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# Complications in Microsurgical Breast Reconstruction: Management and Prevention

Guest Editors:

Dr. Gordon K. Lee

Dr. Bernard T. Lee

Dr. Christine H. Rohde

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## Dr. Gordon K. Lee

Division of Plastic and Reconstructive Surgery, Department of Surgery, Stanford University Medical Center, Stanford, CA, USA.

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# Topic: Complications in Microsurgical Breast Reconstruction: Management and Prevention

Dr. Gordon Lee is a Professor of Plastic Surgery at Stanford University. Dr. Lee completed his undergraduate education at the University of California Los Angeles (UCLA) with a Bachelor of Science degree in Biology and graduated magna cum laude. He attended medical school at Stanford University. He completed a combined residency in General Surgery and Plastic Surgery at UCLA Medical Center, where he was inspired by Dr. William Shaw, a pioneer in microsurgery and breast reconstruction, to pursue a career in academic plastic surgery. After residency, Dr. Lee completed an advanced microsurgery fellowship at the University of Texas M. D. Anderson Cancer Center in Houston, Texas. Dr. Lee is the Residency Program Director for Plastic Surgery, Director of Microsurgery, and the Associate Chief for Clinical Affairs. Dr. Lee is involved in the full range of oncologic reconstructive surgery at the Stanford Cancer Center in performing breast reconstruction, abdominal and pelvic reconstruction, head and neck reconstruction, and extremity reconstruction. Dr. Lee performs approximately 80-100 microvascular free flaps per year, and over 350 breast procedures per year.


## Dr. Bernard T. Lee

Division of Plastic and Reconstructive Surgery, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA.

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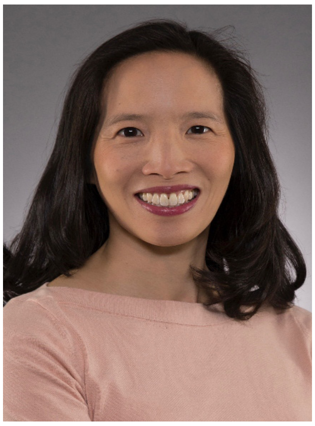
# Topic: Complications in Microsurgical Breast Reconstruction: Management and Prevention

Dr. Bernard T. Lee is a board-certified plastic and reconstructive surgeon, currently serving as the Chief of the Division of Plastic and Reconstructive Surgery and a Professor of Surgery at Harvard Medical School. With a focus on cosmetic surgery, aesthetic breast surgery, facial aesthetic surgery, and reconstructive surgery following breast cancer, Dr. Lee brings extensive expertise in breast implants, perforator flaps (DIEP, SIEA, GAP), facial reconstructive surgery, and managing traumatic facial fractures. His clinical career spans years of dedicated practice, emphasizing innovative techniques and personalized care. Dr. Lee is an accomplished academic, publishing numerous papers in esteemed journals and playing a pivotal role as a reviewer and editor in the field of plastic surgery.



## Dr. Christine H. Rohde

Division of Plastic and Reconstructive Surgery, Department of Surgery, Columbia University Irving Medical Center, New York, NY, USA.

https://columbiasurgery.org/christine-h-rohde-md

# Topic: Complications in Microsurgical Breast Reconstruction: Management and Prevention

Dr. Christine Rohde is the Chief of the Division of Plastic Surgery at Columbia. She graduated from Harvard Medical School in 2000. Following her medical school education, she began her general surgery training at the Brigham and Women's Hospital in Boston. After three years of general surgery training, Dr. Rohde accepted a plastic and reconstructive surgery residency position at Montefiore Medical Center. Interested in microsurgery, Dr. Rohde completed a microsurgical fellowship at New York University Medical School's Institute of Reconstructive and Plastic Surgery in 2006. Her research focuses primarily on outcomes of plastic surgical interventions, particularly as they relate to cancer reconstruction and post-surgical care. In 2013, Dr. Rohde graduated from the Columbia University Mailman School of Public Health with a Masters in Public Health, focusing on comparative effectiveness research.

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**Review**

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# Diagnosis, management and prevention of thrombotic complications in microsurgical breast reconstruction: a review of the literature

**Amy Chen[#], Shannon R. Garvey[#], Asha Nanda, Bernard T. Lee, Ryan P. Cauley**

Division of Plastic and Reconstructive Surgery, Department of Surgery, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA 02215, USA.
[#]Authors contributed equally.

**Correspondence to:** Dr. Ryan P. Cauley, Division of Plastic and Reconstructive Surgery, Department of Surgery, Beth Israel Deaconess Medical Center, Harvard Medical School, LMOB 5A, Boston, MA 02215, USA. E-mail: rcauley@bidmc.harvard.edu

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## Abstract

Autologous free tissue transfer is a safe and effective option for breast reconstruction. It is an increasingly utilized technique with well-demonstrated improved patient satisfaction and quality of life. Microvascular thrombosis is a rare but significant complication of microsurgical breast reconstruction, often resulting in flap failure. Proper diagnosis and timely management of this complication are essential to free flap salvage. While microvascular thrombosis poses a threat to flap survival, several methods may be employed to mitigate its more devastating effects. Here, we present a comprehensive review of arterial and venous thrombotic complications in both the intraoperative and postoperative settings. We discuss preoperative risk assessment, methods for flap monitoring, and operative and medical management of thrombotic complications. We present an updated algorithm for the intraoperative management of microvascular thrombosis adapted to reflect the most recent literature and our novel algorithm for the postoperative management of microvascular thrombosis.

**Keywords:** Breast microsurgery, free flap monitoring, free flap thrombosis, free flap salvage

## INTRODUCTION

Microsurgical autologous free tissue transfer has become a widely practiced technique for breast reconstruction with improved patient satisfaction and quality of life[1-3]. With advances in flap monitoring techniques and medical and surgical management, autologous free tissue transfer is now a safe and effective procedure with high success rates[4,5]. While uncommon, microvascular thrombosis remains a serious complication, occurring in 1.5%-6.2% of breast reconstruction cases, with up to 75% of those cases ultimately resulting in flap failure[6,7]. In this review, we present an overview of the risk factors associated with microvascular thrombosis in free tissue transfer as well as its diagnosis and treatment to facilitate a comprehensive understanding of this potentially devastating complication.

## PREOPERATIVE CONSIDERATIONS

### Risk factors

Risk factors for flap thrombosis can be categorized by their association with one of the three components of Virchow's triad: stasis, endothelial injury, and hypercoagulability. While flap thrombosis is usually attributed to suboptimal intraoperative technique and flap monitoring, acquired or inherited factors that influence the coagulation cascade must be accounted for during patient selection and preoperative optimization. Preoperative consultation should therefore always pay close attention to family and prior medical history suggestive of coagulopathy, potential secondary causes of bleeding disorders, and medications.

While the impact of patient factors on venous thromboembolism has been well studied, data on microvascular thrombosis rates in breast reconstruction are less robust and often discordant. Many studies are limited by small samples and event numbers, inclusion of a single institution, heterogeneity of reconstruction technique, or insufficient controlling of confounding variables[8]. In this section, we summarize the current literature available for commonly encountered patient factors that are often thought to be associated with flap thrombosis, and review management strategies for each.

*Hereditary thrombophilia*

While there have been individual case reports of thrombosis with flap loss in Factor V Leiden patients undergoing microsurgical breast reconstruction, they cannot be used to accurately estimate thrombotic risk[9-11]. In a retrospective study of 2032 consecutive free flaps (not limited to breast reconstruction), 58 of which were performed on patients with prior macrovascular thrombosis and/or known thrombophilia, Wang *et al*. found significantly higher rates of flap thrombosis and flap failure among the hypercoagulable group[12]. However, Pannucci *et al*. noted that this study failed to recognize that flap thrombosis occurred only among hypercoagulable patients with prior history of macrovascular thrombosis or another acquired hypercoagulable disorder[13]. Flap thrombosis did not occur in patients who had known hereditary thrombophilia without any additional history, suggesting that hereditary thrombophilias are less predictive of flap outcomes than acquired thrombophilias or prior history of thrombosis.

Based on these findings, Pannucci *et al*. recommend preoperative screening according to personal and family history of thrombosis, acquired risk factors, and Caprini score; if the patient has elevated risk determined by the screening, they should be referred to a hematologist[13]. This approach deviates from the algorithm previously proposed by Friedman *et al*., who suggest that surgeons should order thrombophilia testing if there is a concern for thrombosis risk and refer to hematology only if the testing is positive[14]. Pannucci *et al*. argue that decisions on thrombophilia testing should be deferred to the hematologist, because there is no evidence supporting hereditary thrombophilia as a risk factor for flap thrombosis[13]. At our institution, all patients with a history of VTE or hereditary thrombophilia are routinely evaluated by

Hematology for risk optimization and operative clearance. Typically, a prophylactic regimen of either an injectable low molecular weight heparin (LMWH) or an oral, direct factor Xa inhibitor is recommended for 1-4 weeks postoperatively. All patients are placed on heparin prophylaxis intraoperatively.

*Obesity*

Obesity in patients undergoing microsurgical breast reconstruction has been associated with increased risks of partial flap necrosis, fat necrosis, and venous congestion[15-17]. In a study of 936 free transverse rectus abdominis muscle (TRAM) flap cases, Chang *et al*. found that obese and overweight patients had a significantly higher overall flap complication rate of 39.1% (compared to 20.4% among normal-weight patients), which included a total flap loss, hematoma, seroma, and skin necrosis[18]. Notably, they did not find any difference in the rate of vessel thrombosis. Hanwright *et al*. found similar results in their analysis of free flap breast reconstruction cases taken from the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database[17]. When classified into class I (BMI of 30 to < 35), class II (BMI of 35 to < 40) and class III (BMI ≤ 40) obesity, Fischer *et al*. found that class III obesity patients had significantly higher rates of flap loss and trended toward higher rates of intraoperative arterial thrombosis[19]. Similarly, Schaverien *et al*. found that class III obesity was associated with a significantly higher risk of complete flap failure, donor-site complications, and overall complications[20].

Given the increased risk of complications associated especially with morbid obesity, careful patient selection is necessary and patients with class III obesity may be advised to reduce their weight prior to surgery[19]. While no studies demonstrate a specific BMI that provides an acceptable risk to proceed with surgery, statistically significant differences in complications tend to increase proportionally as BMI increases[21]. In our practice, we do not use a specific BMI cutoff to assess surgical candidacy, but we candidly discuss the increased risks of partial or total flap failure with all class III patients seeking microvascular breast reconstruction.

*Tobacco use*

Despite experimental evidence on the detrimental effects of tobacco smoke exposure on thrombogenicity, clinical studies on free flap transfers in breast reconstruction have demonstrated conflicting results, with the majority suggesting a less significant effect[22-24]. Khouri *et al*. found that there was no significant effect of tobacco use on flap outcome[25]. Masoomi *et al*. and Arnez *et al*. found no significance in flap loss or vascular thrombosis rates in smokers compared to non-smokers[7,26]. Despite studies showing a weak association between flap thrombosis and smoking, patients should still be advised to cease smoking a minimum of 3 weeks prior to surgery, a widely advocated practice due to the established risk of poor wound healing[27].

*Radiation*

Patients seeking breast reconstruction following post-mastectomy radiation therapy have become increasingly common. Although radiotherapy is known to impair wound healing, its effect on microanastomoses remains an area of ongoing study[28]. Findings from animal studies on irradiated microanastomoses have been variable, with some demonstrating significant change in patency due to intimal hyperplasia as well as increased thrombosis risk, and others showing no such effects[29-32]. Fracol *et al*. and Fosnot *et al*. found a significantly higher risk of any intraoperative vascular complication in radiated fields compared to non-radiated fields, but no significant differences in arterial or venous thrombosis rates both intra- and postoperatively, and no overall difference in the rate of flap loss associated with radiation[33,34].

Complication rates have been shown to be lower in patients who delay breast reconstruction until after radiation is complete[35,36]. Though there is little consensus in the literature regarding the optimal timing of autologous reconstruction following radiation therapy, the majority of surgeons report waiting for 4-6 or 7-12 months after the end of radiation, with patient preference and desire to optimize aesthetic outcomes being the primary drivers of the timing selected[37,38]. Notably, Baumann *et al*. found that among patients receiving delayed abdominal free flap breast reconstruction, flap loss and reoperation rate was higher following reconstruction within 12 months of completion of radiation therapy[39]. At our institution, we routinely delay breast reconstruction for at least 6-12 months after the last radiation treatment, depending on the total radiation dosage, the patient's symptoms, and the effects noted on physical examination.

*Hormonal therapy*

Anti-estrogen therapies used in the adjuvant treatment of hormone-sensitive breast cancers, most notably tamoxifen, have been shown to be associated with venous thromboembolism[40-42]. However, results from studies examining the effect of hormone therapy on flap thrombosis are conflicting[43-47]. Although there are studies suggesting discontinuation of hormone therapy 2 to 4 weeks prior to breast reconstruction, there is no consensus in the literature on whether cessation is necessary[44,46-50]. Until a more definitive conclusion is reached, at our institution, we typically recommend holding hormone therapy for a period of 2 weeks before and after surgery, given the low oncologic risk of short-term cessation.

## Thromboprophylaxis

Administering antithrombotic agents as a prophylactic measure against microvascular thrombosis is a common but non-standardized practice. Protocols for thromboprophylaxis are based largely on individual surgeon preference and opinion, and thus vary widely with regard to agents, dosage, schedule, and duration. In this section, we describe commonly used antithrombotic agents and present an overview of recent evidence on thromboprophylaxis protocols as well as our own institution's regimen.

*Heparin*

Heparin binds and enhances the activity of antithrombin III, which in turn inhibits the coagulation cascade and effectively blocks clot formation and growth. Although animal studies have demonstrated improvement in microvascular thrombosis rates with heparin, clinical findings have been conflicting[51,52]. Lighthall *et al*. and Zhou *et al*. found no significant differences in flap failure rates between patients with postoperative heparin and patients with no postoperative anticoagulants[53,54]. Multiple studies have also found no significant differences in microvascular thrombosis rates between cases performed with and without intraoperative heparin[25,55,56]. However, an earlier study by Kroll *et al*. found that free flap patients dosed with postoperative heparin had lower pedicle thrombosis rates and a trend toward lower flap loss compared to patients with no postoperative anticoagulant agents[56].

*Aspirin*

Aspirin inhibits the production of thromboxane A2 by platelets, which prevents further platelet activation and aggregation. Similar to heparin, the effectiveness of aspirin for flap thrombosis prevention is unclear despite its widespread use. When used alone, aspirin has not been found to be effective for thromboprophylaxis and may be associated with higher complication rates[53]. Interestingly, Ashjian *et al*. found in a retrospective review of 505 microvascular free flap patients that rates of microvascular thrombosis and flap loss were equivalent between patients who received a postoperative 5-day daily regimen of 325 mg of aspirin and patients who received 5,000 units of LMWH until ambulating[57].

*Combination Therapy*

Although many recommendations for thromboprophylaxis have been proposed, there is no consensus on any single regimen. Based on experience and literature review, Conrad *et al*. proposed a protocol consisting of aspirin dosed 1.4 mg/kg/day administered pre- and postoperatively for 2 weeks, with intraoperative heparin as a bolus and local topical agent[58]. Stephan *et al*. and Brinkman *et al*. do not recommend aspirin and instead adhere to heparin monotherapy[59,60]. Overall, current evidence seems to suggest that a more conservative approach to prophylactic antithrombotics is warranted. In a recent systematic review, Liu *et al*. concluded that postoperative antithrombotics including aspirin, dextran, and heparin had no significant effects on flap thrombosis or flap failure, and may increase the risk for hematoma regardless of regimen[61].

At our institution, patients undergoing microsurgical breast reconstruction receive a bolus of heparin 5,000 units subcutaneously, or enoxaparin (40 mg or 0.5 mg/kg if BMI exceeds 40 kg/m$^2$) subcutaneously intraoperatively. Postoperatively, patients receive heparin 5000 units subcutaneously every 8 h, or enoxaparin (same dosing scheme as previously stated) subcutaneously and aspirin 121.5 mg (half a baby aspirin) once per day. In patients deemed at high risk for microvascular thrombosis, enoxaparin is continued for 3-4 weeks postoperatively.

## DIAGNOSIS

### Intraoperative

Intraoperative assessment of anastomotic patency and detection of microvascular thrombosis allows for rapid surgical correction and is imperative for flap survival. Historically, microsurgeons have relied on clinical judgment and patency testing. This includes visual inspection of the flap for bleeding at the flap edges, acoustic sonography over perforators, and examination of the vessel for visible or palpable pulsations distal to the anastomosis. Patency can further be assessed with the Flicker test and Milking test[62].

If questions regarding flow remain after a simple inspection of the pedicle, more advanced techniques can be used[63-65]. Fluorescent Indocyanine Green (ICG) angiography has since been shown to be a reliable, sensitive, and ultimately cost-effective method for evaluating flap perfusion[64-66]. Specifically, the arterial uptake phase in ICG angiography is highly sensitive and has been well-studied in the detection of arterial thrombosis[67]. The venous phase, and the data on its sensitivity, are less clear, and its interpretation is oftentimes influenced by the experience of the surgeon[68]. Yoshimatsu *et al.* report success using ICG angiography to detect venous congestion and Sharaf *et al.* subsequently describe a "pathognomonic heterogeneous or splotchy appearance" within the zone of ICG appearance that is characteristic of venous congestion [Figure 1][69,70].

Flaps can also be interrogated intraoperatively using advanced flap monitoring techniques typically reserved for the postoperative setting-including Near-Infrared Spectroscopy (NIRS) tissue oximetry (eg., ViOptix) or technologies such as FLIR (Forward Looking Infrared) thermal imaging.

### Postoperative

*Flap monitoring techniques*

It is well established in the literature that early detection of and intervention for microvascular thrombosis maximizes the chance of flap salvage[71,72]. Therefore, having a reliable means of flap monitoring is critical. In 1975, Creech and Miller described the ideal flap monitoring technique as one that does not cause harm to the patient or flap and is rapid, accurate, reliable, cost-effective, and applicable to all flap types[73]. Jones further proposed that the ideal monitor be objective, simple to use for inexperienced personnel, and capable of continuous and prolonged monitoring[74]. While no one flap monitoring technique embodies all of these

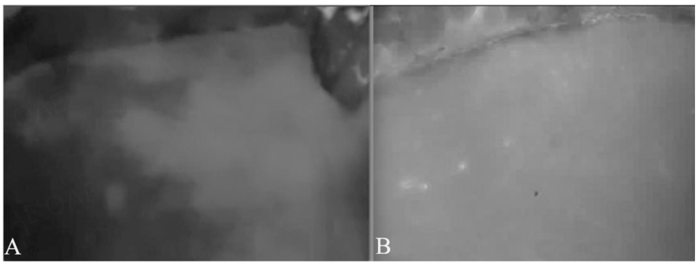


**Figure 1.** ICG angiography of DIEP flaps. (A) Heterogenous ICG appearance consistent with compromised venous outflow; (B) Homogenous ICG appearance consistent with healthy venous outflow; This figure is quoted from Sharaf *et al.* published in Microsurgery by Wiley Periodicals, Inc., copyright 2021[70]. Reprinted with permission from John Wiley and Sons.

qualities, multiple technologies have since emerged, often used in combination with conventional techniques.

*Physical examination*

Physical examination is a commonly practiced method for assessing flap viability. The physical examination should include an assessment of flap color, temperature, turgor, and capillary refill[74,75]. Flap temperature has previously been assessed via touch, temperature probe, temperature-sensitive tape, or handheld contactless thermometer. However, surface temperature monitoring has not been routinely recommended in larger perforator flaps due to its inability to detect changes prior to flap failure or predict reoperation in DIEP flap breast reconstructions[76]. Bleeding is also an important component of the physical examination in flap monitoring. This can be ascertained via needle prick or skin incision; however, both of these techniques can result in transient ecchymosis that may affect accurate flap assessment[74,76].

The physical examination can aid in determining the etiology of flap thrombosis. An arterial thrombosis can be characterized by a cool and pale appearing skin paddle, diminished turgor, and delayed capillary refill. On the contrary, venous thrombosis is often characterized by an edematous and mottled appearing skin paddle with brisk (< 1-2 seconds) capillary refill, increased turgor, and bleeding on needle prick[75].

*Vascular flow*

Physical examination is typically accompanied by a more objective assessment of vascular flow. Currently, the most widely used techniques include those that monitor vascular flow and those that monitor tissue ischemia [Table 1]. The most commonly used objective assessment is intermittent interrogation of blood flow with an acoustic Doppler. While handheld acoustic Doppler sonography is not capable of performing continuous monitoring, it is a widely available, cost-efficient, and non-invasive method for monitoring vascular flow that can be easily operated by house staff[77].

Additional Doppler technologies have since been developed to allow for continuous flap monitoring, including the Cook-Swartz implantable Doppler, flow coupler implantable Doppler, and laser Doppler flowmetry[78]. Given the invasive nature of implantable Doppler, some authors suggest that vessel compression and anastomotic injury by the implanted cuff or wire should be considered[79]. In addition, laser Doppler is a promising non-invasive option but lacks consensus values for detection and thus remains experimental[80].

At our institution, we recommend regularly spaced intervals of acoustic Doppler sonography, ideally in combination with continuous tissue oximetry-based monitoring. However, implantable Doppler is used for

**Table 1. Intra- and postoperative monitoring techniques for the detection of thrombotic complications in microsurgical breast reconstruction**

| Flap Monitoring Technique | Mechanism of Monitoring | Receiver Operating Characteristics | Advantages | Disadvantages | Recommendation for Use |
|---|---|---|---|---|---|
| *Acoustic Doppler Sonography*[77] | The location of the arterial and venous anastomoses is marked on the surface of the flap intraoperatively. A Doppler probe is placed on the surface of the skin paddle overlying the vessel. An auditory pulsatile or continuous hum sound confirms arterial or venous patency, respectively | Sensitivity: 50%<br>Specificity: 100%<br>PPV: 100%<br>NPV: 98.6%<br>Accuracy: 98.6%<br>SR: 100% | Non-invasive, readily available, able to distinguish between venous and arterial flow, ease of operator use, and relatively inexpensive. | Unable to perform continuous monitoring, difficult to determine the source of Doppler signal (recipient *vs* pedicle), no quantitative output, and interpretation dependent on clinical experience | Recommended for routine postoperative monitoring, ideally in conjunction with other continuous/advanced monitoring techniques when available |
| *Cook-Swartz Implantable Doppler*[162-168] | An electrode mounted on a silicone cuff is secured around the vascular pedicle with a thin wire connecting it to an external monitor. Auditory output is similar to that of acoustic Doppler sonography | Sensitivity: 100%<br>Specificity: 88-100%<br>PPV: 33.3-100%<br>NPV: 100%<br>Accuracy: 88.7-100%<br>SR: 80-100% | Capable of continuous monitoring, able to distinguish between arterial and venous flow, and ease of operator use | Relatively more invasive, no consensus on probe placement, no quantitative output, high false-positive rate, risk of anastomotic rupture when pulling the probe, and risk of thrombosis or vessel kinking from the probe/wire | Not recommended if there is a skin paddle, given the preference for non-invasive modalities. Recommend use in buried flaps |
| *Flow Coupler Implantable Doppler*[162,169] | A venous coupler is fitted with a Doppler probe with a thin wire connecting it to an external monitor. Auditory output is similar to that of acoustic Doppler sonography | Sensitivity: 100%<br>Specificity: 94-98.1%<br>PPV: 60-66.7%<br>NPV: 100%<br>Accuracy: 94.7-98.2%<br>SR: 75-100% | Easier to place with reduced operative time compared to implantable Doppler alone, capable of continuous monitoring, and ease of operator use | Relatively more invasive, no quantitative output, monitors venous flow only, and risk of thrombosis or vessel kinking from the probe/wire | Not recommended if there is a skin paddle, given the preference for non-invasive modalities. Recommend use in buried flaps |
| *Color Duplex Ultrasonography*[170,171] | An ultrasound probe and viewing monitor allows direct visualization of vessel patency as well as blood flow velocity and direction | Receiver operating characteristics for the detection of microvascular thrombosis have not been reported in the context of microsurgical breast reconstruction; however, Jacob *et al.* and Arya *et al.* have described its potential use | Non-invasive, readily available, provides real-time imaging of anastomotic patency, and provides quantitative output | Unable to perform continuous monitoring, typically requires a radiology technician to perform and a radiologist to interpret, and no comparative studies available on its use in breast flaps, costly | Can consider adjunctive use in the intraoperative and postoperative setting or in buried flaps. However, should not be used as a primary postoperative monitoring tool due to lack of data and operator dependence |
| *Laser Doppler Flowmetry*[172] | A probe attached to the surface of the skin paddle emits laser light which is reflected back by the movement of red blood cells to calculate their velocity | Sensitivity: 100%<br>Specificity: 100%<br>PPV: 100%<br>NPV: 100%<br>Accuracy: 100%<br>SR: 80% | Non-invasive, capable of continuous monitoring | Monitors at the capillary level only so unable to distinguish between venous and arterial flow, subject to error due to patient movement, no standard criteria for detecting vascular compromise, operator dependent | Not yet advanced enough to be recommended in routine clinical practice |
| *Near-Infrared and Visible Light Spectroscopy*[77,81-83,172-179] | A probe attached to the surface of the skin paddle emits near-infrared or visible light, which is absorbed by chromophores (oxygenated and deoxygenated hemoglobin). The reduction in light intensity is measured to determine tissue oxygen saturation | Sensitivity: 96.5-100%<br>Specificity: 96.4-100%<br>PPV: 50-100%<br>NPV: 99.8-100%<br>Accuracy: 97-100%<br>SR: 66.7-100% | Non-invasive, capable of continuous monitoring, not sensitive to patient movement, provides quantitative output, criteria for detecting vascular compromise defined, and ease of operator use. | Monitors at the capillary level only so unable to distinguish between venous and arterial flow, potential influence of clinical (ex flap type or skin pigment) and environmental (ambient light) variables, and relatively more costly than Doppler devices | Recommended for continuous postoperative monitoring in conjunction with routine acoustic Doppler sonography and clinical assessment if institutional resources allow |

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| | | | | | |
|---|---|---|---|---|---|
| *Microdialysis*[164-168] | A double-lumen microdialysis catheter is introduced into the flap and perfusion fluid is collected. Fluid is subsequently analyzed for products of anaerobic respiration, including low glucose and elevated lactate concentrations | Sensitivity: 100%<br>Specificity: 92.5-100%<br>PPV: 66.7-100%<br>NPV: 100%<br>Accuracy: 93.5-100%<br>SR: 83-100% | Sensitive to flow compromise before clinically apparent, able to monitor buried flaps | Invasive, unable to perform continuous monitoring, sample analysis is not immediate, high false positive rate resulting in unnecessary re-explorations and higher treatment costs, unable to distinguish between venous and arterial flow, and costly | Not yet recommended in routine postoperative breast monitoring, given the presence of other continuous and non-invasive modalities. Can consider use in buried flaps when other forms of monitoring are not feasible |
| *Fluorescent ICG Angiography*[180,181] | ICG is injected intravenously and fluoresces near-infrared light. An infrared-sensitive camera captures these emissions to provide vessel imaging | Sensitivity: 100%<br>Specificity: 86-100%<br>PPV: 100%<br>NPV 100%<br>Accuracy: 100%<br>SR: 100% | Non-invasive, provides real-time imaging of anastomotic patency, and highly sensitive to arterial thrombosis | Unable to perform continuous monitoring, not readily available at the bedside, less sensitive to venous thrombosis, costly | Recommended for intraoperative monitoring but not as a primary monitoring tool postoperatively |

PPV: positive predictive value, NPV: negative predictive value, SR: salvage rate.

continuous monitoring when a skin paddle is not available, such as in buried skin flaps or muscle flaps without a skin paddle.

### *Tissue ischemia*

Near-Infrared Spectroscopy (NIRS) tissue oximetry is an important tool that has been shown to detect flap compromise before it is clinically apparent, decrease rates of flap loss, and improve rates of flap salvage compared to conventional techniques[81]. While more expensive upfront than continuous Doppler techniques, NIRS has demonstrated an overall potential cost benefit across multiple studies[75,82-84]. Pelletier *et al.* found an average reduction of $1,937 per patient when monitored on the surgical floor with NIRS tissue oximetry compared to the surgical intensive care unit (ICU)[82]. Additionally, given the quantitative output of NIRS compared to Doppler technology, an automated text message alert system has been developed, allowing for rapid notification of the surgical team[85]. The potential for decreased time to re-exploration, a critical factor in flap salvage, makes NIRS a promising technology. While NIRS is a valuable tool to continuously monitor flaps with a skin paddle, no single monitoring device should supersede a thorough physical examination and individual clinical experience.

### *Flap monitoring protocols*

Currently, there is no universally recognized protocol or standardized practice for flap monitoring following microsurgical breast reconstruction. Historically, flaps have been monitored in an intensive care or step-down setting for 1 or more days postoperatively, given that the majority of complications occur within the first 24-48 h after surgery[85,86]. With advancements in flap monitoring technologies, many institutions have altered their protocols to allow for early disposition to the floor without increasing the risk of flap failure or postoperative complications[82,83,87-89]. In line with the available literature, we present our institution's flap monitoring protocol in [Figure 2], adapted from Khansa *et al.* to reflect our institution's recommendation for timing and location of monitoring, and criteria for takeback[90]. Nonetheless, we recognize that ultimately a surgeon's approach to flap monitoring should take into account individual patient factors, institutional resources, and the evolving literature.

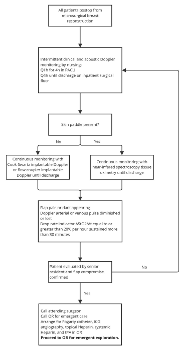


**Figure 2.** Algorithm for postoperative flap monitoring. This figure is adapted from Khansa *et al.* published in Microsurgery by Wiley Periodicals, Inc., copyright 2013[90]. Adapted with permission from John Wiley and Sons.

## MANAGEMENT

### Arterial insufficiency

*Intraoperative management of arterial insufficiency*

Upon intraoperative detection of signs of arterial insufficiency, the anastomosis should promptly be re-examined. The vessel should be inspected for extrinsic compression, vessel spasm, and positional issues such as kinking[91]. The anastomosis should be assessed for the presence or absence of flow with clinical examinations such as the milking test and acoustic Doppler sonography. If arterial thrombosis is suspected, one or more salvage modalities may be attempted[90]. A detailed algorithm for our approach to the intraoperative management of arterial insufficiency is available in [Figure 3A], adapted from Khansa *et al*. to reflect our institution's use of papaverine[90].

*Arterial flow present*

Upon exploration of the pedicle, should arterial Doppler flow be present, a careful clinical examination of the flap and the entire pedicle should be performed. The pedicle should be inspected for any areas that may be prone to twisting, kinking, or external compression. The use of fat grafting over the pedicle can help to maintain the optimal vessel lie. Should the flap appears clinically improved - including the presence of normal capillary refill, turgor, and dermal edge bleeding - it may be carefully re-inset. ICG angiography could be considered to evaluate the flap after inset to ensure the adequacy of flow. If flow is confirmed, close clinical observation in the postoperative period is recommended[90].

*Arterial flow diminished*

If flow is present but diminished, etiologies can include partial microvascular thrombosis, vasospasm, or suboptimal vessel positioning. Vasospasm is best treated through the avoidance of peripheral vasopressors and the local application of topical vasodilators[92-95]. Topical treatments include a wide variety of vasodilators, including alpha antagonists (eg., phentolamine), calcium channel blockers (eg., nicardipine), direct vasodilators (eg., hydralazine), local anesthetics (eg., lidocaine), and phosphodiesterase inhibitors (eg., papaverine)[96]. As multiple vasodilators have been proven to be efficacious, the precise type of vasodilator and the dosing used is more often based on surgeon experience and availability[95-98]. At our institution, vasospasm is often treated with an adventitial injection of papaverine and warm heparinized saline. If there is a specific point of vasospasm identified, these injections can be combined with careful milking of the pedicle using microforceps or the surgeon's pinched fingers, a technique that may provide sufficient intraluminal pressure to break the spasm. Should arterial flow not improve after treatment for vasospasm, the anastomosis should be re-explored, as described in the *Arterial Flow Absent* section.

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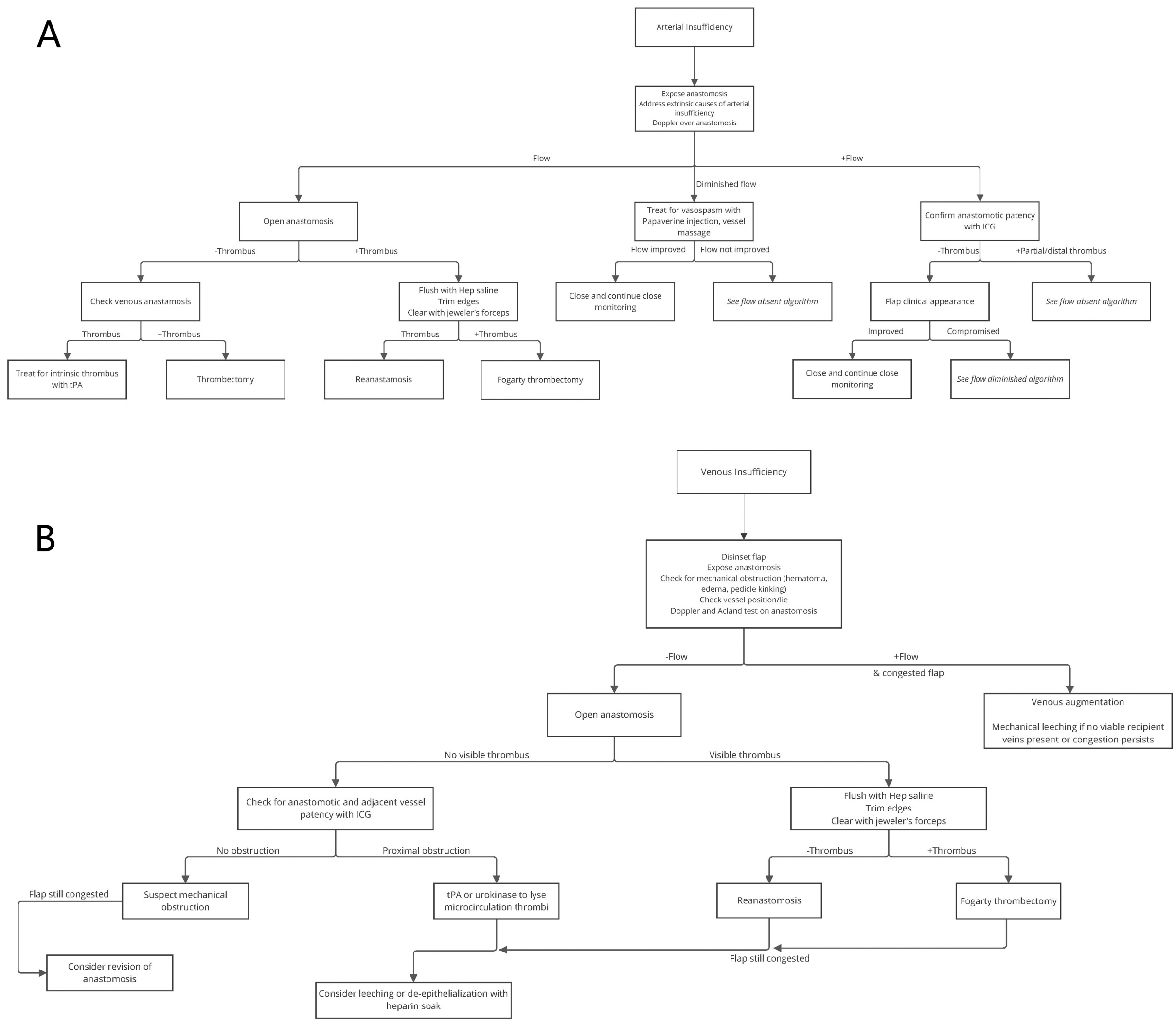


**Figure 3.** Algorithm for intraoperative management of free flap vessel insufficiency. (A) arterial insufficiency; (B) venous insufficiency; This figure is adapted from Khansa *et al.* published in Microsurgery by Wiley Periodicals, Inc., copyright 2013[90]. Adapted with permission from JohnWiley and Sons.

### *Arterial flow absent*

Time to re-exploration and anastomotic revision is critical to flap survival. If the arterial flow is absent or does not respond to treatment for vasospasm, the anastomosis should be opened and promptly explored. If a thrombus is identified upon opening the arterial anastomosis, heparin irrigation and mechanical thrombectomy or chemical thrombolysis may be necessary in addition to revision of the anastomosis. In cases of arterial thrombosis, heparinized saline is used liberally in a 100 I.U./mL concentration to flush the flap and the anastomosis. A review by Couteau *et al*. supports this practice, with 9 of 11 animal studies showing improved free flap survival rates with the use of intraoperative heparin irrigation compared to saline[99].

