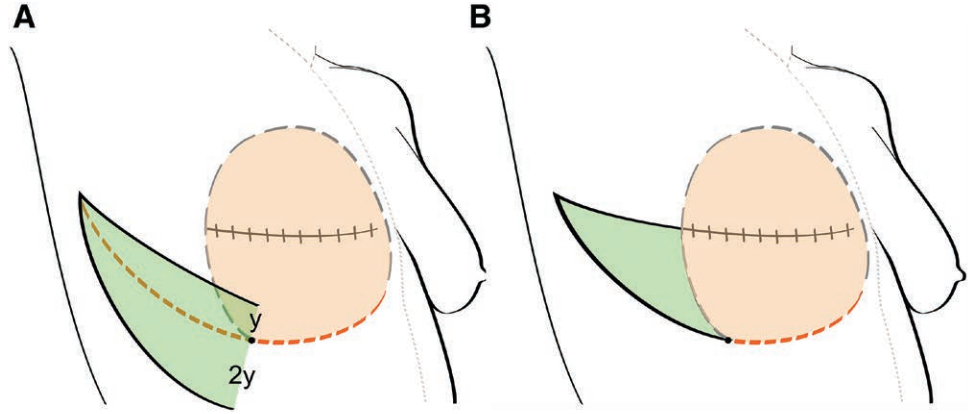

Fig. 1. Preoperative planning of the LICAP flap. A, The original LICAP flap design. B, The modified LICAP design by the authors. Note the change in pivot point to a more cranial position.

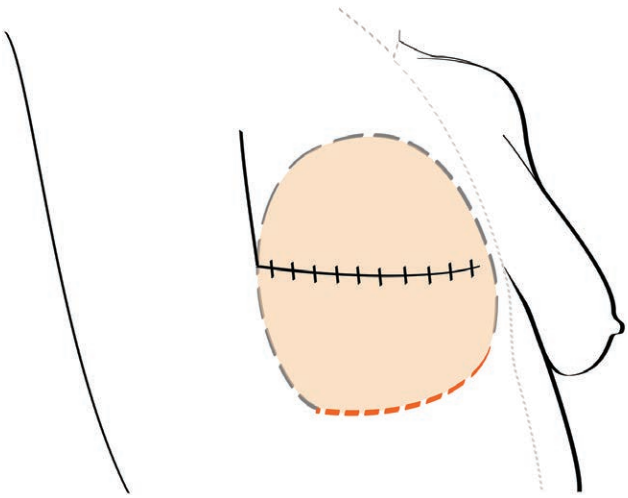

Fig. 2. Extending the transversal postmastectomy scar cranially at the lateral border of the breast site enables transfer of the LICAP flap and reduces scar contracture.

resorbable intracutaneous sutures. The remaining skin incisions on the thorax were closed using only resorbable intracutaneous sutures. A drain was placed beneath the free flap and in the LICAP flap donor site.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics ver. 22 (IBM Corp., Armonk, N.Y.). The following tests were used: independent samples *t* tests (flap size versus BMI class, relative use versus flap type or BMI class, flap weight and relative use versus surgical procedure), 1-way analysis of variance (ANOVA) (age, BMI, or flap size versus flap type) and binary logistic regression (symmetrizing surgery versus procedure type). The significance level was set at $P = 0.05$ in all tests.

RESULTS

During a 6-year period, 109 patients were operated for secondary autologous breast reconstruction, resulting in 121 abdominal flaps. The mean age was 52 years (range, 28–72) and the mean BMI was 26.2 kg/m^2 (20.6–33,5). In addition to prior breast ablative surgery, 74 patients had received radiochemotherapy, whereas 11 patients had only radiotherapy, and 8 patients had only chemotherapy. The number of deep inferior epigastric artery perforator (DIEAP) flaps and muscle sparing transverse rectus abdominis (ms –TRAM) flaps was 100 and 16, respectively. There were 5 superficial inferior epigastric artery flaps. There was no statistical difference in age and BMI between patients grouped by flap type. The ms-TRAM flaps were significantly larger [mean weight 787 g (range, 453–1270)], than the DIEAP flaps [666 g (218–1124)], and the superficial inferior epigastric artery flaps [561 g (470–602)]. Abdominal flap size was also related to patients' BMI; The 42 patients with BMI over 27 kg/m^2 had significantly larger flaps [mean weight, 762 g (250–1270)] compared with the 67 patients with BMI at or lower than 27 kg/m^2 [623 g (218–988)]. Regarding the available lower abdominal tissue, a mean of 75% (45–100%) of the transverse flap was used to reconstruct the breast, with no difference between ms-TRAM and DIEAP flap procedures. There was a tendency to use less of the total transverse flap in patients with BMI over 27 kg/m^2 (mean, 71%) compared with patients with lower BMI (mean, 77%; $P = 0.1$). The range of the relative use was equal for both groups (46–100%).

The free abdominal flap was combined with an LICAP flap in 76 patients (82 LICAP flaps), in 70 unilateral and 6 bilateral reconstructions. The remaining 33 patients with only free abdominal flaps comprised 27 unilateral and 6 bilateral cases. Comparing unilateral breast reconstructions with the LICAP flaps to the ones without, there was no significant difference in mean flap weight (702 versus 682 g) or the amount of abdominal tissue that was used (68% versus 75%). The same held true for bilateral cases, in which each breast was reconstructed with half of the abdominal flap. The mean flap weight was 658 g for patients with the combined procedure compared with 549 g for patients with only free abdominal flap reconstructions. The mean length and width of the LICAP flaps were 11 cm (5–15 cm) and 6 cm (4–9 cm), respectively.

Two ms-TRAM flaps and 2 DIEAP flaps failed completely, and these 4 patients were therefore excluded from the statistical analysis concerning the need for additional symmetrizing surgery. All of them had received both radio- and chemotherapy. In general, all LICAP flaps survived. Sixteen LTD flaps developed a necrotic tip and 5 LTD flaps showed partial epidermolysis. The overall complication rate of the LTD flaps was 26% (21/82). Thirteen of the 21 LTD flap-related complications occurred in patients with previous radiotherapy.

Follow-up data were available for all the 105 patients with successful reconstructions (117 breasts). Additional surgery to improve breast symmetry was needed in 47 of the 79 reconstructions (57%) with the combined procedure compared with 18 of the 38 reconstructions (47%) without LICAP flap. This difference in frequency was not statistically significant. Symmetrizing surgery was also equally frequent for patients, when grouped by BMI class (more or less than 27 kg/m^2). The most commonly performed symmetrizing procedures were contralateral breast reduction for patients with LICAP flaps and fat transfer to the native breast for patients without LICAP flaps.

DISCUSSION

The major goal in breast reconstruction is creating a natural looking breast with adequate volume and shape. Beautiful results can be obtained with the use of a free abdominal flap. However, previous abdominal surgery can reduce the availability of abdominal tissue and will, together with obesity, increase the risk for complications in relation to both donor sites and flaps.[12–14] Furthermore, in patients with thin body configuration and large breasts, the entire lower abdominal tissue might be needed to create an appropriate breast size. There are various surgical techniques to recruit the whole flap, including double pedicle, stacked flaps, and other methods to increase flap projection.[15–18] All these will increase the complexity of the surgery and, thereby put the patient at greater risk for complications. The patients at our institution often prefer to keep their original breast size. Even overweight patients may, for various reasons, not always have an abdominal pannus to achieve that, keeping in mind that these patients often have a large remaining breast to go with their general body habitus. We therefore looked for additional tissue to create a larger neo-mamma without complex harvesting procedures or substantially increased risk for inadvertent results.

General Impression

In this study, we have combined free abdominal flaps with pedicled LICAP flaps, to provide extra volume in secondary breast reconstructions. In addition to larger breast size, we observed increased projection of the reconstructed breast with the combined procedure, as the free abdominal flap could be positioned more medially resulting from the lateral support from the LICAP flap, in comparison to the reconstructions in which we did not use LICAP flaps. Harvesting the LICAP flap did not increase operation time. The LICAP flap tissue lateral to the original breast site is often annoying and many patients ask to have this reduced anyhow. Still, although rather inconspicuous, harvesting a LICAP flap will result in additional scarring in the axilla, which potentially might cause additional postoperative morbidity.

Protecting the Pedicle in Large Reconstructions

Voluminous subcutaneous tissue, in relation to the area of skin surface of the free abdominal flap, can sometimes cause high tension at the suture lines and may result in inadvertent compression on the vascular pedicle after inset. Excision of subcutaneous tissue to reduce the flap volume would result in a smaller breast with less projection. In these situations, the LICAP flap can provide additional skin coverage and thereby reduce the risk for high tension on the sutures and pedicle compression. Furthermore, the skin surplus enables the surgeon to create more ptosis of the reconstructed breast if needed.

Symmetrizing Procedures

The novel combination of flaps presented in this study did not result in a reduced need for breast symmetrization, contrary to our hypothesis. Despite using a mean of 75% of the abdominal tissue and a LICAP flap to augment volume, the majority of patients still asked for additional surgery to achieve symmetry. In the group of patients with the combined procedure, breast reduction of the remaining breast was the most frequently performed procedure. We believe that this can be explained by the fact that many of our patients had a large remaining breast that we could not match with the available flaps. Although we used the entire lower abdominal tissue in some patients, more often we decided to discard zone 4 and a part of zone 3, in situations where the distal flap perfusion was insufficient on peroperative assessment. In a recent article, Wade et al.[19] reported on contralateral breast symmetrization after unilateral DIEP flap breast reconstructions, finding that almost half of their patients had additional surgery done. An interesting finding of our study is the high percentage of patients who asked for the combined procedure. We have the impression that our patients commonly ask for a large-volume breast reconstruction. In patients who had their breast reconstructed with only the free abdominal flap, the most frequently performed additional procedure was fat transplantation to the contralateral native breast to increase its volume. The need for additional surgery in our study was not related to BMI. Although patients with high BMI often have more surplus tissue on the lower abdomen, these patients also commonly wish for larger breast reconstructions. The main indications for symmetrizing surgery were unequal size and ptosis of the non-operated breast.