The simplest form of mechanical thrombectomy is the direct removal of the thrombus with standard microforceps. If the thrombosis is detected prior to propagation, direct removal at the proximal end of the anastomosis can be sufficient. However, if thrombus is suspected to be in the distal pedicle, Fogarty catheter-assisted thrombectomy may be necessary[100]. We typically use a Fogarty catheter with a 1- or 2-mm balloon. The catheter may be introduced via the proximal lumen or a distal side branch if one of sufficient size is available for cannulation. The catheter should be carefully passed until it reaches the perforating vessels entering the flap to ensure that the entire vessel is cleared. Prior to withdrawal, the balloon is typically inflated to half its total capacity to minimize damage to the perforator. Multiple passes may be needed to completely eliminate the propagated thrombus[101]. Once the mechanical thrombectomy is complete, heparinized saline flushes can be used to assess the flap's resistance to flow. If the pedicle can be flushed easily and venous return of the saline is confirmed, a revision of the anastomosis should be attempted. Nevertheless, if resistance to flow is detected, chemical thrombolysis may be needed. At our center, a catheter clearing dose of 1-2 mg of tissue plasminogen activator (tPA) is used. To avoid systemic thrombolysis, we ensure that the flap is isolated from the systemic circulation during the injection of the tPA. After the thrombolytic is allowed to dwell within the flap for several minutes, the flap is again flushed with 300-500 milliliters of heparinized saline to minimize the introduction of systemic tPA after reanastomosis. Furthermore, should an arterial thrombus not be identified after opening the anastomosis, the venous anastomosis should be further explored per the *Intraoperative Management of Venous Insufficiency* guidelines.

Although the above algorithm is used for complete loss of inflow, it is also possible to have partial loss of arterial flow. If the clinical examination or ICG angiography demonstrates inadequate flow to only a portion of the flap, the presence of partial flap thrombosis should be considered. Partial flap thrombosis, especially if it is thought to be intra-flap thrombosis, is often treated with medical management. At our center, we typically attempt to treat partial intra-flap thrombosis with a combination of chemical thrombolysis (e.g., tPA), anticoagulation and/or simple debridement of the thrombosed portion of the flap.

### Postoperative management of arterial insufficiency

*Reoperation*

If arterial thrombosis is suspected in the postoperative period, expeditious return to the operating room to expose the anastomosis is the most appropriate next step[90]. Time to reoperation is consistently shown to be associated with salvage rates after arterial and venous thrombosis[71,72,102]. Likely secondary to delays in management, the rate of flap salvage in postoperative compromise is less than that of intraoperative compromise[90]. It has been shown that the use of careful continuous postoperative monitoring is associated with a decreased time to diagnosis and operative management of flap thrombosis, and thus an increase in the rate of salvage[81]. The approach to anastomotic assessment and revision is discussed in the intraoperative management section above. Our novel algorithm for the approach to postoperative management of thrombotic complications is available in [Figure 4].

*Systemic anticoagulation*

In the setting of postoperative arterial thrombosis, the use of systemic anticoagulation varies by surgeon and institution. Many authors report urgent administration of a 5,000-unit bolus of intravenous heparin at the time of reoperation[71,103]. Others report the use of weight-based dosing to achieve an institution-determined therapeutic PTT level[58,103]. Given higher rates of hematoma with systemic heparin use in free tissue transfer, we typically recommend weight-based dosing of intravenous heparin without the use of a bolus[87]. Once the risk of postoperative hemorrhage is deemed sufficiently low, the patient may be transitioned to a low molecular weight heparin injection (eg., enoxaparin). The duration of anticoagulation after flap thrombosis is often driven by surgeon experience. Although there is no definitive data on the optimal duration of therapeutic anticoagulation in this cohort, Khansa *et al* maintain systemic anticoagulation for at least 4-7 days after reoperation, which is consistent with what other authors report[58,71,90].

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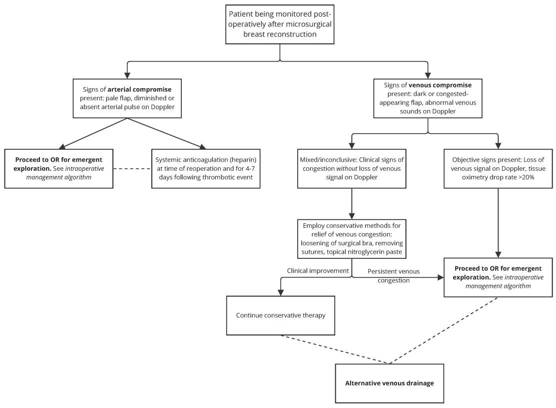


**Figure 4.** Algorithm for postoperative treatment of microvascular thrombosis.

## Venous insufficiency

*Venous congestion and venous thrombosis*

The development of venous congestion can be attributed to several etiologies, the most common of which is venous thrombosis[104]. Mechanical factors such as unfavorable flap position, or kinking and compression of the vascular pedicle are common causes of venous insufficiency. Venous thrombosis can occur secondary to a hypercoagulable state, a technical error at the anastomosis, or from prolonged venous congestion or insufficiency from one of the above mechanical factors[105,106]. Finally, venous insufficiency can result from anatomic variability within the flap, especially if the flap contains portions of two perforasomes. Anatomical studies of DIEP and TRAM flaps have shown that normal venous drainage of the lower anterior abdominal subcutaneous tissue and skin occurs primarily through the superficial inferior epigastric vein (SIEV), which is connected to the deep inferior epigastric vein (DIEV) by choke vessels composed of the vena comitantes of the perforators of the deep inferior epigastric artery (DIEA)[107]. Although the majority of DIEP flaps may survive based on the outflow from the DIEV system alone, the venous outflow of some DIEP flaps may be superficially dominant. In these cases, both the DIEV and the SIEV may require anastomosis for adequate venous drainage[107].

Preoperative imaging with CT angiogram, especially among patients with prior surgery in the region of planned flap harvest, may be beneficial in perforator selection and evaluation of venous anatomy. The presence of the SIEV and its caliber should also be evaluated radiologically and intraoperatively. If the SIEV is noted to be of good caliber (> 1.5 mm), it is prudent to preserve adequate length on this vessel to allow for anastomosis.

*Intraoperative management of venous insufficiency*

As described by Heller and Levin, obstruction of venous outflow can lead to red blood cell extravasation, endothelial breakdown, microcirculation thrombosis, and flap death[108]. Signs of venous congestion in the flap may include rapid capillary refill on the skin paddle (< 1-2 seconds), more profuse dermal bleeding of a darker color, loss of venous Doppler signals in the pedicle and perforators, greater flap turgor, and enlarged secondary veins such as the SIEV. Our algorithm for intraoperative management of suspected venous insufficiency is available in [Figure 3B], adapted from Khansa *et al*. to reflect our institution's use of leeching and de-epithelialization[90].

Suspicion for venous congestion requires release of insetting sutures and diligent assessment of vessel position, flap and pedicle orientation within the breast pocket, and presence of hematoma and/or edema requiring evacuation. This should be paired with the assessment of anastomotic flow using Doppler sonography. Secondary veins, such as the SIEV in the case of a DIEP flap, should be examined closely. These veins should be opened to allow for assessment of their outflow. If the secondary veins are noted to have robust outflow, they should be used for venous supercharging of the flap as described below (*Venous Flow Present*).

Flaps or pedicles can be repositioned to achieve a more favorable lie without kinking. Autologous fat grafts may be used to cushion the pedicle or maintain its position without twists or kinks. Re-evaluation of the venous anastomosis or coupler is critical. A milking test can be used to ensure flow across the anastomosis and throughout the length of the pedicle. If the flap vein was twisted or kinked relative to the recipient vein during anastomosis, the anastomosis may need revision to avoid propagation. Venous vasospasm can cause global congestion, which can usually be resolved by irrigating the vessels with vasodilators (papaverine, lidocaine, verapamil, and nitroglycerin mixture) and warm salinex[109].

*Venous flow diminished or absent*

If there is absent or diminished flow in the anastomosis after mechanical factors and simple vasospasm have been ruled out, the anastomosis should be taken down and inspected for thrombi. As venous supercharging may be necessary, secondary veins should be examined closely as described below. The artery should also be carefully inspected for signs of diminished flow. If the artery is noted to have abnormal flow, this vessel should be treated using the algorithm above (See intraoperative management of arterial thrombosis). If thrombus is noted in the proximal vein, direct thrombectomy with microforceps should be attempted. If the thrombus is too extensive or distant for this approach, a 1-3 mm Fogarty catheter can be used to attempt thrombus removal in the distal pedicle. Although there is concern that the use of Fogarty catheters on microvasculature can increase the risk of endothelial denudation and thrombogenesis, studies on complication rates following Fogarty catheterization so far have been conflicting and limited by small study samples. While some studies have reported successful flap salvage using the Fogarty catheter, others have found a higher rate of failure in flaps undergoing Fogarty catheter thrombectomy[101,110]. However, as there have been no large-scale studies on the use of Fogarty catheters in flap salvage, and all previous studies are subject to significant selection bias, we believe that Fogarty catheters have an important role in the armamentarium of the reconstructive microsurgeon - especially when attempting to salvage flaps with more extensive or proximal thrombi that are not accessible for direct thrombectomy. After the Fogarty catheter is used, the vessels are typically flushed copiously with heparinized saline as per our arterial algorithm.

If no thrombus is visualized upon taking down the anastomosis, it is possible that there is evidence of intra-flap venous insufficiency or thrombosis. Although ICG angiography is typically used to examine inflow to the flap, venous outflow can be assessed using a washout phase. After the arterial flow is confirmed using the ICG, a second examination can be done after a 2-3 min delay. If ICG dye remains in portions of the flap after this delay, it is likely that these portions may be experiencing venous insufficiency. In cases of intra-flap thrombosis, whether arterial or venous, chemical thrombolysis may be needed (see the arterial treatment algorithm above). If only a portion of the flap is determined to suffer from venous insufficiency, this non-viable tissue may simply be debrided.

*Venous flow present*

Evidence of persistent flap congestion in the setting of venous patency indicates the need for venous supercharging, or additional venous flow augmentation. Of the two most common autologous breast reconstructions, DIEP flaps are more likely than free TRAM flaps to be complicated by venous congestion requiring flow augmentation, likely due to DIEP flaps having fewer perforators[107,111,112].

A broad range of techniques for augmenting venous outflow in abdominally-based autologous breast reconstruction has been widely reported in the literature. The vena comitantes of the ipsilateral DIEA, vena comitantes of the contralateral DIEA, ipsilateral SCIV, ipsilateral SIEV, and contralateral SIEV serve as potential sources for donor veins in venous super-drainage, with the ipsilateral SIEV being the most common[113]. The most frequently used recipient vessel is the second internal mammary vein (if available), or the retrograde inframammary vein (IMV) due to their location allowing for optimal flap positioning on the chest. At our institution, for all DIEP flaps, we routinely preserve sufficient length on the SIEV and retrograde IMV to allow for anastomosis if necessary. Given the ease of supercharging the flap during the initial microsurgery, it is prudent to perform this anastomosis early if there is any level of concern for superficial venous dominance. Other potential recipients include the intercostal perforating vein, thoracodorsal vein, cephalic vein, thoracoacromial vein and lateral superficial thoracic vein - however, all of these systems require more time for dissection and may necessitate significant flap rotation to allow for anastomosis[113,114].

According to cadaveric and imaging studies, over 75 percent of females will have both lateral and medial vena comitantes to the inframammary artery (IMA) present above the lower border of the 4th intercostal space (ICS). If the lateral IMV is of adequate caliber for anastomosis, this may be used as the recipient vessel for venous supercharging[115]. Multiple studies have demonstrated that the caudal end of the IMV can accommodate retrograde flow, and have promoted the assumption that the IMV is valveless[116-119]. However, an anatomic study by Mackey and Ramsey on 32 human cadavers found that 1 to 3 valves were present in the IMV of 44% of female cadavers and 42% of male cadavers[120]. Additionally, valves were found between the preferred point of distal anastomosis and the next draining vein in 9% of 2nd ICS and 5% of 3rd ICS. While it is possible that valvular incompetence allowed for retrograde flow in prior studies, the findings by Mackey and Ramsey indicate that retrograde flow may not be guaranteed in the caudal end of the IMV, and that more dynamic studies are required to validate this technique[120]. In our experience, the lateral IMV is often diminutive, even if present. In these cases, we routinely preserve sufficient length on the retrograde end of the medial IMV and utilize this for secondary venous anastomosis. Although some authors may raise concern that retrograde outflow may be diminished due to the presence of valves, we have found that there is sufficient collateralization from the intercostal system and IMV perforators to allow for adequate outflow.

If no other recipient veins are available, it may be possible to perform venous turbo-drainage via an intra-flap anastomosis. Rohde and Keller have described a turbo-drainage technique in which a superficial to deep venous loop is created within the flap by anastomosing the ligated SIEV to the proximal end of one of the vena comitantes of the DIEA[121]. This allows blood from the superficial system to drain directly into the deep system via anterograde venous flow through the vena comitantes, and eventually through the original DIEV-IMV anastomosis. This technique requires minimal additional accommodations for vessel length or flap positioning. It is also suitable for cases in which the superficial venous system is overdominant.

If venous congestion persists despite venous outflow augmentation or there are no viable alternate recipient veins, mechanical leeching can be considered. This method entails intraoperatively placing an angiocatheter in the dominant vein, which is brought up to the skin as a venostomy for controlled manual drainage. The angiocatheter should be flushed periodically and aspirated at hourly intervals for the next 3-6 days based on clinical examination of the flap[122,123]. Bank *et al.* have also reported a case of successful resolution of venous congestion with mechanical leeching guided by ViOptix measurements[124]. Once congestion resolves, the angiocatheter can be removed and the vein can be allowed to clot. Although this method eliminates the infection risks associated with leech therapy, it still requires blood products due to volume depletion by aspiration. Furthermore, studies on mechanical leeching for venous congestion have so far reported high success rates, but given the limited number of studies and their small sample sizes, they are highly likely to be subject to publication bias.

*Postoperative management of venous insufficiency*

Delayed venous thrombosis in the postoperative period is most likely to occur within 3 days of the initial operation[125]. As previously discussed, early detection of a possible venous thrombosis allows for the best chance of ensuring flap survival. Since prolonged venous congestion is often a precursor to venous thrombosis, flap monitoring and timely detection of signs of venous congestion is essential to the prevention of this complication[104].

If clinical signs of venous congestion are present, initial management involves addressing sources of extrinsic compression that may be contributing to poor venous outflow. Common troubleshooting techniques include loosening of surgical bra, removing tight dressings, or removing compressive sutures[113,126-128]. Topical nitroglycerin paste causes both arterial and venous dilation; it may be used as an adjunct to remove extrinsic compression[127,129,130]. If conservative methods fail to relieve congestion, or if venous thrombosis is suspected, reoperation offers the best potential for flap salvage.

The strategy for addressing postoperative venous compromise in the operating room follows a pattern similar to that seen with intraoperative venous insufficiency. One notable exception is the presence of a hematoma that may be compressing the pedicle. Hematoma may be seen in the presence or absence of venous congestion[131]. However, it is more often seen concurrently with venous congestion. When hematoma is suspected as the cause of venous compromise, the hematoma should be evacuated on an emergent basis to avoid further compression of the pedicle[103,131]. In cases of delayed venous insufficiency (i.e., greater than 3 postoperative days) and/or when re-exploration of anastomosis and surgical revision may be impossible, venous insufficiency may be managed medically[128].

While the majority of venous thrombosis events occur within the immediate postoperative period, delayed venous insufficiency and/or thrombosis have been documented up to 5 weeks after initial operation[125,128]. In these later presentations, successful salvage without re-exploration of anastomosis is more common[128]. Yoon and Jones suggest a critical time period for flap survival whereby flaps with delayed thrombosis have a higher rate of survival due to neovascularization and angiogenesis that has already taken place[132].

*Systemic anticoagulation in conjunction with reoperation*

Heparin prevents clot formation by activating antithrombin III, which ultimately prevents the formation of fibrin[133]. While some have utilized antiplatelet therapy in addition to systemic anticoagulation, there is well-documented evidence to show that heparin is favorable to antiplatelet therapy in cases of microvascular thrombosis[134]. Several methods have been reported on the use of systemic heparin in cases of venous thrombosis or congestion, but timing, dosage, and routes of administration vary depending on the institution. Most authors report using the same protocol for systemic anticoagulation in both venous and arterial thrombotic complications. There is currently no standardized recommendation, and no single protocol has been proven to be superior. At our institution, we typically recommend a continuous weight-based heparin infusion titrated with a PTT of 60-80. This can be transitioned to weight-based low molecular weight heparin injections once the patient is deemed to have a sufficiently low bleeding risk. The duration of the treatment may range from 1 week to 4 weeks, depending on our level of concern for thrombosis.

*Alternative venous drainage*

Several methods exist for the medical management of venous insufficiency in free flaps, with varying levels of success demonstrated in the literature[127]. Local injection of subcutaneous heparin has been demonstrated to be effective in several studies. More recently, the use of subcutaneous heparin was discussed by Perez *et al*, who showed that local subcutaneous injection of LMWH is an effective method for flap salvage in cases of venous congestion[135].

Relief of venous congestion may be further facilitated by pricking or de-epithelialization of the flap. Pricking the flap with a needle allows blood loss from the congested area, thereby reducing venous compromise[136]. In a similar manner, de-epithelializing a portion of the flap allows for venous drainage. Heparin may be injected into the de-epithelialized area or a heparin-soaked gauze may be applied to the de-epithelialized area to further increase venous outflow[136,137].

Hirudotherapy, the use of medicinal leeches, may be used in cases of irreparable venous insufficiency and/or flap necrosis secondary to venous compromise. The application of leeches provides temporary relief of venous congestion while a more reliable network for venous drainage is being established[127,138]. The effectiveness of medicinal leech therapy in decreasing venous congestion is two-fold; the initial blood meal by the leech allows for active drainage of ~5-15 mL of congested blood, after which passive blood loss from the bite injury continues to occur. Leech-mediated release of vasoactive substances allows for further local thrombolysis and anticoagulation[139,140]. While leech therapy for free flap salvage has reported success rates ranging from 60-80%, it may be less effective for higher volume flaps such as TRAM or DIEP flaps[127,138]. Primary complications of leech therapy include infection and anemia[139]. The evidence for medicinal leech therapy is limited to case series and retrospective studies. While Pannucci *et al*. found that leech therapy in microvascular breast flaps was associated with higher flap loss rates, this is likely secondary to significant selection bias[141]. Current evidence indicates that leech therapy should be used with discretion and in consideration of patient-specific risk factors[141]. In our experience, leech therapy should be considered as an adjunct in cases with significant intra-flap venous insufficiency that does not respond adequately to other therapies.

Veno-cutaneous catheterization presents another option for the relief of venous congestion. An angiocatheter is placed into a superficial vein at the margin of the flap. Distilled heparin solution is injected into the vein. The catheter is left in place with a valve such that venous drainage may occur as needed. When clinical signs of congestion improve, the catheter may be removed[142-144]. In comparison to leech therapy, veno-cutaneous catheterization is less costly. Further, Mozafari *et al*. showed that veno-cutaneous catheter use is associated with decreased blood loss, wound dehiscence, and flap necrosis compared to leech therapy. It is also associated with high rates of nursing and patient satisfaction[145]. All reported protocols indicate that the catheter must be placed in the operating room, which is a notable disadvantage of this technique[127]. In our experience, venocutaneous catheterization can be difficult to maintain for more than 1-2 days, given the high likelihood of catheter thrombosis with intermittent use.

Negative pressure therapy has also been reported in the literature for the management of venous congestion. However, its use in practice is still rare. Negative pressure therapy is thought to reduce congestion by decreasing edema, increasing drainage and local venous flow, and increasing the rate of neovascularization[146-148]. Negative pressure may also have a compressive effect, making the overall benefit of this therapy difficult to accurately assess[127].

## Special Considerations

### *Management of ischemia-reperfusion injury*

Ischemia reperfusion injury is an important consideration for microsurgeons as tissue damage can persist well after the flow is re-established. Restoration of blood flow to a flap promotes the release of proinflammatory cytokines and reactive oxygen species (ROS), leading to tissue inflammation, coagulation, and necrosis. This cascade can ultimately result in partial or complete flap loss and fat necrosis as well as adverse patient outcomes and healthcare costs[149]. The most dreaded outcome in this scenario is the "no-reflow" phenomenon, whereby tissue damage is so severe that the flap does not perfuse despite the patency of the anastomosis. Several factors have been implicated in an increased risk for ischemia-reperfusion injury, including tissue type, surgical technique, temperature, and ischemia time[150].

Given the pathogenesis of ischemia-reperfusion injury, immunomodulators, antioxidants, and anticoagulants have each been proposed as potential therapeutics. While these therapies have shown promise in animal models, the data on their utility in human patients is unclear[151-157]. For example, while statins have theoretical anti-inflammatory and antioxidant activity, Koolen *et al*. and van den Heuvel *et al*. did not find such benefits in breast microsurgery[158,159]. Additionally, in a retrospective study, Coriddi *et al*. found no significant difference in lost *vs* salvaged flaps and patients who received intra/postoperative steroids or therapeutic anticoagulation for ischemia-reperfusion injury prophylaxis[103]. Ultimately, more research in this area, including randomized controlled clinical trials, is needed before further therapeutic recommendations are made.

### *When flap salvage is not feasible*

When considering approaches to tertiary reconstruction, Baumeister *et al*. recommend the following steps: a sensitive psychosocial approach to the patient and family, an analysis of the cause of the first flap failure, reconsideration of the need for vascularized free tissue transfer, and a change in microsurgical strategy[160]. An investigation into the cause of flap failure should include careful consideration of the following: the preoperative preparations, the recipient vessels and anastomosis, the patient's risk for hypercoagulability and thrombosis, the postoperative care, and the surgeon's individual expertise. Baumeister *et al*. provide a thorough checklist to consider in [Table 2][160].

Hamdi *et al*. broadly classify the causes of flap failure into "technical" (anastomosis errors, pedicle kinking, anatomical variations, and quality and choice of recipient vessels and/or perforator of the nourishing pedicle) and "nontechnical" (one or more hypercoagulability disorders) etiologies[161]. In the event of "nontechnical" flap failure, alternative options, including a pedicled flap, should be strongly considered, given the high risk of another failure. However, for patients whose free flap failed due to a presumed technical error, another free flap may be reasonably considered.

In the rare case of non-salvageable total flap failure, an in-depth and empathetic discussion with the patient and family is essential. A description of possible alternative forms of breast reconstruction will provide necessary reassurance. We recommend debriding all non-viable tissue in the operating room soon after the diagnosis is assured. The mastectomy skin flaps should be closed if possible. If the skin flaps cannot be closed primarily, a negative pressure therapy dressing may be used temporarily. In a case of partial flap failure, debridement of the non-viable tissue should take place only after demarcation. The timing of future efforts at breast reconstruction should be dictated by the patient's preferences, psychosocial needs, and the state of the wound after flap debridement.

**Table 2. Checklist to be reviewed by surgeon after free flap failure. This figure is quoted from Baumeister *et al.*[160] published in *Plastic & Reconstructive Surgery* by the American Society of Plastic Surgeons, copyright 2008. from Wolters Kluwer Health, Inc**

| *Preoperative preparations* |
|---|
| Did I know enough about the recipient vessels (artery and vein)? |
| Did I need an angiogram? |
| Did I adequately assess the patient's coagulation potential? |
| Did I need to exclude a venous thrombosis? |
| Did I know about any previous operations, scars, or irradiation? |
| Were the type, size, and positioning of the flap properly planned? |
| ***Recipient vessels/anastomosis*** |
| Were there atherosclerotic changes? |
| Was there poor arterial outflow suggesting a proximal problem? |
| Did I need to perform the Fogarty maneuver on the artery? |
| Was it necessary to go more proximal using an interpositional graft to avoid the zone of injury? |
| Did I injure the vessel during preparation? |
| Was I satisfied with my technical performance during the anastomosis? Did I see every stitch? |
| Was it possible to improve the exposure of the vessels during anastomosis? |
| Was end-to-end or end-to-side anastomosis the best option? |
| Was there any tension or kinking of the vessels? |
| Did I irrigate with heparin? |
| Was there any vasospasm? |
| Should I have used papaverine or Xylocaine? |
| Was the room/patient warm enough? |
| Was the patient's blood pressure adequate? |
| Were there any external constricting fascial bands or muscles compressing the vessels? |
| ***Coagulation/thrombosis*** |
| Was the operation performed in the acute posttraumatic period? |
| Was I satisfied with the coagulation of bleeding points? |
| Was there any thrombosis? |
| Intraoperative positioning |
| Were the exposure and approach to the vessels optimal? |
| Was it possible to operate in two teams and thus shorten the operating time? |
| Was it possible to improve the positioning of the surgeon during anastomosis? |
| ***Postoperative care*** |
| Was the patient hypovolemic, hypotonic, or hypothermic? |
| Was patient/flap positioning appropriate? |
| Was there any pressure on the proximal extremity/vessels? |
| Would it have been preferable to use an external fixator? |
| Was there pressure on the flap's pedicle? |
| Were the flap's perfusion and positioning adequately monitored (hourly)? |
| Would it have been preferable to use a Cook Doppler probe or a similar device? |
| Was the anticoagulation therapy adequate? Would full heparinization have helped? |
| Were there problems with patient compliance? |
| ***Revision*** |
| Was the thrombosis recognized early enough? |
| Was the revision performed immediately? |
| Would a different revision strategy have been preferable? |
| ***Surgeon*** |
| Would referral to another surgeon be appropriate? |

*Flap alternatives*

Much of the decision-making regarding the next steps following flap failure depends on what was found following troubleshooting of the prior failed flap, anatomical limitations of the patient, and the patient's preferences. The decision to pursue another reconstruction should be made only after a thorough reassessment of the patient's medical and familial history for hypercoagulability and other potential risk factors. Following their review of 14 patients who underwent tertiary breast reconstruction after a prior failed reconstruction, Hamdi *et al*. recommend that, based on their experience, the latissimus dorsi flap and the thoracodorsal artery perforator flap with or without an implant are associated with lower morbidity compared to free flaps, and should be considered if the patient is at high risk of complications[161]. At our center, pedicled options such as the latissimus flap are essential for patients at high risk for microsurgical thrombosis. If the patient displays a strong preference for a free flap and they are deemed a candidate for a second attempt at free tissue transfer, preoperative planning should include CT and color Duplex imaging to assess alternative donor sites and viable recipient vessels, hematologic consultation for assessment of thromboembolism risk and application of thromboprophylaxis measures, and preparation of secondary options in case the second free flap fails.

## CONCLUSION

Microvascular thrombosis continues to pose challenges in autologous breast reconstruction. Reconstructive surgeons should be mindful of obtaining relevant patient history, assessing risk factors, and consulting anatomical imaging when necessary during preoperative planning, and vigilantly monitor signs of flap compromise during the operative and postoperative phases. Cases of suspected thrombosis should be approached systematically to ensure proper management, using algorithms such as the ones we have presented in this review. Nevertheless, further investigation into individual techniques is necessary to optimize the prevention and management of thrombotic complications in breast reconstruction.

## DECLARATION

### Author's contributions

Made substantial contributions to manuscript conception, literature review, manuscript preparation, and manuscript editing: Chen A, Garvey SR, Nanda A, Lee BT, Cauley RP

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### Conflicts of interest

All authors declare that there are no conflicts of interest.

### Ethical approval and consent to participate

Not applicable.

### Consent for publication

Not applicable.

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# Complications in microsurgical breast reconstruction: thrombosis prevention and management

**Suzanne M. Inchauste**

Department of Surgery, Division of Plastic and Reconstructive Surgery, University of Washington Medical Center, 1959 NE Pacific Street, Seattle, WA 98195, USA.

**Correspondence to:** Dr. Suzanne M. Inchauste, Department of Surgery, Division of Plastic and Reconstructive Surgery, University of Washington Medical Center, Seattle, WA 98195, USA. E-mail: sinchaus@uw.edu

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## Abstract

Breast reconstruction is one of the largest components of plastic and reconstructive surgery. Autologous free flap breast reconstruction continues to grow due to exceptionally high flap success rates. It provides patients with a durable and natural reconstruction with high patient satisfaction. A patent microvascular anastomosis is a key component to a successful autologous free flap breast reconstruction. Thrombus within the vascular anastomosis or the distal flap microcirculation is the most common cause of flap failure. This review aims to discuss microsurgical techniques including atraumatic handling of vessels, appropriate magnification, suture styles, anastomotic techniques, recipient vessel selection, the role of anticoagulation and antiplatelet therapy used to minimize the risk of thrombotic events. When microvascular thrombus occurs, early reoperation and reperfusion is imperative to flap survival. This review will discuss specific maneuvers and intraoperative interventions to maximize flap salvage.

**Keywords:** Microsurgery, autologous free flap breast reconstruction, thrombosis, microsurgical anastomosis, thrombus prevention

## INTRODUCTION

The first free tissue transfer by McLean and Buncke in 1972[1] was the birth of microsurgery. Autologous free flap breast reconstruction has gained popularity since it was first described in 1979[2]. In 1979, Holmström studied the vascular supply of abdominoplasty tissue using angiography and identified the superficial and deep inferior epigastric vascular systems. He then performed the first autologous free flap breast reconstruction using a free abdominoplasty flap in a patient with a prior radical mastectomy. Holmstrom designed the flap based on the dimensions of an abdominoplasty, umbilicus to pubic region and between the anterior superior iliac spines. Holmstrom visualized the perforators within the rectus abdominus muscle, piercing the anterior rectus sheath, and traveling into the abdominoplasty tissue. He raised the flap on these perforators, including the ipsilateral rectus muscle and vascular pedicle, transferring the flap 5 days later. Holmstrom completed the arterial anastomosis to the axillary artery, and the two venae comitans and the contralateral superficial inferior epigastric vein to the axillary and thoracodorsal veins. Improvements in microvascular free tissue transfer techniques over the past 50 years have made autologous free flap breast reconstruction widely accepted. After reading this review, the participant will gain knowledge about how to successfully perform a microvascular anastomosis. This review will discuss microsurgical techniques including atraumatic handling of vessels, appropriate magnification, suture styles, anastomotic techniques and the role of anticoagulants and antiplatelet therapy in minimizing the risk of thrombosis to improve any microsurgical anastomosis. It will specifically discuss autologous breast free flap recipient vessel selection, alternative options, and maneuvers to manage thrombotic complications.

## PREVENTION

The percentage of women electing to have breast reconstruction after mastectomy continues to increase. Overall, autologous free flap breast reconstruction is less common than implant-based breast reconstruction. However, it has steadily increased and accounted for 23% of all breast reconstruction procedures in 2020[3]. Autologous microvascular free flap breast reconstruction continues to grow with advancements in technology, increasing experience and comfort of surgeons with microsurgery, expanding indications, and new donor sites such as lumbar artery perforator flaps[4] and omental fat-augmented free flap for breast reconstruction patients with inadequate abdominal or thigh tissue[5]. In addition, autologous free flap breast reconstruction has excellent patient-reported outcomes and satisfaction[6]. Autologous free flap breast reconstruction provides a durable, natural aesthetic reconstruction. Autologous free flap breast reconstruction has been associated with high satisfaction and lower long-term failure[6]. Drawbacks to autologous free flap breast reconstruction include a secondary donor site with associated donor site morbidity, longer surgery, and recovery with a higher risk of thromboembolic complications, and specialized operative instruments that can be expensive and not available at every site providing breast reconstruction. Implant-based reconstruction does not require specialized equipment, limits surgery to the breast only with shorter operative times and recovery, but has lower patient satisfaction, higher longer-term failure rates and thus more explant procedures[7]. Successful autologous free flap breast reconstruction requires appropriate patient selection, adequate preoperative planning, meticulous flap dissection, and patent microvascular anastomosis. Autologous free flap breast reconstruction has exceptionally high success rates ranging from 97%-99%, with flap failure most associated with a thrombus[8-14]. Patient selection, flap selection and design, and complete preoperative evaluation with appropriate imaging are important. The goal of this review is to discuss surgical techniques and maneuvers of microsurgery to maximize success.

Microsurgical technical points:

Excellent surgical technique is key to the success of any surgery; microsurgery is no exception. Meticulous dissection of the flap perforators, flap pedicle and recipient vessels is equally important. Autologous free flap breast reconstruction relies on the patency of very small vessels to be successful. Extreme care must be taken during vessel dissection to minimize tension on vessels and avoid avulsion or intimal injury. The same care is required during the preparation and handling of vessels during microvascular anastomosis.

Endothelium is the inner cellular lining of all vessels and constitutes the intima layer. The endothelium controls vascular relaxation and constriction[15]. Injury to the endothelium can result in vasospasm or constriction as well as platelet adherence and clot formation. Studies have shown that damage to the intima increases the risk of thrombus and flap loss[16]. It is important to minimize instrumentation to both the recipient and flap vessels, especially within the lumen of the vessel. The lumen of the vessels should be visualized under high magnification and carefully inspected for any tears or separation of the intima. This is especially critical when the patient has a history of radiation. Radiated vessels are more friable and prone to intimal injury. Prior radiation therapy is not a contraindication but awareness of the potential damage to recipient vessels is needed. Compared to implant-based reconstruction and immediate autologous free flap breast reconstruction in postmastectomy radiation patients, delayed autologous free flap breast reconstruction is associated with higher patient satisfaction, fewer revision surgeries and lower long-term complications[17]. If an intimal injury is seen, the vessel needs to be trimmed back until healthy, uninjured intima prior to proceeding with the anastomosis. Further dissection of the vessels may be needed to achieve appropriate exposure to healthy-appearing vasculature. In the setting of poor vessel quality, such as radiation damage or atherosclerotic disease, the use of alternative vessels or vein grafts may be warranted, as discussed below.

Once the vessel is trimmed back to a healthy lumen and appropriate length, the outside of the vessel is prepared. The vessels are separated, and surrounding fatty tissue removed. The outer layer of connective tissue surrounding a blood vessel is the tunica adventitia or tunica externa. Adventitia is comprised of collagen, elastic fibers, and perivascular nerves. The adventitia plays an important role in controlling lumen size through the regulation of the smooth muscle tone. Activation of sympathetic fibers within the adventitia causes vasoconstriction and lumen narrowing. Interruption of these sympathetic fibers within the adventitia leads to decreased activation of smooth muscle tone and vasodilation[18]. Limited resection of the adventitia around the artery during vessel preparation has been shown to reduce vascular tone and increase lumen size, and vascular flow during microvascular anastomosis[18]. Vasodilation and increased flow improve anastomotic patency and decrease thrombosis. Care must be taken to not over-resect the adventitia and weaken the vessel. Limited adventitiectomy around the circumference of the vessel edge with microscissors can provide the desired sympathectomy without compromising the vessel integrity.

Magnification:

Visualization is crucial to performing a successful microvascular anastomosis. It is critical to see all the structures of the vessel and suture placement. The use of surgical microscopes for appropriate visual magnification to perform microvascular anastomoses remains the predominant method. The magnification achievable with most operating microscopes is between 6× and 40×. More recent publications have shown microsurgical anastomoses performed with loupes magnification to be safe and effective for free flap breast reconstruction[10,19,20]. Loupes provided 3.5× to 5.5× magnification[20]. Small vessel diameters equal to 1.5 mm or less still require operative microscope magnification[20]. One must consider that the authors of most publications regarding loupes microsurgery are very experienced microsurgeons. Novice surgeons learning microsurgery may not have equivalent outcomes. The operative microscope allows for significantly better visualization with magnification twice to forty times as powerful as loupes. Newer operative microscopes are equipped with integrated near-infrared illumination systems that can be used to evaluate intraoperative flap perfusion and anastomotic patency[21]. Operative microscopes provide better visualization of vessel intima to evaluate damage or tears, management of small side branches, or dissection within fibrotic or radiated fields. This is especially important when first learning microsurgery.

Suture technique:

Now it is time to perform the vascular anastomosis. There has been debate regarding the ideal suture technique. Simple interrupted suture for microvascular anastomosis remains the gold standard, but numerous techniques have been described. The six most published suture techniques are simple interrupted, continuous, locking continuous, continuous horizontal, horizontal interrupted with eversion, and sleeve anastomoses[21]. Publications comparing anastomotic suture techniques have shown no difference in short and/or long-term patency rates. Each technique has been found to be successful if microsurgical principles of suture line eversion with direct intima-to-intima contact and minimal tension are maintained. The suture technique is less important than maintaining the above principles. Suture style depends more on surgeon preference and experience than the superiority of one technique over another.

Hand sewn versus coupler anastomosis:

Vascular anastomoses were historically handsewn with sutures. Nakayama first described a microvascular anastomotic coupling device in 1962[22]. Microvascular anastomotic coupling device (MACD) is a well-established alternative to hand-sewn venous anastomosis. The device has an interlocking ring-pin design to complete the anastomosis with reliable vessel eversion and intima-to-intima contact. The coupling device ring acts as a rigid stent and protects against vessel collapse. However, the rigid ring can act as a potential twisting or kinking point as well if not positioned appropriately. Hand-sewn venous anastomosis is technically demanding due to the thin, fragile nature of vein walls. Studies comparing venous anastomosis techniques (coupler versus hand sewn) show comparable revision and thrombosis rates[9,22,23] but do demonstrate shorter anastomosis times with the use of MACD[22,23]. The use of a coupling device to complete a venous anastomosis is successful in approximately 99% of attempts with a less than 1% conversion rate to hand-sewn anastomosis[23]. The shorter anastomosis time translates to shorter operative time and potential cost savings. A study compared the cost of disposable products and operating room time between hand-sewn venous anastomosis and MACD. This study demonstrated cost saving due to decreased operative time despite the higher disposable cost with MACD[24]. The use of a coupler device for venous anastomosis has been widely adopted as the standard.

Microsurgeons have reported the use of MACD for arterial anastomosis as well. Studies demonstrate anastomotic completion rates with MACD are lower with a higher conversion to hand-sewn anastomosis compared to venous anastomosis[25]. Vessel size mismatch, end-to-side anastomosis, thicker arterial wall, or nonpliable artery were the most common reasons surgeons reported for failure to complete an arterial anastomosis with a coupling device. The literature also describes intimal cracking or tearing during eversion onto the coupler ring pins as reasons for conversion as well[25]. The use of a coupling device for arterial anastomosis can be done, but proper vessel selection is critical. Successful arterial coupling requires adequate vessel size, minimal vessel size mismatch, and a pliable vessel that can be everted. Hand-sewn anastomosis remains the most popular technique for arterial anastomosis.

End-to-end versus end-to-side anastomosis:

End-to-end anastomosis remains the standard technique for microsurgical autologous free flap breast reconstruction. This is especially true in the case of more novice microsurgeons, as this provides the best visualization of the vessel lumen and most pedicle freedom. When end-to-end and end-to-side were compared, rates of anastomotic thrombosis and flap failure were not significantly different[26-28]. Surgeon preference and experience with each technique play a role in selection. End-to-end anastomosis does allow for more freedom of rotation with flap positioning and inset. End-to-side anastomosis can create a tether point at the anastomosis, which may be a point of possible avulsion injury. End-to-side can be technically more difficult but allows for continuity of the recipient vessel and maintains distal perfusion.

Some authors describe the use of end-to-side microvascular anastomosis when a significant vessel caliber mismatch exists. When SIEA flaps are used for autologous free flap breast reconstruction, the superficial inferior epigastric artery diameter is smaller, usually less than 1.5 mm. This can be less than 50% the diameter of recipient IM artery, creating a significant size mismatch. The use of either end-to-side microvascular anastomosis or the use of the thoracodorsal artery as an alternative for a better size match has been described[29].

Internal mammary perforators or end-to-side anastomoses have been described to preserve the internal mammary vessels[30-32]. The use of internal mammary perforators is limited by the size of the perforators and is found to be adequate in less than 10% of cases[32]. Internal mammary perforators have limited use due to their small size and risk of kinking, therefore, should be reserved for use by experienced microsurgeons. End-to-side anastomosis for the internal mammary vessels can be considered in cases when preservation of distal perfusion is desired, such as in patients with coronary artery disease. This allows preservation of the internal mammary artery for coronary artery bypass grafting[31,33].

Vessel selection:

One of the key elements of successful microvascular anastomosis is the appropriate selection of the recipient artery and vein. The thoracodorsal vessels were the first described recipient chest vessels for free flap breast reconstruction[34]. In early autologous free flap breast reconstruction, axillary lymph node dissection was more common, so surgeons routinely used thoracodorsal vessels due to the ease of access within the operative field. Innovations in breast cancer surgery meant more sentinel lymph node biopsy and less frequent axillary lymph node dissection. This influenced a change in recipient vessel selection to the internal mammary (IM) vessels. By contrast, thoracodorsal vessels had a higher rate of conversion compared to internal mammary vessels in autologous free flap breast reconstruction patients[35]. History of axillary lymph node dissection and preoperative radiation were significantly associated with thoracodorsal vessel conversion[35].

Currently, the internal mammary vessels are the predominant recipient vessel of choice due to their larger size, need for shorter pedicle length, better access for microvascular anastomosis and more central placement of the flap in the breast pocket[35-38]. The use of internal mammary vessels has also been advocated because it preserves the thoracodorsal vessels as a backup option for recipient vessels in salvage reconstruction or pedicled myocutaneous latissimus dorsi flap. Dissection of internal mammary vessels does have some special considerations. It often requires removal of a small segment of rib cartilage for adequate exposure. During this dissection, there is potential for pneumothorax, given that only a thin layer of pleura exists between the IM vessels and the lung. Chest wall movement with respiration and radiation fibrosis can make recipient vessel exposure and microvascular anastomosis more challenging. The IM vessels have been found to be the largest at the third intercostal space, which is the most common access point.

Studies have shown that size of the right and left internal mammary arteries did not differ significantly[39]. However, studies have shown left internal mammary vein is significantly smaller than the right[39]. The left internal mammary vein has been shown to have higher rates of thrombosis, venous thrombosis-related flap loss, and higher rates of conversion to an alternate vein compared to the right internal mammary vein[39]. Studies have shown higher rates of venous thrombosis associated with smaller vein diameters.

If a small caliber vein is seen, the first step is to dissect the vessel more proximal to look for a larger caliber. Consideration should be taken if the recipient vein diameter is less than 2 mm, particularly in delayed reconstruction in an irradiated chest, to look for an alternate recipient vessel. Alternate recipient vessels include the vena comitans, retrograde IM vein, contralateral IM vein, or thoracodorsal vein. Other alternative recipient venous outflow options include cephalic vein transposition[40]. Cephalic vein transposition (CVT) is used more frequently in patients undergoing delayed reconstruction and with a history of radiation[40]. CVT can be used as an alternative for the primary recipient vessel or to supplement flap venous insufficiency. Contralateral internal mammary vessels are another option in the setting of unilateral reconstruction [Figure 1], which requires adequate pedicle length or vein graft in flaps with shorter pedicles such as a transverse upper gracilis flap (TUG). Adequate dissection is needed to avoid kinking the vessel and one should appropriately line the course of the pedicle with adipose tissue to prevent compression from the underlying sternum. Thoracodorsal vessels were the original recipient vessel choice of free flap breast reconstruction and are often considered a reliable alternative vessel choice when the IM vessels are not usable, but it does require a longer pedicle. The use of the thoracodorsal vein as an alternative recipient vessel when the IMA anastomosis is patent may require a long vein graft. It can also potentially limit the use of a pedicled latissimus dorsi myocutaneous flap for salvage reconstruction. The thoracodorsal vessels may not be usable in up to a third of all patients with a history of axillary lymphadenectomy and radiation[35].

Venous insufficiency:

After the primary microvascular anastomosis, the flap can demonstrate venous outflow insufficiency with hyperemic appearance of the flap skin and dark red bleeding from the edges. If the flap demonstrates venous congestion, the first step is a complete evaluation of the arterial and venous anastomosis for patency. If the anastomoses are patented, the next step is to augment the venous drainage of flaps with additional venous anastomosis. If the recipient vein is small and the concern is inadequate deep venous flow, the primary option is augmentation of the deep venous system by completing a second venous anastomosis to the other vena comitans of the deep venous system of the flap to IM vena comitans, retrograde IM vein or an alternate vein.

It is rare to develop intraoperative venous congestion in the setting of patent adequate deep venous anastomosis, as this occurs less than 1% of the time[41]. This is most commonly due to superficial dominant venous drainage of the flap [Figure 2]. Most surgeons routinely dissect the superficial inferior epigastric vein at a length of 5-8 cm during DIEP flap harvest. In the setting of flap venous congestion, if the SIEV is engorged and congestion improves with drainage of the superficial system, then augmenting the venous outflow with a separate venous anastomosis to the SIEV is necessary. A second recipient vein such as second IMV, retrograde IMV, internal mammary or intercostal perforator, lateral thoracic vein, thoracoacromial vein, external jugular, cephalic vein transposition, thoracodorsal vein or to a proximally dissected vena comitans of the flap with and without vein graft has all been described[40-43]. Early recognition of flap venous insufficiency at the time of primary reconstruction with intraoperative correction has shown exceptional intraoperative salvage rates[41].

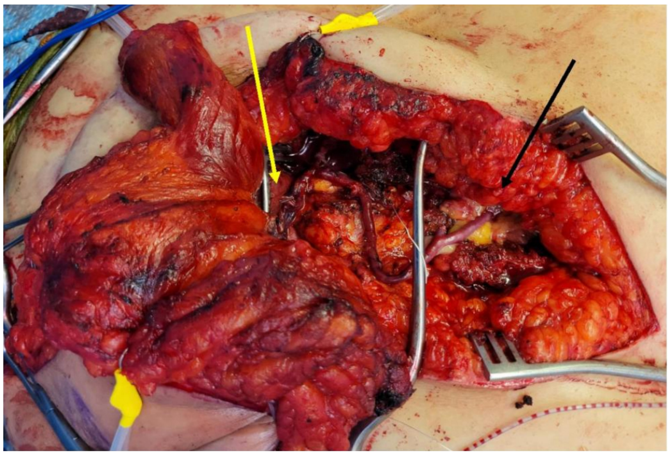

**Figure 1.** TUG flap with vein graft to the contralateral IM artery. The patient had a history of a failed DIEP flap. Yellow arrow points to the anastomosis of TUG artery to the vein graft. Black arrow points to the anastomosis of the vein graft to contralateral IMA. IM: internal mammary; DIEP: deep inferior epigastric perforator; IMA: internal mammary artery.

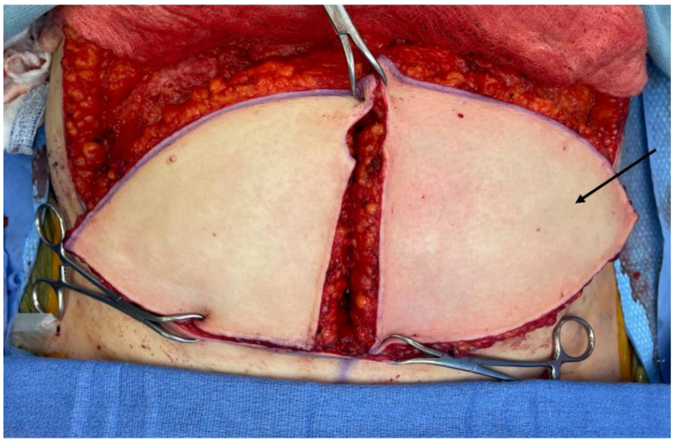

**Figure 2.** Arrow pointing to the left hemiabdomen in a bilateral DIEP with superficial dominant venous system. The left hemiabdomen demonstrated mild hyperemia compared to the right hemiabdomen prior to microvascular anastomosis. A second venous anastomosis to the SIEV was done at the initial microsurgical anastomosis. DIEP: deep inferior epigastric perforator; SIEV: superficial inferior epigastic vein.

Vein grafts:

If a vein graft is needed for a second venous anastomosis, several vein graft donor sites have been described. One must consider vessel size match, donor site morbidity, and ease of donor site access within the surgical field. The contralateral SIEV [Figure 3] or superficial circumflex iliac vein can be used, particularly in the setting of unilateral reconstruction. These vessels are within the abdominal sterile field, easy to access and harvest, and have a good vessel size match. Other options include the dorsal foot veins. They are easy to access, can be prepped quickly without disrupting the chest and abdominal field, and have adequate size match. Superficial veins in the forearm have been described in a similar way. It is important when harvesting a vein graft to ligate all the side branches and mark the proximal end to orient the direction of flow.

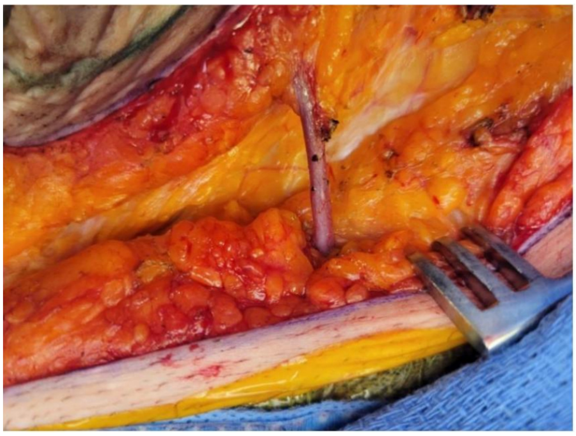

**Figure 3.** SIEV dissected 8 cm to length during DIEP flap elevation. DIEP: deep inferior epigastric perforator; SIEV: superficial inferior epigastic vein.

Vein grafts can be used to increase pedicle length for either the arterial or venous anastomosis, augment flap venous outflow with a second venous anastomosis through either the deep or superficial system, or during flap salvage. Vein grafts are more commonly used during primary reconstruction to troubleshoot intraoperative concerns[40]. For example, if the recipient or flap vessels have scar or fibrosis, then cutting back the vessels to more healthy tissue may shorten the vessel length resulting in the need for a vein graft. If the primary recipient vessels are insufficient and pedicle length is needed to access alternative recipient vessels, a vein graft may also be required [Figure 1]. If a second venous anastomosis is needed to augment flap venous drainage, a vein graft may be needed to perform the second venous anastomosis. Vein grafts can be used during flap salvage to restore flow after thrombosis or avulsion injury as well. Studies have shown that primary reconstruction with the use of vein graft has success rates as high as 95%, but there are significantly higher rates of thrombosis compared to primary reconstruction without vein graft[44]. Longer vein grafts are associated with higher rates of thrombosis and failure[45]. Vein grafts are an important tool in one's armamentarium when confronted with difficult microsurgical free flap reconstructions but are associated with higher rates of thrombosis and flap failure.

Once the free flap surgery is complete, postoperative flap monitoring protocols that are diligent, rigorous, and timely are essential for successful free flap breast reconstruction. The first and most important flap monitoring system is the physical exam. Flap assessment evaluating the skin color, temperature, turgor, capillary refill, and bleeding with pinprick is the gold standard. Any signs of concern such as pale flap color, cool to the touch, absent capillary refill or blood on pinprick are concerns for an arterial or inflow thrombosis. Brisk capillary refill, hyperemic or purple skin color, swollen or boggy turgor, or brisk dark red blood with pinprick are physical exam findings consistent with venous congestion or venous thrombosis [Figure 4]. Monitoring systems including acoustic Doppler sonography, implantable Doppler devices, and continuous near-infrared spectroscopy that complement physical exam can prompt early detection of vascular compromise and facilitate expeditious return to the operating room. Studies have shown higher salvage rates with a shorter time from detection of compromise and return to the operating room with the use of a monitoring system in addition to serial physical exams[46].

Anticoagulation:

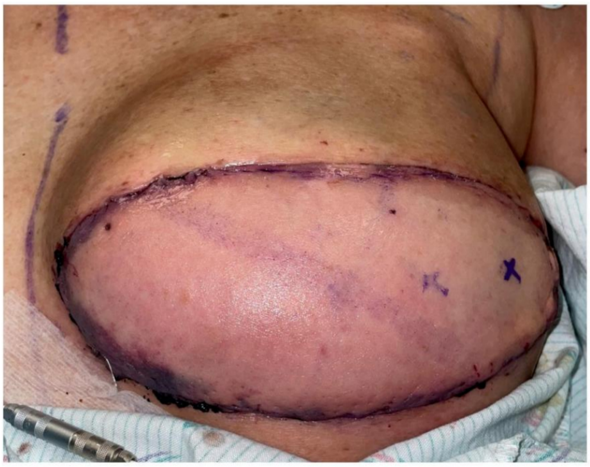

**Figure 4.** Left breast DIEP flap venous congestion seen on post operative. Please change to left breast DIEP flap with venous congeston on post operative day 2. DIEP: deep inferior epigastric perforator.

Medications to prevent and treat thrombus have been given to patients for decades. One of the oldest and most widely used anticoagulants is heparin[47]. McLean discovered heparin in 1916, but its clinical inception was not until 1935[47]. Heparin activates antithrombin III which inhibits thrombin, thus preventing conversion of fibrinogen to fibrin and inhibiting clot propagation. Heparin aids in the migration of endothelial cells while increasing negative charge, disturbs the fibrin lattice, and prevents platelet binding[16]. Heparin is an effective treatment for both arterial and venous thrombosis.

Heparin can be used locally as an irrigation solution or given to the patient as a systemic anticoagulant during microsurgery. Most microsurgeons use a heparinized saline solution at concentrations of 100 unit/mL as a local irrigation solution during microvascular anastomosis[48]. The heparinized saline solution as an irrigation solution during microvascular anastomosis has shown lower rates of thrombus formation compared to saline and lactated ringers. It provides high concentrations of heparin locally to the site of microvascular anastomosis to prevent thrombus formation without systemic anticoagulation effect. It can be used liberally during the primary anastomosis, during any anastomotic revision, or at the time of take back since the systemic absorption is minimal.

Numerous intraoperative and postoperative protocols with the use of pharmacologic anticoagulants exist in the literature, but there is no consensus on an ideal protocol. Systemic heparin given as a bolus at the time of microvascular anastomosis was routine in early microsurgery history. The studies report a range of doses from a flat 5,000 units up to 160 units/kg[46,49]. Although systemic heparin did not significantly increase flap survival or decrease thrombus formation, it did increase the risk of flap hematoma[48]. More recently, systemic heparin has not been given routinely but is reserved for patients with a history of thromboembolic events or in patients with extensive thrombosis at the time of flap salvage. Operative intervention for thrombectomy is the standard and systemic anticoagulation can be used to supplement flap salvage but does not replace operative exploration.

Dextran is a polysaccharide that is a product of fermentation with a molecular weight of 40 or 70. Dextran 40, a low molecular weight dextran, is a non-protein colloid given intravenously to expand plasma volume, cause hemodilution, and impair platelet function[50]. Dextran 40 was used for venous thrombosis prophylaxis and was typically given as 50-100 g the day of surgery and then a fixed dose of 500 mL daily for 2-5 days postoperatively in autologous free flap breast reconstructions infancy[50-52]. Later studies demonstrated free flap survival and thrombotic complication did not improve with routine use of dextran 40 and had an increased risk of other systemic complications[50,52,53]. Dextran 40 is no longer routinely used during standard autologous free flap breast reconstruction. However, for patients with a known hypercoagulable state, Dextran 40 has been described for thrombosis prevention[52].

Antiplatelet medication:

Antiplatelet therapy such as aspirin has been used as prophylaxis against thrombus in microvascular free flap surgery. Aspirin or acetylsalicylic acid inhibits cyclooxygenase, decreasing the production of arachidonic acid metabolism, including TxA2, a potent platelet aggregator and vasoconstrictor, thus inhibiting thrombus formation. Aspirin has been effective in the prevention of thrombus formation associated with cerebrovascular events and myocardial infarction[16]. Most recent studies demonstrated no significant reduction of thrombosis or flap failure with the use of aspirin but did increase the risk of hematoma[54,55]. These more recent studies have shifted the routine use of antiplatelet therapy to more restricted use for high-risk patients.

Patients with a history of unprovoked thromboembolic events, multiple miscarriages, or a known hypercoagulable state can successfully undergo autologous free flap breast reconstruction. However, the patients should be counseled on the risk of flap failure, reoperation, prolonged hospitalization, need for systemic anticoagulation, use of antiplatelet therapy, increased risk of bleeding complications, and significant risks of other thromboembolic events such as DVT, PE or stroke[56]. Consideration of hematology consultation and coagulopathy work-up before surgery can aid in the formulation of a proper anticoagulation plan to maximize success in this patient population. Hypercoagulability is a relative contraindication for autologous free flap breast reconstruction but not an absolute contraindication.

## MANAGEMENT

Up to about 5%-6% of autologous breast free flap reconstructions require operative exploration for vascular compromise[26,57]. Venous thrombosis is the most common cause of flap compromise, followed by arterial compromise, then hematoma or infection[48,57]. Timely recognition of vascular compromise is critical to flap survival, and early intervention is associated with higher flap salvage rates[16,57-59]. Intraoperative recognition and revision have significantly better prognoses and lower flap loss rates[48]. However, flap salvage rate has been shown to be highest within the first 24 h of the initial surgery with close to 94% salvage rates[26] and drops considerably further during the postoperative period, down to 12.1% salvage rate by postoperative day 3[12,26]. Improved salvage rates are associated with early intervention, the use of alternative recipient vessels, and fewer microsurgical revisions[60]. Close flap monitoring is most crucial in the first 24 h postoperatively to detect flap compromise [Figure 4], and if vascular thrombosis is suspected, then immediate return to the operating room is indicated.

Troubleshooting a failing free flap starts with distinguishing between arterial and venous compromise. The next step is to identify the cause of the problem and the mechanisms to correct the problem. The anastomosis can have technical issues such as intimal injury, a back walled suture in the anastomosis or inadequate recipient vessel. Mechanical problems such as hematoma, seroma, tight inset, pedicle kink or twist can all impair vascular flow. Problems within the flap include damaged perforators or pedicle, superficial dominant venous system with engorged SIEV and venous congestion with dark dermal bleeding.

The first step is to evaluate the arterial and venous anastomosis for adequate flow. This can be assessed with a strip test, intraoperative Doppler, or angiography with the use of indocyanine green[61]. If arterial or venous thrombosis is identified, maneuvers to remove the thrombus, correct the problem and reestablish perfusion are performed.

Direct thrombectomy:

When a thrombus within the vessel is suspected, the first step is to open or cut out the anastomosis. The vessels should be inspected for intimal injury or technical errors, such as a suture catching the vessel backwall that may be the source of thrombus. Direct thrombectomy can be performed at the anastomosis. Jewler's forceps can be used to gently milk the clot out of the vessel in an atraumatic fashion. The vessel is then copiously irrigated with heparinized saline irrigation. The vessel lumen is inspected again for any intimal injury and cut back to healthy tissue. Adequate flow of the recipient artery is evaluated to ensure complete removal of a possible proximal thrombus. The anastomosis is then revised, and the flap reassessed for perfusion.

Fogarty:

If the thrombus cannot be directly removed from the vessel using Jewler's forceps, then a Fogarty catheter can be used to perform the thrombectomy in free flap salvage[62]. The Fogarty catheter is passed distal to the thrombus, gently inflated the balloon to fill the lumen of the vessel without overexpansion, then slowly and gently pulled back to remove the clot. Fogarty catheters can damage the vessel lumen; therefore, it is imperative to limit the number of passes and not overexpand the balloon. Improper technique can denude the endothelium and cause intimal dissection, vessel rupture, or balloon rupture inside the vessel, leaving foreign material within the vessel lumen[63,64]. Once the thrombus has been removed, it is critically important to carefully inspect for any intimal injury before proceeding with anastomotic revision.

Thrombolysis:

If thrombectomy cannot be accomplished or distal thrombosis in the microvascular circulation is suspected, then targeted thrombolytic therapy is a crucial next step. Tissue plasminogen activator (TPA) is an enzyme that catalyzes the conversion of plasminogen to plasmin and breaks down fibrin in thrombus. TPA is a thrombolytic that can be used in flap salvage. Thrombolytics are often given when there is extensive clot burden, incomplete thrombectomy and evidence of microvascular thrombosis in the capillary system seen with no-reflow phenomenon. No reflow phenomenon occurs when arterial inflow has been reestablished and adequate venous thrombectomy has been performed, but there is inadequate venous flow from the flap vein.

Thrombosis at the level of anastomosis is adequately treated with thrombectomy and does not require thrombolytic intervention. However, distal arteriolar and capillary thrombus cannot be manually or mechanically evacuated but instead require chemical thrombolysis[65,66]. TPA is typically injected into the flap arterial system and allowed to marinate within the flap, then drain out the flap venous system. The goal is to target thrombolytic therapy within the flap without introduction into the systemic circulation. This allows higher doses of TPA to be administered without systemic complications. The typical dilution dose of TPA given during flap salvage is 1 mg/mL. A slow injection of 2-10 mg of dilute TPA is performed over a one-to-two-minute period[46,48,66,67], followed by a 10-15 min rest in the flap microcirculation. TPA administration can be repeated immediately thereafter until adequate venous flow has been accomplished[16,66,68]. TPA is directly administered to the flap during flap salvage and has not demonstrated an increased risk of hematoma to either the flap or abdomen[28,48]. Flap salvage rate with the use of thrombolytics is lower, likely due to the increased thrombus burden that necessitated thrombolytic therapy[48]. When salvaging a failing flap with significant clot burden, this is typically the last maneuver that can be done to void the flap of thrombus and reestablish perfusion.

## CONCLUSION

Reconstructive autologous free flap breast reconstruction is a growing field with innovation, technological advancements, broader application, and increased availability to patients. Core principles of microsurgery such as meticulous dissection, atraumatic vessel handling, adequate magnification, appropriate recipient vessel selection, and tension-free anastomosis with direct intima to intima contact are key maneuvers for a successful microsurgical reconstruction. Identification and correction of inflow or outflow problems intraoperatively can prevent thrombus formation and flap compromise. If vascular compromise is suspected postoperatively, immediate return to the operating room for exploration is a must. Every microsurgeon must develop an algorithm to first diagnose the problem, then implement a stepwise plan to execute the maneuvers needed to reestablish perfusion to the flap in order to successfully salvage a failing flap.

## DECLARATIONS

### Authors' contributions

The author contributed solely to the article.

### Availability of data and materials

Not applicable.

### Financial support and sponsorship

None.

### Conflicts of interest

The author declared that there are no conflicts of interest.

### Ethical approval and consent to participate

The University of Washington Medical Center stated that the study does not need to complete an IRB since the figures are examples of surgical techniques similar to a case report. The author states that there is no ethical concern since the photos do not include any PHI or patient identifiers such as a face or unique tattoos.

### Consent for publication

All patients gave consent for participation and publication.



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**Plastic and Aesthetic Research**

Review

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# Detecting flap compromise: an updated review of techniques to monitor microsurgical flaps post-operatively in breast reconstruction

**Priscila C. Cevallos[1,4,#], Daniel Najafali[1,3,#], Thomas M. Johnstone[1,#], Mimi R. Borrelli[1,2], Oscar J. Manrique[5], Gordon K. Lee[1], Rahim S. Nazerali[1]**

[1]Division of Plastic & Reconstructive Surgery, Department of Surgery, Stanford University School of Medicine, Palo Alto, CA 94304, USA.
[2]Division of Plastic & Reconstructive Surgery, Department of Surgery, The Warren Alpert Medical School of Brown University, Providence, RI 02903, USA.
[3]Carle Illinois College of Medicine, University of Illinois Urbana-Champaign, Urbana, IL 61801, USA.
[4]Geisel School of Medicine, Dartmouth University, Hanover, NH 03755, USA.
[5]Division of Plastic & Reconstructive Surgery, Department of Surgery, Strong Memorial Hospital, University of Rochester Medical Center, Rochester, NY 14642, USA.
[#]Authors contributed equally.

**Correspondence to:** Dr. Rahim S. Nazerali, Division of Plastic & Reconstructive Surgery, Stanford University School of Medicine, 770 Welch Road, Suite 400, Palo Alto, CA 94304, USA. E-mail: rahimn@stanford.edu

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## Abstract

Breast reconstructive surgery utilizing free tissue transfer has revolutionized the restoration of aesthetic and functional outcomes for patients. Even for the most routine free flap procedures, substantial hospital resources and costs are necessary. The effectiveness of free flap surgery, along with any reconstructive procedure, hinges upon meticulous patient selection, thorough pre-operative planning, well-informed peri-operative decision-making, and diligent post-operative monitoring and care for the patient. This article presents a review of standard clinical care monitoring techniques during the post-operative period, as well as the diverse strategies currently employed for post-operative flap monitoring.

**Keywords:** Flap monitoring, flap salvage, peri-operative monitoring, post-operative monitoring

## INTRODUCTION

Microvascular free flap surgery represents an innovative reconstructive technique that has greatly broadened the possibilities of surgical breast reconstruction[1-3]. Recently, microsurgery has seen a surge in popularity, accompanied by the introduction of new flap types and expanded indications for their use[4]. Nonetheless, the occurrence of flap loss remains a dreaded outcome, with reported failure rates ranging from 2% to 5%[5-7]. The considerable effort, time, and cost invested in microvascular breast reconstruction, spanning from pre-operative planning to post-operative follow-up, intensify the impact of such losses. Pre-operative planning, including possible imaging, may begin several months in advance. Post-operatively, patients are admitted to the intensive care unit (ICU) for hourly flap checks during the first 48 hours, when the flap is most vulnerable[8]. However, evidence has emerged suggesting that patients can be safely managed in step-down units instead of ICUs, allowing for accelerated discharges without an increased risk of flap loss[9]. Nevertheless, the costs associated with autologous breast reconstruction remain high. According to the Healthcare Cost and Utilization Project National Inpatient Sample dataset, the average cost of a deep inferior epigastric artery perforator (DIEP) flap for autologous breast reconstruction amounts to $22,677[10]. Flap failure amplifies this already high cost by 50% to 77%, primarily due to extended hospital stays and the need for secondary operations, thereby further compromising aesthetic and/or functional outcomes for patients[11,12].

Free flaps fail when tissue perfusion is compromised and unable to meet the metabolic demands of the tissue. This occurs from inadequate inflow, inadequate outflow, or intrinsic issues. Among these causes, venous insufficiency is the most frequently encountered, as veins are delicate structures prone to compression or damage from trauma or pressure[13-15]. Certain intraoperative decisions can increase the post-operative risk to the vasculature, such as the presence of perforators with long or tortuous courses. Additionally, elevated tissue pressure, resulting from factors like edema, hematoma, or external compression (e.g., positioning), can surpass perfusion pressure. Certain patient factors (e.g., age, disease, body weight, smoking, pharmacological history), as well as the specific flap type, can further contribute to the risk of experiencing any of these causes[16].

The initial 48-hour period following surgery poses the highest risk for flap failure, emphasizing the importance of employing sensitive strategies for early detection. Timely identification of flap failure can be instrumental in salvaging compromised flaps by prompting an urgent return to the operating room for diagnostic assessment and salvage attempts[8,17-21]. Flaps can be successfully salvaged in 28% to 90% of cases, but this range is highly dependent on the time of detection and take-back[22-25]. As the field of breast reconstruction continues to expand with various options, the challenge of early detection has necessitated the concurrent evolution of advanced flap monitoring techniques. For example, the introduction of nipple-sparing mastectomy, which may involve immediate reconstruction using a buried free flap without a skin paddle, requires the development of reliable monitoring methods independent of cutaneous visualization. In addition to thorough clinical examinations conducted by experienced professionals, several adjunctive post-operative monitoring technologies have been developed to complement physical examinations and contribute to reducing failure rates. This narrative review summarizes the techniques employed to facilitate early detection of threatened flaps in breast reconstruction, encompassing post-operative protocols, clinical examinations, and supplemental technologies. We also highlight novel advancements and future directions in plastic and reconstructive surgery.

## POST-OPERATIVE FLAP MONITORING

Most institutions follow specific protocols to ensure standardized care during the vulnerable post-operative period (48 h), typically in the ICU with trained staff and immediate access to the operating room if indicated. However, protocols vary significantly between institutions and flap types, and there remains no national consensus on the frequency or duration of monitoring. Recent discussions have emerged regarding the necessity of ICU monitoring for free flaps and the utility of monitoring beyond the initial 48 h[26,27]. A meta-analysis of head and neck microvascular reconstruction indicated that immediate post-operative ICU care did not lead to a decrease in flap failure or complication rates[28]. Frequent monitoring with hourly flap checks in the first 24 h is ideal, and this frequency can be decreased to every 4 h for the subsequent 2-3 days[29]. Shorter intervals, such as 30-minute intervals for the first 24 h, are considered optimal but can be time-consuming for surgeons, residents, or nursing staff. Additionally, microsurgical flaps carry the potential for infection and vascular trauma, which, when combined with manual examination and dressing procedures, may result in the development of hematoma and seroma[30]. Nevertheless, the primary objective of any post-operative monitoring protocol should be to optimize the patient's recovery and expedite their return to pre-operative status, thereby reducing hospital length of stay, the risk of infection or deep venous thrombosis, and costs of care[27]. Emerging research suggests that the implementation of an enhanced recovery after surgery (ERAS) program, which incorporates a transdisciplinary comprehensive approach to peri-operative care, may effectively reduce post-operative complications, shorten the length of stay, and minimize the need for morphine equivalent dosing[31]. High-volume institutions and greater provider experience have been associated with lower rates of flap failure, indicating the beneficial role of protocols[32,33]. Typically, patients are placed on strict bed rest and "nothing by mouth" for the first 24 h to prevent mechanical complications and allow for prompt re-exploration, if necessary. Volatile hemodynamic disturbances are avoided by using appropriate anesthetic/pharmacologic agents[20,34,35]. The use of anticoagulation remains controversial due to the delicate balance between undesirable bleeding and the risk of thrombosis[36]. However, prophylactic administration of heparin can be employed for deep-vein thrombosis prevention. Aspirin can be given for up to 30 days to inhibit platelet aggregation[37]. Low-molecular-weight heparin and aspirin, either alone or in combination, have shown similar efficacy in reducing macrovascular graft occlusion after surgery[36]. Lastly, patient education about the planned monitoring can help to manage their expectations, improve compliance, and enhance both flap outcomes as well as the overall patient experience[38].

### Bedside clinical evaluation

The clinical exam remains the cornerstone of flap monitoring after breast reconstruction, offering high sensitivity and effectiveness in detecting failing flaps without incurring the expenses associated with advanced monitoring technologies or specialized personnel. The clinical exam comprises four essential components: color, capillary refill, tension/turgor/swelling, and temperature [Table 1][39]. Unlike software-based techniques, the clinical exam has the capability to discern between adequate inflow (arterial) and outflow (venous) problems[39]. While not all patients will have a drain post-operatively, checking the drain's functionality, output color, and amount remains an important aspect of the clinical exam.

The effectiveness of the clinical exam relies heavily on the experience of the provider, who may assign varying importance to specific exam findings. Furthermore, patient-specific factors, such as skin tone and flap location, can influence findings; color changes, for instance, may be less pronounced in patients of different races and/or ethnicities[40,41]. The clinical exam has limitations in cases where flaps lack a cutaneous component (e.g., musculocutaneous flaps and other buried flaps). In such instances, surgeons may opt to expose a small portion of the flap at the skin surface temporarily to facilitate monitoring. Advanced monitoring technologies are particularly valuable when the clinical exam yields ambiguous or inconclusive results[42].

**Table 1. Clinical examination findings**

| | Characteristics | Arterial | Venous |
|---|---|---|---|
| Visual | Color | Pale | Cyanotic, dusky |
| | Capillary Refill | Delayed (> 3 secs) | Shortened (< 2 secs) |
| | Pinprick | Decreased | Dark venous outflow |
| Tactile | Temperature | Cold | Warmth |
| | Tension/Swelling | Mild swelling (late finding) | Increased turgor |

### Adjunctive techniques

Medical devices manufacture is an evolving field and an area of ongoing research. The objective of developing flap monitoring devices is to create compact, portable techniques that can provide consistent, real-time quantitative data on flap viability and perfusion[43-47]. The data obtained should be objective and not provider-dependent[48,49]. This data can assist surgeons in assessing flow patterns, quality, severity, and determining the need for reoperation[50].

Typically, techniques for flap monitoring are categorized as either non-invasive [Tables 1 and 2] or invasive [Table 3]. Multiple devices can be used in combination as adjuncts to the clinical exam. Generally, non-invasive techniques are more user-friendly, readily available, and cost-effective. Quantitative results that can be tracked over time enhance the sensitivity of detecting flap failure. Monitoring devices may enable flap monitoring without direct contact with providers, which was advantageous during the COVID-19 pandemic[51]. However, it is important to note that absolute values may have limitations and lack consistency between patients. Further, the use of monitoring machines may entail costs and require specialized expertise[48].

### Non-invasive techniques

*Photoelectric assessment with Doppler monitoring*

Doppler ultrasonography is widely recognized as one of the most effective and commonly used non-invasive methods for flap monitoring, with acoustic Doppler devices being the most predominant choice. Acoustic Dopplers operate by emitting sound waves of a specific frequency, phase, and amplitude into the tissue. These sound waves reflect off moving matter, primarily the red blood cells within the intravascular arterial and venous system in flaps. The movement of these cells leads to a slight shift in the frequency of the reflected sound waves, known as the Doppler effect, hence the term “Doppler”. The machine converts and transmits these reflections into an audible noise, which exhibits a pulsatile pattern in arterial flow and a quieter, more consistent pattern in venous flow[52-54]. Marking arterial and venous acoustic signals at the conclusion of the procedure with a single stitch can facilitate post-operative monitoring[55]. Acoustic Doppler sonography is a user-friendly technique that requires minimal training, and the devices are widely available, cost-effective, and highly portable[54]. However, it is important to note that the absence of a signal does not always indicate inadequate blood supply for flap viability, and the signal from key perforators may be difficult to distinguish from background noise caused by other vessels[53].

Laser flowmetry is another Doppler-based method employed for flap monitoring, although it differs from acoustic Doppler by measuring in *light* waves instead of *sound* waves[56]. Laser flowmetry probes are secured to the skin surface overlying the target vessel using dressings or sutures[57,58]. The data output provides real-time measurements of skin surface blood velocity and blood flow, which are accurate up to a depth of 8 mm[13]. However, these values only serve as relative indicators of blood flow, and while trends within the same patient are reliable, the data can be significantly influenced by various patient- and device-related factors[57,59]. As a result, there is no clear “cut-off” value suggestive of vascular compromise. Instead,

**Table 2. Non-invasive techniques for flap monitoring including main benefits and limitations**

| Non-invasive technique | Benefits | Limitations |
|---|---|---|
| Physical examination | ● Combines several signs (visual, tactile, drain output) to determine the risk of flap failure<br>● Opportunity for patient interaction to counsel, manage anxiety and concern, provide answers to questions, and participate in shared decision making post-operatively (e.g., ensuring bed rest and "nothing by mouth") | ● Subjective to provider's gestalt and experience<br>● Not quantitative<br>● Limited in flaps without cutaneous portion<br>● Lack of continuous monitoring |
| Acoustic doppler ultrasonography | ● Minimal training required<br>● Highly portable, bedside utilization<br>● Cost effective<br>● Intra- and post-operative use<br>● Simple to pair with concurrent physical examination | ● Accuracy can be impacted by noise from vessels near the target vessel<br>● Blood flow detected is not always sufficient to sustain flap<br>● Unsuitable for buried flaps |
| Laser doppler flowmetry | ● Intra- and post-operative flap use<br>● Relatively easy to interpret and can be monitored by many members of the care team<br>● Blood flow velocity readings are continuously reported, giving a quantitative picture of blood flow<br>● Accurate flow and velocity measurements in vessels up to 8 mm deep | ● Blood flow measurements are not absolute but relative, depending on specific device and patient parameters, making a definitive threshold for vascular compromise elusive<br>● Many of the pieces of the laser flowmeter apparatus are fragile and can be easily broken by patients and providers alike<br>False reports of inadequate flow can be reported when a blood clot or other obstruction blocks the laser's path |
| Color duplex ultrasound | ● Improved sensitivity for detection of vascular compromise compared to other Doppler methods<br>● Can detect and discern discrete vascular pathologies | ● Large and unwieldy<br>● Requires expert operation by a technician as well as the presence of an attending microsurgeon or resident to orient the device<br>● Expensive to acquire and maintain<br>● Not as useful in the intraoperative setting |
| Surface temperature monitoring with/without infrared thermal device | ● Cost effective<br>● Bedside<br>● Real-time<br>● Not provider dependent<br>● Can be non-contact<br>● Quantitative<br>● Trends can be monitored overtime | ● Limited value in isolation without combined clinical judgment (spurious results possible, e.g., if not in contact)<br>● Cannot be used in flaps without cutaneous portion |
| Tissue oximetry | ● Bedside<br>● Real-time<br>● Not provider dependent<br>● Quantitative<br>● Trends can be monitored overtime<br>● Highly portable | ● Readings influenced by ambient light<br>● Readings influenced by patient movement<br>● Readings can vary by device type<br>● Different skin colors have been reported to produce different results<br>● Does not directly assess vascular patency (measures end tissue oxygenation)<br>● Cost |

significant drops or variations in measurements are used to indicate changes in flap perfusion, and this can be easily discerned by healthcare personnel and family members. It should be noted that laser Dopplers employ delicate fiber optic cables that are easily damaged. Finally, false reports of inadequate flow are not uncommon, even when the tissue is well-perfused, such as in cases when a blood clot or other obstruction disrupts the laser's path[50].