Complications

A few patients developed early postoperative complications and required secondary revisions. The risk for complications in autologous breast reconstruction are well known and relate to flap type, length of surgery, and patient characteristics.[20–22] Our complication rate did not differ from previous reports.[12] Regarding LICAP flap-related complications, our early complication rate at 26% falls within the previously reported incidence at 12–36%.[2,22,23] These flap complications can be considered minor and are easily treated at the outpatient clinic. Commonly reported risk factors are high BMI, smoking, and lengthy flaps. Because the LICAP flap does not have a true axial perfusion, the distal flap circulation is difficult to predict, resulting in an increased risk for partial epidermolysis and tip necrosis. We therefore limited the length of the LICAP flaps to maximally 15 centimeters, in accordance with previously reported recommendations.[23] Still we observed tip necrosis in 16 LICAP flaps, mainly in patients who had received radiotherapy. This has also been reported by others.[24] Contrary to some studies, we did not find any correlation between BMI and LICAP flap complications.[22]

Novel LICAP Flap Design

We modified the LICAP flap design as compared with the description by Lossing et al.[25] In our hands, the combination of the original flap outline and a free abdominal flap resulted in an unsightly box-form appearance of the new breast (Fig. 3). A similar square shape was also reported by Hudson[3], when using the combination of a pedicled TRAM and a LICAP flap. This is related to the LICAP flap pivot point being at the inferolateral border of the breast. Our modification transposes the pivot point more superiorly due to the fact that the inferior border of the LICAP flap is placed at the anticipated submammary fold. The result is a more natural contour in the inferior and lateral part of the breast (Fig. 4). In any case, the perforators arising from the serratus anterior muscle need to be protected, when the base of the LICAP flap is reached during the subfascial dissection.

Postoperative Considerations

It is important to avoid using a tight bandage or bra postoperatively, since this might cause inadvertent compression on the lateral intercostal perforators. Following mastectomy, some patients will experience unsightly and

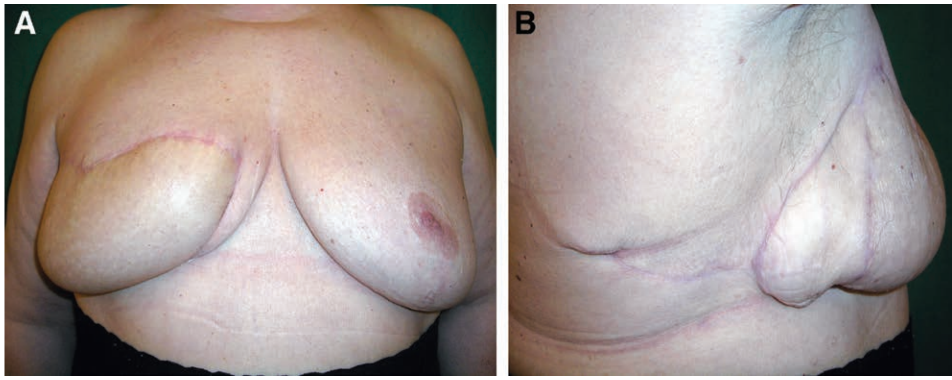

Fig. 3. Postoperative result in a 69-year-old patient after breast reconstruction with a free ms-TRAM flap combined with an LICAP flap, using the original LICAP design. Lateral (A) and anterior view (B). This design can result in an unsightly box-form, as illustrated.

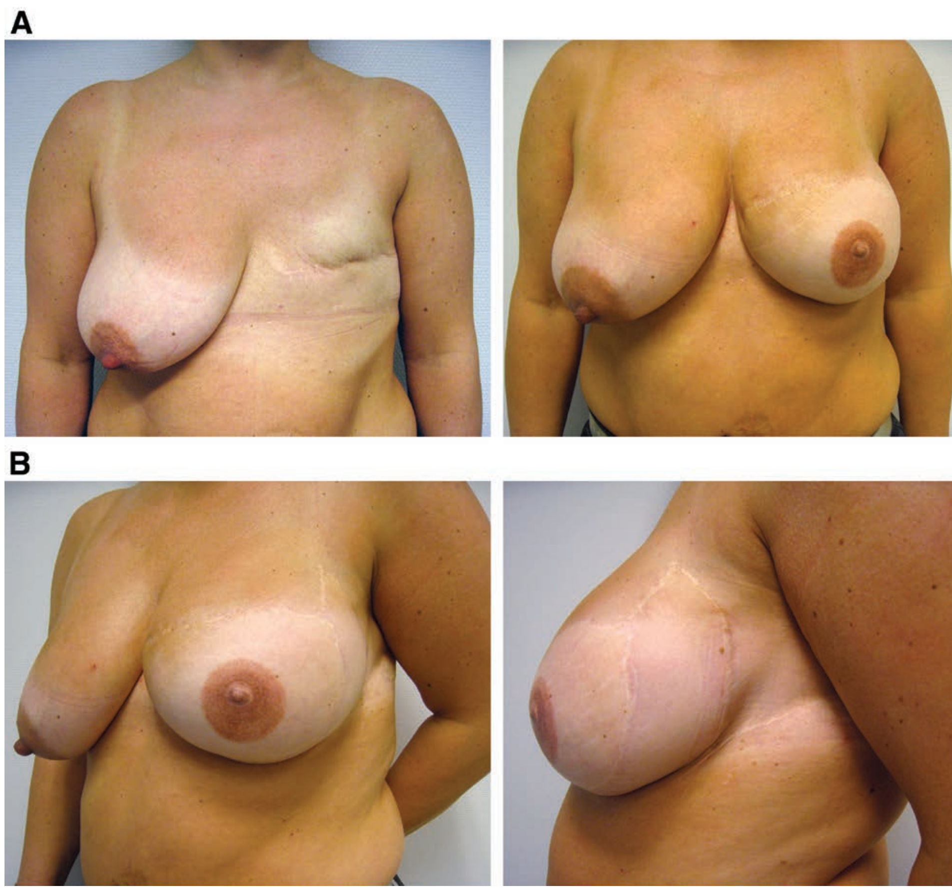

Fig. 4. Postoperative result in a 41-year-old patient after breast reconstruction using a DIEAP flap combined with an LICAP flap of the modified design. Lateral (A) and anterior view (B). Note the improved lateral contour and ptosis.

tense contracture of the transversal scar. Since this scar is intersected laterally with soft skin and subcutaneous tissue from the LICAP flap, the tension is reduced and the esthetical appearance improved. The transposed LICAP flap also allows for more tension free inset of the free abdominal flap beneath the raised mastectomy skin flaps. Finally, the distal part of the LICAP flap can contribute to recreate the lateral cranial fullness seen in a natural breast. The scars in the axilla and in the lateral part of the neo-mamma can be easily hidden using regular clothing and were well tolerated by our patients. It is worth noticing that the scars after the LICAP flap procedure do not reach onto the back, as would be the case when using a latissimus dorsi or thoracodorsal artery perforator flap. Esthetically, the LICAP flap enabled us to create a breast with a more natural shape, more ptosis, and an improved lateral contour, even in patients with inadequate abdominal flap volume to match their preoperative desires.

CONCLUSIONS

The combination of a free abdominal flap and a pedicled LICAP flap allows for the reconstruction of larger breasts in patients with marginal tissue redundancy on the abdomen. The LICAP flap provides a natural lateral contour to the reconstructed breast and can contribute to more projection as well as increased ptosis. The procedure is simple and safe without adding extra operative time or unsightly scars. To minimize postoperative complications, the length of the LICAP flap and previous local radiotherapy need to be considered. Many patients still opt for additional procedures to achieve optimal breast symmetry.

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Paper II

OPEN

PRS GLOBAL OPEN

ORIGINAL ARTICLE

Reconstructive

The Value of Dynamic Infrared Thermography in Pedicled Thoracodorsal Artery Perforator Flap Surgery

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Background: Dynamic infrared thermography (DIRT) is a noninvasive imaging technique that can provide indirect and real-time information on skin perfusion by measuring skin temperature. Although used in flap surgery, there are no reports on its value in procedures using a pedicled thoracodorsal artery perforator (TDAP) flap. The aim of this study was to assess the usefulness of DIRT in preoperative perforator mapping and in monitoring intra- and postoperative flap perfusion of pedicled TDAP flaps.

Methods: This prospective study comprised 21 patients (21 flaps) scheduled for reconstructive surgery with a TDAP flap. Perforator mapping was done by DIRT, handheld unidirectional Doppler ultrasound, and computer tomography angiography. Intra- and postoperative flap perfusion was assessed by clinical signs and with the use of DIRT and handheld unidirectional Doppler ultrasound.

Results: Perforator mapping with DIRT showed that first-appearing bright hotspots were always associated with arterial Doppler sounds and suitable perforators intraoperatively. Computer tomography angiography presented useful information on the thoracodorsal artery branching pattern but was less beneficial for perforator mapping. Intra- and postoperative flap monitoring with DIRT was more useful than handheld unidirectional Doppler ultrasound and clinical signs to detect early arterial and venous perfusion problems. DIRT demonstrated that TDAP flap perfusion is a dynamic process with an increase in perfusion during the first operative days. Nineteen flaps survived, of which 3 sustained distal necrosis. Two flaps were lost due to inadequate blood perfusion.

Conclusion: DIRT provides valuable real-time information for perforator mapping and for monitoring TDAP flap perfusion intra- and postoperatively. *(Plast Reconstr Surg Glob Open 2020;8:e2799; doi: 10.1097/GOX.0000000000002799; Published online 15 July 2020.)*

INTRODUCTION

The thoracodorsal artery perforator (TDAP) flap is a frequently used pedicled flap in breast reconstruction.[1] Unlike the myocutaneous latissimus dorsi flap, no muscle is harvested, and donor site morbidity is thereby reduced.[2] However, abandoning the muscle comes at the expense of less robust blood flow. Preoperative perforator mapping to locate dominant perforators and to optimize perforator flap design can be helpful to ensure adequate tissue perfusion.[3,4] The most frequently reported mapping techniques are handheld unidirectional Doppler ultrasound, computer tomography angiography (CTA), and color Doppler ultrasound. Intra- and postoperative assessment of flap perfusion is commonly accomplished by clinical examination and handheld unidirectional Doppler ultrasound.[5]

Thermography is widely used in medicine as a noninvasive technique to measure skin temperature.[6] Dynamic infrared thermography (DIRT) is based on the relationship between dermal perfusion and the rate and pattern

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Table 1. Local Protocol for Preoperative TDAP Flap CTA

Scanner: Siemens Somatom Definition Flash
Slice thickness: 128 detector row × 0.6 mm, pitch 1.3
Rotation speed: 0.5 s
Contrast medium: Ominpaque 350 mg I/mL
Flow rate: 4 mL/s
Total volume: 80 mL contrast medium + 50 mL saline
Scanning range: Clavicle to xiphoid process
Scanning direction: Cranial to caudal
Bolus tracking: >100 HU at aortic arch with 5 s delay
Image reconstruction: 0.4 mm overlapping axial images

Patient in supine position with arms stretched above the head.
HU, Hounsfield units.

of skin rewarming following a cold challenge. The use of DIRT has been reported in flap surgery.[7,8] To our knowledge, however, there are no reports on DIRT in reconstructive surgery using pedicled TDAP flaps. The aim of this study is to assess the usefulness of DIRT in preoperative perforator mapping, as well as in intra- and postoperative monitoring of perfusion in TDAP flaps.

MATERIALS AND METHODS

This prospective study was performed in accordance with the principles outlined in the Declaration of Helsinki and in-house rules of the University Hospital of North Norway. All patients were nonsmokers or had stopped smoking at least 3 months before surgery and consented to participate in the study.

Preoperative Assessment of Flap Perfusion

Preoperative perforator mapping was done by CTA, handheld unidirectional Doppler ultrasound, and DIRT. The CTA protocol is presented in Table 1. Doppler ultrasound and DIRT examinations were performed in the lateral decubitus position, similar to during flap harvest. Arterial perforator sounds were detected using a handheld 8 MHz unidirectional Doppler ultrasound (Multi Dopplex II; Huntleigh Healthcare, Cardiff, United Kingdom) and marked with a red dot on the skin (Fig. 1). DIRT was performed in a dedicated laboratory (room temperature 21°C–23°C) using an infrared camera (FLIR ThermaCAM S65 HS or FLIR T 420; FLIR Systems, Boston, Mass.) with thermal emissivity set to 0.98. After a 10-minute acclimatization period, the donor site was exposed to a mild cold challenge for 2 minutes using a desktop fan blowing air at room temperature over the skin surface. The rate and pattern of skin rewarming were registered for 3 minutes. First-appearing hotspots were marked with a black cross (Fig. 1). All data were electronically stored for analysis using designated software (FLIR Research IR, ver. 3.0.11; FLIR Systems).

Surgical Technique

Our surgical technique followed previously established methods.[9,10] In short, the patient was operated on in a lateral decubitus position, with the ipsilateral arm abducted and supported by an arm table. The deep fascia was included in the flap. A propeller flap design was used in the majority of cases.[11] If a longer pedicle was needed, the perforator was mobilized further by including a small muscle cuff surrounding the vessels. Most frequently, the skin bridge between donor and recipient site was divided to avoid compression on the pedicle, although subcutaneous tunneling was used in a few cases. In breast reconstructions, TDAP flaps were combined with submuscular implants in all but 2 patients.

Intraoperative Assessment of Flap Perfusion

Flap perfusion was evaluated by clinical signs (color, refill, and temperature), Doppler ultrasound, and DIRT. The intraoperative cold challenge was effectuated by washing the flap surface for 30 seconds with gauze soaked in saline at room temperature (22°C–23°C), after which the skin was dried with a gauze.

At first, DIRT was repeated to confirm the preoperative findings regarding the rate and pattern of skin rewarming of the flap at the donor site. After flap and perforator dissection, skin perfusion by each potentially suitable perforator was assessed, leaving the selected perforator open, while the other perforators were temporarily closed using microclamps. After flap transposition and at the end of the surgery, flap perfusion was evaluated again.

Postoperative Assessment of Flap Perfusion

Postoperative flap monitoring was done by clinical evaluation, Doppler ultrasound, and DIRT. Clinical signs and Doppler ultrasound were checked every 2 hours

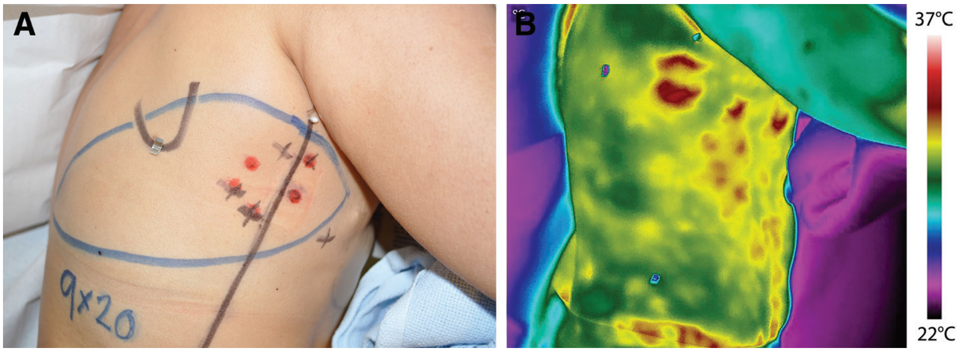

Fig. 1. Routine procedure for preoperative perforator mapping. A, Perforators localized by Doppler ultrasound (red dots) and DIRT (black crosses). B, Thermal image showing several hotspots (bright red color) representing the localized heat radiation conveyed by the subcutaneous perforators. Note the scale on the right side of the image explaining the relation between temperatures and color.

during the first 24 hours and every 6 hours thereafter for 2 days. DIRT was done on postoperative days 1, 2, 3, and 6.

RESULTS

Twenty-one patients (1 male), mean age 50 years (21–65 years) and mean body mass index 23.0 kg/m^2 (17.4–30.3 kg/m^2), were included. Nineteen female patients were scheduled for secondary breast reconstruction. Twelve of these had received adjuvant radiochemotherapy, whereas 5 had received radiotherapy only. The average time interval between radiotherapy and TDAP flap surgery was 59 months (median, 39 months; range, 11–209 months). One female patient required scar release due to childhood flame burns to the axilla and thorax. The male patient had a scar contracture in the axilla following surgery for hidradenitis.

Preoperative Findings

Preoperative CTA was accomplished in all but 5 patients, whereas DIRT and Doppler ultrasound were performed in all patients. CTA visualized the thoracodorsal artery (TDA) and its branching pattern in all patients. Although intramuscular perforators could be visualized on CTA in many patients, the continuation of an intramuscular perforator into the subcutaneous layer could be detected in only one. This result did not change when using maximum intensity projection reconstructions with a slice thickness of 10 mm. DIRT showed large variability in the locations and numbers of hotspots between patients. Rapidly appearing hotspots with progressive rewarming were always associated with arterial Doppler sounds. In some patients, arterial Doppler sounds were detected on locations without a hotspot on DIRT.

Intraoperative Findings

The results of perforator mapping with DIRT were similar intra- and preoperatively. Surgery confirmed that the locations of selected hotspots corresponded with the locations of suitable perforators. In 7 flaps, intramuscular dissection was required to obtain a longer pedicle to optimize flap transposition. The mean flap length was 19 cm (15–24 cm) and the mean width was 9 cm (7–10 cm). In 17 breast reconstructions, 6 silicone implants [mean volume, 283 mL (200–355 mL)] and 11 expander implants (range, 300–450 mL) (Mentor Worldwide LLC, Santa Barbara, Calif.) were used.

Analyses of the rate and pattern of rewarming at each hotspot showed that the brightest hotspot, with the largest rewarming area, was always associated with a suitable perforator. Rewarming always started at the brightest hotspot with an increase in temperature of the surrounding area. Other hotspots then appeared near the first-appearing hotspot in the area where the vascular pedicle entered the flap. The distal part of the flap showed a slower, more homogenous rewarming without hotspots (Fig. 2).

Although the pattern of hotspots remained largely unchanged directly after flap transposition, the observed rewarming at the hotspot(s) was somewhat slower. In cases of a major decrease in rewarming, repositioning the flap to its donor site resulted in an increased rate of rewarming and brighter hotspots within approximately 3 minutes. Repeated transposition and reposition appeared to enhance flap perfusion in general. Such a cycle of transposition and reposition and back to the recipient site took approximately 6 minutes.

In some cases, flap transposition resulted in a colder flap and the disappearing of hotspots within a few minutes. Such findings were also associated with less audible or loss of arterial Doppler sounds and were related to impaired arterial inflow, caused by kinking, torsion, tension, or compression on the pedicle. DIRT and ultrasound findings always preceded clinical signs of a pale flap (Fig. 3). After proper adjustments were made, rewarming improved and hotspots reappeared.

In some cases, DIRT showed a homogenous rewarming pattern without a clear pattern of hotspots after flap transposition. The arterial Doppler sounds gradually weakened. Clinically, the flap showed a bluish discoloration. This pattern of rewarming was always related to venous congestion. Manipulation of the pedicle or, in one case, removal of the implant normalized the flap perfusion.

Postoperative Findings

Two flaps were lost due to insufficient flap perfusion postoperatively. In both patients, the preoperative CTA showed a thin TDA. Although DIRT and Doppler investigations at the end of surgery indicated normal perfusion, postoperative DIRT showed a slow rate of rewarming at the hotspots and in the periphery. Finally, the hotspots and arterial Doppler sounds disappeared, the flaps became pale, and the skin temperature dropped on DIRT. Both patients had received adjuvant radiotherapy as part of their prior cancer treatment.