Color duplex ultrasound is a less commonly employed Doppler-based method for non-invasive flap monitoring, utilizing a device that emits and detects the entire visual spectrum of light[60]. The device detects the Doppler effect, which is the change in frequency between the emitted and reflected visible light waves. These light waves are transduced to create a grayscale ultrasound image that is augmented with color to indicate the direction and position of blood flow. Color duplex ultrasound has proven successful in monitoring various flaps with different vessel sizes, including fasciocutaneous perforators for DIEP flaps[61]. A variant device known as "power Doppler imaging" uses higher frequency waves to detect vessels with smaller diameters, reaching as low as 0.2 mm[62]. Color Doppler ultrasound is highly sensitive in detecting compromised vessels, enabling the assessment of vessel caliber, patency, flow characteristics, anomalies, and

**Table 3. Invasive techniques for flap monitoring, including main benefits and limitations**

| Invasive technique | Benefits | Limitations |
|---|---|---|
| Implantable doppler & venous coupler | ● Cost effective<br>● Usable on all types of flaps<br>● Ease in signal reading | ● May cause vessel damage<br>● Complex operative technique<br>● High false positive rates |
| Transcutaneous oxygen tension monitoring | ● Very sensitive to declines in tissue oxygenation<br>● Easy to monitor<br>● Can be used for monitoring of buried flaps<br>● Provides a direct measurement of oxygen availability at the cellular level | ● Invasive, requires tunneling with some extra dermal components<br>● May be unreliable in large cutaneous flaps or flaps with large within-flap temperature gradients |
| Biochemical markers | ● Cost effective<br>● Reflect the flap's local environment<br>● Patterns of known metabolites exist to direct thresholds and clinical decisions | ● Limited efficacy among diabetic patients<br>● Not applicable for buried flaps |
| Microdialysis | ● Can be used when clinical examination is not possible<br>● Detects flap failure hours before it becomes clinically evident<br>● Gives a quantitative metric | ● Causes local tissue trauma<br>● Cost<br>● High false-positive rates<br>● May require an equilibrium period<br>● Securing the catheter can be difficult |
| Fluorescence imaging | ● Broadly used with clinical applications beyond plastic surgery<br>● Can leverage different fluorophores<br>● Handheld devices and probes have been developed<br>● Ease of use | ● Additional staffing requirements are not as high as other techniques<br>● Continuous monitoring is difficult<br>● Repeat injections of dyes may be required<br>● Limited circulation of fluorophores |
| Technetium-99m sestamibi scintigraphy | ● Can monitor muscle flap viability reliably<br>● Reveals distal ischemia or hypoperfused area in muscle tissue<br>● Short half-life of ~6 h | ● Limited to a majority of case reports and series with the need for more robust studies<br>● May need to be combined with other techniques, such as Doppler, to visualize the blood vessel integrity |
| Perfusion-weighted MRI | ● Is relatively non-invasive, and risks to the patient are limited to those imposed by the administration of contrast<br>● Provides a picture of entire-flap perfusion | ● Resource intensive<br>● Requires support staff at each step<br>● Requires serial studies if flap is to be monitored over time |

pathologies[54]. However, its specificity in identifying vascular compromise, like other Doppler devices, is limited. Color duplex ultrasound machines are more expensive, less portable, and require trained personnel for operation. Typically, the presence of a microsurgeon is necessary to aid in the anatomical orientation of the transmitter, while a radiology technician is required for consistent image acquisition and interpretation.

*Surface temperature monitoring*

In addition to tactile assessment in the clinical exam, flap temperature can be measured and monitored using temperature probes placed on the skin surface. The arterial blood supplying the flap carries heat, which is released into the surrounding extravascular tissue through convection[63]. Congested flaps exhibit distinct temperature drop patterns compared to ischemic flaps. A temperature drop of 3 °C (37 °F) at the center of a skin paddle indicates arterial thrombosis, while a uniform temperature drop of 1-2 °C (33.8-35.6 °F) across the skin surface of a flap suggests venous compromise[64]. Typically, surface temperature monitoring can detect flap compromise starting from the eighth hour post-operation[65]. Measurement of flap temperature can be easily performed using inexpensive strips (~1$ per strip) placed on the surface of free flaps, and the values can be compared to the temperature of adjacent non-operated skin[66].

Recently, infrared thermography has emerged as a novel method of post-operative flap monitoring in breast reconstruction[67,68]. This thermal imaging technology converts the detected temperature values through infrared radiation into pixel values, resulting in a visual display of cutaneous blood flow. Infrared thermography has demonstrated a sensitivity of 96% and a specificity of 75%, indicating its potential as a valuable adjunct to clinical assessment[67].

Surface temperature monitoring has its limitations when applied to buried and intraoral flaps[69], and it can be influenced by various external factors, including ambient room temperature and air flow. Research suggests that in patients who have undergone DIEP breast reconstruction, surface temperature monitoring using a dual-channel digital thermometer (Raytek, Norway) lacks sensitivity and is inferior to clinical examination conducted by trained nurses[70]. In the case of large perforator flaps such as DIEPs, the temperature difference between the flap surface and adjacent non-flap surface may be minimal, reducing the utility of surface temperature monitoring. However, it may still have value in monitoring perfusion in scenarios like digit replantation and small free flap reconstruction[71].

*Mobile smartphone monitoring technology*

Given the widespread use of smartphones, leveraging this technology to enhance communication and enable remote post-operative monitoring through adjunct devices presents a rapid, cost-effective, and non-invasive option for early detection of free flap failure.

Innovative text messaging systems that alert surgical teams of post-operative monitoring tissue oximetry readings below a certain threshold show promise in identifying potential flap loss and facilitating prompt notification[72]. With smartphones equipped with advanced digital photography capabilities, earlier discharge and continued remote flap monitoring at home with improved communication between patients and healthcare staff may soon become possible. Studies suggest that the use of remote digital photography may even lead to reduced response time to re-exploration and improved flap salvage rates[39,73]. The usefulness of digital photography by patients becomes even more apparent when uploaded through dedicated post-operative monitoring platforms, enabling easy comparison with previous images[74]. By employing free applications on smartphones, continuous real-time streaming of free flap tissue to surgeons for decision-making can be achieved[75]. Kiranantawat *et al*. developed a smartphone application that identifies color changes indicative of compromised flaps for monitoring purposes[76]. Furthermore, the integration of machine learning algorithms holds the potential to reveal previously undetectable findings to the human eye[77].

Digital thermographic cameras, such as the FLIR ONE ™ device (FLIR systems, Wilsonville, Ore), can be attached to a smartphone to capture thermal images of a free flap, enabling the detection of temperature differences with high sensitivity. These images can be easily transmitted to healthcare providers for evaluation and early identification of flap failure. While this device has primarily been used by trained operators in the peri-operative setting for DIEP flap reconstruction, advancements in technology and reduced costs hold the potential for future remote use by patients[78]. However, it is important to note that this device is influenced by external factors such as vasoconstriction, warming blankets, or low ambient temperature, which may impact its accuracy.

*Tissue oximetry*

Tissue oximetry utilizes both near-infrared spectroscopy (NIRS) (wavelength: 800-2,500 nanometers) and visible light (wavelength: 40-700 nanometers) to non-invasively measure flap perfusion[79-83]. Examples of tissue oximeters commonly used in the post-operative setting include Spectros T-Stat (Houston, TX, USA) and ViOptix T.Ox (Newark, CA, USA) [Figure 1A]. The functioning principle of most oximetry systems follows a standard pattern: the oximeter devices emit light towards the flap tissue, a portion of which is absorbed by the blood. The remaining light is reflected and captured by the sensors in the oximeter. Oxygenated and deoxygenated blood reflect and emit light differently, and the oximeter probes utilize these properties to estimate the percentage of oxygenated and deoxygenated hemoglobin within the underlying tissue[13,69]. A decrease in tissue oxygenation detected by NIRS has shown high specificity and sensitivity in

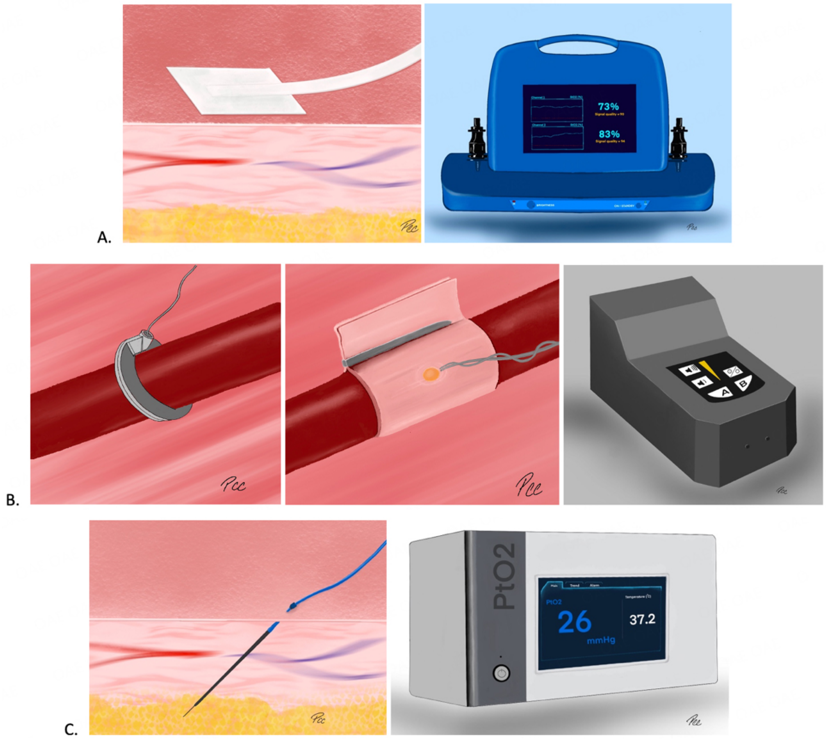


**Figure 1.** Types of non-invasive and invasive techniques used for flap monitoring. (A): Example of a non-invasive tissue oximetry device; (B): Example of an invasive venous coupler and implantable Doppler monitoring device; (C): Example of an invasive transcutaneous oxygen tension monitoring device.

detecting flap failure[84]. However, conflicting reports regarding time-based trends in post-operative flap oximetry exist, with some observing transient decreases, increases, or stable flap oxygenation. These trends may be attributed to fluctuations in hemodynamic status (i.e., pulse oximetry) rather than perfusion status[85].

Tissue oximetry devices serve as valuable adjuncts for flap monitoring due to their high portability, user-friendliness, and ability to provide continuous monitoring. Rather than focusing on absolute values, observing the individual oximetry trend of a flap provides greater insight into perfusion. It is important to note that while oximetry indicates organ tissue oxygenation, which directly reflects flap viability as opposed to vascular patency[80], there can be delays in detection of up to 1-5 h[86]. Additionally, environmental light and variations in skin tones can potentially interfere with accurate readings[40-41,87]. In a recent study involving over 1,000 free flaps for breast reconstruction, tissue oximetry offered no benefit over clinical judgment, although other reports present contradictory evidence[88,89]. Bai *et al.* conducted experiments using porcine models to test the use of NIRS in flaps without cutaneous paddles. NIRS probes were buried into muscle tissue to provide continuous monitoring of local tissue oxygen saturation, demonstrating the capability of heat convection probes to detect changes in tissue microcirculatory blood flow[43,90].

Implementation of tissue oximetry for routine monitoring incurs additional costs, with equipment expenses amounting to $16,500 and disposable sensor costs of $150 per unit[13]. These initial costs must be weighed against the estimated savings, which have been reported to reach as high as $1,667 with the utilization of NIRS monitoring protocols in DIEP flap reconstruction[91].

### Invasive techniques

Invasive techniques for free flap monitoring are utilized for buried flaps when surface monitoring is not feasible. An ideal implantable device should possess the following characteristics: (1) enable continuous real-time monitoring of anastomotic patency; (2) reliably distinguish between arterial and venous occlusions; and (3) be applicable for monitoring both cutaneous and buried flaps. Various devices have been developed for invasive flap monitoring and ongoing research focuses on device refinement[42-47]. Current electronic flap monitoring techniques offer qualitative and quantitative information on flap perfusion, including flow patterns and quality[48-50]. However, there are limitations associated with the use of invasive monitoring techniques, such as the requirement for expert interpretation of results, inadequate equipment designs and potential malfunction, and high costs[48].

*Implantable Doppler & venous coupler*

Swartz *et al*. were the first to publish on the utilization of an implantable probe for continuous monitoring of microvascular anastomoses[92]. Their study employed a 20-MHz ultrasonic Doppler probe encased in a silicone sleeve positioned distal to an anastomosis, demonstrating the probe's effectiveness in monitoring patency and occlusion up to 4 weeks post-operatively[92]. This system, now referred to as the Cook-Swartz implantable Doppler (Cook Medical®, Ireland), has since become a valuable tool in clinical post-operative monitoring, particularly for buried flaps, such as those in nipple-sparing mastectomy procedures [Figure 1B]. Apart from the Cook-Swartz implantable Doppler used in buried flaps, an external transcutaneous Doppler signal can be marked on the mastectomy skin intra-operatively, following temporary clamping of the flap vascular pedicle, to minimize potential signals confusion between the mastectomy skin and the flap. In 1994, Swartz *et al.* discovered that Cook monitoring of venous anastomoses exhibited greater sensitivity to both venous and arterial thrombosis compared to solely detecting arterial anastomoses[92,93]. Since its introduction, there have been numerous advancements aimed at enhancing the monitoring of capabilities of Cook Doppler devices, which heavily rely on their positioning. These improvements encompass non-attachment around a venous pedicle, microclip fixation, suture fixation, and elongation of the silicone cuff. The success of these developments has varied, and their implementation may lead to prolonged operating times and necessitate technical expertise to ensure proper intraoperative placement[94,95]. Additionally, complications associated with Cook Dopplers include retained wires, pedicle laceration during extraction, and signal interruption due to clot formation around the probes[96].

The Flow Coupler is an additional invasive post-operative monitoring device designed to detect the patency of microsurgical anastomoses [Figure 1B]. Developed by Synovis Life Technologies in 2010, this device consists of a removable 20-MHz Doppler that provides real-time data on vessel patency. Preliminary data suggests that the Flow Coupler is both effective and reliable. However, studies comparing the results of the Cook-Swartz implantable Doppler and the Synovis Flow Coupler have not identified any significant differences in false positive or false negative results, or the need for salvage procedures[97]. The Flow Coupler may have a higher false positive rate and a higher incidence of vascular thrombotic events compared to non-flow coupler devices[98]. A pooled meta-analysis revealed that the use of a Cook-Swartz Doppler in combination with clinical monitoring is associated with significantly higher rates of flap survival but also increased Incidence of false positive results[96]. When compared to microdialysis, the implantable Cook-Swartz Doppler demonstrated earlier detection of flap compromise by 60 min and reduced time to re-exploration compared to external Doppler monitoring[99,100].

*Transcutaneous oxygen tension monitoring*

Tissue oxygen tension monitoring is a commonly used invasive method to assess flap perfusion and viability [Figure 1C][101]. This technique involves the use of probes that compare the partial pressure gradient between oxygen delivered at the capillary level and mitochondrial consumption, providing a direct estimation of oxygen availability at the cellular level[102,103]. To achieve tissue oxygen tension monitoring, an implantable probe and microcatheter are typically used, with the microcatheter containing an electrode functioning as an oxygen sensor[104]. When the apparatus is placed in the flap, it measures the reduction of molecular oxygen using a cathode and polarized circuit[101,105]. Rapid declines in oxygen tension detected by these sensors indicate potential vascular compromise[106].

Oxygen tension monitoring devices offer real-time measurements of oxygenation, allowing for trend analysis over time. These measurements are easily understandable by all members of the care team and are considered highly sensitive indicators of end-organ tissue perfusion[107-109]. However, these devices require invasive procedures for placement and removal of probes, which carries the risk of flap infection. Furthermore, the temperature calibration of probes makes them susceptible to the influence of external environmental factors and subtle temperature variations within the flap. Consequently, some authors have suggested that these systems may be more prone to bias and could benefit from the integration of other flap monitoring approaches, particularly in cases involving large areas of skin or significant temperature gradients within the flap[101,110].

*Fluorescence imaging*

Fluorescein angiography was one of the early applications of fluorescence in measuring flap perfusion[111]. Depending on the specific use case, different fluorophores can be leveraged to monitor perfusion quality and flap viability. Indocyanine green fluorescence angiography (ICG-FA) has been extensively used for peri-operative assessment of anastomotic patency and has found applications in various fields, such as cardiac function monitoring, liver function testing, neurosurgery, and ophthalmology. As a non-toxic, water-soluble dye with a half-life of 3-4 min, ICG can be safely injected into patients to visualize microvascular patency and tissue perfusion. Adelsberger *et al.* conducted a study involving 210 free flaps to assess vascular thromboses post-operatively. They used a handheld infrared camera in a dark room to visualize the distribution of the dye after injection over a 4-hour interval for the first 72 h[112]. The combination of ICG-FA and clinical examination yielded an 85% success rate in detecting vascular thromboses. Revision rates decreased from 19% to 12%, with a false negative revision rate of 4.8% over a span of 3 years, accounting for a training and habituation period. Others have combined ICG injection with scanning of flap using a near-infrared camera with an additional pinprick test to evaluate perfusion status by fluorescent imaging of bleeding. This approach facilitates the need for repeated pinpricks and may lead to subsequent complications, such as hematoma. However, it is particularly useful in patients with questionable perfusion[113]. Hitier *et al.* determined that intraoperative fluorescence after anastomosis to the recipient vessels serves as a reliable predictor of post-operative flap viability, capable of indicating abnormal values 16 hours prior to clinical evidence of flap failure using fluorescence signal thresholds[114]. Despite its usefulness, ICG-FA has certain limitations. It does not allow for continuous monitoring and requires repeat injections. Exploring other fluorophores with increased circulation time may enable continuous monitoring and provide activation at different wavelengths.

*Other monitoring techniques*

Given the significant advancements in post-operative monitoring techniques for autologous breast reconstruction proven to have a high sensitivity and specificity, there has been a shift away from more outdated and costly monitoring techniques. These include the use of biochemical markers, microdialysis, technetium-99m sestamibi scintigraphy, and perfusion-weighted MRI. While we include them here for a comprehensive perspective, it is important to note their limitations in terms of invasiveness, cost, and lack of continuous monitoring.

*Biochemical markers*

Using a femoral vessel anastomosis rodent model, Su *et al*. reported in 1982 that both venous and arterial occlusion decreased tissue glucose content and increased lactate content. Venous occlusion was found to have a more detrimental effect on flap survival[115]. The theory behind this observation suggests that vessel occlusion impairs perfusion, resulting in decreased tissue oxygenation and glucose delivery, leading to a shift from aerobic to anaerobic metabolism[116-118].

Since then, tissue biomarkers such as glucose with or without lactate have been successfully used for flap monitoring in the clinical setting[119-122]. These biomarkers have been utilized at different threshold values and rates of change to indicate venous occlusion, showing variable sensitivity and specificity. Measurement of flap tissue glucose levels is a simple, inexpensive, and rapid option for post-operative flap monitoring compared to other techniques[13]. However, the efficacy of glucose measurements in detecting arterial occlusion and in diabetic patients is limited, and this technique lacks applicability in buried flaps[123-125].

*Microdialysis*

Microdialysis has been employed as a method for microinvasive monitoring of flap ischemia in various flap types, including myocutaneous, buried flaps and TRAM flaps[126-129]. This technique involves a double-lumen catheter with a semipermeable membrane at the end, which draws fluid from the flap through the membrane into the catheter. By continuously assessing small molecules in the dialysate, such as glucose, lactate, pyruvate, and glycerol, microdialysis provides a measure of the flap's metabolic activity. These values can be compared values to a baseline value or ratios, non-flap tissue away from the operative site, or reference values. The analysis of the interstitial fluid contents allows for flap examination without the need for direct clinical examination and can potentially detect ischemia one to two hours before clinical evidence of flap failure[130]. This technique is limited by its high cost and relatively high false-positive rate. Additionally, widespread adoption is restricted by the requirement for a skilled nursing team and clinical familiarity with microdialysis.

*Technetium-99m sestamibi scintigraphy*

Technetium-99m (99mTc) sestamibi, a metabolically inactive radionuclide, is injected and measured by scintigraphy to visualize areas of tissue hypoperfusion and evaluate microvascular anastomotic patency. It has been employed to assess free muscle flap viability, particularly in detecting a delayed secondary thrombosis caused by microemboli, which may not be evident using other techniques relying on more obvious signs[131-133]. Additionally, this technique permits visualization of partial necrosis, providing important information of surgical significance in the case of future surgical debridement[131].

*Perfusion-weighted MRI*

Several reports have described the use of contrast-enhanced magnetic resonance imaging (MRI) as a method for analyzing flap perfusion, with parameters optimized for vascular contrast uptake[134,135]. Compromised flaps exhibit significantly reduced signal intensity on MRI[134,135]. Perfusion-weighted MRI can assess the overall perfusion of the entire free flap. The drawbacks of this technique are mostly resource-related: the financial and time-based costs of MRIs are high. Additionally, perfusion-weighted MRI does not directly evaluate vascular pathology and necessitates specialized support staff throughout the process.

## Future directions

In the past 40 years, post-operative flap monitoring technologies have advanced to provide continuous, remote, highly sensitive, and non-invasive options for surgeons. Lee *et al*. developed a new dual-camera flap monitoring system that combines mask region-based convolutional neural networks in the visible-light system with infrared systems to address lower image resolution challenges posed by illumination changes and patient movement[136,137]. This study demonstrated earlier detection of vascular congestion compared to manual observation. Kim *et al.* utilized a novel negative pressure wound therapy technique using a transparent film to monitor the entire flap, allowing for the examination of flap color changes, capillary refilling status, and flap warmth without missing any portions of the flap[30]. This technique has been shown to reduce monitoring time and costs[30]. Videocapillaroscopy technology shows further promise in evaluating circulatory changes on the skin surfaces of free flaps while deliberately clamping pedicle vessels[138]. Bucknor *et al.* described a novel, non-invasive, optical oxygen-sensing liquid bandage for post-operative monitoring in autologous breast reconstruction[139]. This technique uses a camera to continuously capture the intensity of oxygen phosphorescence and fluorescence. Hummelink *et al.* used a "free flap patch" adherent to a flap to continuously measure temperature and tissue saturation[140]. The development of novel, patient-friendly wearable wireless monitors is ongoing, promising rapid and real-time insights into tissue perfusion.

## CONCLUSION

Careful post-operative monitoring of free flaps following breast reconstructive surgery is crucial for determining procedural success. While the clinical examination remains the gold standard for post-operative flap monitoring, various adjuncts exist to complement and enhance our understanding of flap perfusion.

## DECLARATIONS

### Authors' contributions

Made substantial contributions to the conception and design of the study and performed data analysis and interpretation: Cevallos PC, Najafali D, Johnstone TM

Performed data acquisition, as well as provided administrative, technical, and material support: Borrelli MR, Manrique OJ, Lee GK, Nazerali RS

### Availability of data and materials

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### Conflicts of interest

All authors declared that there are no conflicts of interest.

### Ethical approval and consent to participate

Not applicable.

### Consent for publication

Not applicable.



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Review

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# Mitigating the impact of skin necrosis in reconstruction after nipple-sparing mastectomy

**Grant G. Black**[#], **Yunchan Chen**[#], **Marcos Lu Wang**, **Karina Condez**, **David M. Otterburn**

Division of Plastic and Reconstructive Surgery, NewYork-Presbyterian/Weill Cornell Medical Center, New York, NY 10065, USA.
[#]Authors contributed equally.

**Correspondence to:** Dr. David M. Otterburn, Division of Plastic and Reconstructive Surgery, NewYork-Presbyterian/Weill Cornell Medical Center, 525 East 68th Street, New York, NY 10065, USA. E-mail: dmo9004@med.cornell.edu

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## Abstract

Skin flap necrosis is a common postoperative complication after breast reconstruction, with an incidence of up to 43.4% among patients undergoing nipple-sparing mastectomy. Necrosis can adversely impact aesthetics due to the need to excise nonviable tissue, and increase the risks of infection, implant loss, nipple-areola complex sacrifice and malposition. Patient-specific factors including age, body mass index, and breast size may affect the risk of necrosis. Mastectomy and reconstruction techniques (i.e., choosing between skin- and nipple-sparing mastectomy, and between autologous and alloplastic reconstruction) may also influence necrosis rates. Intraoperative measures such as indocyanine green angiography and autologous skin banking, and the postoperative use of nitroglycerin paste for high-risk patients and warming blankets for autologous reconstruction are methods to help prevent and minimize the morbidity of skin necrosis. Herein, we share our institution's approaches to predicting and mitigating skin necrosis, and methods of optimizing outcomes for breast reconstruction patients.

**Keywords:** Mastectomy, breast reconstruction, necrosis, autologous flap, implant

## INTRODUCTION

Breast cancer is one of the most common forms of neoplasia in women; approximately 1 in 8 will develop it in their lifetime[1]. The number of mastectomies performed each year is rising both as a factor of the growing incidence of breast cancer and the number of patients seeking prophylactic mastectomies for risk reduction[2,3]. As such, over 137,000 breast reconstructive procedures following mastectomy were performed in the United States in 2020[4]. Roughly 75% of these surgeries involved implant-based, or alloplastic, reconstruction, while the other 25% utilized autologous reconstruction.

The types and incidences of complications following both mastectomy and reconstruction are well-documented. Among the most prevalent of these adverse effects is mastectomy skin flap necrosis, caused by disruption of the vascular supply to the breast. Damage to the subdermal plexus and its deep perforators with subsequent skin necrosis has a documented incidence ranging from 1.4% to 43.4%[5-9]. This wide range is attributed in part to a lack of uniform definition of necrosis; different studies classify necrosis by various criteria, including the intervention needed, the timing of occurrence, the depth of necrosis, or the surface area of tissue involved[6].

Though the framework for determining necrosis may be up for debate, the negative impact is clear: while mild necrosis can be managed with local wound care, moderate to severe skin flap necrosis often requires debridement and reoperation in both alloplastic and autologous reconstructions[8,10,11]. Necrosis can lead to infection and/or implant exposure, ultimately resulting in reconstructive failure[6]. Prior studies have shown that mastectomy skin necrosis greater than 6 $cm^2$ after autologous reconstruction benefits from operative management due to prolonged healing with conservative care, and that necrosis exceeding 10 $cm^2$ can lead to severe breast distortion[11,12]. Revision for breast reconstruction is also costly and resource intensive[13,14].

The risk of developing mastectomy skin flap necrosis is influenced by a myriad of factors, including patient demographics and comorbidities, mastectomy technique, and reconstructive pathway. This review paper will detail each of these known risk factors, as well as the intraoperative techniques used to anticipate skin necrosis. We will also review postoperative strategies to prevent skin necrosis. Lastly, we will discuss the future directions of necrosis detection and treatment.

## PREOPERATIVE PLANNING

### Patient-specific risk factors

A number of both retrospective and prospective studies have identified potential risk factors for developing breast skin necrosis after mastectomy. Independent of both mastectomy technique and reconstruction type, these established determinants include increased body mass index (BMI), older age, diabetes mellitus, and tobacco use[10,12,15-18]. A history of breast irradiation and surgery, including augmentation and reduction, has also been shown to increase the risk of skin necrosis[5,9,17]. Based on our ten-year institutional cohort of 530 patients and 902 breast reconstructions, obesity (BMI > 30 $kg/m^2$) and hypertension were risk factors across all patients[19].

Increased breast size has also been implicated in skin necrosis, as measured through proxies such as mastectomy specimen weight and volume on mammograms[7,9,20]. However, we have shown that direct anatomic measurement in the preoperative period provides similar predictive power. During the initial consultation, we routinely collect five anatomic breast measurements: nipple-sternal notch distance, nipple-inframammary fold distance, chest width, breast height, and breast circumference [Figure 1]. In our experience, the risk of necrosis increases significantly with a nipple-sternal notch distance > 27 cm, nipple-inframammary fold distance > 8.5 cm, chest width > 15 cm, breast circumference > 29 cm, and breast height > 10.5 cm[21].

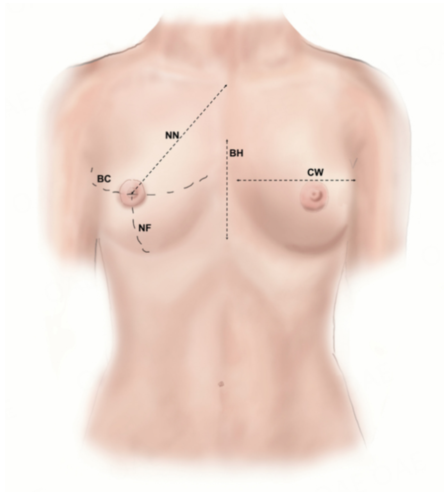


**Figure 1.** Breast size measurements that our institution takes preoperatively and uses to anticipate the risk of breast skin necrosis after mastectomy. BC: breast circumference; NN: nipple-notch distance; NF: nipple-inframammary fold distance; BH: breast height; CW: chest width.

These measurements not only provide valuable information during reconstruction, such as when selecting tissue expander size or determining DIEP flap dimensions, but they also allow us to calculate breast skin surface area through geometric approximations. In a prior study, we approximated surface area using a cone without its base and a half ellipsoid, and showed that the risk of necrosis increases significantly with surface area > 212 $cm^2$ on conical estimation and > 308 $cm^2$ on half ellipsoid estimation[21].

### Mastectomy technique

Nipple-sparing mastectomy (NSM) has been shown to lead to psychosocial and sexual well-being compared to skin-sparing mastectomy (SSM)[22]. However, while NSM is oncologically safe, poor vascularity of the nipple-areola complex (NAC) can negatively impact overall results[23]. There is still inconclusive evidence that NSM leads to higher rates of skin necrosis than SSM; Matsen *et al.* and Lee *et al.* demonstrated a significant difference between the two, but Andersen *et al.* and Gould *et al.* found equal rates of skin necrosis[7,17,18,20]. The decision to pursue NSM *vs.* SSM is thus one that must take into account the balance between the risk of complications and quality of life, the comfort level of the breast surgeon performing the procedure, and the risk of skin necrosis at each practitioner's institution as surgical technique will vary.

One of the most significant contributors to breast skin necrosis, particularly in NSM, is the thickness of the mastectomy skin flap. Prior studies have reported that mastectomy skin flaps less than 5-8 millimeters in thickness place patients at increased risk of necrosis[13,15]. Frey *et al.* even introduced an incremental range of ideal flap widths as a function of patient BMI[24]. However, a predetermined thickness can be difficult to implement practically due to benign variations in anatomy; the thickness of breast skin and subcutaneous fat may not correlate with weight or age, and a distinct layer of superficial fascia may be present in only up to 56% of patients[15,25]. As reconstructive surgeons, we rely on our breast surgery colleagues' expertise in determining the appropriate skin flap thickness, treading a fine line between adequate oncologic resection and risking postoperative skin necrosis.

There are several surgical approaches for NSM, notably via inframammary fold (IMF), radial horizontal, radial vertical, and periareolar incisions. Periareolar incisions encompassing more than 30% of the areolar circumference are an independent risk factor for necrosis[26]. In fact, periareolar incisions have been shown to result in necrosis more than radial horizontal, vertical and IMF incisions[5,15,27]. Carlson *et al.* reported an odds ratio of 9.69 ($P$ = 0.014) when studying nipple necrosis after periareolar incision compared to all other incision types. After mastectomy, the branches of the internal mammary and lateral thoracic vessels that normally perfuse the NAC are disrupted; periareolar incisions further damage the subdermal plexus supplying the NAC, resulting in skin necrosis that particularly impacts this region. Our institution, like many others, preferentially uses IMF incisions when possible due to the reduced rates of skin necrosis, improved surgical access to the breast pocket, and aesthetic benefits of concealing the scar below the lower pole of the breast.

#### Reconstructive options

Patients deciding to pursue either implant-based or autologous reconstruction must consider oncologic treatment regimens, patient comorbidities, aesthetics, and recovery time, among other factors. Though skin necrosis is not the only outcome of interest, it is highly influenced by this choice; Sue *et al.* demonstrated a threefold difference in necrosis rates between autologous flaps and implants (30.4% in flaps, and 10.6% in implants), and Lee *et al.* found a higher rate of necrosis in free flaps compared to pedicled flaps, with an odds ratio of 1.575[18,28]. This increased risk is attributed to the acute stress placed on the breast skin during the microvascular reconstruction, compared to the often-employed two-stage alloplastic technique of slowly inflating tissue expanders (TE) before transitioning to permanent implants. Supporting this theory, higher initial TE fill volumes have been shown to predispose patients to skin necrosis[10,20]. A study by Sue *et al.* found that initial TE volumes greater than 200 mL were associated with an 11.4% risk of necrosis, compared to 5.4% in TEs filled less than 200 mL initially ($P$ = 0.02)[10].

Our own study of 902 breasts across 530 patients found a significant difference between breast skin necrosis rates after immediate reconstruction with either DIEP flaps (373 breasts, 26.8% necrosis) or tissue expanders (529 breasts, 15.5% necrosis). However, after controlling for BMI and patient comorbidities, this difference became insignificant[19]. As our DIEP cohort had a significantly higher BMI, mastectomy specimen weight, and prevalence of diabetes, it is possible that these factors, rather than the procedure itself, may be to blame for increased rates of skin necrosis. Higher-BMI patients are better suited for autologous reconstruction than low-BMI patients given the need for sufficient donor tissue, leading to a selection bias that would be difficult to study in a controlled setting. Nevertheless, skin necrosis following autologous reconstruction is easier managed by banking skin during the index operation than in an alloplastic setting which may require a more aesthetically deforming surgery due to the risk of device extrusion and infection[8,28]. The timing of reconstruction can also impact the likelihood of skin necrosis. Though studies have shown that delayed alloplastic reconstruction is associated with reduced rates of necrosis[10], this method subjects all patients to an additional procedure, rather than just those who develop necrosis. These patients differ from those who undergo two-stage DIEP flap reconstruction with skin banking (discussed below) because the additional intermediate operation to place tissue expanders offers no new opportunity to improve cosmesis, as this can be done during the placement of a permanent implant.

We routinely perform delayed DIEP flaps with intermediate, or "babysitter", tissue expanders for patients undergoing post-mastectomy radiation therapy, so as to avoid irradiating the healthy flap. In our study of 344 immediate DIEP flaps and 99 delayed flaps, we found lower rates of skin necrosis in the delayed group compared to the immediate group (2.0% *vs.* 16.0%)[29]. There were no differences in other measured postoperative outcomes. Ultimately, we did not use these findings as an argument to perform delayed DIEP flaps on all patients, as the skin banking technique has provided adequate reconstruction without an additional procedure[13].

## INTRAOPERATIVE STRATEGIES

### Indocyanine green angiography

Though the incidence of skin flap necrosis is high, there are ways in which surgeons can both anticipate and even mitigate the effects of necrosis intra-operatively. Fluorescent imaging can aid in assessing mastectomy flap skin perfusion in real time, which can help predict the possible extent of skin necrosis[30]. The intra-operative use of fluorescence-guided imaging with indocyanine green (ICG) has been used in clinical practice for over fifty years to assess vascular perfusion. Specialties such as ophthalmology and cardiology have made ICG fluoroscopy a routine part of assessing pertinent vessels, such as retinal and coronary arteries[31]. ICG has multiple benefits in that it is nontoxic to the patient, remains contained within the circulatory system, and is cost-effective[32].

For the past 15 years, ICG fluoroscopy has been implemented to help assess mastectomy flap perfusion intra-operatively to predict skin flap viability[33]. Fluoroscopy can be used during autologous reconstruction to assess the patency of any free-flap microvascular anastomoses and subsequent flap perfusion, both intraoperatively and postoperatively[34]. It can also be particularly beneficial in pre-pectoral implant-based reconstruction where preservation of mastectomy skin is of utmost importance due to the risk of device extrusion.