Clinical signs of venous congestion and a diffuse homogeneous rewarming pattern on DIRT, with no hotspots, were observed in 2 other breast reconstructions. Implant removal, on postoperative days 1 and 2, respectively, immediately resulted in a rewarming pattern with hotspots and a gradual return of normal skin color (Fig. 4). Both flaps survived, although 1 developed necrosis at the distal end. Partial tip necrosis also occurred in 2 other patients. One of these flaps was a bi-lobed flap used to correct burn scars. In these cases, DIRT results indicated a normal flap perfusion, apart from the most distal part, which was slightly colder after the surgery. The remaining patients had complete flap survival. There were no donor site complications.

DISCUSSION

Adequate tissue perfusion is essential in perforator flap surgery. Preoperative imaging can provide information on the location and quality of perforators. Such information can simplify the surgical procedure and reduce operating time.[12] This is particularly important in anatomical locations with large interindividual variability in vascular anatomy and in cases where previous surgery may have altered the normal anatomy. Handheld unidirectional Doppler ultrasound is the most commonly used technique in perforator mapping due to its easy handling and availability. However,

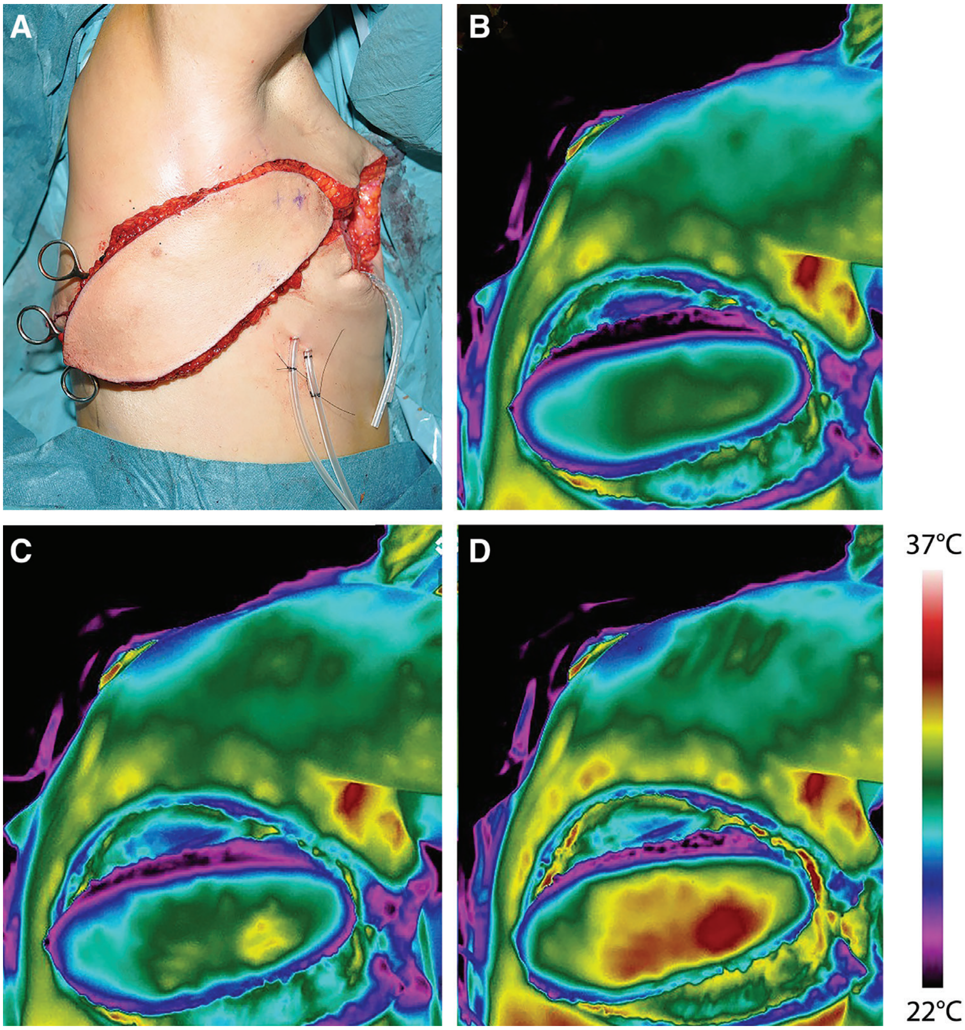

Fig. 2. Intraoperative images of a TDAP flap raised and isolated on a perforator, illustrating the information gained from the cold challenge. A, Isolated flap. B, Thermal image immediately after the cold challenge with reduced heat radiation and no hotspots. C, Thermal image 3 minutes after the cold challenge with increased heat radiation and a bright hotspot at the proximal end of the flap. D, Thermal image after complete rewarming of the flap. Note reduced heat radiation at the distal end of the flap.

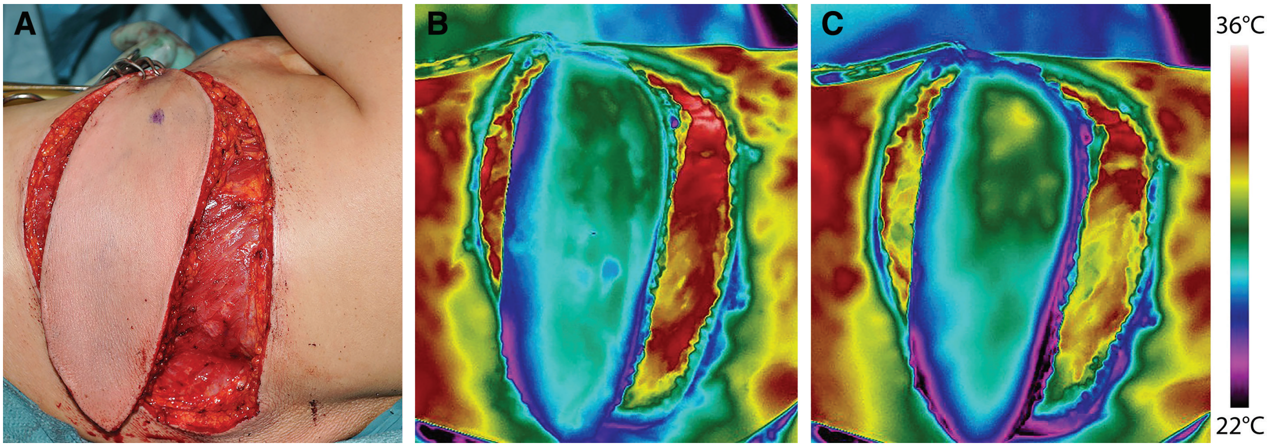

Fig. 3. DIRT revealing impaired flap perfusion before clinical signs are visible. A, This flap cooled down after transfer to the recipient site and was therefore relocated to the donor site. The thermal image shows the flap immediately after return to the donor site. B, The flap at the donor site showing no clinical signs of impaired perfusion. C, Thermal image 2 minutes after figure A, with reappearance of hotspots in the proximal part of the flap, confirming perfusion through the perforator.

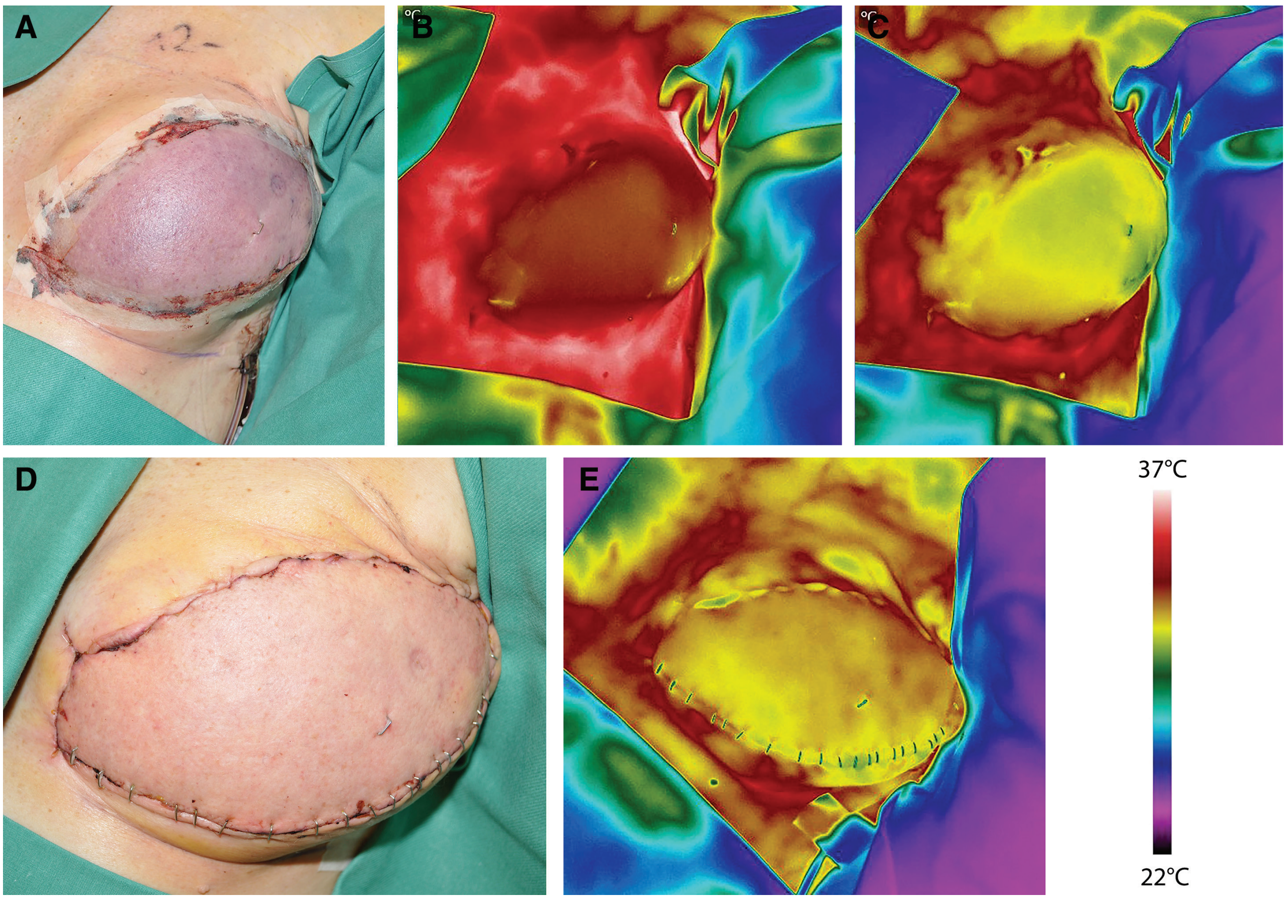

Fig. 4. This series of images shows venous congestion of the flap caused by a breast implant. A, The flap shows clinical signs of venous congestion. B, The thermal image shows a homogenous temperature pattern. C, Thermal image of the congested flap 3 minutes after the cold challenge shows no hotspots. D, The flap after removal of the implant showing normal skin color. E, Thermal image following implant removal showing re-appearing hotspots within few minutes after the cold challenge.

Stekelenburg et al[13] found poor interobserver reliability and almost 50% false-positive results when handheld unidirectional Doppler ultrasound was compared with color Doppler ultrasound. The false-positive results were mainly related to axial or intramuscular vessels. This could explain why the location of some arterial Doppler sounds could not be correlated to hotspots in our preoperative assessment. However, the perforators that were detectable by both DIRT and Doppler ultrasound preoperatively were all associated with perforators on surgical exploration. Hence, DIRT can enhance the reliability of perforator mapping with handheld unidirectional Doppler ultrasound. Furthermore, perforator mapping with DIRT produced reproducible results, as the preoperative results were identical to those obtained immediately before flap harvest.

Skin rewarming after a cold challenge is related to the quality of the perforator. First-appearing hotspots with a progressive, rapid skin rewarming are related to transport of warm blood through perforators with a large diameter and well-developed vascular network. The cold challenge makes it easier to locate such perforators and assess their ability to rewarm the skin.[14,15] Although Theuvenet et al[16] already in 1986 published an article on thermographic assessment of perforating arteries using a cold challenge, it was not until recently that DIRT has gained popularity in perforator mapping. Our results show that DIRT can also be used for perforator mapping of TDAP flaps. A disadvantage of DIRT, in comparison to CTA, is that it cannot provide detailed information on the anatomical course of the perforator.[17] A few studies support the use of CTA in TDAP flap surgery.[3,4,18] However, TDAPs are smaller, and the overlying subcutaneous layer is often thinner compared with, for example, deep inferior epigastric artery perforators and abdominal flaps, where CTA is a commonly used imaging technique. This can make the interpretation of the CTA more challenging in TDAP flap surgery.[4] Indeed, Feng et al[19] reported on perforator mapping in the lower extremities, where the thickness of the subcutaneous layer often resembles that of the back, and found that color Doppler ultrasound was superior to CTA. In our study, CTA was not very useful for TDAP mapping, although the protocol was similar to those in previous studies.[3,4,18] However, CTA clearly demonstrated the branching pattern of the TDA and, to some extent, its intramuscular course. Elzawawy et al[20] showed that the branching pattern of the TDA varies considerably among patients. Information on detailed vascular anatomy may therefore still be useful when intramuscular dissection is required. In addition, a TDA with a small caliber on CTA might be associated with reduced flap perfusion. We had the impression that the TDA as seen in 2 of our patients with total flap loss had a small caliber. The intramuscular course of perforators can perhaps be used to estimate the location of perforators in the subcutaneous tissue, even without detectable subcutaneous continuation. However, different patient positions during CTA and surgery may reduce the reliability of CTA for perforator mapping.

Intraoperative evaluation of the perforator is most frequently done with a handheld unidirectional Doppler ultrasound despite the mentioned limitations. Our results show that assessment of tissue perfusion after flap dissection can be easily performed with DIRT, allowing for selective quality assessment of individual perforators by clamping other possible perforators. This technique was described by Kalra et al[21] for intraoperative selection of a dominant deep inferior epigastric artery perforator.

Perforator flap surgery demands meticulous surgical technique, as inadvertent damage to the perforator can easily occur. Torsion, kinking, or external compression of the pedicle may cause impaired flap perfusion after flap transposition. In our study, DIRT revealed these events even before clinical signs of impaired flap perfusion became visible. The rate of rewarming at the hotspot overlying the perforator rapidly decreased in case of reduced inflow. Repositioning the flap back to its donor site improved the rate of rewarming at the hotspot and the flap. After correcting the obstruction, the flap could be relocated to its recipient site without affecting the normal rewarming. Interestingly, in some flaps, this procedure had to be repeated more than once, but flap perfusion improved every time as if some flap preconditioning occurred. While an arterial inflow problem became visible by a decreased rate of rewarming or disappearance of hotspots, venous outflow problems were characterized by a homogenous rewarming pattern without hotspots. This may be explained by the pooling of warm blood in the flap due to venous congestion.

Following flap transposition, the number of hotspots at the proximal part of the flap gradually increased, while the distal part of the flap showed a homogeneous rewarming pattern without hotspots and was cooler than the proximal part. Hotspots became visible in the distal part only during consecutive postoperative days. In cases with partial flap necrosis, this always occurred in the distal part of the flap. A possible explanation may be found in the angiosome concept by Taylor and Palmer.[22] Perforators within the same angiosome are linked by direct vascular connections, whereas adjacent angiosomes are connected by choke vessels that can open on demand to increase the vascular territory of each source vessel. The TDA is the dominant blood supply to the latissimus dorsi muscle and its overlying skin.[23] However, at its most medial extension, blood supply to the skin territory is provided by intercostal arteries.[24] A horizontal TDAP flap design up to the midline therefore consists of 2 angiosomes. The TDAP flaps for breast reconstructions in our study were designed with a horizontal orientation to conceal the scar under the bra strap. At the end of the surgery, hotspots were only seen in the angiosome corresponding with the TDA. However, during the consecutive postoperative days, hotspots became visible in the adjacent angiosome of the intercostal arteries. In such case, DIRT revealed that the perfusion of the TDAP flap is a dynamic process, explained by the opening of choke vessels between the angiosomes, resulting in gradually expanding perfusion of perforators in the distal part of the TDAP flap. Flap necrosis is most likely to occur in this distal part, as was seen in several TDAP flaps. As reported by others, designing the TDAP flap over the vertical angiosome of the descending branch of the TDA may reduce the risk for such complications.[25–27]

In 2 cases, the flaps showed a bluish discoloration within hours after the operation, and DIRT showed a homogenous rewarming pattern without hotspots. We assumed that the venous congestion resulted from compression by the breast implants. Flap perfusion improved rapidly with re-emerging hotspots on DIRT and normalized flap color after implant removal. The 2 flaps that failed had initially audible Doppler sounds, but a slow rewarming pattern during the first postoperative days. During the following days, DIRT showed a progressive decrease in flap temperature starting at the periphery; the Doppler sounds became gradually weaker and finally disappeared. The vascular pedicle in one of these flaps was dissected over a rather long distance through the muscle and might have been injured. Both flaps had a small caliber TDA on CTA. Although no intraoperative explanation was obvious in the other case of total flap failure, this was probably caused by injury to the perforators following dissection or postoperative tension on the pedicle.

One of the limitations of DIRT is that it only provides indirect information on skin perfusion. However, Miland et al[28] showed a good correlation between the results from DIRT and direct visualization of blood vessels using indocyanine-green fluorescence angiography (ICG-FA). Nevertheless, an animal study using DIRT and ICG-FA to predict partial flap necrosis in a pedicled flap demonstrated that intraoperative DIRT findings overestimated flap survival by 5%–6%, while intraoperative images of ICG-FA underestimated flap survival by 6%–10%.[29] When this limitation is acknowledged, DIRT may be useful to assess distal flap perfusion. Unlike CTA and ICG-FA, DIRT does not require intravenous injection or exposure to ionizing radiation. Furthermore, DIRT provides real-time information on skin perfusion without the need for physical contact with the patient. Recently, low-cost handheld thermal cameras and thermal cameras for smartphones have shown to be promising alternatives to expensive cameras in perforator mapping, making DIRT available at a lower cost.[30,31]

In summary, this study showed that DIRT was useful for perforator mapping in pedicled TDAP flaps, as it provides valuable information on the hemodynamic quality of perforators and their location. DIRT was also useful for intraoperative and postoperative monitoring of TDAP flap perfusion. DIRT provided more accurate information on inadequate flap circulation than clinical judgment or handheld Doppler ultrasound. DIRT showed that flap perfusion of the transversely designed TDAP flap is a dynamic process with a progression of perfusion during the first postoperative days.

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Paper III

OPEN

PRS GLOBAL OPEN

ORIGINAL ARTICLE

Breast

Liberal versus Modified Intraoperative Fluid Management in Abdominal-flap Breast Reconstructions. A Clinical Study

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Anmar Numan, MD†‡
Louis de Weerd, MD, PhD*†

Background: The outcome of reconstructive microsurgery is influenced by the intraoperative anesthetic regimen. The aim of this study was to compare the impact on the intra- and postoperative complication rates of our modified fluid management (MFM) protocol with a previously used liberal fluid management protocol in abdominal-flap breast reconstructions.

Methods: This retrospective study analyzed adverse events related to secondary unilateral abdominal-flap breast reconstructions in two patient cohorts, one with a liberal fluid management protocol and one with a MFM protocol. In the MFM protocol, intravenous fluid resuscitation was restricted and colloid use was minimized. Both noradrenaline and propofol were implemented as standard in the MFM protocol. The primary endpoints were surgical and medical complications, as observed intraoperatively or postoperatively, during or shortly after the hospital stay.

Results: Of the 214 patients included in the study, 172 patients followed the MFM protocol. Prior radiotherapy was more frequent in the MFM protocol. Surgical procedures to achieve venous superdrainage were more often used in the MFM cohort. Intraoperative as well as postoperative complications occurred significantly more frequently in the liberal fluid management cohort and were specifically associated with partial and total flap failures. Prior radiotherapy, additional venous drainage, or choice of inhalation agent did not have an observable impact on outcome.