One prospective study compared intraoperative skin perfusion using ICG-guided imaging to areas of the breast affected by postoperative skin necrosis and found that breast skin with < 25% perfusion intraoperatively was not viable 90% of the time, and areas with > 45% of perfusion on ICG imaging survived 98% of the time[33]. Surgeons can use this intraoperative information to remove any potentially nonviable skin at the time of mastectomy and to guide patient expectations postoperatively. Our imaging protocol calls for an injection of 10 mg of reconstituted dye (or 4 mL of solution) followed by a 20 mL normal saline flush. The imaging device of choice (e.g., Stryker Spy, Medtronic VisionSense) is brought onto the field and run for at least 2 min to allow sufficient time for visualization of contrast media in the mastectomy flaps. The false positive rate of ischemia is almost zero, but areas of delayed or poor perfusion on laser angiography may still be clinically viable. With NSM, excising even a small amount of skin near the incision may lead to nipple malposition and deformity. Therefore, it may be best to take a conservative approach if the area to be excised may lead to deformity. This requires patient handholding and preoperative counseling, as partial skin necrosis will take several weeks to mature and can appear alarming to the uninitiated. In our practice, all patients with potentially compromised skin have a warming blanket and nitroglycerin paste on the mastectomy flaps postoperatively, as discussed below.

### Skin banking during autologous reconstruction

While fluorescent imaging using ICG may help predict the occurrence and extent of skin necrosis, skin banking during autologous reconstruction helps address the loss of tissue due to necrosis. Skin loss can significantly alter breast shape, nipple position, and overall breast symmetry[12]. Although skin grafting may mitigate these sequelae, it creates a color and texture mismatch to the bordering native breast skin and can be costly. In cases of skin necrosis in implant-based reconstruction, converting to an autologous reconstruction may be the sole option to address large areas of skin loss.

However, autologous reconstruction affords the surgeon the ability to bank donor skin in the event of skin loss from necrosis or if further resection is needed due to positive margins at the NAC. The use of banked skin to revise an autologous reconstruction has been demonstrated with abdominal flaps (TRAM, DIEP, SEIA) and with transverse myocutaneous gracilis flaps[35,36]. A recent retrospective study from our institution found that managing skin necrosis using banked skin was more cost-effective than using skin grafts with or without acellular dermal templates when the incidence rate of skin loss exceeding 10 $cm^2$ surpassed 25.3%[13].

At our institution, DIEP reconstruction is performed in two stages following all NSM approaches: the first involves harvesting the flap and anastomosing it to the internal mammary vessels in a standard fashion. During the first stage, a large elliptical skin paddle is preserved on the flap for both banking and Doppler ultrasound monitoring of vascular patency [Figure 2]. After two weeks (ample time for skin necrosis demarcation and final pathology), we return to the operating room to completely remove the DIEP flap skin - both the banked portion as well as the monitoring paddle - if tumor margins are negative or if there is no skin necrosis. If tumor margins are positive or if there are significant amounts of full-thickness mastectomy skin flap necrosis, the banked skin is used to reconstruct the skin defect due to oncologic re-excision or necrosis. This technique provides a plan to manage necrosis and allows for improved cosmesis. Although a second procedure is not without its risks, such as flap hypoperfusion during induction of general anesthesia, we have not had any instances of flap failure attributed to the second stage banked skin excision in our ten-year experience. Standardizing these methods for all patients undergoing NSM can lead to increased patient satisfaction, cost-effectiveness, and overall stronger reconstructive outcomes. We have found that we use banked skin in 18% of cases: 15% from skin necrosis and 3% from positive margins on final pathology. With NSM, if the skin from the areola cannot be replaced, the circular areola will be excised and closed as an ellipse. Typically, the areola is 20% of the height of the breast and this leads to a profound asymmetry between breasts. The banked skin easily replaces the excised areola and ultimately ends up with a seamless reconstruction following nipple reconstruction and areola tattooing.

## POSTOPERATIVE MANAGEMENT

For patients undergoing implant-based reconstruction, intraoperative indocyanine green angiography helps determine the postoperative management strategy. In those with patchy perfusion, significant secondary bruising, or atherosclerotic and vascular comorbidities, topical nitroglycerine is used to increase vasodilation and improve tissue blood flow[37]. In randomized controlled trials, this technique showed efficacy in reducing mastectomy flap necrosis rate[38-40]. At our institution, we use a 2% nitroglycerin ointment when clinical suspicion of potential necrosis is high. It is applied to the entire mastectomy skin flap at the end of the procedure and once more at 12 h postoperatively. As a general principle, nitroglycerin application is discontinued at the time of discharge to avoid systemic hypotension.

We have also explored other modalities of reducing partial- and full-thickness skin flap necrosis in a rodent model. Tacrolimus has been previously shown to increase lymphatic collateral drainage and reduce the incidence of lymphedema and venous congestion[41]. Our study randomized Sprague Dawley rats to receive either topical tacrolimus or placebo daily for one week before and one week after a dorsal skin flap was raised[42,43]. On histological evaluation and image analysis, the tacrolimus group showed significantly increased tissue viability, as well as reduced skin ischemia and full-thickness necrosis. Topical tacrolimus is a possible alternative or auxiliary ointment that may be trialed in high-risk patients, reducing lymphatic congestion and arterial insufficiency to prevent mastectomy skin flap necrosis. Given our promising experience with topical tacrolimus in a rodent model, future studies will examine its application and efficacy in humans, particularly in comparison to our current treatment algorithm with nitroglycerin ointment, as described above.

Aside from topical medications, warming blankets are used at our institution for patients at risk of mastectomy skin flap necrosis. The goal of their use is to attempt to further improve tissue perfusion through heat-induced vasodilation. Other centers have cited the use of space heaters, water-circulation blankets, and heating lamps to have similar effects. These adjunctive tools are widely used in the post-

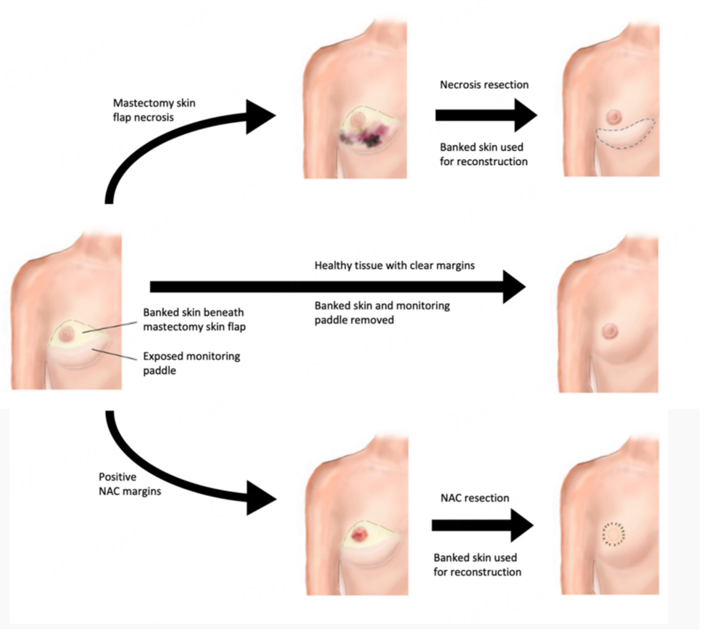


**Figure 2.** Skin banking during stage 1 of NSM with DIEP flap reconstruction. During stage 2, banked skin can be removed, or used to replace native breast skin in the event of necrosis or additional oncologic resection.

surgical management algorithm for maintaining core body temperature[44]. Heat-induced vasodilation not only improves skin perfusion following both alloplastic and autologous reconstruction, but also helps mitigate microvascular compromise in flap-based reconstructions[19,44]. However, care should be taken, as denervated skin lacks some of the protective vasodilatory effects of normally innervated skin and is therefore at higher risk of suffering thermal burns. Patients should not treat themselves with warming devices after discharge.

## CONCLUSION

Skin flap necrosis is a common complication after mastectomy. It is influenced by patient factors such as age, BMI, diabetes, tobacco use, prior surgery, and irradiation. Larger breast size, both in terms of volume and surface area, also increase risk. In the operating room, nipple-sparing mastectomies, thin skin flaps, periareolar incisions, and autologous reconstructions may also promote skin necrosis. However, indocyanine green angiography can assist surgeons with early detection and management of necrosis, and banking skin flaps during autologous reconstruction can provide a cost-effective and aesthetically pleasing option for revision. In the postoperative period, topical nitroglycerin and external warming can improve skin flap perfusion and mitigate the severity of necrosis. In the future, other topical agents such as tacrolimus may be used in similar clinical settings without the systemic effects on blood pressure that limit the use of nitroglycerin. Clearly, while much is known about the risk factors, prevention, and treatment of skin necrosis after mastectomy, more studies must be done to further this field of knowledge and thus improve patient well-being.

## DECLARATIONS

### Authors' contributions

Made substantial contributions to the design of the study: Black GG, Otterburn DM

Made substantial contributions to manuscript writing: Black GG, Chen Y, Wang ML, Condez K
Made substantial contributions to figure illustration: Chen Y

### Availability of data and materials
Not applicable.

### Financial support and sponsorship
None.

### Conflicts of interest
All authors declared that there are no conflicts of interest.

### Ethical approval and consent to participate
Not applicable.

### Consent for publication
Not applicable.



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**Plastic and Aesthetic Research**

Review

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# Strategies for prevention and management of partial flap loss or fat necrosis in microvascular autologous breast reconstruction

**Gabriela D García Nores, Angela Cheng**

Department of Surgery, Division of Plastic and Reconstructive Surgery, Emory University, Atlanta, GA 30322, USA.

**Correspondence to:** Dr. Angela Cheng, Department of Surgery, Division of Plastic and Reconstructive Surgery, Emory University, 1364C Clifton Rd NE, Atlanta, GA 30322, USA. E-mail: angelacheng@emory.edu

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## Abstract

Partial flap loss (skin involved) or fat necrosis following autologous breast reconstruction remains a dreaded postoperative complication despite significant advances in microsurgical techniques. Several strategies have been proposed in the preoperative and intraoperative period to prevent this complication ranging from preoperative imaging, intra-operative tissue perfusion assessment, appropriate perforator selection (location and number), maximizing inflow and outflow with additional anastomoses and/or pedicles, and minimizing ischemia time. Postoperative management of partial flap loss (when there is skin involvement) and fat necrosis remains a challenge, with very little published data focusing on classification, timing, and techniques. Early intervention versus close observation may depend on multiple patient factors and the degree or volume of necrosis. Secondary intervention options include hyperbaric oxygen therapy, fat aeration with a needle, liposuction, fat grafting, addition of another flap or implant, depending on the nature of the defect. This review summarizes the current evidence for each of these strategies to help the current surgeon understand their options in preventing and managing patients suffering from partial flap loss.

**Keywords:** Partial flap loss, fat necrosis, prevention of fat necrosis

## INTRODUCTION

Autologous free tissue transfer is considered a safe, common, and highly successful technique for breast reconstruction. The historical evolution from the pedicled transverse rectus abdominis muscle (pTRAM) to free TRAM (fTRAM), then muscle-sparing TRAM (msTRAM), and finally deep inferior epigastric artery perforator (DIEP) or superficial inferior epigastric artery (SIEA) flaps has been remarkable but also introduced new challenges. Important advancements in preoperative flap planning, harvest, and postoperative monitoring have significantly decreased the rate of major complications such as total flap loss. Furthermore, working in multidisciplinary teams when planning for immediate autologous reconstruction allows for better planning and therefore better outcomes. However, several minor complications are still routinely encountered, including donor site morbidity (e.g., bulge/hernia and wound dehiscence) and partial flap loss or fat necrosis. While the reported incidence of fat necrosis ranges widely due to inconsistent postoperative assessment and lack of standardization, a systematic review of 70 articles conducted by Khansa *et al.* found a reported incidence of 3.0%-37.9% and the mean rate of fat necrosis to be 11.3%[1]. Widely accepted risk factors include smoking, obesity [BMI (kg/m$^2$) > 30], postoperative radiation therapy, and ischemia[2]. While some factors are clearly beyond our control at the time of surgery, there are certain techniques we can employ to minimize the risks of complications. In this article, we aim to provide a summary of the current literature on strategies for the prevention and management of partial flap loss (skin involved) and fat necrosis to best guide today's surgeon.

## PREVENTION

### Preoperative imaging

Numerous studies on the value of preoperative imaging for DIEP and other autologous flaps have been published[3,4]. Preoperative imaging to map perforator location and intramuscular course has been reported to decrease operative time, total flap loss, and fat necrosis[5]. This is based on the knowledge that a better understanding of perforator course will help delineate vascular territories and therefore minimize fat necrosis in under-perfused areas. The most common imaging modality utilized is CT Angiography (CTA), but similar benefits have been reported using MR Angiography (MRA) and even ultrasound[6]. There is always a concern for the cost of imaging, additional radiation exposure, and possible incidental findings leading to delays in care and additional workup[7]. MRA is a strong competitor against CTA, as it does not have any radiation exposure (although the radiation dose of a CTA can now be reduced to as low as 5 millisieverts, which is the equivalent of two abdominal X-Rays) and has a safer contrast allergy profile. MRA has been described as having a clearer definition of the intramuscular perforators, whereas CTA is superior in evaluating subcutaneous course. Davis *et al.* even describe using preoperative imaging to identify atypical venous connections and predict venous congestion[8].

### Intraoperative perfusion assessment

The introduction of indocyanine green laser angiography (ICG or SPY angiography) has also proven to be beneficial for more than mastectomy flap evaluation. This technology allows the surgeon to assess perforator location and intraoperative tissue perfusion during flap harvest, aiding in perforator selection. The surgeon can also evaluate tissue perfusion after anastomosis to detect early signs of ischemia or venous congestion, which could lead to partial or complete flap loss. SPY angiography technology can be employed intraoperatively to assess the perforasome territory based on the selected perforator for a DIEP flap. The authors routinely clamp the other perforators temporarily to gauge the perfusion of the skin paddle and/or adipose tissue. Additional perforators can be harvested if the perforasome territory is deemed inadequate. Once the flap is transferred and anastomosed, repeat SPY angiography objectively confirms that the flap is well perfused. This technology is also useful in identifying early or partial venous congestion which may lead to complete or partial flap necrosis and has been demonstrated to decrease postoperative complications[9]. Routinely, we repeat the SPY assessment after 15-20 min to assess for fluorescein clearance.

We strongly recommend trimming any portion of the skin paddle and/or sub-Scarpal fat that is clearly hypoperfused during arterial phase as well as poorly draining on the venous phase evaluation. A flap with superficially dominant venous drainage can also become apparent during this stage and should prompt the surgeon to perform a second venous outflow anastomosis. This is supported by Hembd *et al.*, who reported on 506 DIEP flaps with decreased odds of fat necrosis with the use of indocyanine green angiography, without a reduction in flap failure rates. Overall incidence was 13% and the use of ICG was independently associated with a decrease in the odds ratio[10]. Similarly, Momeni also reported a series of 80 patients, 137 flaps, and an overall incidence of 14.6% of fat necrosis. ICG angiography was used to guide debridement in one cohort, reducing the incidence of fat necrosis from 18/79 to 2/58[11]. Another group similarly demonstrated a decreased rate of fat necrosis from 59.5% to 29% with ICG as well as a reduced rate of second surgery from 45.9% to 20.8%[12]. Parmeshwar *et al.* performed a systematic review of the use of ICG angiography. Based on the analysis of 9 articles and a comprehensive review involving a total of 355 patients and 824 free flaps, the researchers concluded that there was a significant disparity in flap fat necrosis, but no difference in total or partial flap loss. They suggest that ICG angiography is a more effective and efficient technique to reduce fat necrosis and is more sensitive than clinical assessment[13]. However, most recently, Yoo *et al.* reported their experience with 353 DIEP flaps, revealing a 10.9% incidence of fat necrosis and no difference with the use of ICG angiography[14]. Other less common intraoperative imaging techniques include Doppler, dynamic infrared thermography, and hyperspectral imaging.

### Perforator selection (Medial *vs.* lateral)

Saint-Cyr has published numerous studies on the perforasome theory, which help us understand and maximize flap perfusion. He reports the majority of perforators are located in the periumbilical region[15]. However, this eccentric location has led other authors to question whether the medial row perforators were indeed the optimal choice. Kamali *et al.* reported a nearly 3-fold higher incidence of fat necrosis in flaps, based solely on the medial row *vs.* lateral row (24.5% *vs.* 8.2%) and no difference with flaps based on lateral only *vs.* both medial and lateral. They suggested increasing the number of perforators harvested along the same row to minimize fat necrosis[16]. However, Garvey *et al.* reviewed 228 patients with 120 medial and 108 lateral perforator flaps with similar rates of fat necrosis and partial flap necrosis[17]. In another study by Saint-Cyr, he offered further insights into the zones of perfusion based on medial *vs.* lateral row and effects on flap harvest and design. The authors reported that lateral row perforators rarely crossed midline so unilateral DIEP flap which require more than hemi-abdominal volume should be harvested based on medial row perforators[18]. Lastly, Hembd *et al.* reviewed 409 DIEP flaps and noted an incidence of 14.4% fat necrosis with a decrease in the odds ratio for this endpoint when using lateral row, or both medial and lateral row perforators. They recommend using larger caliber perforators and lateral row perforators alone, or in addition to medial row perforators, rather than just harvesting more perforators due to the increased risk of abdominal bulge[19].

### Number of perforators

To minimize donor site morbidity, the surgeon often strives to minimize the number of perforators harvested while maintaining adequate flap perfusion. Khansa *et al.* reported the most important predictor of fat necrosis was flap type, with the lowest degree of fat necrosis in the Free TRAM flaps (6.9%), then the SIEA flaps (8.1%), followed by the pedicled TRAM (12.3%), and finally the DIEP flap at 14.4%[1]. A 2010 study by Baumann *et al.* found less fat necrosis in msTRAMs or multiple perforator DIEPs than single perforator DIEPs. The lowest incidence of fat necrosis was actually reported in flaps with 3-5 perforators (predominantly msTRAMs)[20]. Their findings were validated by Garvey *et al.*[21]. Bhullar *et al.* also concluded that medial row perforators had a wider perfusion zone and suggested harvesting at least 2-3 perforators of substantial caliber[22]. Both Wu and Saint-Cyr reported increased rates of fat necrosis in single-perforator DIEP flaps by 3-fold and 2-fold, respectively[23,24]. However, it is well known that increasing the number of harvested perforators potentially risks higher donor site morbidity. Taking all the aforementioned into consideration, surgeons must carefully balance these factors in the decision making of flap harvest and perforator selection to maximize flap perfusion and minimize donor site morbidity[25].

### Maximize perfusion (APEX/supercharging)

A novel option to maximize perfusion by incorporating both medial and lateral row perforators yet minimizing the donor site morbidity was described by Dr. Allen *et al.* The abdominal perforator exchange (APEX) flap allows harvest of two perforators while sparing the intervening rectus fibers by adding an additional anastomosis to reconnect the medial and lateral division prior to division of the primary pedicle. DellaCroce *et al.* reported his 6-year experience with 364 flaps and nearly eliminated abdominal bulge/hernia. The operative time was 34 min longer on average. Only one patient presented with diffuse fat necrosis[26]. Other surgeons have also advocated supercharging by harvesting a second or third pedicle (SIEA, SCIA, and/or DCIA) to improve the perfusion of the flap. Both these options require increased technical difficulty and complexity, but in experienced hands, they can optimize flap perfusion without an increase in donor site morbidity. Further studies are needed to better understand appropriate patient selection and long-term evidence on these refinements.

### Additional venous outflow

Some incidences of fat necrosis may not be due entirely to ischemia but are rather a result of progressive venous congestion. For example, superficially dominant venous drainage may not be apparent during the index operation. We strongly recommend dissecting the superficial inferior epigastric vein (SIEV) routinely during DIEP flap harvest to serve as an indicator of risks of venous congestion and a secondary outflow as needed. Engorgement of the SIEV during DIEP harvest is an early indicator of possible superficial dominance. ICG angiography can often confirm this anatomical variant with delayed drainage of the dye until the SIEV is vented. Ming-Huei Cheng often routinely augments his venous outflow using the SIEV through a variety of configurations to connect to the DIEV or a secondary recipient vein. He elects to routinely dissect a length of at least 7-10 cm of SIEV. He reported 32 episodes of venous congestion in 162 patients undergoing unilateral DIEP flap reconstruction. Salvage consisted of either venous augmentation or SIEV substitution with no statistical difference in flap salvage. This was mostly done by anastomosis of the SIEV to either the 2nd vena comitantes or the internal mammary vein with the use of a vein graft or DIEV[27].

### Minimize ischemia time

The easiest and quickest way to prevent partial flap necrosis is to minimize flap ischemia time. High-volume surgical centers with dedicated surgical teams and experienced surgeons have demonstrated remarkable efficiency with DIEP flaps, and there are anecdotal reports of DIEP flaps being routinely performed now in under 2 h. Lee *et al.* reported 86 patients with a mean ischemia time of 89 min and an incidence of fat necrosis at 17.4%. Ischemia time was found to be significant in both univariate and multivariate analyses. The authors report the threshold of 99.5 min as a cutoff for higher rates of fat necrosis[28]. Ideally, a microsurgical operative team would include dedicated and experienced nurses, surgical technicians, anesthesiologists, and surgeons. In other surgical subspecialties (i.e., transplant, bariatrics, hepatobiliary), designated centers of excellence have lower complication rates and patients are occasionally funneled by their insurance to these facilities to receive their care. There are already several large private groups in the USA dedicated solely to breast reconstruction with good outcomes. Whether this model or designation of excellence is applicable to microsurgical breast reconstruction remains to be seen.

### Flap inset

Blondeel *et al.* have already published excellent guides on aesthetic breast reconstruction based on the footprint, conus, and skin envelope. Often, for patients with extremes in body mass index, maximizing the volume harvested results in flap design where the distal portions of the flap may have questionable perfusion. Wade *et al.* reported a statistically significant relationship between the incidence of fat necrosis and BMI ($kg/m^2$) as a continuum as well as BMI ($kg/m^2$) > 35 as an independent variable[6]. For these situations, we strongly recommend careful consideration of flap orientation during inset to bury any questionable portion of the flap. An oblique or vertical inset permits the area of maximal perfusion on a medial row perforator to be utilized as the visible skin paddle inset along the inframammary fold. Careful attention should be given to insetting the healthiest portion of the flap along the "social breast" or cleavage area, ensuring that any fat necrosis that may develop will form along the lateral and inferior regions of the breast. Patients tolerate fat necrosis in these areas much better, because it is less likely to cause visible deformity when wearing a brassiere or clothing. If a buried partial flap loss occurs, it typically evolves into fat necrosis, which can be more easily managed than a necrotic skin paddle with underlying tissue ischemia.

## MANAGEMENT

### Indications for intervention/classification

There is currently only one proposed classification system for fat necrosis. Similar to the well-known Baker grading scale for capsular contracture, the authors based this classification on whether the fat necrosis is palpable, visible, and/or painful. Not surprisingly, the most severe Type IV (painful) always requires surgical intervention. Type II (palpable but not visible) was mostly observed (48%), with 17% undergoing biopsy and 35% debridement. For Type III (visible and palpable), 11% underwent biopsy and 89% underwent debridement[29].

Classification systems may be useful in many conditions but should not be considered a definitive guide for management. Breast cancer patients may be hypersensitive and anxious about any palpable masses or lumps in their reconstructive breasts due to concern for cancer recurrence. Additionally, our breast surgeons and non-surgical colleagues (hematology/oncology or radiation oncology) may be less familiar with the diagnosis and management of fat necrosis, which can lead to concern when a palpable firm nodule or mass is noted during examination in the postoperative period. Open communication between all providers is crucial to avoid unnecessary interventions and to provide appropriate reassurances and workup. It is of utmost importance to educate all multidisciplinary team members in recognizing fat necrosis from other differential diagnoses, in order to provide timely onset of therapy and avoid unnecessary tests or interventions. In the study by Haddock *et al.*, the authors reported per single incidence of fat necrosis, 0.69 revisions, 1.22 imaging studies, 0.77 biopsies, and 1.7 additional oncologic office visits[3]. The cost and psychological toll on the patient for additional imaging, biopsy and surgery is not trivial and often overlooked. The majority of management for this issue is conservative and symptom-oriented. If fat necrosis is only diagnosed via imaging and is asymptomatic, no intervention is indicated. Some of these patients may need a lower threshold for treatment of areas of fat necrosis to avoid further unnecessary worry and/or evaluation.

### Timing of intervention

Ellis *et al.* performed a systematic literature review to develop an algorithm for the management of fat necrosis based on six articles with level 3 evidence. Again, the incidence varied from 12.7%-40.4% in clinical diagnosis. The authors noted clinical examination to be the most homogenous diagnostic approach for fat necrosis, identifying it as a palpable lump or mass of any size. Ultrasound should demonstrate a solid mass with increased echogenicity of the subcutaneous tissues or a simple cyst not consistent with tumor recurrence, and further investigation should be conducted 12 months post-mastectomy, once flap swelling has resolved and flap softening has occurred[30].

Many astute clinicians and patients often notice mild discoloration or firm areas of a flap postoperatively, especially along the periphery. These areas are likely mild ischemia and/or congestion, which may evolve into partial flap loss or fat necrosis. Routine imaging is not recommended, as these smaller areas of fat necrosis are likely to resolve spontaneously and do not require any intervention. For any patients where there is a palpable mass with significant concern, ultrasound is a cost-effective and simple tool to confirm the benign post-surgical change and calm their fears. Our general recommendation is expectant observation, massage, and providing reassurance that any persistent areas of concern can be addressed in the future. Tenderness is expected, and some patients with mild or moderate discomfort can be offered non-steroidal analgesics and careful observation. Narcotics may be necessary for patients suffering from severe flap necrosis and severe pain until surgical intervention can be scheduled.

Hyperbaric oxygen (HBO) has been studied in animal models extensively, but there is more limited data on human clinical use due to a lack of standardization and availability. Baynosa and Francis summarized the recent studies which demonstrated utility in salvage of compromised grafts/flaps and improved flap survival. The mechanism of action is likely related to improved tissue oxygenation, fibroblast function, neovascularization and minimizing ischemic-reperfusion injury, which theoretically would also minimize fat necrosis or partial flap loss[31]. HBO may be relatively contraindicated in select patients due to the risk of pneumothorax if there was any concern for iatrogenic injury during recipient vessel exposure. Further research is needed to better understand the role of HBO for our autologous breast reconstruction patients.

Anecdotal reports have described a successful technique of aeration of fat necrosis under local anesthesia after breast reduction. The authors recommend early intervention using an 18-gauge hypodermic needle to puncture the area of fat necrosis multiple times. This technique is similar to lawn aeration done to minimize soil compaction and maximize penetration of air, water, and nutrients to grass roots. Theoretically, this technique introduces new channels into the threatened area of ischemia tissue to either deliver blood, oxygen and/or nutrients, as well as creating channels for macrophages to access and break down the necrotic fibrosis. The exact mechanism requires further study but is an interesting option to consider for the management of areas of early fat necrosis. Obviously, this should be judiciously used near the pedicle to avoid inadvertent damage to the entire flap perfusion.

In our experience, even moderately large areas of firmness and fat necrosis often fully or partially resolve enough to become acceptable to patients after 3-6 months. For these smaller zones of fat necrosis that are truly bothersome to the patient (visible, painful, and/or palpable), elective removal can easily be performed during second stage revision, usually after 3 months.

For the management of more significant partial flap loss, the clinical evaluation must distinguish between fat necrosis occurring within a fully buried portion of a flap or "partial flap necrosis" where a visible superficial skin flap is necrotic. For an exposed area, earlier intervention with surgical debridement may be necessary if there is a large volume of flap loss (> 25%) and concern for infection. However, these situations can often be successfully managed conservatively with wound care and reassurance to minimize deformity. In our experience, these rarely require a return to the operating room unless a majority of the flap is necrotic and poses a significant risk of gangrenous necrosis. Aggressive debridement should be avoided as this may actually expose tenuous tissue that would otherwise recover, and instead convert these tenuous areas into additional volume loss, thereby creating a secondary deformity that is extremely difficult to correct without further surgery or additional flap(s). Topical antimicrobials such as silver sulfadiazine can be applied to minimize the risk of infection until the tissue fully demarcates. Patients should be advised to expect wound dehiscence and development of an eschar and home health care may be useful to arrange. Once the tissue is fully demarcated, debridement of the eschar and underlying dead fat is easy to perform in the clinic as this area is usually insensate. Wet-to-dry dressings and/or negative pressure therapy can also be applied to facilitate wound closure via secondary intention. It is often not necessary to fully debride all the fat necrosis as the healthy portion of the flap will granulate and cover deeper fat necrosis. Deep areas of fat necrosis are often not palpable or noticeable to the patient and do not require any further intervention. Secondary correction of the smaller resulting deformity can be performed with scar revision, flap repositioning or advancement, and/or fat grafting once the wound is fully healed.

### Small *vs.* moderate *vs.* large size deformity

The size of the defect must be considered when discussing treatment options to correct the deformity. Small areas adjacent to the scars can be directly excised. Deeper areas or more remote areas from the scar (i.e., the upper medial breast) can be removed with liposuction rather than reopening the entire incision for exposure and risk creating a large dead space. Autologous fat transfer is the most minimally invasive treatment which can readily correct minor deformities. A more aggressive cutting tip cannula may be necessary for very dense areas of fibrosis. Ultrasound-assisted liposuction (UAL) can facilitate the removal of moderately large areas. A larger area may require multiple sessions to slowly scrape out the fat necrosis and replace it with autologous fat transfer. Hassa *et al.* successfully treated 54 breast reconstructions with fat necrosis with UAL. The average size was 2.72 cm and half the patients only required one session. Thirty-seven percent (20 patients) required two sessions, and the remaining 13% (7 patients) required three sessions. Complete resolution was confirmed in 44 patients (81.5%) and only one thermal burn complication was noted[32]. We personally believe it is not necessary to fully remove the fat necrosis with direct liposuction, as simply breaking up a larger fibrotic mass facilitates the body's natural lytic process. During liposuction for moderately large zones of fat necrosis, our group's primary goal is to soften the area of concern and minimize visible deformity prior to transfer of autologous fat. Patients must be warned to expect multiple sessions to fully address moderately large zones of fat necrosis.

Larger volume loss can also be corrected with the addition of an implant if the soft tissue envelope is adequate and the patient is amenable. Care must be taken to avoid damaging the pedicle during pocket dissection for the implant. We would strongly encourage waiting at least 3 months to maximize the revascularization from the surrounding soft tissue before risking injury to the primary pedicle. In larger defects where both skin and volume are deficient, a secondary flap and/or expander-implant may be necessary. The thoracodorsal artery perforator flap (Tdap), latissimus flap and epigastric perforator flaps are great local flap options that can be advanced, rotated, or transferred as propeller flaps into the defect. In the most severe scenarios, it may be beneficial to consider another free flap. Common alternative secondary free flaps include the transverse upper gracilis, profunda artery perforator, lumbar artery perforator, lateral thigh perforator, and gluteal free flaps. Careful evaluation of the remaining donor sites and discussion with the patient is needed to address the defect with the most appropriate flap.

## DISCUSSION

Despite significant advances in preoperative and intraoperative surgical technology and a better understanding of flap perfusion, partial flap necrosis and fat necrosis remain persistent nemesis for surgeons performing autologous breast reconstruction. The majority of studies are retrospective and limited in size. Current evidence supports the use of both preoperative imaging and intraoperative ICG Angiography to maximize flap perfusion and debride poorly perfused tissue. The choice of which perforators to harvest remains a challenge to maximize perfusion and minimize donor site morbidity. Both the introduction of the APEX flap or a secondary venous outflow have shown promise in improving flap physiology to improve outcomes, but require slightly more technical effort with additional anastomoses and an unclear benefit. Minimizing ischemia time is an easy goal for all surgeons and often can be achieved by creating dedicated microsurgical care teams.

The current evidence is often inconclusive and poor in quality (level 3 or lower evidence). This calls for the need to standardize the diagnosis of fat necrosis, evaluate the timing of intervention and techniques, and establish a classification grading system to allow for prospective large-volume studies to better understand the true incidence of fat necrosis and the most appropriate management strategies. Consideration during flap inset to bury any areas of questionable perfusion can avoid partial flap necrosis and convert this into fat necrosis which is easier to manage. HBO and fat aeration have been suggested to improve fat necrosis in the postoperative period with limited evidence. Mild to moderate partial flap necrosis or fat necrosis can often be conservatively managed successfully to minimize deformity. Ultimately, most patients with symptomatic fat necrosis due to pain or deformity require secondary correction with a combination of techniques, including fat transfer, liposuction, flap advancement, addition of local or secondary free flaps for soft tissue, and addition of an expander or implant for volume.

## CONCLUSIONS

As Benjamin Franklin wisely stated, "An ounce of prevention is worth a pound of cure", and that certainly still holds true in dealing with partial flap failure and fat necrosis following autologous breast reconstruction. As such, the majority of the suggested strategies are focused on pre-surgical planning and intraoperative decision-making to successfully harvest a maximally perfused flap. Navigating this complication remains a complex challenge for even the most skilled of microsurgeons, and often requires multiple additional procedures to remove the necrotic tissue and restore the deficiency using fat transfer, additional flaps, and/or placement of an expander or implant.

## DECLARATIONS

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Contributed to the article: Garcia Nores GD, Cheng A

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Review

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# Management after flap failure: a narrative review

**Paige L. Myers, Sherry Y. Q. Tang, Noah H. Saad, Adeyiza O. Momoh**

Section of Plastic Surgery, Department of Surgery, University of Michigan, Ann Arbor, MI 48109, USA.

**Correspondence to:** Adeyiza O. Momoh, Section of Plastic Surgery, Department of Surgery, University of Michigan, 1500 E. Medical Center Drive, Ann Arbor, MI 48109, USA. E-mail: amomoh@med.umich.edu

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## Abstract

Autologous free tissue transfer for breast reconstruction is a well-established and reliable form of reconstruction for women undergoing mastectomies. These surgeries are performed with high rates of success; however, the consequences of flap failure can be devastating to patients and surgeons. Breast reconstruction decision making following flap loss is a uniquely individualized process, based on considerations of safety, patient goals and preferences, as well as the surgeon's skillset. The first priority following flap failure is to provide thoughtful patient counseling and support through this difficult time. The aims of reconstruction salvage after flap loss are to excise unhealthy tissue and restore a breast mound of normal anatomical shape. We present an algorithm as a possible approach to managing flap failures. We also review the management of breast reconstruction following free flap failure, including the role of hematologic investigation, anticoagulation recommendations and secondary or tertiary reconstruction with both prosthetic and autologous techniques.

**Keywords:** Microsurgery, breast reconstruction, flap failure

## INTRODUCTION

Autologous free tissue transfer for breast reconstruction is a well-established and reliable form of reconstruction for women undergoing mastectomies. Free tissue flaps provide a versatile and natural reconstructive option, with greater longevity of results and evidence of improved patient-reported quality of life compared to implant-based reconstruction[1,2]. Free flap breast reconstructions are performed with high rates of success, estimated at > 96% in high-volume centers[3-9]; however, the consequences of flap failure can still be devastating to patients and surgeons[10]. Specific patient and non-patient related factors have been identified that can PREDISPOSE PATIENTS to a greater risk for flap failures. Patient factors include hypercoagulable conditions, prior radiotherapy, and obesity[11,12]. Beyond patient factors, flap failures can also be IMPACTED by flap and perforator choices, and technical problems in all phases of the procedure including the flap harvest, microvascular anastomoses, flap inset and postoperative incidents.

Breast reconstruction decision making following flap loss is a uniquely individualized process, contingent upon considerations of safety, patient goals and preferences, as well as the surgeon's skillset. The aims of reconstruction salvage after flap loss are to excise unhealthy tissue and restore a breast mound of normal anatomical shape[13]. There are well-described management algorithms for other types of failed microvascular reconstruction, such as for lower extremity[14] or head and neck reconstructions[15], but there is a paucity of information on this topic in breast reconstruction. We present an algorithm as a possible approach to managing flap failures [Figure 1]. We also review the management of breast reconstruction following free flap failure, including the role of hematologic investigation, anticoagulation recommendations and secondary or tertiary reconstruction with both prosthetic and autologous techniques.

## PATIENT COUNSELING IN THE SETTING OF FLAP FAILURE

However difficult the conversation may be, clear and thoughtful patient communication is imperative in the event of a flap failure. Complications from surgery have a significant impact on quality of life, including mental health conditions[16]. This can be particularly devastating to women undergoing secondary autologous reconstruction after failed alloplastic reconstruction, as there are potential feelings of losing the breast twice[17]. Having a complete preoperative discussion to set realistic expectations is the first step. This is true for not only complete flap loss, but the range of breast complications as well as those that involve the donor site. Informing patients of the likelihood of adverse events is necessary while also discussing individual factors that place them at higher risk, such as obesity or hypercoagulability. It can be helpful to discuss flap loss rates reported in the literature and, if available, failure rates at the specific treating institution. It is also beneficial to educate patients on the secondary (or tertiary) options for reconstruction, such as implant-based, and additional autologous reconstruction options. While knowledge of the possibility of flap failure can cause some concern for patients, most are placed at ease knowing that alternate options exist in the unlikely event of flap failure and that they will be supported and guided through each step of the process. In patients who do not wish to undergo further reconstructive surgery, the option of an aesthetic flat closure should be offered[18]. In fact, Lineaweaver *et al.* found that nearly half of patients opted to forgo further breast reconstruction following their flap failure[19].