Conclusions: The incidence of adverse events during and after autologous breast reconstructive procedures was reduced with the introduction of an MFM protocol. Strict intraoperative fluid control combined with norepinephrine and propofol was both beneficial and safe. *(Plast Reconstr Surg Glob Open 2021;9:e3830; doi: 10.1097/GOX.0000000000003830; Published online 17 September 2021.)*

INTRODUCTION

The anesthetic goals in flap surgery are to provide optimal tissue perfusion and oxygenation.[1] Intraoperative hypotension is a well-known risk for postoperative complications and is commonly counteracted by intravenous crystalloid infusion.[2,3] Intravenous colloids can provide additional support to prevent hypotension.[4] Besides normal insensible water loss and urine production, there is a constant physiological fluid transfer from the intravascular to the interstitial compartment.[5] Ischemia-reperfusion injury (IRI) can induce increased capillary leakage, leading to excessive fluid entrapment in the tissue.[6] Superfluous intraoperative fluid resuscitation causes interstitial fluid overload and results in an increased risk for complications.[4,7,8]

Vasopressors can be used to maintain adequate blood pressure and reduce the need for additional fluid infusion. In reconstructive microsurgery, there has been skepticism toward using vasoactive agents due to concern of vasospasm and reduced flap perfusion.[9]

Inspired by studies on restrictive fluid administration in elective gastrointestinal surgery, we introduced in 2005 a modified fluid management (MFM) protocol in abdominal-flap breast reconstructions, aiming to reduce intraoperative fluid volumes and complications.[10] Vasopressors were used liberally to maintain normotension, and propofol (Propofol-Lipuro, B. Braun, Melsungen AG, Germany) was introduced to minimize the impact of

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IRI.[11] The aim of this study was to compare the impact of our MFM protocol with a previously used liberal fluid management (LFM) protocol on intra- and postoperative complications in secondary unilateral abdominal-flap breast reconstructions.

PATIENTS

This retrospective study included patients scheduled for secondary unilateral abdominal-flap breast reconstruction over a period of 20 years (1999–2018). The study was approved by the regional ethical committee and accomplished in accordance with the Helsinki declaration. Patients were allocated to two cohorts, corresponding to which of the two protocols was followed. The MFM protocol was fully implemented in 2005, which therefore served as a dividing time-point between cohorts. Exclusion criteria were patients with obstructive pulmonary disease, coronary artery disease, peripheral arterial disease, or use of nicotine products within three months before admission. A complete anesthesia record was mandatory.

METHODS

The Liberal Fluid Management Protocol

The LFM comprised isoflurane or sevoflurane inhalation anesthesia at the discretion of the anesthesiologist. Crystalloids were used to maintain normotension (mean arterial pressure ≥ 65 mm Hg). Intravenous colloids were added on demand to correct hypotension irresponsive to increased crystalloid fluid infusion. Vasopressors were occasionally utilized to correct hypotension, unless manageable with intravenous fluids and colloids.

The Modified Fluid Management Protocol

The MFM comprised sevoflurane as the predominant inhalation anesthetic. Crystalloids combined with vasoactive agents were used to maintain mean arterial pressure of 65 mm Hg or greater. Colloids were used very restrictively and only to correct hypotension irresponsive to boluses of norepinephrine and crystalloids. Inhalation anesthesia was replaced by propofol infusion after completion of the microvascular anastomoses.

Surgical Treatment and Follow-up

Pedicled transverse rectus abdominis musculocutaneous flaps were performed by a single team, whereas free flap surgery was accomplished by a two-team approach using the internal mammary vessels as the preferred recipient vessels. Venous superdrainage was performed if venous congestion was suspected, based on intraoperative assessment by infrared thermography and clinical signs.

Hemoglobin and hematocrit levels were measured preoperatively and 1 and 2 hours postoperatively. Postoperative flap monitoring was accomplished by handheld Doppler ultrasound and clinical evaluation every hour until 24 hours after surgery, and thereafter every two hours until postoperative day 3 and every 6 hours until discharge. Hypotensive episodes were defined as mean arterial pressure less than 65 mm Hg. Relevant surgical and medical information was obtained from the patient records.

Primary endpoints were surgical and medical complications (Table 1). Postoperative complications were registered during hospital stay and until 2 weeks after discharge. Wound infection was diagnosed based on local and systemic clinical signs, and/or unexplained rise in inflammatory markers (CRP, WBC).

Statistical Analysis

Differences between cohorts were determined using chi-Square or Fisher's exact tests (FET) for binominal categorical variables and independent sample *t*-test for normally distributed ordinal continuous variables. Significantly different variables were included in a multivariate logistic regression model to assess independent association with outcome. Data were analyzed using SPSS statistical software (IBM Corp. IBM SPSS Statistics for Windows, Version 25.0., Armonk, N.Y.). Statistical significance was defined as a P value less than 0.05.

RESULTS

The LFM cohort contained 42 patients, and the MFM cohort, 172 patients. There were no significant differences between cohorts regarding age or body mass index (Table 2). Prior radiotherapy was more frequent in the MFM cohort ($P < 0.05$).

Anesthesia and Medical Treatment

The anesthesiologic results are summarized in Tables 3 and 4. Sevoflurane was the most common anesthetic agent in both cohorts. Propofol was much more frequent in the MFM cohort, as expected ($P < 0.05$).

Intraoperatively, the LMF cohort received more fluid but had lower urine output. The end-surgery fluid accumulation in the LFM cohort was 53.8 ± 22.0 ml/kg

Table 1. Assessed Complications by Category

Intraoperative Complications	Postoperative Surgical Complications	Postoperative Medical Complications
Bleeding > 500 ml	Bleeding > 500 ml	Cardiac arrythmia
Inadequate flow in recipient artery on surgical exploration	Wound infection Wound rupture	Congestive heart failure Myocardial infarction
Arterial anastomotic thrombosis	Partial flap loss	Pulmonary embolism
Venous congestion	Total flap loss Hernia at abdominal donor site	Deep vein thrombosis Acute renal failure
		Respiratory distress Urinary tract infection

Table 2. Patient and Case Characteristics

	LFM Protocol (n = 42)	MFM Protocol (n = 172)
Age (y ± SD)	50.6 (± 8.6)	51.3 (± 8.9)
BMI (kg/m² ± SD)	26.1 (± 3.1)	26.0 (± 2.6)
Prior radiotherapy, n (%)	17 (40.5%)	126 (73.3%)
Prior chemotherapy, n (%)	26 (61.9%)	132 (76.7%)

Table 3. Intraoperative Data on Anesthesia and Fluid Management

	No. Patients (%)	
Intraoperative Procedures	**LFM Protocol (n = 42)**	**MFM Protocol (n = 172)**
Inhalation agent		
Isoflurane	16 (38.1)	38 (22.1)
Sevoflurane	25 (59.5)	133 (77.3)
Other	1 (2.4)	1 (0.6)
Propofol		
Not used	27 (64.3)	5 (2.9)
Throughout the procedure	1 (2.4)	45 (26.2)
Final 2 h	11 (26.2)	100 (58.1)
Final 3 h		16 (7.5)
Final 4 h		5 (2.3)
Single bolus	1 (2.4)	1 (0.6)
Multiple boluses	2 (3.2)	
Vasopressor agent		
Not used	41 (97.6)	13 (7.6)
Norepinephrine		158 (91.9)
Dopamine	1 (2.4)	1 (0.6)
Colloid type		
Not used	14 (33.3)	164 (95.3)
Macrodex	21 (50.0)	8 (4.7)
Voluven	2 (4.8)	
Macrodex + Voluven	4 (9.5)	
Other	1 (2.4)	
Hypotensive episodes		
None	18 (42.8)	154 (89.5)
One	11 (26.2)	10 (5.8)
Several	13 (31.0)	8 (4.7)

compared with 29.6 ± 10.6 ml/kg for the MFM cohort ($P < 0.05$).

In the LFM cohort, 28 patients (66.6%) received colloids (Macrodex, Meda AS, Asker, Norway or Voluven, Fresenius Kabi Deutschland GmbH, Bad Homburg, Germany) compared with eight patients (4.7%) in the MFM cohort. While 159 patients (92.5%) in the MFM cohort received vasopressors, only one (2.4%) did so in the LFM cohort ($P < 0.05$). Multiple hypotensive episodes occurred in 13 patients (31%) of the LFM cohort compared with eight patients (4.7%) in the MFM cohort ($P < 0.05$).

Preoperative hemoglobin and hematocrit levels did not differ significantly between cohorts. The average intraoperative blood loss was higher in the LFM cohort than in the MFM cohort, at 443.8 ± 250.2 ml and 201 ml ± 124.1 ml, respectively ($P < 0.05$). Eight patients, of which five (11.9%) were in the LFM cohort, needed blood transfusion, all postoperatively, mainly because of dizziness during mobilization.

Surgical Parameters

Data related to surgical procedures are presented in Table 5. The deep inferior epigastric perforator flap (DIEP) was the most frequently used flap in both cohorts. Contrarily, pedicled transverse rectus abdominis musculocutaneous flaps and free superficial inferior epigastric artery flaps comprised over 40% of the flaps in the LFM cohort. Procedure time or flap weight did not differ significantly. Venous superdrainage was more common in the MFM cohort (73.8%) compared with the LFM cohort (35.7%) ($P < 0.05$).