Higgins *et al.* interviewed women who experienced complete flap loss for breast reconstruction to better understand the psychosocial detriment of this outcome[10]. Not surprisingly, women expressed difficulty with body image and coping with emotions after flap loss. Another notable theme that emerged, however, was the impact the relationship with the surgeon had on the patient's overall experience. The study showed that women who reported a strong relationship with their surgeon also reported easier acceptance and coping with their flap loss. Similarly, patients who felt unsupported or dismissed by their surgeon expressed greater emotional distress and questioning after flap loss[10]. Many women suggested increasing emotional support resources in the setting of flap failure, including social workers and psychiatrists. Given that a multidisciplinary approach results in better outcomes in breast reconstruction[20] a similar holistic approach to the management of the patient who has experienced a flap loss may be beneficial. Li *et al.* found that with dedicated nursing attention, surgical breast cancer patients reported lower depression scores and greater satisfaction postoperatively[21]. Even with ancillary support, the surgeon is ultimately responsible for the

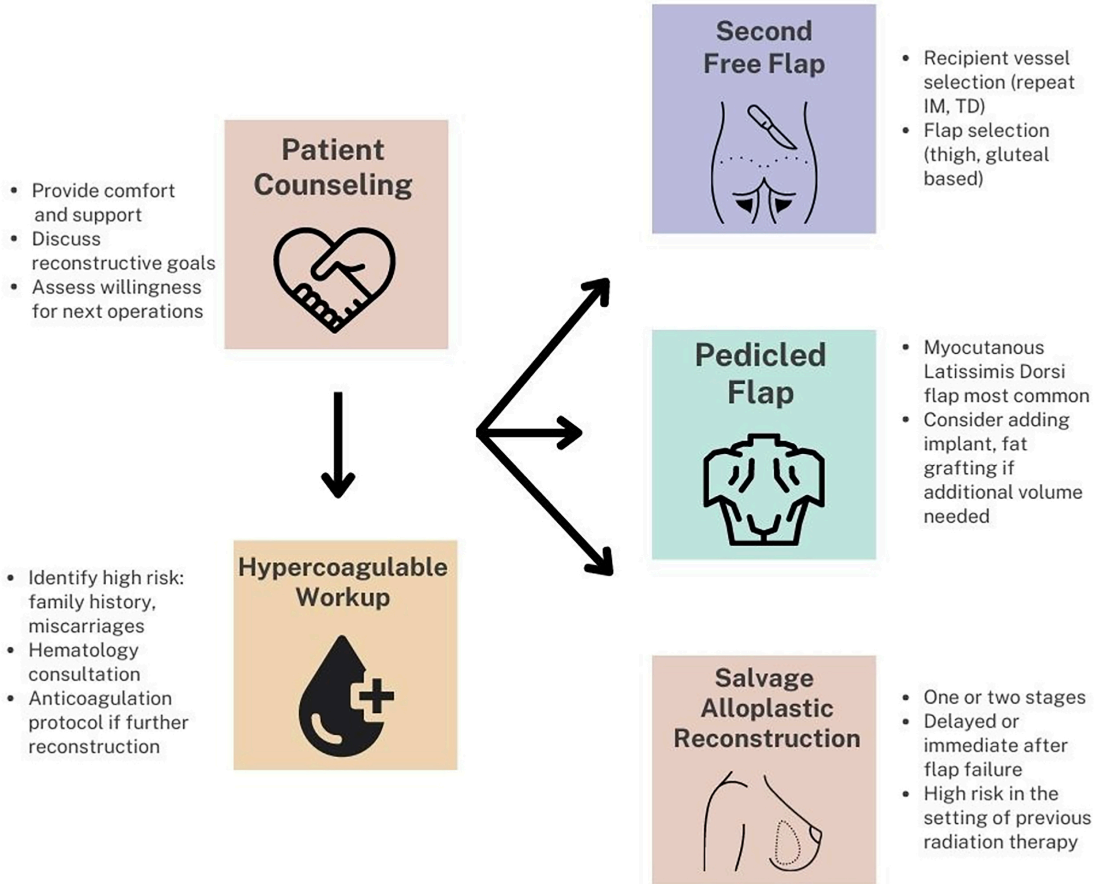


**Figure 1.** Algorithm for management after flap failure.

management of the patient and has the most influential impact on helping patients through this difficult time.

## HEMATOLOGICAL INVESTIGATION

A hematology workup should be considered if risk factors for clotting are identified during the preoperative evaluation, or if unexplained clotting resulting in failure is encountered postoperatively. While free flap transfer can be successfully performed in patients with underlying thrombophilias, hypercoagulability has traditionally been described as a relative contraindication to free tissue transfer. A recent systematic review performed by Kotamarti *et al.* found an 18.4% thrombosis rate with a pooled 12.2% flap failure rate in breast reconstruction patients concerning patients with hypercoagulability[22]. Many patients with hereditary or acquired thrombophilia experience their first complication in the setting of surgery[23]. Additionally, when thrombosis is discovered postoperatively in these patients, the salvage rate is near zero[23,24].

Thrombophilia is reported to have a prevalence rate of 5 to 27% of the population, with even higher prevalence in oncologic patients and patients undergoing lower extremity reconstruction[22,25,26]. Hypercoagubility disorders can be hereditary or acquired. Hereditary disorders include factor V Leiden, prothrombin G20210A mutation, methylenetetrahydrofolate reductase (MTHFR) mutations, protein C deficiency, protein S deficiency, antithrombin III deficiency, and elevated factor VIII. Acquired conditions include antiphospholipid syndrome (anticardiolipin, lupus anticoagulant), and some forms of hyperhomocysteinemia. Hypercoagulable states pose a challenge in autologous free flap reconstruction because they are frequently undetected preoperatively and are often only brought on by a precipitating event, such as a microvascular procedure[25,27].

Free flap thrombosis more commonly occurs in the postoperative period than intraoperatively in patients with known hypercoagulability disorders[22]. Multiple studies have also demonstrated that flap salvage rates are significantly higher if flap thrombosis and re-exploration occur early in the postoperative period[28-31]. Wang *et al.* found that the failure rate approaches 100% when flap thrombosis occurs on postoperative days 4 and 5 in hypercoagulable patients[28]. For these reasons, it is imperative to screen patients for hypercoagulable disorders preoperatively to minimize the risk of postoperative flap thromboses that are difficult to salvage. Perioperative risk assessment can significantly reduce the occurrence of flap thrombosis[32]. During the initial preoperative consultation, it is important to obtain a thorough history by asking questions regarding (1) personal history of blood clots, including deep vein thrombosis or pulmonary embolism; (2) personal history of miscarriages; (3) personal history of strokes at a young age; and (4) family history of clotting or previously diagnosed coagulation disorders[28,32]. If hypercoagulability is suspected based on history, referral to hematology for further workup is warranted. Patients who were referred to a hematologist have shown a higher flap success rate compared to patients who did not, as administration of an appropriate perioperative anticoagulation regimen can mitigate risk[28]. For instance, Kalmar *et al.* discovered that a platelet count of > 250 K/mcL ($P$ = 0.004) is associated with a higher rate of flap failure[33]. The authors suggest there may be a role for personalized anticoagulation protocols for thrombocytosis with agents specifically targeting platelets, such as aspirin, ticlodipine, and dipyramidole[33]. Genetic testing should also be considered, especially in patients with a family history of clotting episodes. It is recommended that a formal hypercoagulable workup be performed at a minimum of 4-6 weeks after a traumatic event such as surgery, as coagulation factors remain elevated during this time, specifically thrombin, that will alter the results of the testing[13,34]. After a patient is confirmed to have a hypercoagulable disorder, surgeons can collaborate with hematologists to determine a perioperative anticoagulation regimen, especially if salvage free-tissue transfer is to be attempted. Literature is sparse on success and failure rates for breast reconstruction of an attempted second flap after an initial failure in a patient with a known hypercoagulable condition. In a series described by Hamdi *et al.*, two patients with hypercoagulable conditions underwent a second free flap with a successful free tissue transfer with appropriate anticoagulation[17].

## ANTICOAGULATION REGIMEN

In patients without hypercoagulable disorders, prophylactic antithrombotic therapy is used to minimize the risk of venous thromboembolic events but can also decrease the incidence of microvascular thrombosis after free flap surgery[25]. There is no consensus on anticoagulation protocols and relevant studies are generally lacking. For example, at the authors' institution, it is typical to administer subcutaneous heparin 5,000 units preoperatively, aspirin 300 mg rectal suppository at the end of the case, followed by Lovenox 40 mg QD starting postoperative day 0 and aspirin 325 mg starting on the first postoperative for 30 days for patients without increased risk of thrombosis. Liu *et al.* reported a regimen of intraoperative heparin bolus of 2,000 units intravenously followed by five days of heparin infusion at 500 unit/hour in patients who are at risk of hypercoagulability[35]. Wang *et al.* presented four different anticoagulation protocols based on surgeon preference at a single institution[28]. It is apparent that prophylactic antithrombotic regimen has varied through the decades amongst different institutions and surgeons.

When it comes to patients who have already experienced a thrombotic event or patients who are likely to have an underlying hypercoagulable condition, the use of therapeutic anticoagulation remains controversial. A retrospective review by Senchenkov *et al.* described an algorithm of anticoagulation for patients both with and without a history of hypercoagulability[25]. They concluded that in patients without hypercoagulable history, additional anticoagulation beyond routine VTE prophylaxis is not indicated. Based on available data in the cardiovascular literature, Senchenkov *et al.* recommend that in patients with a hypercoagulable history, a heparin bolus prior to flap ischemia, ex-vivo irrigation of the flap with heparinized saline prior to anastomosis, and systemic anticoagulation should be considered[25]. Additionally, in the setting of recurrent flap thrombosis, heparin drip, intraoperative ASA, Plavix via nasogastric tube, and dextran-40 infusion should be considered[25].

The use of thrombolytic agents after free flap failure can be considered, but their efficacy has not been well established. Thrombolytic agents used in free flap salvage include streptokinase, urokinase, and tissue-plasminogen activator (tPA)[29,36,37]. tPA is the most commonly used agent and is generally injected via the arterial pedicle at a concentration of 1 mg/mL[37]. Urokinase is generally infused in an anterograde manner through the arterial pedicle at a concentration of 5,000 units/mL. Streptokinase can be injected into the arterial pedicle at 7,500 to 250,000 units diluted in 10-30 cc of normal saline[37]. Thrombolytics should be used with caution and only as a last resort due to their associated complications, including bleeding events and allergic reactions. With this in mind, they can be injected just proximal to the arterial anastomosis to increase their bioavailability at the site of the thrombus. Some have also reported taking down the venous anastomosis to avoid the systemic spread of the thrombolytic agent, though the risk of complications from systemic spread of the doses used in flap salvage is not entirely clear[37].

## SALVAGE FREE FLAP: RECIPIENT VESSEL SELECTION

A significant challenge facing the reconstructive surgeon following the failure of free flaps for breast reconstruction is the availability of recipient vessels in the chest. There is no consensus on the optimal timing of secondary free flap reconstruction following the failure of the initial flap, though some surgeons advocate for immediate free flap reconstruction at the time of debridement of the original flap as the mammary arteries and veins may still be salvageable. Hamdi *et al.* advocate for color Duplex imaging to assess the internal mammary system following free flap failure if considering another flap[17]. If the anterograde system is thrombosed, the retrograde system should be interrogated as it is a robust and reliable recipient vessel option for secondary free flap reconstruction[38,39]. Alternative vessel choices can be based on the subscapular system, which comes off of the axillary vessels, namely the thoracodorsal or serratus vessels[40] [Figure 2]. To identify the thoracodorsal and serratus vessels, the lateral pectoralis border is first found. Within the axillary fat, the lateral thoracic vein is found and can be followed proximally to the axillary vein. Carefully dissecting bluntly through the axillary fat posterior to the origin of the lateral thoracic vein reveals the proximal thoracodorsal vessels. The serratus branch can be found two to three cm from the origin of the thoracodorsal artery, supplying the serratus muscle[40]. The thoracodorsal artery must be ligated distally to avoid a caliber mismatch of secondary flap pedicle[41]. Moran *et al.* conducted a prospective cohort study and found no significant outcome differences between the internal mammary and thoracodorsal vessels as recipient sites for autologous breast reconstruction, concluding that both are safe options with acceptable results[42].

Other less common venous outflow options have been described, such as the cephalic and external jugular veins[43]. Additionally, if the failure is not due to thrombosis of the pedicle and the anastomosis remains patient, the initial flap artery and vein can be used for secondary flap salvage recipient vessels[44,45]. The thoracoacromial vessels have also been described for recipient vessels for autologous breast reconstruction,

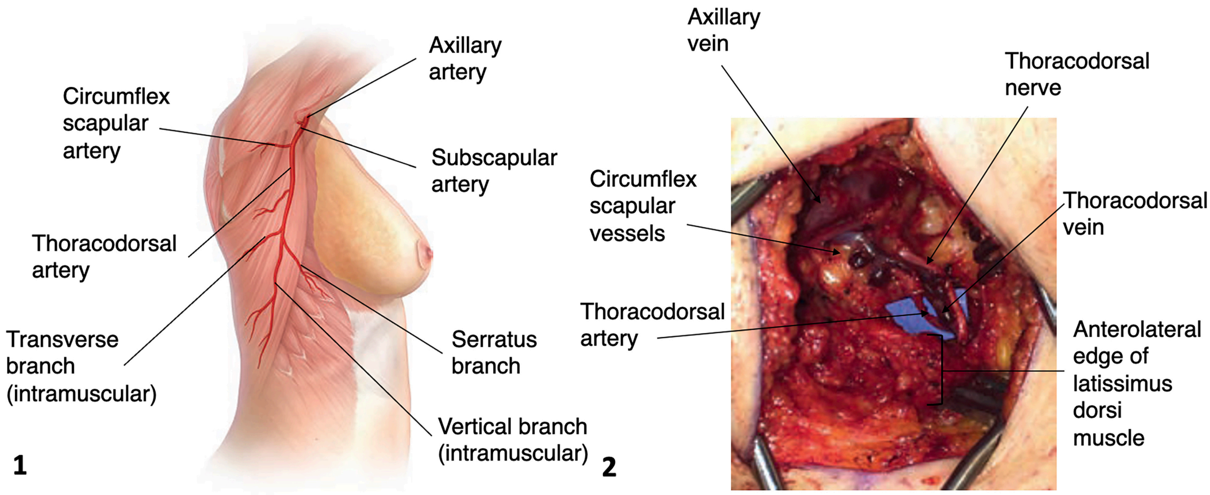


**Figure 2.** Illustration of the thoracodorsal vessels arising from the subscapular system (Image 1). Exposure of the thoracodorsal artery, vein, and nerve prior to their entry into the latissimus dorsi muscle. The nerve should be dissected free to prevent any kinking of the vessels after anastomosis (Image 2). Reproduced with permission from TA Kung, AO Momoh, Ch 24: Recipient Vessel Exposure--Internal Mammary and Thoracodorsal, Operative Techniques in Breast Surgery, Trunk Reconstruction and Body Contouring. Publication Date: June 3, 2019. Wolters Kluwer.

with the added benefit of not sacrificing any rib and possibly less pain[46]. Yamamoto *et al.* compared thoracoacromial vessels to the internal mammary vessels for breast reconstruction found a significantly smaller size artery (1.70 ± 0.26 mm) and vein (1.64 ± 0.24 mm) compared to the internal mammary artery (2.27 ± 0.31 mm) and vein (2.33 ± 0.29 mm) ($P < 0.001$)[46]. Even less commonly, contralateral internal mammary vessels as recipient options have been described[47,48].

## SALVAGE FREE FLAP: SECONDARY FLAP SELECTION

As the DIEP flap remains the gold standard for autologous breast reconstruction, in the scenario of a failed initial free flap reconstruction, secondary free flap options require alternative donor sites. These include the thigh (myocutaneous gracilis flaps, profunda artery perforator flap, lateral thigh flap) and trunk (lumbar artery perforator flap, superior and inferior gluteal artery perforator flaps).

A myocutaneous gracilis flap (either transverse, diagonal, or vertical skin paddle orientation) is a reliable option with high patient satisfaction for secondary free flap salvage[49]. As this flap does not require perforator dissection, it can be performed expeditiously if attempting in the setting of an immediate flap loss. The profunda artery perforator (PAP) flap is another medial thigh-based flap with similar advantages to the myocutaneous gracilis flap but a muscle-sparing alternative[50] [Figure 3]. The lateral thigh perforator (LTP) flap, renovated for breast reconstruction by Robert Allen, Sr. is a secondary option for patients with the “saddlebag” deformity[51,52]. Based on the ascending lateral circumflex femoral artery, dissection is relatively simple due to the septocutaneous location of the perforators between the tensor fascia lata (TFL) and the gluteus medius (GM) muscles[53]. The LTP has a short pedicle, often necessitating vein grafting in salvage cases. The lumbar artery perforator (LAP) flap perforasome includes the soft tissues commonly referred to as the “love handle” region[54]. Like the LTP flap, this also has a short pedicle. Gluteal artery perforator flaps (superior and inferior)[55] are additional trunk-based options for alternative flap options. Historically, the SGAP and IGAP flaps were preferred second-line options, though now mostly replaced by

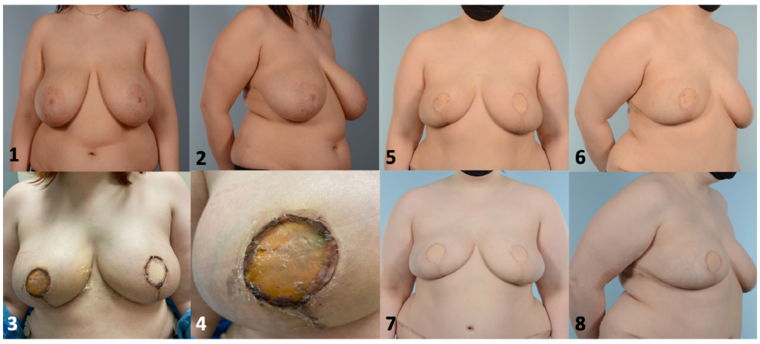


**Figure 3.** Patient with a genetic predisposition for breast cancer (Images 1 and 2) who underwent bilateral skin- sparing mastectomies and immediate reconstruction with a left DIEP flap and a right SIEA flap. Three weeks postoperatively, she presented with a discoloration of the right flap skin paddle, brisk capillary refill, and firmness at the inferolateral quadrant of the breast (Images 3 and 4). While not frankly necrotic, the entire breast ultimately was very firm (Images 5 and 6). The right SIEA flap was debrided and replaced with a PAP flap using a more proximal portion of the same antegrade internal mammary vessels (Images 7 and 8).

medial thigh-based flaps due to reliable anatomy, availability of donor site tissue, ease of harvest, and lower complication rates[53,56].

Though typically utilized in a pedicled fashion, a contralateral latissimus dorsi myocutaneous free flap can be performed in the setting of tertiary reconstruction[57]. This has a reliable anatomy with generally adequate donor site tissue, especially if a large area of skin is needed. An additional consideration for this option would be if the ipsilateral thoracodorsal dorsal pedicle was previously sacrificed during an axillary lymph node dissection. While this may not be the first choice for a free flap tertiary salvage breast reconstruction, a contralateral free latissimus is an option if needed.

Non-abdominally based flaps may not provide enough tissue in the setting of a DIEP flap failure. Challenges with alternative flaps include less volume with a smaller skin paddle and an inability to restore the breast footprint or skin envelope, especially when working to match a relatively large contralateral breast (native or reconstructed)[58]. With smaller flaps, a dependable solution is to combine two flaps for single breast reconstruction in a "stacked" fashion[39]. When recipient vessels are limited due to previous thrombosis after flap failure, flaps can be stacked using the "daisy-chain" technique: anastomosing one flap to a branch of the pedicle of the other flap[59].

Performing a second free flap after an initial failure can be a reasonable option shown to be effective in the literature. Hamdi *et al.* retrospectively reviewed their series of repeat free flap breast reconstruction after an initial free flap failure[17]. In this series, 688 patients experienced 14 failures of autologous reconstruction requiring salvage. Of these 14, eight patients underwent nine microvascular breast reconstructions, with two of these nine experienced failures of the second flap. This information is useful when discussing options with patients after free flap failures. Baumeister *et al.* similarly retrospectively reviewed 902 free flaps, identifying 13 patients who underwent a second flap surgery[60]. Microsurgical free tissue transfers were successful in 11 of the 13 patients. The authors outline their approach in the setting of a failed flap which includes a reconsideration of the need for autologous tissue, sensitive patient counseling, thorough analysis of the cause of failure, and change in microsurgical strategy[60].

## PEDICLED FLAP OPTIONS

Pedicled flaps are an alternative option to performing free flaps for salvage in clinical situations where vascularized tissue is required, such as in the setting of radiation. Implant reconstructions in the setting of prior radiation result in increased rates of major complications such as implant extrusion, capsular contracture, and reconstruction failure compared to similar reconstructions in non-irradiated breasts[61]. As such, many reconstructive surgeons opt to use autologous reconstruction in these patients. The latissimus dorsi flap (LD)[62] is the most common pedicled flap option for autologous tissue salvage following free flap failure, as it does not require microsurgery and has a reliable anatomy with a versatile skin paddle that results in a high reconstructive success rate[13,63] [Figure 4]. Though first described for postmastectomy reconstruction by D'Este in 1912[63], it was popularized in the late 1970s as a method of autologous breast reconstruction. The latissimus dorsi flap allows for the harvest of a large skin paddle, useful in situations where there was a loss of skin from the prior failed free flap.

Aesthetic results are often excellent, and the LD flap permits the use of healthy, non-radiated tissue to cover an implant if one is needed to achieve a size match[64]. If greater volume is required, an implant or tissue expander can be placed under the flap, in one or two stages, either above or below the pectoralis muscle[65]. In appropriate candidates, autologous fat grafting at the initial time of the LD flap can provide significant volume enhancement as needed[66,67]. This is known as the Latissimus Dorsi and Immediate Fat Transfer (LIFT) procedure, where upwards of 500 cc of fat can be added for increased volume. When considering this option, ensure the thoracodorsal pedicle has not been injured from previous interventions, such as an axillary lymph node dissection or radiation[68]. A recent retrospective review of 248 patients by Wattoo *et al.* showed long-term overall patient satisfaction from latissimus flap reconstruction[69]. While minor complication rates were high in the short term (seroma 58% and wound infection 13%), chronic complications were low (shoulder stiffness 1.9%, pain 11.5%), highlighting the utility of this procedure. These results are consistent with another retrospective review of 277 patients by Yezhelyev *et al.*, with higher short-term complications (seroma 19.5%), but overall low risk in the long term[70].

## CONVERSION TO ALLOPLASTIC

Alloplastic or implant-based reconstruction is another effective option for salvage, particularly in non-radiated breasts. When contemplating conversion to implant-based reconstruction, the psychological and emotional toll experienced after free flap failure should be considered, especially in women who specifically chose autologous tissue to avoid implants[71,72]. The benefits of conversion to prosthetic reconstruction include a shorter hospital stay and a lower complication rate in the short term [Figure 5][73]. Factors that influence the decision to choose alloplastic reconstruction include the amount and quality of mastectomy skin available, the desired size of the breast and ultimately the patient's wishes. Decisions about implant pocket placement (prepectoral or subpectoral) and use of a biologic mesh (coverage and support with or without acellular dermal matrix) need to be made. A history of radiation must be considered if choosing alloplastic reconstruction.

The timing of initiation of expansion in the outpatient clinic is variable, depending upon surgeon preference and healing of the incision. The timing of adjuvant therapies must also be considered. If initial flap failure occurs in the immediate postoperative setting with several days to weeks of complications, a full course of tissue expansion may not allow for timely receipt of adjuvant radiation or chemotherapy. Expansion can begin as quickly as 10-14 days without an increase in complications[74], though a common protocol is to begin expansion 3-4 weeks after tissue expander placement with exchange to permanent implants 3-6 months from tissue expander placement. Patients can then undergo revisions including fat grafting as needed to achieve optimal aesthetic results.

## CONCLUSION/RECOMMENDATIONS

While less common in high-volume centers[75], autologous free tissue transfer failures can be devastating in

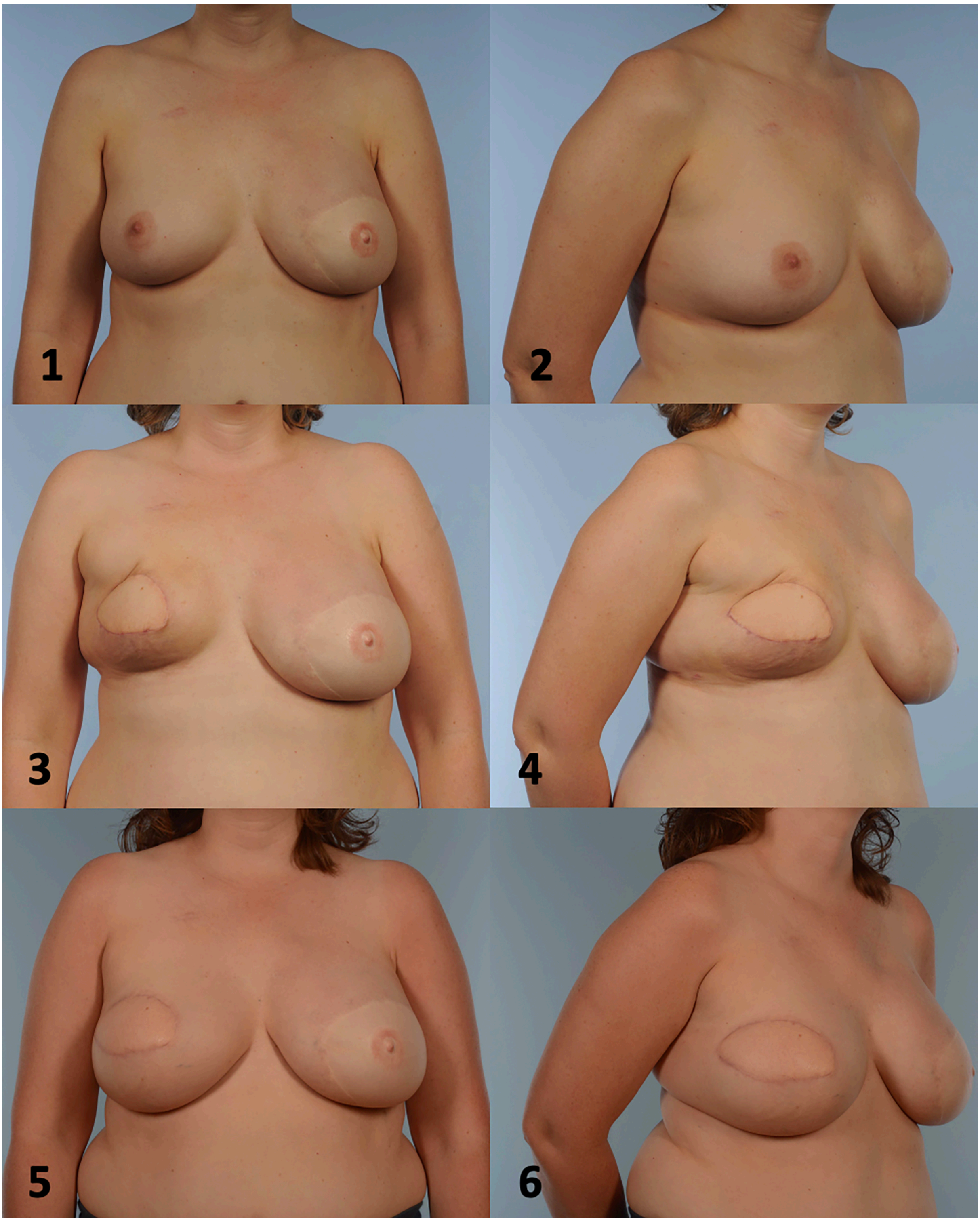


**Figure 4.** Patient with previous left breast cancer and latissimus dorsi flap reconstruction with new right breast cancer (Images 1 and 2). Salvage reconstruction was performed with right latissimus dorsi flap + tissue expander placement reconstruction (Images 3 and 4). Final postoperative result following implant exchange (Images 5 and 6).

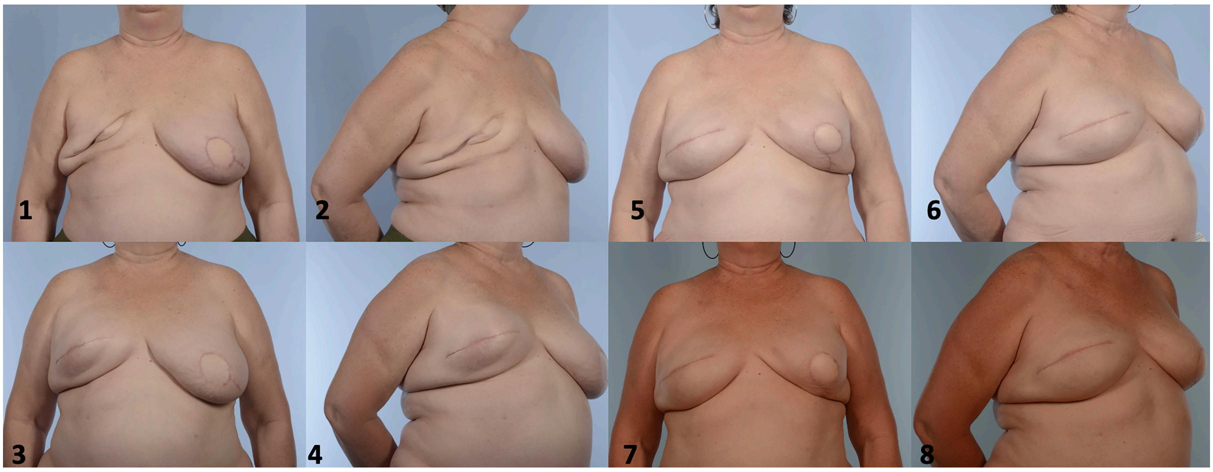


**Figure 5.** Patient with left breast cancer who underwent bilateral mastectomies and immediate reconstruction with DIEP flaps. The right flap failed (Images 1 and 2). After debridement and a period of healing, the breast was reconstructed with a subpectoral tissue expander (Images 3 and 4). The expander was later exchanged for a 700 cc silicone implant (Images 5 and 6).

breast reconstruction; it is important to have secondary (and tertiary) options available. It is imperative to discuss the risks and benefits of the procedure with patients, including the availability of secondary options in the event of failure. Efforts should be made to build a trusting relationship with patients preoperatively and to provide emotional support postoperatively when failures occur. Second-line options, including free and pedicled flaps, implants, or a combination of both, should be entertained based on the clinical scenario with a balance of safety and achieving the patient's overall reconstructive goals.

## DECLARATIONS

### Authors' contributions

Substantial contributions to the conception and design of the review paper, including clinical recommendations, literature review, manuscript writing, and figure creation: Myers PL, Tang SYQ, Saad NH, Momoh AO

### Availability of data and materials

Not applicable.

### Financial support and sponsorship

None.

### Conflicts of interest

All authors declared that there are no conflicts of interest.

### Ethical approval and consent to participate

All participants provided written informed consent.

### Consent for publication

Written informed consent for publication of patient photographs was obtained, specifically for external not-for-profit educational purposes such as lectures, presentations at professional conferences and publication.

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**Plastic and Aesthetic Research**

Review

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# Chest complications in autologous breast reconstruction

**Candice M. Leach, Meredith S. Collins**

Department of Plastic and Reconstructive Surgery, University of Kansas Medical Center, Kansas City, KS 66160, USA.

**Correspondence to:** Dr. Meredith S. Collins, MD, FACS, Department of Plastic and Reconstructive Surgery, University of Kansas Medical Center, 4000 Cambridge Street, MS 3015, Kansas City, KS 66160, USA. E-mail: mcollins7@kumc.edu

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## Abstract

Complications from autologous free flap reconstruction of the breast can present with both common surgical complications and unique complications at the chest recipient site. This review covers complications at the chest recipient site, including chest wall deformity, chronic pain, mastectomy skin flap necrosis, infection, pyoderma gangrenosum, bleeding complications, pneumothorax, chyle leak, and positive internal mammary lymph node metastasis.

**Keywords:** Autologous breast reconstruction, complications, chest wall deformity, pneumothorax, mastectomy skin flap necrosis, chyle leak, internal mammary node metastasis

## INTRODUCTION

The deep inferior epigastric artery perforator (DIEP) flap remains the gold standard in autologous breast reconstruction. DIEP flap surgery poses many challenges and potential for complications, which can be related to the flap itself, the flap donor site, the chest recipient site, or systemic. This review will focus on complications of the chest from the internal mammary recipient vessel dissection, including chest wall deformity from rib resection and chronic pain, mastectomy skin flap necrosis, infection, pyoderma gangrenosum, bleeding complications, pneumothorax, chyle leak, and positive internal mammary lymph node metastasis. Each topic will explore current literature and recommendations based on clinical experience.

## CHEST WALL DEFORMITY AND PAIN ASSOCIATED WITH RIB RESECTION

Use of the internal mammary artery and vein as the flap recipient site traditionally includes the removal of rib cartilage for exposure of the vessels[1,2]. With excision of the rib cartilage, two main primary concerns include chronic pain and chest wall deformity[3-7]. Several techniques have been subsequently described to try to alleviate these issues, including rib-sparing[3,8-15], simultaneous rib-sparing[16], and anastomosis to intercostal perforator vessels[14,17,18] to avoid or minimize rib resection. Additionally, consideration can be given to the utilization of alternative recipient vessels, such as the thoracodorsal vessels. With removal of the rib cartilage, techniques to reduce the chest wall deformity include the use of a pectoralis flap[19,20], placement of the medial portion of the flap over the defect[5], and replacement of the cartilage[4].

First described in 2008 by Parrett, the rib-sparing technique involves resection of the intercostal muscles as well as the perichondrium on either side of the third intercostal space (ICS), allowing for 2 to 2.5 cm of internal mammary vessel pedicle length[3]. Rosich-Medina *et al.* reported results of 178 free flaps in 167 patients with no postoperative chest wall pain or concerns over chest wall contour after rib-sparing exposure of the internal mammary vessels[13]. Sacks *et al.* reported the results of 100 microvascular reconstructive cases using the rib-sparing technique with no noted contour deformities[12]. Mickute *et al.* looked at patient-controlled anesthesia (PCA) morphine use postoperatively in 12 rib-sparing versus 12 rib removal patients and found significantly less morphine use (mean 11.0 mg *vs.* 28.6 mg) in the rib-sparing group, which held true when accounting for patient weight[21].

Computed tomography (CT) has been used to measure intercostal spaces preoperatively, with the finding that increased patient height correlated to increased ICS width[8]. In the patients with preoperative CT scan, the mean ICS width was $2.65 \pm 0.54$ cm in rib-sparing patients compared to $2.25 \pm 0.38$ cm in a rib resection group[8]. Khoo *et al.* published results of intra-operative clinical measurement of the second ICS width performed with a surgical ruler in 95 patients/109 breasts, and found a mean of $2.03 \pm 0.331$ cm, and a very weak positive correlation with patient height[9]. Sasaki *et al.* found similar measurements of $2.06 \pm 0.359$ cm for the second ICS (290 evaluated) and $1.40 \pm 0.420$ cm for the third ICS (30 evaluated)[10]. A retrospective chart review of 400 patients performed by Hamilton *et al.* found conversion to or initial attempt with rib resection for patients when the ICS was less than 12 mm[11].

If ICS dissection does not provide adequate space for anastomosis, the ribs may be trimmed with a rongeur and the microscope can be tilted to visualize the vessels as they pass under the rib for continued dissection[8,10,12,14]. Darcy *et al.* described resection of the posterior portion of the cartilage to improve exposure while leaving the anterior surface intact 30% of the time after increased experience with this technique[14]. Another technique includes the exposure of two contiguous ICSs (second and third) without rib resection as described by Oni *et al.*[16]. This method provided for additional exposure of the internal mammary vessels in cases such as bipedicled flaps, stacked free flaps, anastomotic redo, and salvage. Successful completion of this technique provided for antegrade and retrograde anastomoses in 15 patients with no flap failure. They noted mean second ICS width of 2.07 cm and third ICS width of 1.20 cm[16].

Consideration should also be given to the ICS that is selected. One concern with rib-sparing techniques when the second ICS is utilized is shorter cephalad vessel length if revision of the anastomosis is required[13,15].

Direct anastomosis of the free flap to internal mammary perforator branches (IMPB) has been described by several authors[14,17,22]. Munhoz *et al*. reported on five patients who underwent anastomosis of SIEA flaps to the 2nd intercostal space IMPB with no immediate complications[17]. All patients were evaluated with preoperative CT scan to evaluate both the donor superficial inferior epigastric artery and vein, as well as the recipient pectoralis muscle perforators and their course[17]. Rad *et al*. discussed a series of nine patients who underwent IMPB anastomosis using a coupler for both arterial (1.5 mm-2.0 mm) and venous (2.0 mm to 3.0 mm)[18]. Handheld Doppler was used to preoperatively map perforators which were then explored for suitability for anastomosis, typically at the second and third ICS[18].

The concern for chest wall deformity may be alleviated with suturing of the flap over the area of rib resection, utilizing a rib-sparing technique, or using intercostal perforators as recipient vessels. While contour deformity and chronic pain have been described, these have not been noted in the senior author's practice with rib-resection at the 3rd or 4th rib and suturing of the flap medially to the chest wall to cover the defect. This allows for a widened exposure, which can be beneficial in the case of microsurgical education of trainees as it facilitates the ease of anastomosis.

## MASTECTOMY SKIN FLAP NECROSIS

Evaluating the viability of mastectomy skin flaps prior to reconstruction is important to try to minimize mastectomy skin flap necrosis (MSFN) or massive skin necrosis (> 30% of the breast), as these complications can lead to prolonged healing and the need for additional interventions. In autologous reconstruction, this is particularly important during an immediate reconstruction. Risk factors that have been identified to contribute to MSFN include smoking[23-25] and increased BMI[25,26]. Nykiel *et al*. reviewed 944 autologous breast reconstructions including 204 free flaps and radiation was not a significant factor in the development of MSNF which occurred in 30% of the free flap cases[25]. Patel *et al*. discussed the treatment of 12 patients (of 805 reviewed), including 15 breasts (of 1,076 reviewed), who developed massive MSFN after autologous breast reconstruction between 1997 and 2010[23]. Of the patients who developed MSFN, 41.7% were current smokers and 16.7% were former smokers at the time of preoperative evaluation. Treatment initially started with allowing an eschar to form and separate. Antibiotics were only started for secondary cellulitis. Wound healing varied from 30 to 300 days, with 87% of the patients requiring late scar revision at an average of 8.9 months after initial surgery[23]. Nykiel *et al*. published a treatment algorithm for MSFN in 2014, recommending surgical intervention if wound healing was anticipated to be greater than 3 weeks[25]. Regression analysis showed full-thickness wounds greater than 6 $cm^2$ and partial-thickness wounds greater than 5 $cm^2$ took longer than 21 days to heal without clinical debridement and closure[25].

Given the significant impact on healing time, increased clinical care, potential for additional procedures, and impact on patient satisfaction caused by MSFN, several modalities have been evaluated to try to decrease the incidence. The use of indocyanine green fluorescence angiography (ICGFA) has been demonstrated to reduce the rate of MSFN to 13% from 23.4% in skin-sparing mastectomies undergoing reconstruction, effectively reducing those requiring reoperation from 14% to 6%[27]. A 2018 systematic review evaluated publications reporting clinical judgment versus indocyanine green (ICG) or fluorescein for rates of MSFN and reoperation. Clinical judgment had a mean of 19.4% MSFN and 12.9% reoperation. ICG and fluorescein had mean rates of MSFN of 7.9% and 3%, and mean rates of reoperation of 5.5% and 0%, respectively. Of note, only a single study evaluating the use of fluorescein was included in the review (34 breasts) compared to 13 studies using ICG (652 breasts)[28]. Additional imaging modalities that have been explored include hyperspectral imaging, which found a cutoff of tissue oxygenation at a depth of 1 mm (StO2%) < 36.29% led to a greater than 50% chance of mastectomy skin flap necrosis[29].

At our institution, the preferred method for evaluation of mastectomy skin flaps, in addition to clinical judgment, for immediate flap reconstruction is ICG fluorescence angiography (ICGFA). We also utilize ICGFA for flap evaluation and perforator selection. The majority of flaps at our institution are performed in a delayed fashion, which eliminates this issue. In the case of immediate flap reconstruction, if there is a concern for significant MSFN, then a delayed inset of 5-7 days can be performed. We have also used nitroglycerin paste when there is a concern about the perfusion of the nipple-areolar complex following nipple-sparing mastectomy with immediate DIEP flap reconstruction.

## INFECTION

Postoperative infections can be classified as surgical site, deep surgical site, or organ space infection. A retrospective American College of Surgeons (ACS) National Surgical Quality Improvement Project (NSQIP) database analysis in 2021, which included 1924 free flap breast reconstructions, found adjusted rates of 2.3%, 1.3%, and 0.3%, respectively, within 30 days of surgery[30]. The effects of radiation on infection rates have been mixed, with some studies showing increased infection rates versus non-radiated fields (4% *vs.* 0.5%)[31], while other studies have demonstrated no difference in placing a flap in a previously irradiated field[32]. Active smoking and body mass index (BMI) have also been reported as risk factors for postoperative infection[33]. In 2010, Reiffel published the results of a survey of the American Society for Reconstructive Microsurgery related to the use of peri-operative antibiotics. It was found that for microsurgical breast reconstruction, the first choice was a first-general cephalosporin for patients with no known allergies (93.5%), and clindamycin (79.5%) or vancomycin (20.5%) as the choice for patients with a penicillin allergy. Duration of antibiotic coverage varied greatly from a single dose (5.3%), < 24 h (26.7%), 1 to 3 days (33.3%), 4 to 5 days (12.0%), > five days (4.0%), and until drain removal (18.7%)[34]. Liu *et al.* compared a cohort of peri-operative antibiotics for 24 h versus greater than 24 h (median 10 days) in microsurgical breast reconstruction and found no difference in surgical site infection (15.5% *vs.* 19.5%, $P$ = 0.47)[35]. Additional studies have yielded similar results with no significant difference in SSI for patients receiving 24 h of antibiotics versus greater than 24 h in autologous breast reconstruction[36] and DIEP flap reconstruction specifically[37].

The current practice at our institution is continuing antibiotics until drain removal. This remains an uncommon complication of autologous breast reconstruction in our practice, even with the use of mesh for reconstruction of the abdominal donor site. We presently require three months of preoperative smoking cessation, a BMI of less than 35 $kg/m^2$, and a hemoglobin A1C of < 7.0 with the goal of reducing the incidence of postoperative surgical site infection.

## PYODERMA GANGRENOSUM

Pyoderma gangrenosum (PG) is a rare complication in free autologous breast reconstruction. First described by Brunsting in 1930, PG is a neutrophilic dermatosis characterized by ulcers, bullae, and/or pustules[38]. It can present very similar to a surgical site infection and even mimic a necrotizing soft tissue infection, making diagnosis difficult. Traditionally, PG has been a diagnosis of exclusion. Several diagnostic criteria have been proposed to aid in the diagnosis of PG. Su *et al.* proposed two major criteria and four minor criteria, with diagnosis requiring both major and at least two minor criteria[39]. A Delphi consensus in 2018 proposed one major and eight minor criteria, with a diagnosis made when the one major and four of eight minor criteria were met[40]. Table 1 summarizes the major and minor criteria for each.

A 2016 review of published cases of postoperative pyoderma gangrenosum (PPG) found a lower association with systemic disease than other forms of PG. Additionally, it was noted PPG is often misdiagnosed, which may lead to initiation of antibiotic drug therapy and debridement with possible subsequent morbidity[41].

**Table 1. Major and minor criteria for diagnosis of pyoderma gangrenosum**

| | Major criteria | Minor criteria |
|---|---|---|
| Su *et al.*[39] | (1) Rapid progression of painful, necrolytic cutaneous ulcer with an irregular, violaceous, and undermined border<br>(2) Other causes of cutaneous ulceration have been excluded | (1) History suggestive of pathergy or clinical finding of cribriform scarring<br>(2) Systemic diseases associated with PG<br>(3) Histopathologic findings (sterile dermal neutrophilia, ± mixed inflammation, ± lymphocytic vasculitis<br>(4) Treatment response (rapid response to systemic steroid treatment |
| Delphi consensus[40] | (1) Biopsy of the ulcer edge demonstrating neutrophilic infiltrate | (1) Exclusion of infection<br>(2) Pathergy (ulcer occurring at sites of trauma)<br>(3) Personal history of inflammatory bowel disease or inflammatory arthritis<br>(4) History of papule, pustule, or vesicle that rapidly ulcerated<br>(5) Peripheral erythema, undermining borders, and tenderness at sites of infection<br>(6) Multiple ulcerations (at least one occurring on an anterior lower leg)<br>(7) Cribiform scars at sites of healed ulcers<br>(8) Decrease in ulcer size within one month of initiating immunosuppressive medications |

A 2017 case report and systematic review by Zelones *et al*. of PG in autologous breast reconstruction identified 16 prior cases of PG with the average onset at 10 days postoperatively with a range of two days to two months[42]. Seven cases included fever and six included leukocytosis. Nine cases involved both donor and recipient sites, five cases involved the recipient breast only, and two did not specify. Only two cases reported positive wound cultures. Treatment modalities included steroids, cyclosporin, hyperbaric oxygen, tacrolimus, calcineurin inhibitor, and zinc oxide. The reported case also demonstrated fever, leukocytosis, erythema, bullae, and crepitus[42]. Due to difficulty in making a diagnosis, initial treatment with antibiotics and debridement prior to diagnosis of PG is common[42-48].

In 2019, Li *et al*. published a series of eight cases of postoperative PG after free abdominal tissue transfer for breast reconstruction[48]. The mean presentation was 3.9 days postoperatively, and symptoms included fever in six of eight, and leukocytosis in five of eight. As a component of PG is pathergy, or an exaggerated response to trauma/debridement, early diagnosis is important to break the cycle and initiate the appropriate treatment. Li proposed three factors that should raise suspicion for PG, including violaceous rash and ulceration at skin paddle inset and mastectomy flap, multi-site involvement (bilateral breasts or breast and abdomen), and finally a dramatic and immediate response to steroids or other immunosuppressive agents[48].

Pyoderma gangrenosum can be difficult to diagnose and suspicion should remain high in patients presenting with ulcerations and erythema of surgical sites, especially if more than one site is involved. Early biopsy of the wound edge can aid in diagnosis by evaluating for neutrophilic infiltration. Once there is a concern for possible PG, biopsy of the wound edge and consultation with Dermatology should be initiated.

## BLEEDING COMPLICATIONS

A 2019 NSQIP analysis of 4,143 patients undergoing free flap reconstruction of the breast noted a bleeding complication rate of 12%, defined as receipt of at least one unit of packed or whole red blood cells from the start of the procedure to 72 h postoperatively. The rate was highest in immediate bilateral reconstruction (16.6%), followed by delayed bilateral reconstruction (12.8%), unilateral immediate reconstruction (10%), and finally unilateral delayed reconstruction (9.4%)[49]. A 2021 NSQIP analysis of patients undergoing breast reconstruction including 1924 patients undergoing free flap reconstruction found an adjusted rate of bleeding complications of 12.3%[30]. Chen *et al.* evaluated the intraoperative use of heparin during microsurgical free flap reconstruction in 2008 and found that intravenous heparin administration prior to anastomosis did not lead to increased rates of hematoma or bleeding, but also did not decrease the rate of microvascular thrombosis[50].

In addition to requiring transfusions, bleeding may lead to hematoma formation and the need to return to the OR for evacuation. In order to try to reduce bleeding complications, the use of tranexamic acid (TXA) has been evaluated. In 2018, a meta-analysis of surgical trials evaluated the safety and effectiveness of TXA. The study showed the risk for transfusion was reduced by 38% in the TXA groups with no significant differences in mortality or thrombotic events[51]. Lardi *et al.* evaluated the use of TXA in microsurgical breast reconstruction[52]. The study compared patients who received up to 3 g of intravenous TXA intraoperatively and postoperatively to those that received no TXA. The use of TXA was determined by intraoperative and postoperative blood loss. Analysis of the two groups showed decreased blood loss in the TXA group (158.4 mL) versus control (231.5 mL) ($P < 0.001$) and a trend towards decreased hematoma of the breast (10.0% TXA versus 18.2% control), but this was not statistically significant ($P = 0.332$). There was no statistical difference in blood transfusions, deep venous thrombosis, or thrombosis of anastomosis[52].

Hematoma of the chest recipient site can be related to venous congestion. Chu *et al*. discussed the results of a retrospective review of reoperation for hematoma and/or venous congestion in head and neck reconstruction and breast reconstruction patients[53]. Of the 15 patients who developed both, 8 were separate occurrences, while 4 patients developed compression of the pedicle vein from the hematoma, and in the remaining 3 patients, it was believed that the venous congestion was the cause of the hematoma. For breast reconstruction, venous congestion leading to hematoma was more common than hematoma preceding venous congestion[53].

Meticulous hemostasis at the time of free flap reconstruction is vital to minimize hematoma formation or bleeding complications requiring transfusion. We have not adopted the routine use of TXA in microsurgical breast reconstruction. We administer a preoperative dose of aspirin, which is continued daily for 30 days, in addition to low-molecular-weight heparin while inpatient. The combination may contribute to bleeding in some patients. While hematomas do occur, in our experience, this seems to be most common in the setting of continuous heparin infusion following microsurgical thrombosis, anastomotic redo, or deep venous thrombosis/pulmonary embolism. Prompt identification and treatment of hematomas is important as it may be related to another issue, such as venous congestion or compression of the pedicle.

## PNEUMOTHORAX

Dissection of the internal mammary vessels as recipients of autologous breast reconstruction poses a risk of injury to the parietal pleura and subsequent development of pneumothorax (PTX). The rate is overall low in autologous reconstruction, with literature primarily composed of case reports and case series[54-56]. Darcy *et al.* reported one pneumothorax in a series of 463 rib-sparing free flap reconstructions[14]. Clinical symptoms of pneumothorax can include decreased oxygen saturation, tachycardia, tachypnea, dyspnea, and difficulty ventilating the patient. Progression to tension pneumothorax will result in hypotension. Reekie *et al.* reported a case of tension pneumothorax after an extended latissimus dorsi flap with noted venous congestion of the flap in combination with progressive hypotension, tachycardia, low pulse oximeter readings, and increased ventilatory pressures[54]. The patient was treated with needle decompression and subsequent chest tube placement with noted rapid improvement in the flap venous congestion concurrent with physiologic improvement[54].

Several treatment algorithms have been published for the management of suspected pneumothorax intra-operatively[55,56]. The first step is to perform a bubble test by filling the cavity with saline followed by a breath hold by anesthesia. In a series of four pneumothoraces during free flap breast reconstruction identified at a single institution, this test was only noted to be positive in one patient diagnosed with pneumothorax based on postoperative chest X-ray[55]. If the bubble test is negative, then no additional intervention is required. If the bubble test is positive, the injury should be repaired by direct suture of the pleural tear, fascial graft or muscle/fascia flap, or fat plug as needed[55,56]. Repair should be performed over a catheter which is removed during positive pressure breath hold as the last suture is tied down. Bubble test should then be repeated to confirm the repair. Postoperative chest X-ray and clinical monitoring for signs of pneumothorax should be performed. If clinically significant pneumothorax develops postoperatively, the patient will require a chest tube. Careful coordination with the team placing the chest tube is vital as placement of a postoperative intercostal drain for pneumothorax was reported to occur immediately adjacent to the internal mammary vascular pedicle and vascular anastomosis[56].

Intraoperative concern for pneumothorax should prompt a bubble test and repair as needed. Venous congestion in a flap may be a sign of pneumothorax in an otherwise healthy flap[54] and is considered during the evaluation for the cause of venous congestion. Patients with concern for intra-operative pneumothorax should have postoperative chest x-ray completed. If chest tube placement is needed postoperatively, the microsurgical reconstruction team needs to carefully coordinate the placement of the chest tube to minimize potential injury to the flap and/or vascular pedicle.

## CHYLE LEAK

With dissection of the internal mammary vessels, identified lymph nodes are typically removed. Removal of these lymph nodes interrupts the lymphatic channels, and in 2019, Long *et al*. reported a case of a chyle leak after delayed-immediate bilateral DIEP flaps[57]. The patient had a history of invasive ductal carcinoma of the right breast and was treated with a right modified radical mastectomy and left simple mastectomy with immediate placement of acellular dermal matrix wrapped tissue expanders followed by adjuvant radiation. On postoperative day five following the DIEP flaps, the left breast drain changed to cloudy but low volume output and she was discharged home. The next day, she had significant swelling of the left breast surgical site, which improved after 600 mL of milky fluid spontaneously decompressed through the left-sided drain. Chyle leak was suspected and confirmed after testing the fluid for triglycerides and chylomicrons (> 1300 mg/dL and present). She had foam tape applied to the area to try to compress the leak and was started on a low-fat, high-protein diet with resolution of the milky drainage on postoperative day 12. Her drain was subsequently removed on postoperative day 16 and she remained on a low-fat diet for 3 weeks. Their recommendation is to deal with lymphatic vessels and nodes deliberately with the use of clips as opposed to cautery or sharp dissection during internal mammary vessel dissection[57].

For a patient who is otherwise clinically doing well without evidence of infection but experiences milky output from a drain after starting a regular diet, chyle leak should be suspected and evaluated with fluid testing for triglycerides and chylomicrons (> 110 mg/dL and presence is confirmatory) as was done in this case. Treatment may start with a diet low in long-chain triglycerides with supplementation of medium-chain triglycerides[58] as well as the addition of somatostatin or octreotide. If the leak persists beyond 2 weeks or the volume is greater than 500 to 100 mL per day, more aggressive measures may be required, such as a percutaneous approach with coiling of the thoracic duct or surgical intervention to identify the leak and ligate the offending vessels.

## POSITIVE INTERNAL MAMMARY NODE METASTASIS

The internal mammary vessels are a popular choice as recipient vessels for autologous free flap breast reconstruction. During the dissection of the internal mammary vessels, lymph nodes may be identified, and for patients with a history of breast cancer, the concern for possible metastasis is present. In 2011, Yu *et al*. discussed their institution's experience with opportunistic internal mammary lymph node biopsy during microsurgical breast reconstruction[59]. They noted 3 prior studies reporting biopsy of internal lymph nodes, with a total of 9 containing metastasis out of 49 biopsied. Of 293 free flap breast reconstructions, 43 patients had internal mammary lymph nodes identified during dissection of the internal mammary vessels, with a total of 6 of these patients having metastasis in the sampled nodes. The treatments varied in their patients, from radiation to the chest wall and internal mammary lymph node chain, with some patients also receiving radiation to the supraclavicular fossa, chemotherapy, or no additional treatment. Of the 38 sampled nodes in the remaining 37 patients, which were negative for metastasis, five were noted to have silicone granulomas in patients with prior implant-based breast reconstruction, and the remaining 33 showed inflammatory changes only. It was noted that there was no macroscopic difference identified between these nodes[59]. Wright *et al*. reported on routine internal mammary lymph node sampling in 264 autologous breast reconstructions (204 patients)[60]. All removed lymph nodes were clinically unremarkable without macroscopic evidence of tumor involvement. Six patients had positive metastatic disease, resulting in an alteration of their adjuvant treatments[60].

We recommend a pathologic examination of any lymph nodes identified during the dissection of the internal mammary vessels and referral to our oncology colleagues for treatment options in the event of positive nodes.

## CONCLUSION

Complications at the recipient site of autologous breast reconstruction can include common surgical complications (infection, bleeding), recipient site-specific issues (contour deformity, mastectomy skin flap necrosis), and uncommon complications (pneumothorax, pyoderma gangrenosum, chyle leak, positive internal mammary nodes). It is important to understand the risks, contributing factors, and treatments for each. Our hope is this review reinforces treatment options for more common complications as well as increases awareness of less well-known complications. High clinical suspicion for uncommon complications can reduce the time to diagnosis and potential additional morbidity from delay in diagnosis and appropriate treatment.

## DECLARATIONS

### Authors' contributions

Literature review and compilations for each topic, introduction, and conclusion: Leach CM
Personal and institutional experiences and recommendations for each topic, introduction, and conclusion: Collins MS

### Availability of data and materials

Not applicable.

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All authors declared that there are no conflicts of interest.

**Ethical approval and consent to participate**

Not applicable.

**Consent for publication**

Not applicable.

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Systematic Review

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# A systematic review on embodiment and breast reconstruction: a patient-centered framework for evolving breast outcome measures

**Madeline G. Chin[1], Sahand C. Eftekari[2], Steven P. Moura[2], D' Andrea T. Donnelly[2], Ellen C. Shaffrey[2], Lucas Sears[2], Aaron M. Dingle[2]**

[1]Division of Plastic Surgery, The Warren Alpert Medical School of Brown University, Providence, RI 02903, USA.
[2]Division of Plastic Surgery, University of Wisconsin School of Medicine and Public Health, Madison, WI 53705, USA.

**Correspondence to:** Dr. Aaron M. Dingle, Division of Plastic Surgery, University of Wisconsin School of Medicine and Public Health, 5107 Wisconsin Institutes for Medical Research, 1111 Highland Avenue, Madison, WI 53705, USA. E-mail: dingle@surgery.wisc.edu

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## Abstract

Embodiment describes the sense of one's own body, encompassing dimensions of being, having, and using a body. Regarding breast reconstruction, embodiment can be understood as how effectively the reconstructed breast replaces the patient's missing breast. While there has been increasing attention in recent decades on understanding and measuring embodiment in the prosthetic limb, there is limited literature applying embodiment to the context of breast reconstruction. We posit that the literature on prosthetic embodiment can be applied to evolving discussions on breast reconstruction outcomes and patient satisfaction. As breast reconstruction techniques continue to evolve, such as advances in nerve coaptation and reinnervation of the breasts, the concept of embodiment may help broaden the scope of how patient outcomes can be more holistically evaluated. This systematic review examines existing literature on embodiment after breast reconstruction, summarizes embodiment and its subcomponents, and discusses how embodiment can be a helpful framework for the future of breast reconstruction outcome measures.

**Keywords:** Embodiment, breast reconstruction, prosthetic embodiment

## INTRODUCTION

Advances in postmastectomy breast reconstruction techniques have led to increasingly nuanced methods of assessing reconstructive outcomes[1-3]. While historically breast cancer surgery centered solely on successful resection of malignancy, rising survival rates of breast cancer patients have led to increased attention to quality of life metrics following breast reconstruction[4-6]. While alloplastic interventions have been the most common form of reconstruction over the past twenty years, developments in tissue-based, autologous approaches have led to the possibility of a softer, more natural-appearing breast mound and, in turn, improved long-term patient satisfaction[7-10].

In the context of breast reconstruction, the BREAST-Q is the current gold standard patient-reported outcome measures (PROMs) instrument[11]. The BREAST-Q measures physical, psychosocial, and sexual well-being, in addition to patient satisfaction with breasts, outcome, and overall care. The BREAST-Q has evolved considerably since its inception in 2004, notably with the recent addition of a sensation module[12]. However, as breast reconstruction techniques continue to evolve, investigating patient outcomes utilizing research approaches from reconstruction and prosthetic replacement of other areas of the body may be useful. Within the prosthetic limb literature, the advancement of neural interfaces that allow improved control and sensory feedback from prostheses has spurred new outcome measures centered on dimensions of embodiment[13-15].

Embodiment describes the sense of one's own body, or with respect to prostheses, how effectively the prosthesis replaces a patient's absent or altered body part[13]. The primary domains of embodiment for prosthetic limbs are motor, sensory, postural, and psychosocial domains. These domains shape a sense of ownership and agency, which facilitate the embodiment of the prosthesis. Regarding breast reconstruction, we suggest that embodiment encapsulates existing quality-of-life measures, including psychosocial well-being, sexual well-being, and sensation, and expands on them to offer a more holistic and personal framework for understanding one's sense of self post-reconstruction.

Given the extensive literature on prosthetic embodiment, we propose its incorporation into discussions on improving and evaluating breast reconstruction outcomes[13-15]. This systematic review aims to summarize existing literature on breast reconstruction and embodiment, and discuss how embodiment can be a helpful framework for the future of breast reconstruction outcome measures.

## METHODS

This literature review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[16]. To review existing literature on breast reconstruction and embodiment, we queried the PubMed/MEDLINE, Web of Science, Embase, and Cochrane databases with relevant search terms, including combinations of "embodiment" and "breast reconstruction," "breast implant," or "breast" [Figure 1]. Our search strategy included all articles published in the years 1977 to August 2023. Studies not available in the English language were excluded.

## RESULTS AND DISCUSSION

### Breast embodiment framework

The literature search on embodiment in the context of breast cancer surgery yielded 320 articles, of which 21 were ultimately included [Figure 1]. The majority of these studies applying "embodiment" to assessments of patients' experiences following breast reconstruction utilized qualitative methodologies, predominantly semi-structured patient interviews [Table 1]. Many of these patient interviews centered on the broad research question of how women experience oncoplastic breast surgery, and then "embodiment" served as a

**Table 1. Summary of included articles on breast embodiment**

| Author (year) | Assessment methods | Domain(s) | Key findings/embodiment definitions |
| --- | --- | --- | --- |
| Adams *et al.*[53] (2011) | Literature review 17 qualitative studies included | PSYCH | This review article examined the experiences and concerns of women under the age of 45 diagnosed with breast cancer. Key issues identified included feeling 'out of sync' and fear of recurrence. These articles were analyzed with a framework of altered embodied subjectivity. Beyond visual changes, the participants underscored the *feelings* of *being* in an altered body |
| Cheng *et al.*[20] (2018) | Qualitative 8 semi-structured interviews | PSYCH | This study interviewed women who decided to undergo delayed breast reconstruction. Four embodiment themes were highlighted: losing a sense of self, living with an altered body, reclaiming the body/self, and rebuilding the body/self |
| Chuang *et al.*[19] (2018) | Qualitative 8 interview participants, 20 transcripts | PSYCH | This study evaluated perceptions of the body from women diagnosed with breast cancer and treated with a mastectomy more than 5 years prior. Main themes from the interviews included abandoning objectification, restoring body image, and redefining the self |
| Boer *et al.*[40] (2015) | Qualitative 10 women, 26 interviews at different stages of reconstruction | PSYCH + SENS | This study interviewed women prior to undergoing breast reconstruction regarding their expectations of their body post-reconstruction. The women were also interviewed after reconstruction. In the analysis, their expectations were categorized as dealing with their "gazed body," their "capable body," and their "felt body." After reconstruction, these expectations had to be reconfigured and many had to adjust to the unexpected, namely altered feeling of the reconstructed breast |
| Esplen *et al.*[52] (2020) | Review | PSYCH | This review summarized various body image interventions for women with breast cancer, with a particular focus on online interventions. The authors outlined a construct of "embodied body image" in cancer in which body image is multifaceted and linked to patients' early history, self-identity, and self-worth |
| Graham *et al.*[60] (2018) | Qualitative 4 semi-structured interviews, 5 online forums, 3 online newspaper articles | PSYCH | This article explored women's decision processes for risk-reducing mastectomy, highlighting social and political factors that shape the process. The analysis highlights how a sense of "embodied selves" is often gendered and culturally shaped by conceptions of womanhood and feminity |
| Greco[59] (2015) | Qualitative 12 interviews, analyses of policy documents of French/EU regulatory agencies, medical literature, and an online forum | PSYCH + SENS | This article examined the 2010 controversy in France regarding the use and eventual recall of silicone breast prostheses. The mixed methods article includes interviews with patients who received these breast implants during post-mastectomy reconstruction. The article analyzed the patients' experiences of both physical and psychological pain utilizing the concept of "embodied risk," insofar as the risks derived from prostheses and implants are literally embodied by patients |
| Hansen *et al.*[18] (2022) | Qualitative 7 women, 14 interviews | PSYCH | This article assessed women's experiences of oncoplastic breast surgery and how treatment affected body image. Participants discussed how the reconstructed breast restored a sense of normalcy, in particular with maintaining interpersonal relationships. The findings were framed by a theory of embodiment defined by philosopher Merleau-Ponty, insofar as the altered body is an essential part of the subjective being, and time and transition are needed before the altered body is integrated into an individual's embodiment |
| Holmberg[21] (2014) | Qualitative Interviews with 17 first-time breast cancer patients, 4 oncologists, and 10 nurses | PSYCH | This article examined the nature of persistent worry that women may experience after breast cancer treatment, particularly mistrust towards their own bodies. The authors described how cancer diagnoses impact a patient's sense of embodiment, given these diagnoses are often received before a physical sense of illness, therefore leading to an experience of shock. The authors conceive of post-treatment worry as an "embodied sense of risk" |
| Hopwood *et al.*[17] (2019) | Review | PSYCH | This article offers a novel framework for embodied body image in cancer patients. The approach consists of three dimensions of embodiment: "being a body, having a body, using a body." Applications of the framework were illustrated through three case examples of breast cancer patients |
| Lende *et al.*[58] (2009) | Qualitative 15 semi-structured interviews | PSYCH | This article examines the decision-making of African-American women regarding breast cancer screening. The article describes an "embodied approach," which highlights the significance of subjective experience and of understanding the body as relational and meaningful |
| Lindau *et al.*[38] (2020) | Review | SENS + PSYCH | This article describes bionic technologies for the restoration of sensation in the nipple-areolar complex. The authors highlight that mastectomy often leads to numbness of the chest, which can impact sexual well-being and lead to the "disembodiment" of the breasts. The authors discuss their sensor technologies, which can be placed under the skin of the nipple-areolar complex, to detect touches |
| Loaring *et al.* | Qualitative | PSYCH | This study focused on couples' experiences of mastectomy with |

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| [42] (2015) | 8 semi-structured interviews, with 4 long-term heterosexual couples | | reconstruction, and its impact on sexual intimacy and body image. The results highlighted how heteronormative sexual scripts and gendered coping styles may influence couples' intimacy after an experience of 'altered embodiment'. The authors stressed how the altered body involved both *personal* adjustment, and *relational* adaptation in the context of these intimate relationships |
| Parton *et al.*[56] (2016) | Qualitative<br>16 semi-structured interviews | PSYCH | This study examined how woman understand their own bodily experiences and sexuality in the context of cancer, as well as their sexual relationships. A dominant theme was describing the "abject body" after cancer, outside of normality and ideal femininity |
| Piot-Ziegler *et al.*[41] (2010) | Qualitative<br>19 women, 3 semi-structured interviews each | PSYCH + SENS+ POST | This study examined the impact of mastectomy on women's identity. Participants discussed how breast reconstruction is often viewed as a potential restoration of altered body integrity and physical symmetry. Many described how grieving the past body and having to accept a new body can lead to an identity crisis. Modified touch and sensation, altered postural balance, and impact on relationships were discussed |
| Quixadá *et al.*[51] (2022) | mixed methods:<br>-likert questionnaires on pain, self-esteem, fatigue, depression, anxiety, stress, and exercise self-efficacy<br>-posture: vertical spine and vertical head angles<br>21 women included | POST + PSYCH + SENS | This study evaluated the practicality of measuring posture objectively, and explored the correlation between posture and affect in patients with breast cancer-related postsurgical pain who underwent a 12-week course of Qigong mind-body training. The majority of participants who improved in fatigue and anxiety scales had better vertical head values. Pain severity decreased when vertical spine angle improved |
| Reid-de Jong[55] (2022) | Qualitative<br>6 women interviewed | PSYCH | This study evaluated the experiences of women who underwent post-mastectomy tattoos. Many women described feelings of being damaged following mastectomy. The tattoos often served as an embodied representation of self, and helped women regain confidence in a symbolically meaningful way |
| Slatman[25] (2014) | Review | PSYCH | This review explored various understandings of embodiment from a patient's perspective, focusing on experiences after breast surgery. The author proposes that an analysis of embodiment requires including both individual-level and social group-, or societal-level |
| Slatman *et al.*[39] (2016) | Qualitative<br>multiple interviews with 19 female breast cancer patients | PSYCH + SENS | This study addressed how women give meaning to their bodies' scars after breast cancer surgery. Beyond the physical marking of scars, women also highlighted experiences of pain/functional impairment and changes in sensation |
| Thomas-MacLean[54] (2005) | Qualitative<br>12 women, interviewed twice each | SENS + PSYCH | This study explored women's experiences of bodily changes and subsequent embodiment after breast cancer, utilizing a feminist perspective. Key themes that impacted the altered sense of embodiment included altered or loss of sensation and the management of appearances (e.g., wearing prostheses) |
| Trachtenberg *et al.*[57] (2022) | Likert questionnaires<br>4 measures of gender socialization: gender role socialization scale, mental freedom scale, objectified body consciousness scale, and silencing the self scale<br>2 measures of psychosocial well-being: experience of embodiment scale and functional assessment of cancer therapy-breast<br>113 women included | PSYCH | This study examined the correlation between gender socialization and psychosocial well-being in young women treated for breast cancer. Women who reported more normative gender socialization were associated with poor well-being scores. Women who described greater resistance towards gender-role expectations and objectification pressures correlated with greater well-being scores. Body shame, body surveillance, and mental freedom were significant predictors of variance within a regression analysis of the Experience of Embodiment Scale scores |

PSYCH: Psychosocial; POST: postural; SENS: sensation.

key framework for interpreting their findings.

Embodiment encompasses the dimensions of "being, having, and using a body," and has been measured through sensation, posture, and psychosocial outcomes[17]. These subcomponents of embodiment can be articulated by patients and evaluated independently; however, they all contribute to an overall sense of being and belonging in one's body. A recurring theme from the literature was that alterations to these dimensions require both personal and relational adaptations. Another over-arching theme was embodiment post-reconstruction requires time and transition. One patient described the breast reconstruction experience,

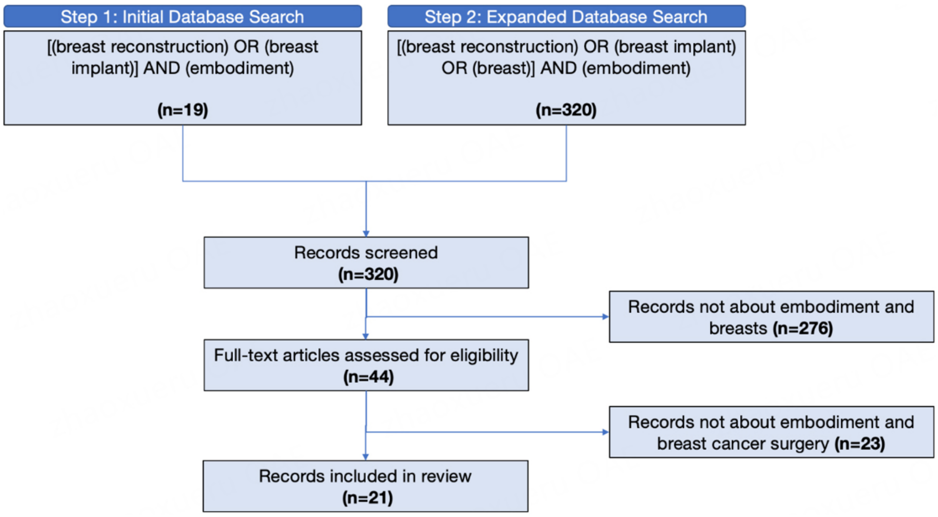


**Figure 1.** Diagram of the literature review process.

saying, "I think it is comparable to giving birth…the body is a completely different universe until it is healed[18]." Given that embodiment describes the sense of one's body, the process of embodiment post-reconstruction is a process of acceptance of a new, altered body. Embodiment post-reconstruction can include a redefinition of self in the context of the altered body and abandoning self-objectification of the body[19-21]. In patients' descriptions of seeking and undergoing reconstruction, they linked the physical reconstruction to the process of striving to redefine the self, amongst their cancer diagnoses[18,20].

These studies offer a starting point for outlining a framework for breast embodiment. However, there is more extensive literature on measurements of prosthetic limb embodiment compared to breast embodiment[13,14,22]. While breast reconstruction, autologous or implant-based, is not universally described as a "prosthesis", the prosthetic embodiment framework can be extended to breast reconstruction to describe how effectively the reconstructed breast replaces a patient's missing breast. There are parallels between these contexts, insofar as alloplastic implants are analogous to prostheses, while autologous breast reconstruction represents a reconstructive approach similar to limb salvage with bone allograft or vascularized composite allotransplantation of the limb. In both contexts, "prosthesis" and reconstructive approaches are intended to restore the normal form and functions of the missing body part. Therefore, we sought to merge the themes from this literature review with established embodiment conceptions outlined in the prosthetics literature to suggest a framework of "breast embodiment".

## PRIMARY DRIVERS OF EMBODIMENT

Within existing frameworks of *prosthetic* embodiment, two primary drivers of embodiment are ownership and agency[13,14,22]. The proposed outline for understanding *breast* embodiment overlaps considerably with prosthetic embodiment. However, there are a few key distinctions given their anatomic and functional differences. We propose that "ownership" and "body representation" are the two main drivers of breast embodiment, both of which are influenced by three domains of embodiment: sensation, posture, and psychosocial [Figure 2].

Ownership is the sense that an implant or prosthetic belongs to oneself, or is "part of my body" or "part of me[14,23,24]." Ownership includes explicit and implicit subcomponents. Explicit ownership describes a patient's conscious sense of the implant/prosthesis as instinctively part of their own body. A decreased sense of

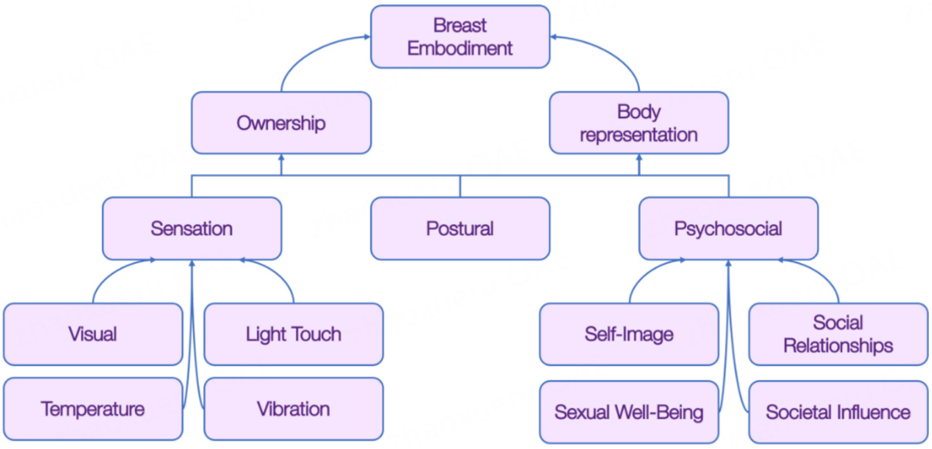


**Figure 2.** Breast embodiment framework.

ownership, or feeling of estrangement from one's own body post-reconstruction, can lead to decreased embodiment. One patient who underwent breast reconstruction noted, "At least there is something to fill in the bra, so I guess people will never notice that the breast is *not mine*" (emphasis added)[18]. In contrast, implicit ownership represents a patient's unconscious behaviors towards the implant/prosthesis. In the context of breast prostheses or reconstruction, sometimes forgetfulness of the breast prosthesis can promote a sense of ownership, insofar as if the person is constantly cognizant of the prosthesis, by feeling pain or constantly feeling, these sensations may highlight the foreignness of the prosthesis[25]. Thus, these subconscious behaviors facilitate a sense of ownership.