Table 4. Intraoperative Fluid Measures and Data on Blood Parameters

Measures	LFM Protocol (n = 42)	MFM Protocol (n = 172)
Total fluid volume (ml ± SD)	4618.3 (± 1857.8)	3141.5 (± 768.3)
Total fluid per weight (ml/kg ± SD)	64.3 (± 24.3)	43.8 (± 10.5)
Fluid/weight/procedure time (ml/kg/h ± SD)	11.0 (± 5.7)	6.8 (± 1.7)
Colloid in treated population (ml ± SD)	741.1 (± 391.6)	443.8 (± 140.0)
Colloid/weight in treated population (ml/kg ± SD)	10.2 (± 5.3)	6.5 (± 2.0)
Total urine output (UO) (ml ± SD)	769.3 (± 516.6)	1019.0 (± 662.0)
Total UO per weight (ml/kg ± SD)	10.5 (± 6.5)	14.3 (± 9.3)
Fluid balance	3849.0 (± 1608.7)	2122.6 (± 791.4)
Fluid balance per weight (ml/kg ± SD)	53.8 (± 22.0)	29.6 (± 10.6)
Intraoperative blood loss (ml ± SD)	443.8 (± 250.2)	201.0 (± 124.1)
Preoperative hemoglobin (gr/dl ± SD)*	13.1 (± 0.9)	13.5 (± 0.9)
Preoperative hematocrit (% ± SD)†	37.2 (± 3.5)	40.6 (± 2.9)
Postoperative hemoglobin (gr/dl ± SD)‡	9.9 (± 1.2)	11.4 (± 1.1)
Postoperative hematocrit (% ± SD)§	28.7 (± 3.7)	34.4 (± 3.3)
Δ Hemoglobin (gr/dl ± SD)	−3.2 (± 1.2)	−2.1 (± 1.0)
Δ Hematocrit (% ± SD)	−8.1 (± 4.3)	−6.1 (± 2.8)

*Missing data from 2/172 (1%) patients in MFM cohort.
†Missing data from 16/42 (38%) in LFM cohort and 20/172 (11%) in MFM cohort.
‡Missing data from 7/42 (18%) patients in LFM cohort and 4/172/151 (2%) in MFM cohort.
§Missing data from 22/42 (52%) patients in LFM cohort and 10/172 (6%) in MFM cohort

Table 5. Intraoperative Data on the Surgical Procedures

	LFM Protocol (n = 42)	MFM Protocol (n = 172)
Procedure time (min ± SD)	372.1 (± 106.0)	398.2 (± 82.3)
Flap weight (g ± SD)	717.7 (± 220.7)	686.1 (± 180.4)
Flap type, n (%)		
DIEP	23 (54.8 %)	138 (80.2 %)
MS-1 TRAM	2 (4.8 %)	25 (14.5 %)
Pedicled TRAM	13 (31.0 %)	4 (2.3 %)
SIEA	4 (9.5 %)	5 (2.9 %)
Venous drainage, n (%)		
DIEV to IMV	27 (64.3 %)	45 (26.2 %)
Double DIEV to IMV	1 (2.4 %)	30 (17.4 %)
SIEV to CV	14 (33.3 %)	56 (32.6 %)
Double DIEV to IMV + SIEV to CV		18 (10.5 %)
SIEV to IMV		13 (7.6 %)
Other		10 (5.8 %)

CV: cephalic vein; DIEV: deep inferior epigastric vein; IMV: internal mammary vein; MS-TRAM: muscle sparing transverse rectus abdominalis myocutaneous flap; SIEA: superficial inferior epigastric artery perforator flap; SIEV: superficial inferior epigastric vein.

Outcome

Outcome data are presented in Table 6. Intraoperative complications were more frequent in the LFM cohort compared with those in the MFM cohort, at 28.6% and 14.5%, respectively ($P < 0.05$). Intraoperative blood loss (>500 ml) was the most frequent complication in the LFM cohort and vascular pedicle problems in the MFM cohort.

Postoperatively, surgical and medical complications were more frequent in the LFM cohort. The higher incidence of surgical complications, observed in 27 patients (42.9%), when compared with in 33 patients (21.9%) in the MFM cohort, was mainly related to partial and total flap failures ($P < 0.05$). Postoperative flap complications due to vascular insufficiency occurred in 38 patients. Emergent exploration was performed in 12 flaps, of which three were salvaged. Other postoperative surgical complications were scarce, apart from a significantly higher occurrence of postoperative hematoma in the MFM cohort [12 patients (7%)], mainly related to the abdominal donor site. Medical complications, mostly respiratory distress, were reported in six patients (14.3%) in the LFM cohort and four patients (2.3%) in the MFM cohort ($P < 0.05$). Mean length of stay (LOS) was significantly longer in the LFM cohort at 12.7 (± 6.5) days compared with 10.5 (± 2.7) days for the MFM cohort ($P < 0.05$).

Logistic regression analysis showed a statistically significant association between the applied fluid management protocol and intraoperative and postoperative complications (Table 7). The MFM protocol was more beneficial, resulting in reduced odds for complications in the range of 57%–85% compared with the LFM protocol. Propofol was not independently associated with outcome. Likewise, prior radiotherapy, type of inhalation agent, or venous superdrainage did not have a statistically significant impact on outcome. Post-hoc analysis within the LFM cohort found no significant association between flap type and the incidence of surgical complications.

Table 6. Observed Adverse Events and LOS

	LFM Protocol (n = 42)	MFM Protocol (n = 172)
Intraoperative complications, n (%)		
None	30 (71.4%)	147 (85.5%)
Bleeding (>500 ml)	8 (19.0%)	2 (1.2%)
Inadequate flow in recipient artery	3 (7.1%)	7 (4.1%)
Arterial thrombosis		11 (6.4%)
Venous congestion	1 (2.4%)	1 (0.6%)
Other		4 (2.3%)
Postoperative surgical complications, n (%)		
None	20 (47.6%)	134 (77.9%)
Bleeding		12 (7.0%)
Infection	1 (2.4%)	5 (2.9%)
Wound rupture		4 (2.3%)
Partial necrosis	14 (33.3%)	11 (6.4%)
Total flap loss	6 (14.3%)	6 (3.5%)
Hernia	1 (2.4%)	
Postoperative medical complications, n (%)		
None	36 (85.7%)	168 (97.7%)
Pulmonary embolism	1 (2.4%)	
Respiratory distress	3 (7.1%)	3 (1.7%)
Urinary tract infection	1 (2.4%)	
Other	1 (2.4%)	1 (0.6%)
Length of stay, d (± SD)	12.7 (± 6.5)	10.5 (± 2.7)

Table 7. Regression Analysis of Outcome per Fluid Management Protocol

	No. Patients (%)			
Complications	LFM Protocol (n = 42)	MFM Protocol (n = 172)	P	Odds Ratio (95% CI)
Intraoperative	12 (28.6)	25 (14.6)	0.034	0.425 (0.192–0.939)
Postoperative surgical	22 (52.3)	33 (22.1)	0.000	0.284 (0.140–0.573)
Postoperative medical	6 (14.3)	4 (2.3)	0.004	0.143 (0.038–0.532)

Postoperative complications reduced considerably after 2003, associated with a concurrent reduction of intraoperative fluid resuscitation and end-surgery fluid accumulation. The complication rate was further reduced with full implementation of the MFM protocol in 2005 (Fig. 1).

DISCUSSION

The MFM protocol resulted in fewer complications for unilateral autologous breast reconstructions compared with the LFM protocol. Plausible explanations are discussed.

Fluid Resuscitation

Insensible loss and fluid shifting have been the rationale for large volume resuscitation in the past. Recent studies have found these estimations incorrect.[12,13] Intraoperative fluid overload results in tissue edema and an increased risk of postoperative complications and prolonged recovery.[13] Flap-related complications are more common when using a LFM.[7,8,14,15] Intraoperative crystalloid volumes exceeding 7 L, or 130 ml/kg/day have been associated with major medical and surgical complications.[7] The ideal intraoperative crystalloid infusion rate is reported to be in the range of 3.5–6 ml/kg/h.[8]

The mean intravenous fluid volume in the LFM cohort was 11 ml/kg/h, versus 6.8 ml/kg/h in the MFM cohort (Table 4). More noteworthy, as the intraoperative urine output was lower in the LFM cohort, the net fluid accumulation at the end of surgery was significantly larger in the LFM cohort. We think that fluid accumulation is more important that the fluid infusion rate, as the end-surgery interstitial edema should be directly correlated to the actual fluid uptake. Karamanos et al observed a positive impact on outcome with strict fluid management during free flap breast reconstructions.[15] The fluid accumulation in their restricted cohort (4.8 ml/kg/hr) mirrors the findings in our MFM cohort (4.6 ml/kg/h). Furthermore, in a goal-directed fluid therapy (GDFT) study on pedicled and free flap breast reconstructions, Polanco et al registered a net fluid accumulation of 317 ml/h for patients following an enhanced recovery after surgery (ERAS) protocol.[16] This was almost similar to the end-surgery fluid balance in our MFM cohort (325 ml/h). Extracellular colloid leakage may contribute to such fluid entrapment and prolonged edema.[17,18] The more frequent colloid use

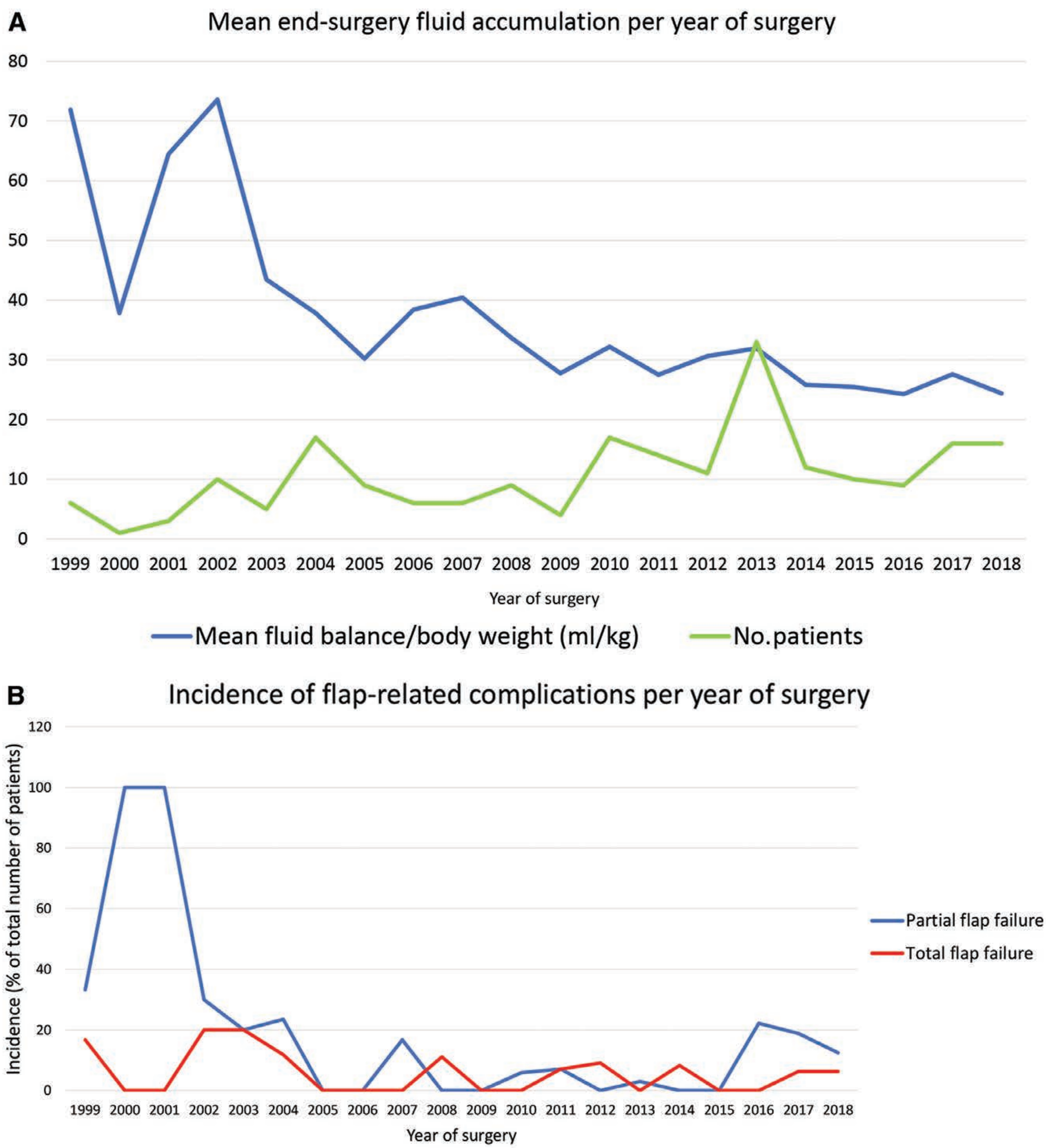

Fig. 1. Fluid accumulation and flap complications. A, Yearly distribution of mean end-surgery fluid balance in the patient population during the study period. A notable reduction is seen after 2002. B, Distribution of the incidence of flap-related complications per year during the study period. The incidence of partial flap failure (blue line) is generally higher than the incidence of total flap failure (red line). Flap-related complications were remarkably fewer after 2002/2003.

in the LFM cohort could be a plausible explanation for the larger fluid accumulation compared with the MFM cohort, although statistical analysis did not find an independent association between the use of colloids and outcome in the present study. Post-hoc analysis showed that intra- or postoperative bleeding (>500 ml) was significantly more common among patients who had received colloids, which are known to alter hemostasis.[19] No other adverse events associated with colloids were observed.[5,20] Others reported that colloids are safe to use in flap surgery.[14,21,22]

Fluid resuscitation using small volumes may be insufficient to correct hypotension, resulting in an increased risk for complications, especially in patients with preoperative comorbidities.[13,23] An individualized GDFT can therefore be a beneficial fluid management strategy in autologous breast reconstructions.[16]

Ischemia-reperfusion Injury

IRI in free flap surgery can be a significant risk factor for adverse events.[6] Prolonged duration of ischemia is associated with increasing risk of flap loss.[24] Propofol inhibits platelet aggregation, induces vasodilation, and protects against adverse effects of free radicals after flap reperfusion.[25,26] Propofol was an essential part of the MFM protocol and might have had a beneficial impact on the outcome, although not detectable on statistical analysis.

Anesthesia

Isoflurane and sevoflurane preserve a high cardiac output and adequate microcirculatory flow.[27] Sevoflurane is particularly beneficial in flap surgery, as it reduces capillary leakage of plasma into the interstitial space and protects against IRI, thereby limiting tissue edema.[28,29] The combination of sevoflurane and propofol was essential in the MFM protocol. Independent association with outcome was not observed for either drug, but we believe that a synergistic effect of these contributed to the beneficial outcomes in the MFM cohort.

Vasoactive Agents

At the time of introduction of our MFM protocol in 2005, few reports supported the use of vasoactive drugs in free flap surgery. Prior animal studies presented contradictory results regarding the impact of vasoconstrictive agents on flap perfusion, resulting in a general notion that vasopressors could increase the risk of peripheral vasospasm, thrombosis, and flap failure.[9] Yet, some studies reported findings of increased flap perfusion when utilizing inotropic drugs.[30,31] We included norepinephrine in the MFM cohort to maintain adequate blood pressure, the benefits of which have later been advocated by Eley et al in a study comparing the effect of several vasoactive drugs on flap perfusion.[32]

The short half-life of most vasopressors facilitates a more precise intraoperative control of the blood pressure, which in turn will contribute to reduce the risk of poor outcome.[2] The higher urine output in the MFM cohort can partially be explained by the effect of norepinephrine, promoting increased kidney perfusion. Norepinephrine also mitigated intravenous fluid resuscitation, as adequate blood pressure could be upheld without the need for additional intravenous fluid. The safety of vasoactive agents in reconstructive microsurgery observed in this study falls in line with the findings of several recent publications.[9,33,34]

Postoperative Hemodilution

The impact of reduced oxygen-carrying capacity resulting from hemodilution or anemia has been debated. Velanovich et al and Mlodinow et al found no association between low hematocrit and flap failure.[35,36] Others have demonstrated a negative effect of a hematocrit level at 24%.[8,37] Sigurdsson et al recommended a hematocrit level at 30%–35% to achieve optimal viscosity and oxygen-carrying capacity.[38] In our study, postoperative hematocrit levels were at 31.1% in the LFM cohort and 34.5% in the MFM cohort. The difference between pre- and postoperative hematocrit levels was larger in the LFM cohort, which can be explained by hemodilution due to higher volumes of crystalloid infusion and more frequent use of colloids.

Surgical Factors

Pedicled flaps were more frequent in the LFM cohort. Pedicled or free TRAM flaps were chosen when perforators were insufficient to allow for DIEP breast reconstruction. Although some reports have found free flaps to be an independent risk for ischemic flap complications, others have found no such association.[39–41] Addressing surgical site complications specifically, Masoomi et al found no correlation with different flap types (free or pedicled).[42] No association between flap type and complications was observed on intracohort analysis among patients following the LFM protocol. However, the more frequent intraoperative bleeding in the LFM cohort might have been related to the more traumatic dissection in pedicled transverse rectus abdominis musculocutaneous flaps when compared with the delicate dissection in DIEP flaps.

Insufficient venous drainage is the most frequent cause of flap complications.[43,44] Venous superdrainage was more frequent in the MFM cohort compared with the LFM cohort, but venous superdrainage per se did not have an independent impact on the postoperative outcome of flap complications. In a recent meta-analysis, Lee et al did not find sufficient evidence to advocate such procedures in autologous breast reconstruction.[45] Thus, one could postulate that an overzealous use of venous super-drainage was performed in the present study.

Radiation Therapy

Although prior radiation therapy in breast reconstructions has been associated with an increased risk of complications, the present study found no significant impact of prior radiotherapy on outcome.[46]

Length of Stay

Several reports from different surgical disciplines state that shorter length of stay (LOS) can be achieved with multimodal analgesia, patients of lower American Society of Anesthesiologists class, and implementation of ERAS protocols. Correspondingly, long-lasting surgery and anesthesia as well as excessive fluid administration are known to lengthen hospitalization.[47,48] A recent publication assessing ERAS in free flap breast reconstructions demonstrated a significantly shorter LOS, with less opioid and antiemetic use and with no increase in the rate of major complications.[49] Polanco et al in their study on ERAS with goal-directed fluid therapy also noted a decrease in LOS after the implementation of ERAS, but stated that the preoperative counseling on shorter hospitalization itself might have influenced patients' expectations in terms of LOS.[16] Although we did not specifically implement preoperative counseling in the MFM protocol, we observed a reduced LOS in this patient cohort. Patients in the MFM cohort were mobilized earlier, whereas patients in the LFM cohort were more frequently hindered by dizziness and peripheral edema. We anticipate that the restrictive fluid management was the main factor influencing LOS. The geographical nature of our catchment area, with many patients traveling long distances to our hospital, may have mitigated the potential difference in LOS between cohorts.

Limitations

The retrospective approach of this study is an obvious limitation. The small number of patients, especially in the LFM cohort, limits the validity of our findings. The follow-up period of our patients was short. The multimodal nature of our modifications to the fluid management protocol did not allow assessment of the independent impact of certain variables, such as colloids or norepinephrine. We still postulate that the synergistic effect of these modifications contributed to the improved outcomes in the MFM cohort.

An obvious source of bias is the learning curve related to complex procedures. This relates to both technical details of flap surgery and to a general know-how in the surgical and anesthetic team. The higher complication rate in the LFM cohort could be partially attributed to inexperience. Several studies report a higher incidence of adverse events during the first 30 cases.[50,51] In contrast, Grinsell et al reported that the complication rate did not differ between early and late cases and attributed this to a more widespread knowledge on flap surgery during recent years.[52] Even if no significant difference in procedure time between cohorts was observed in the present study, the advantage of skilled staff without doubt supports successful outcome and might therefore have resulted in unjust acclaim for the MFM protocol. Yet, the rather "dramatic" improvement in complication rates with the introduction of the MFM protocol seems more likely related to the modifications in fluid management than to the expected improved prognosis plainly due to increased team-competence.

CONCLUSION

Reduced intraoperative fluid resuscitation combined with optimized blood pressure control by using norepinephrine and propofol can result in fewer complications in unilateral abdominal-flap breast reconstruction.

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