While "ownership" applies to both prosthetic and breast embodiment, the driver of "agency" is less pertinent to the context of breast reconstruction. In regards to prosthetic limbs, agency refers to a patient's capacity to start and terminate their actions to control their prosthesis in a deliberate manner[14], which is outside the scope of breast embodiment given the lack of motor actions as a primary function. Instead of agency, we suggest that body representation is a second key driver of breast embodiment. Previous literature has included body representation as a major component of embodiment, alongside ownership and agency[13,26,27]. The integration of a reconstructed breast into one's body representation facilitates embodiment, in so far as the foreign object or reconstructed tissue becomes part of the neural structures that guide awareness and perception of the body[14].

Body representation encompasses the experiences, understandings, and knowledge of the physical structure of one's body[13,28]. Similar to ownership, there are explicit and implicit subcomponents of body representation. Explicit body representation refers to conscious experiences of the body, which include its shape, size, location, and physical properties. "Body image" is often defined as these explicit experiences of "body representation[13,28,29]". Whereas implicit body representation is often referred to as "body schema[29]". Body schema refers to the body's spatial properties, and the subconscious or unconscious mechanisms that direct posture and movement. At this implicit level of body representation, an object becomes embodied if its properties are cognitively processed similar to the properties of biological body parts[30]. In the context of breast reconstruction, the integration of a reconstructed breast into one's body representation supports the sense of embodiment.

## THE THREE EMBODIMENT DOMAINS

The established domains that shape and create the drivers of *prosthetic* embodiment are motor, sensory, postural, and psychosocial[22]. These domains are integral to *breast* embodiment, with the exception of the motor domain. Embodiment outcome measures typically assess one of these three domains-sensation, posture, or psychosocial. In embodiment research, these domains are the interface for assessing how an intervention can alter a patient's embodiment level, given that these domains act as a gateway to influence the higher drivers of embodiment.

The sensory domain encompasses the visual, tactile, vibratory, and temperature inputs that allow a patient to receive feedback from the implant/prosthesis[31-33]. The postural domain describes the proprioceptive features of an implant/prosthesis and the positioning a patient develops following reconstruction. The psychosocial domain includes the self-image and social integration of an implant/prosthesis into a patient's life. A key difference in breast embodiment compared to prostheses is the emphasis on sexual well-being within the psychosocial domain. Sexuality is more commonly addressed in breast embodiment, which may be attributed to societal roles in gender identity and breast sensation as it relates to sexual function, which underscores the overlapping nature of the embodiment domains. Thus, the proposed framework of breast embodiment offers a conceptual schema, rather than a rigid outline [Figure 2]. While sensation and motor domains of embodiment are the most prevalent domains discussed within the current literature on limb prosthetics, the psychosocial domain (including sexual function) is underrepresented[22,34]. Conversely, many breast reconstruction outcomes focus on the psychosocial domain, with more recent increasing attention to the sensation domain given advances in neurotization during breast reconstruction[35-37]. We identified the relevant domains for each article included in our literature review on embodiment and breast reconstruction [Table 1]. All included articles assessed psychosocial dimensions, while one-third included sensation, and two articles included impacts on posture [Figure 3].

### Sensation

The complete or partial desensitization of the chest following mastectomy and breast reconstruction is a common phenomenon and contributing factor to altered embodiment[38,39]. Altered embodiment refers to the disruption of one's sense of self, or the experience of self-alienation from one's body[25]. However, expectations for loss of breast sensation after mastectomy may not be clearly set for patients during their course of care, which can lead to distressing outcomes[38,40]. Sensation was often tied to influencing ownership and, in turn, embodiment. One patient described, "It seems as though [the breast] was not yours, because, first of all, you have no sensations anymore[41]".

Furthermore, a few articles highlighted the impact of altered sensations on intimate relationships[38,42]. In response to numbness of the breasts following mastectomy, some women report aversion towards sex or a feeling of frustration or detachment during sexual interactions[38,42]. Lindau *et al.* proposed leveraging technology utilized in restoring sensation in bionic hands to restore sensation to the nipple-areolar complex[38]. They posit that providing sensation to the reconstructed breast fosters its embodiment and may reduce post-mastectomy sexual dysfunction[38]. Additionally, these relational impacts of altered sensation extend beyond intimate partners. In one study, patients discussed the fear of modified touch and sensations before undergoing mastectomy; however, they reported that modification of sensitivity and sensuality was seldom discussed in medical contexts[41]. This literature on the sense of touch in relational contexts, such as hugging one's child or partner, highlights how sensation is a crucial domain of breast embodiment.

### Posture

Postural changes following breast reconstruction also impact embodiment. Particularly for patients

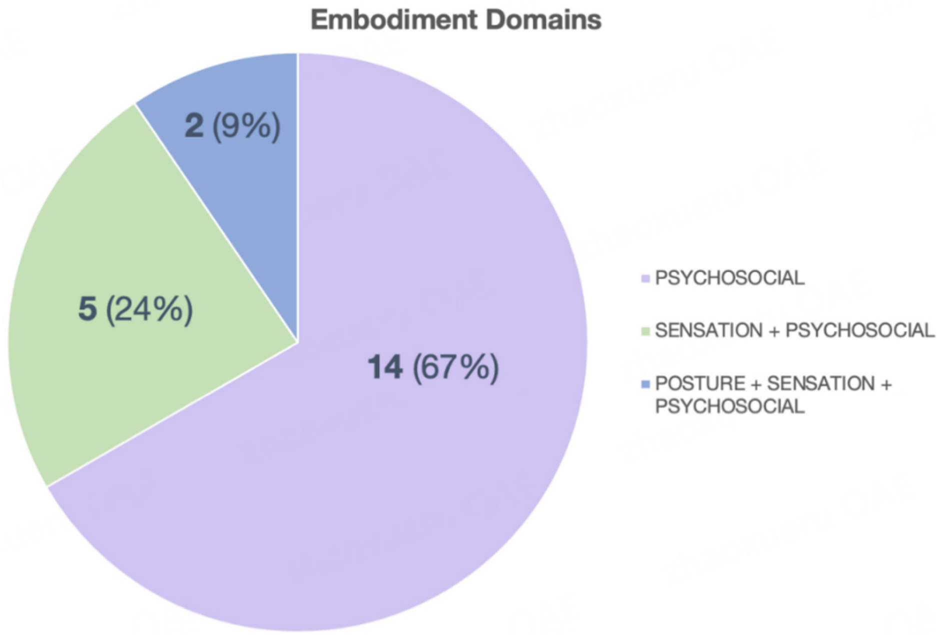


**Figure 3.** Domain analysis of included articles in embodiment and breast reconstruction literature review.

undergoing unilateral mastectomy, postural control and balance can be altered[43-46]. In evaluations of mastectomy-induced spinal deformities, several studies have reported on the correlation between immediate breast reconstruction and the prevention of spinal postural changes[47-49], though delayed breast reconstruction has not demonstrated significant improvement in this regard[50]. In our review, some women reported postural imbalance following mastectomy, thus highlighting the integral role of immediate reconstruction in attempting to restore postural symmetry[41]. Quixadá *et al.* objectively measured posture through vertical spine and vertical head angles in a 3D motion capture system and examined the correlation between posture and affect in breast cancer survivors who underwent a therapeutic course of Qigong mind-body training[51]. Notably, patients who improved in fatigue and anxiety scales had better vertical head values, suggesting a connection between posture and affect within an embodied paradigm[51]. Overall, the postural domain was the least captured within this embodiment literature review, which suggests future work is needed to assess the influence of measurements of posture on embodiment.

### Psychosocial

The psychosocial dimensions of embodiment were the predominant focus of the identified literature on breast embodiment. In addition to the impacts on sexual well-being and social relationships discussed previously, much of the literature raised the effect of breast reconstruction on self-image, which included traditional conceptions of body image, as well as a broader sense of self-identity[52]. Multiple articles discussed how patients undergoing breast cancer surgery are often left in a state of altered embodiment[18,25,41,42,53,54]. Beyond the visual anatomical alterations, patients' language around self-conceptualization following mastectomy described insecurities related to sexuality, gender identity, beauty, and femininity[55-57].

These broader questions around self-identity highlight how psychosocial dimensions of breast embodiment include the patient's experience within a given societal context[58]. While breast reconstruction is a lived experience from within, the impact of its visual representation on others influences body image and, in turn, embodiment. The breast embodiment literature brings attention to how reconstructive breast surgery is often driven by the desire for a "normal" feminine appearance[59]." One patient explicitly described how "the breast and shape do imply a femininity which I have always had," demonstrating how breasts often serve as a cultural symbol for femininity[18,25]. Thus, embodiment can often be a matter of societal adaptation to gender norms and/or a negotiation of one's femininity. Women are often situated between individual and cultural perceptions of what it means to be a woman, which further complicates an individual's negotiation of their own sense of identity[60].

While many existing outcome evaluations of breast reconstruction focus on the "natural look" of the breasts or how the breast physically "feels to touch" relative to preoperatively, the qualitative results from our literature analysis highlight the patient's *feeling* of how the implant/prosthesis "fills a void in her chest[25]." From this perspective, the implant/prosthesis not only restores an empty space but also provides psychological comfort in the face of this recent loss[25]. Beyond the outward appearance of the breasts, embodiment examines the deeper, inner function of the breast implant/prosthesis as filling a void and fitting into one's body representation.

This literature review offers insight into how "embodiment" allows for a more capacious understanding of patients' subjective experience of their bodies following reconstruction. These studies and this proposed framework of breast embodiment provide a foundation for incorporating embodiment into existing evaluations of patients' quality of life post-reconstruction.

## INCORPORATING EMBODIMENT INTO PATIENT-REPORTED OUTCOME MEASURES

The embodiment framework extends the scope beyond current breast reconstruction outcome measures while still centering patients' experiences and perspectives. In designing and implementing outcome evaluations for breast reconstruction, capturing the first-person perception of the embodied experience is critical to understanding reconstructive goals and the patient's experience postoperatively. Traditionally, evidence-based medical sciences have given primacy to quantitative data, which, in the case of subjective matters, has given rise to a variety of "quality of life" scales[25]. These quantitative tools are valuable for the collection of large data samples to offer generalizable outcomes.

Within the field of breast reconstruction, the BREAST-Q is the gold standard patient-reported outcome measurement instrument[11,61]. The BREAST-Q measures three quality of life domains (physical, sexual, and psychosocial well-being) and three satisfaction domains (satisfaction with breasts, outcome, and care)[11]. The BREAST-Q questionnaire has demonstrated high reliability and has been independently validated[11,62].

Since its inception in 2004, the BREAST-Q has evolved considerably, with the addition of multiple new modules and scales to address identified gaps[12,63-65]. When the content validity was recently re-examined to determine relevance and comprehensiveness, additional scales for breast sensation, cancer worry, fatigue, work impact, and upper extremity lymphedema were developed[66]. These changes reflect the increasing trend in the literature on functional outcomes, in addition to the traditional paradigms in post-mastectomy breast reconstruction focusing on aesthetic outcomes[38,67].

As breast reconstruction techniques continue to advance, we believe that embodiment offers a helpful framework for formulating additional questions that can capture patients' values. The developments in breast neurotization have already been paralleled with evolving sensation measures[12,35,36,67]. Previous focus on breast sensory outcomes focused on symptomatic complications following surgery, such as pain, burning, or tightness. Numbness, or loss of sensation, was largely overlooked in patient-reported outcome scales. In 2021, the BREAST-Q incorporated new sensation modules to evaluate how the loss of sensation in the breast area has affected the quality of life and to quantify the amount of sensation felt in the breast during certain activities (i.e., when pressing, bumping something, showering, touched sexually, hugging)[12]. The concept of embodiment can offer additional dimensions to future iterations of outcome evaluations. Newer tools such as the Prosthesis Embodiment Scale may serve as inspiration[15]. The Prosthesis Embodiment Scale includes thirteen items that correlate with measurements of embodiment, including ownership ["The prosthesis is my (body part)"], belongingness ("The prosthesis belongs to me"), affiliation ("The prosthesis is part of my body"), and completeness ("My body feels complete"). Other items such as integrity, self-observation, posture, touch, and vividness are also relevant to breast reconstruction outcome measures and could serve to enhance existing BREAST-Q metrics.

This literature search was predominantly comprised of qualitative patient interviews. The BREAST-Q and other patient-reported outcome measure tools are also developed through in-depth qualitative interviews before quantitative field testing. We suggest that embodiment may be a helpful concept for widening and diversifying the scope of conversation during such interviews. Furthermore, it is essential to recognize the limitations inherent to questionnaires and other quantitative measurement tools. These tools are often confined to discrete information about aspects of one's body at a specific moment and, therefore, can be limited in accounting for the diverse multitude of bodily experiences[25]. There is growing recognition of the role of qualitative research in the field of plastic and reconstructive surgery[68-70]. Given the complexity of breast embodiment as a conceptual framework, we suspect qualitative data will continue to play an integral role in eliciting these patient perspectives.

### Limitations

There were limitations to this review. Since the concept of embodiment has been sparsely discussed within existing surgical literature, this systematic review utilized a wide inclusion criterion, including articles from outside the field of plastic surgery, primarily psychology and qualitative health journals. Given our aim to introduce the concept of breast embodiment more broadly, this review included literature describing patient experiences with multiple forms of breast reconstruction. We did not elucidate differences in embodiment between the different types of mastectomies (i.e., total, skin-sparing, nipple-sparing, *etc.*) and different forms of reconstruction (i.e., autologous, alloplastic). It is likely that there are embodiment differences between autologous and alloplastic reconstruction, and thus future work analyzing breast embodiment and measurements of its domains within these two different contexts is warranted.

While we mainly focused on breast embodiment in the context of reconstructive surgery, it is worth noting that using an external breast prosthesis, or artificial breast form, remains an option in the United States and worldwide. Future literature review on the embodiment of an external breast prosthesis could also contribute to the overall discussion on breast embodiment.

Lastly, given that the embodiment framework seeks to give space to an individual's subjective experience, it also opens space for alternative choices and narratives for patients who opt out of the decision to have reconstruction or utilize prostheses. The Going Flat movement has brought attention to the option of mastectomy alone, and outcomes on patient satisfaction have increasingly been explored[71]. Evaluating embodiment following mastectomy in this patient population warrants further investigation.

## CONCLUSION

As advances in breast reconstruction progress, the goals of reconstruction may extend beyond anatomic similarity and restoring sensation; these advances may also further patients' goals of having an increased sense of being one's own breast. This review explored how the concept of embodiment can be understood and applied to patients undergoing breast reconstruction. While qualitative studies have examined embodiment following mastectomy and breast reconstruction, further research is needed to measure the dimensions of breast embodiment, including ownership, body representation, sensation, posture, and psychosocial outcomes. Studies in the prosthetics literature may serve as a guide for applying these measures to breast reconstruction outcomes. The breast embodiment framework builds upon existing patient-reported outcome measures and expands the plastic surgeon's tools for evaluating patients' experiences following reconstruction. Beyond post-mastectomy reconstruction, the embodiment framework may also be useful in outcome evaluations of other reconstructive surgeries, such as gender-affirming surgery.

## DECLARATIONS

### Author's contributions

Concept and design: Dingle AM, Chin MG, Eftekari SC, Moura SP, Donnelly DAT, Shaffrey EC, Sears L
Literature review and analysis of data: Chin MG
Drafting of the manuscript: Chin MG
Critical revision of the manuscript for important intellectual content: Chin MG, Eftekari SC, Moura SP, Donnelly DAT, Shaffrey EC, Sears L, Dingle AM

### Availability of data and materials

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### Conflicts of interest

All authors declared that there are no conflicts of interest.

### Ethical approval and consent to participate

Not applicable.

### Consent for publication

Not applicable.



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# Comparing microsurgical breast reconstruction outcomes following postoperative monitoring techniques: a systematic review and meta-analysis of 2529 patients

**Jose A. Foppiani[1,#], Lauren Valentine[1,#], Angelica Hernandez Alvarez[1], Allan Weidman[1], Stephen Stearns[1], Lacey Foster[2], Karthika Devi[3], Khaled Albakri[4], Samuel J. Lin[1]**

[1]Division of Plastic Surgery, Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, MA 02215, USA.
[2]Keck School of Medicine, University of Southern California, Los Angeles, CA 90033, USA.
[3]Sri Manakula Vinayagar Medical College and Hospital, Puducherry, TN 605107, India.
[4]Faculty of Medicine, The Hashemite University, Zarqa 13133, Jordan.
[#]Authors considered joint first authors.

**Correspondence to:** Dr. Samuel J. Lin, Division of Plastic Surgery, Beth Israel Deaconess Medical Center/Harvard Medical School, 110 Francis Street Suite 5A, Boston, MA 02215, USA. E-mail: sjlin@bidmc.harvard.edu

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## Abstract

Aims: This paper aims to assess the existing evidence regarding oximetry and thermography by comparing postoperative rates of complications following microsurgical breast reconstruction.

Methods: A systematic review of PubMed, Web of Science, and Cochrane was completed. A qualitative and quantitative analysis of all included studies was then performed.

Results: Fourteen studies were included with a total population of 2,529 female patients who underwent microvascular breast reconstruction, ultimately totaling 3,289 flaps. The mean age for the cohorts included in this study ranged from 48.9 to 57 years of age. A total of 15 complete flap losses were reported. Furthermore, this meta-analysis of proportion showed that total flap loss experienced was 0% (95%CI 0%-100%) for patients monitored with thermography compared to 0% (95%CI 0%-1%) for those monitored with oximetry. Partial flap loss occurred at a frequency of 1% [95% confidence interval (CI) 0%-73%] for patients monitored with thermography compared to 1% (95%CI 0%-2%) for those monitored with oximetry. Furthermore, the results of this study showed that thermography prompted a return to the operating room (OR) in 1% (95%CI 0%-73%) of the patients compared to 5% (95%CI 3%-9%) for oximetry. Lastly, the overall complication rate was 12% (95%CI 1%-54%) for patients monitored with thermography compared to 10% (95%CI 4%-21%) for those monitored with oximetry.

Conclusion: Ultimately, this meta-analysis concludes that while oximetry monitoring currently has strong evidence for improving flap outcomes, trends in the current data indicate that further studies may demonstrate that thermography may be comparable to oximetry in achieving similar patient outcomes.

**Keywords:** Microsurgical breast reconstruction, oximetry, thermography, flap monitoring, flap take back, flap outcomes

## INTRODUCTION

Flap failure is a devastating complication after microvascular free tissue transfer for breast reconstruction. Despite advancements in microvascular techniques, rates of take-backs to the operating room for complications leading to flap compromise have been reported at around 0%-10% for microsurgical breast reconstruction[1-10]. Historically, surgeons have relied on physical examination to assess flap viability by assessing color, warmth, capillary refill, and turgor[11]. Physical examination is also often used in conjunction with a handheld Doppler ultrasound[11]. Evidence has shown that early detection of vascular compromise in a threatened flap is essential for increasing rates of flap survival[1-8]. Given the need for timely diagnosis, several noninvasive methods of flap monitoring have emerged as useful adjuncts to conventional methods of evaluation of flap compromise.

In the past, authors described the ideal characteristics of a monitoring technique that is benign to both the patient and the free flap[12]. They determined that the ideal monitoring method would be rapid, repeatable, reliable, recordable, rapidly responsive, accurate, inexpensive, objective, and applicable to all kinds of flaps[12]. They also felt it should be equipped with a simple display that could alert relatively inexperienced personnel to the development of circulatory impairment[12]. Despite this thorough postulation of an ideal system, there is no standard of care for flap monitoring devices and no high-impact evidence that favors one technique over another.

Two technologies commonly mentioned in the literature for flap monitoring post-microsurgical breast reconstruction are oximetry and thermography. One available device utilizing oximetric monitoring is the ViOptix T.Ox Tissue Oximeter (ViOptix, Inc., Fremont, Calif.); this device is a noninvasive monitor of real-time flap perfusion that uses the emission of near-infrared light to measure local tissue oxygen saturation[13,14]. This technology has been shown to provide an increase in flap salvage rate and early detection of flap compromise. Another monitoring method is thermal imaging or dynamic infrared thermography (DIRT)[14]. Thermal imaging detects infrared radiation from an object and produces an image based on the local temperature, which can be used as a surrogate marker for cutaneous blood flow. Several studies have shown thermography's efficacy in preoperative planning to identify perforating vessels, but until more recently, technological impediments limited its use[14]. Handheld thermal imaging devices are now commercially available (FLIRONE, Flir Systems, Inc., Wilsonville, OR) and are becoming more affordable[14]. Further, they can be paired with most smartphones, making this technique very appealing for convenient postoperative monitoring[14]. However, despite its high potential, no studies have shown DIRT technology to be superior or comparable to other flap monitoring methods. The purpose of this systematic review was to clarify the existing evidence regarding oximetry and thermography by comparing postoperative rates of complications following microsurgical breast reconstruction.

## METHODS

This study protocol was prospectively registered with PROSPERO (Study # ID: CRD42022360392)[15]. This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement guidelines[15].

### Eligibility criteria

Criteria for included studies were defined as adult female patients who underwent autologous breast reconstruction and were monitored with either oximetry or thermography. The full eligibility criteria are accessible at PROSPERO and are as follows:

Inclusion criteria:

· Adult female patients
· Patients who underwent autologous breast reconstruction (microvascular)
· Patients who were monitored with oximetry or thermography
· Observational studies and clinical trials
· Case Series and Case Reports with greater than 15 patients
· Studies in English, French, and Spanish

Exclusion criteria:

· Editorials;
· Commentary reports;
· Case series/Case Report with < 15 patients
· Abstracts with no full text available
· Letters to the editors; · Animal studies
· Cadaveric Studies
· Studies where breast flap-related outcomes could not be identified

### Search strategy

A comprehensive research review using subject headings, controlled vocabulary, and keywords was conducted on 25 September, 2022, on MEDLINE (in Ovid), Web of Science, and the Cochrane Central Register for studies published until 2021. Our full-text search strategy is accessible at PROSPERO.

### Study selection

The search results were uploaded into the online systematic review program Covidence to conduct study selection[16]. Six independent reviewers performed a two-screening process for study selection. (Hernandez Alvarez A, Valentine L, Weidman A, Devi K and Foppian JA). First, titles and abstracts were screened. A third reviewer ( Foppian JA) moderated and if discordances were present, resolved the conflict. Next, a full-text analysis was performed by four of the reviewers (Foppian JA, Hernandez Alvarez A, Valentine L and Weidman A). If conflicts arose between reviewers, the third reviewer moderated a discussion to come to a joint decision.

### Data extraction/synthesis

Data extraction was guided by a predetermined checklist: first author's last name, year of publication, total sample size, gender, type of flaps, the device used for monitoring, monitoring protocol, identification of threatened flaps, flap take back, rates of flap salvage, flap loss, complication including but not limited to: congestion, ischemia, infection, necrosis, and hematoma, etiology of complication and treatment of complication, time to identification of complications, and intervention for treatment of the complications.

### Outcomes

The primary outcomes were detection of complications, identification of threatened flaps, patient return to the operating room (flap "take-back"), flap salvage, flap loss, and time to identification of complications.

### Quality assessment

To assess the risk of bias, we utilized the National Institute of Health (NIH) quality assessment tool. Each article was categorized as follows: "low risk," "moderate risk," or "high risk" of bias.

### Statistical analysis

A comprehensive qualitative analysis was made. For the quantitative analysis, the binomial data was analyzed. Each complication rate's pooled prevalence was estimated using a proportion meta-analysis with Stata statistical software (STATA Corp., College Station, TX version 16.1)[17]. Due to the heterogeneity among studies, a logistic-normal-random-effect model was conducted. Ninety-five percent exact confidence interval (CIs) and 95% Walds CIs were performed for study-specific and overall pooled prevalence, respectively. Additionally, the Freeman-Tukey double arcsine transformation was used. The percentage of weight and effect size of each individual study were presented[17,18]. To assess heterogeny, $I^2$ statistics were used. Significant heterogeneity was considered if pp-value < 0.05 or $I^2 > 50\%$.

## RESULTS

### Study selection and characteristics

A total of 614 studies were initially retrieved following the removal of duplicates. Of those, 18 met all inclusion criteria. However, 4 of the 18 articles contained duplicate or already published patient information and were removed. Therefore, 14 articles were ultimately included for qualitative and quantitative analysis [Figure 1][19-32]. Of the 14 articles, 11 were focused on oximetry, and 3 were focused on thermography. When using the NIH quality assessment tool, 7 were found to be at low risk of bias, 6 at moderate risk, and 1 at high risk based on the NIH quality assessment tool [Table 1][19-32]. The Prisma Flow diagram is seen in Figure 1.

### Patient and flap characteristics [Table 1]

From all 14 included studies, a total of 2,529 female patients who underwent microvascular breast reconstruction were included in this analysis, which ultimately totaled 3,289 flaps overall[19-32]. The mean age for the cohorts included in this study ranged from 48.9 to 57 years of age. The most common flap used in the patient population was the deep inferior epigastric (DIEP) flap with 2,372 total flaps, followed by 96 transverse rectus abdominis (TRAM) flaps, 43 superior gluteal artery perforator (SGAP) flaps, 17 superficial inferior epigastric artery (SIEA) flaps, 8 profunda artery perforator (PAP), 6 diagonal/transverse upper gracilis (DUG/TUG) and 1 latissimus dorsi (LD) flap. The remainder of the flaps included 746 flaps described only as "abdominal-based flaps" and stacked flaps, which can be seen in Table 1[19-32].

### Diagnostic tools and monitoring protocols

The studies included in this review used a variety of diagnostic tools for thermography and oximetry, each with its own nuances in terms of application and protocols.

In the realm of thermography, the study by Saxena *et al.* employed the FLIR A320 IR thermal camera, a specialized device designed for thermal imaging, while the research conducted by Phillips *et al.* utilized the FLIR One device, which is connected to a mobile smartphone for ease of use[20,21]. On the other hand, the study by Thiessen *et al.* did not explicitly indicate which tool was employed for dynamic infrared thermography[19]. Notably, the approaches to measurement in these studies showed some variation. Both Thiessen *et al.* and Saxena *et al.* conducted two measurements within the initial 1-2 days post-procedure,

**Table 1. Study characteristics and flap demographics**

| Author | Type of study | NIH quality assessment | Number of participants | Mean age | Number of flaps | Type of flap |
|---|---|---|---|---|---|---|
| Thiessen *et al.*[19] 2020 | Prospective observational | Moderate | 21 | 56.7 | 33 | 1 TRAM<br>32 DIEP |
| Saxena *et al.*[20] 2019 | Prospective observational | Moderate | 32 | 51.9 | 32 | 32 TRAM |
| Phillips *et al.*[21] 2020 | Prospective observational | Low | 19 | 54.6 | 30 | 30 DIEP |
| Lindelauf *et al.*[22] 2021 | Prospective observational | Moderate | 30 | 51 | 42 | 42 DIEP |
| Johnson *et al.*[23] 2021 | Retrospective observational | Low | 460 | 50.7 | 740 | 740 "abdominal-based flaps" |
| Pelletier *et al.*[24] 2011 | Randomized control | Low | 50 | 49.2 | 50 | 14 TRAM<br>21 DIEP<br>9 SIEA<br>3 DIEP/SIEA double stacked flaps<br>3 DIEP/SIEV turbocharged flaps<br>1 DIEP + DIEP double stacked flap |
| Ricci *et al.*[25] 2017 | Retrospective observational | Low | 900 | 50.3 | 900 | 3 TRAM<br>872 DIEP<br>2 SIEA<br>23 SGAP |
| Ozturk *et al.*[26] 2014 | Prospective observational | Moderate | 20 | 49.3 | 30 | 4 TRAM<br>24 DIEP<br>2 SIEA |
| Saad *et al.*[27] 2020 | Retrospective observational | Moderate | 120 | 53 | 120 | 35 TRAM<br>85 DIEP |
| Salgarello *et al.*[28] 2018 | Retrospective observational | Moderate | 45 | 52.6 | 45 | 45 DIEP |
| Carruthers *et al.*[29] 2019 | Retrospective observational | Low | 196 | 50.7 | 301 | 301 DIEP |
| Tran *et al.*[30] 2021 | Retrospective observational | Low | 175 | 50.9 | 286 | 3 MS-TRAM<br>266 DIEP<br>3 SIEA<br>6 TUG/DUG<br>8 PAP |
| Kumbasar *et al.*[31] 2021 | Prospective observational | High | 10 | 57 | 10 | 1 TRAM<br>8 DIEP<br>1 LD |
| Koolen *et al.*[32] 2016 | Retrospective observational | Low | 451 | 48.9 | 670 | 3 TRAM<br>646 DIEP<br>1 SIEA<br>20 SGAP |

NIH: National Institute of Health; DIEP: deep inferior epigastric; TRAM: transverse rectus abdominis; SGAP: superior gluteal artery perforator; SIEA: superficial inferior epigastric artery; PAP: profunda artery perforator; DUG/TUG: diagonal/transverse upper gracilis; LD: latissimus dorsi.

providing a short-term perspective on thermal changes[19,20]. Conversely, the study by Phillips *et al.* did not furnish details on their protocol for measurements, leaving some ambiguity in their approach[21].

Regarding oximetry, several studies-including those by Pelletier *et al.*, Ricci *et al.*, Ozturk *et al.*, Carruthers *et al.*, Tran *et al.*, Koolen *et al.*, and Johnson *et al.*-relied on the ViOptix tissue oximetry technology to monitor oxygen levels in tissue[23-26,29,30,32]. In contrast, Lindelauf *et al.* employed the Foresight MC-2030 oximeter, Saad *et al.* used the T-Stat tissue oximeter by Spectros, Salgarello *et al.* utilized the Somanetics INVOS 5,100 C Cerebral/Somatic Oximeter (Covidien), and Kumbasar opted for the INVOS 700 cerebral oximetry monitoring system[22,27,28,31]. The protocols for the use of these diagnostic tools exhibited some

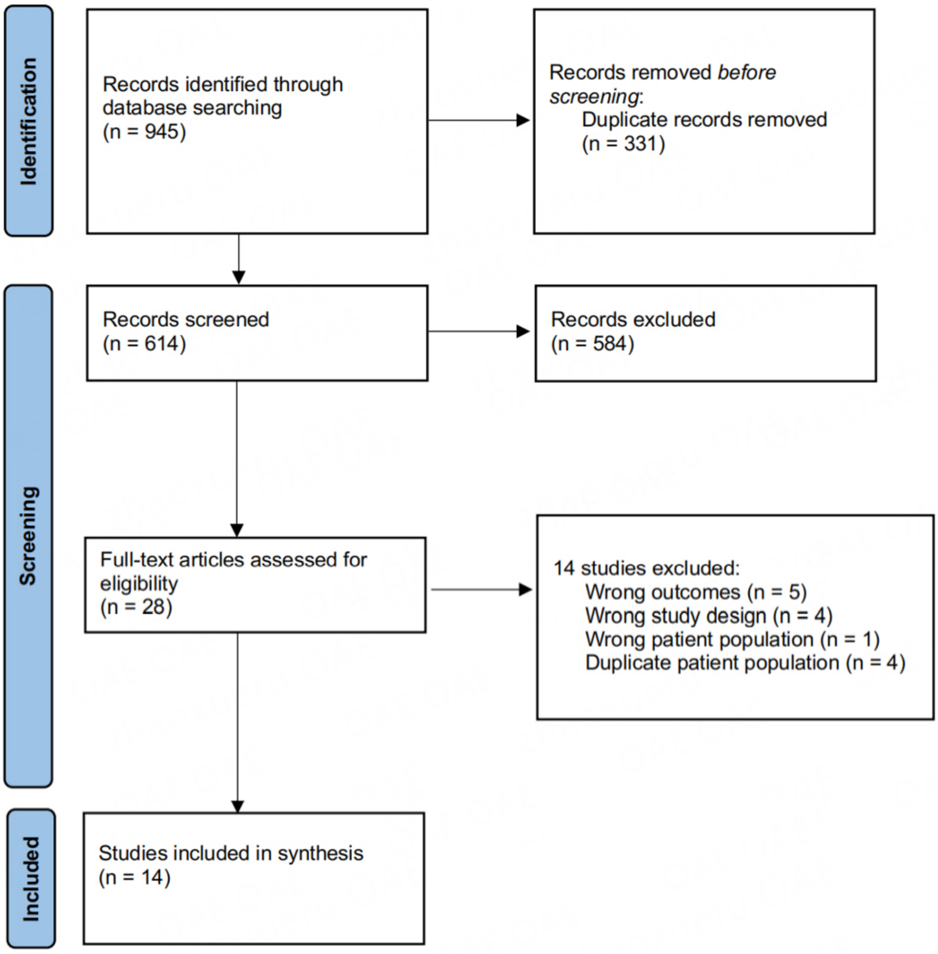


**Figure 1.** Systematic Reviews and Meta-analysis (PRISMA) guidelines flow diagram.

variance among the studies. Salgaretto *et al.*, Kumbasar *et al.*, and Koolen *et al.* recorded measurements continuously for a minimum of two days after the conclusion of the procedure, providing a continuous record of tissue oxygenation[28,31,32]. The remaining studies, meanwhile, opted for interval readings, though the specific timing of these readings differed slightly between studies [Table 2].

### Meta-analysis of complications [Table 3]

The pooled prevalence of complication-related outcomes was calculated through a meta-analysis random effects model of proportion. The pooled prevalence of flaps determined to be threatened was 0.05 (95%CI 0.03-0.10) for studies using oximetry and 0.10 (95%CI 0.02-0.11) for those using thermography [Supplementary Digital 1]. In studies using oximetry, the pooled prevalence of partial flap loss was 0.01 (95%CI 0.00-0.02) and 0.00 (95%CI 0.00-0.01) for complete flap loss. In those using thermography, the pooled prevalence of partial flap loss was also 0.01 (95%CI 0.00-0.73) and 0.00 (95%CI 0.00-1.00) for complete loss. With regards to the rate of flap salvage, the pooled prevalence of salvage in studies using oximetry was 0.06 (95%CI 0.03-0.11) compared to 0.23 (95%CI 0.14-0.35) in those using thermography, indicating that thermography was superior in facilitating salvage to compromised flaps [Supplementary Digital 2]. The pooled prevalence of the rate of return to the operating room was 0.05 (95%CI 0.03-0.09) for studies using oximetry and 0.01 (95% CI 0.00-0.73) for thermography [Supplementary Digital 3]. Further, in studies using postoperative oximetry, the pooled prevalence rates of the remaining flap complications

**Table 2. Monitoring protocols in thermography and oximetry groups**

| Lead author and publication date | Diagnostic method | Diagnostic tool | Time frame of use | Protocol for diagnostic tool | Cut-off values used for concern | Length of monitoring period |
|---|---|---|---|---|---|---|
| Thiessen *et al*[19]. 2020 | Thermography | Unspecified | Preoperative, intraoperative and postoperative | Once preoperative to determine perforators. Intraoperatively, first after perforator dissection to confirm patency, then a second after the microvascular anastomosis, then a third after flap inset Postoperatively, 2 measurements taken 1-2 days following surgery | N/a | 24-48 h |
| Saxena *et al*.[20] 2019 | Thermography | FLIR A320 IR thermal camera | Postoperative | Measurement immediately after the procedure and one day (24 h) after the procedure | N/a | 24 h |
| Phillips *et al*.[21] 2020 | Thermography | FLIR one device connected to an iPhone 7 smartphone | Intraoperative, postoperative | Intraoperatively after isolation on its vascular pedicle, at max ischemia before anastomosis, in 5-minute intervals after completion of microvascular anastomosis, and before leaving the OR Postoperatively, used whenever there was concern for flap viability | N/a | N/a |
| Lindelauf *et al*.[22] 2021 | Oximetry | Foresight MC-2030 oximeter | Preoperative and postoperative | Preoperative baseline measurements were performed. A new sensor was positioned postoperatively on the transplanted tissue. In unilateral procedures, postoperative StO2 values of the native breast were also obtained. Measurements were continued for 24 h | N/a | 24 h |
| Johnson *et al*.[23] 2021 | Oximetry | ViOptix | Intraoperative and postoperative | Intraoperatively following anastomosis. Postoperatively, hourly checks by nursing staff until the second postoperative morning, followed by every other hour monitoring for the second to third postoperative days, and every fourth-hour monitoring from the third postoperative morning through discharge | Any change 10% or greater | Though discharge with a mean of 4.8 days |
| Pelletier *et al*.[24] 2011 | Oximetry | ViOptix | Postoperative | Measurements every 4-6 h until discharge | An StO2 level below 30% or a drop in StO2 level of > 20% per hour lasting for 30 minutes | Until discharge with a mean of 3.1 days (ICU group) and 2.7 days (floor group) |
| Ricci *et al*.[25] 2017 | Oximetry | ViOptix | Postoperative | Monitored continuously with tissue oximetry for three consecutive days, beginning immediately following the procedure | A rapid 20-point drop from baseline in 1 h or an absolute recording < 30 percent | 72 h |
| Ozturk *et al*.[26] 2014 | Oximetry | ViOptix | Intraoperative and postoperative | Readings were recorded prior to extubation, after extubation and every 4 h for the next 36 h | N/a | 36 h |
| Saad *et al*.[27] 2020 | Oximetry | T-Stat tissue oximeter by Spectros | Postoperative | Tissue oximetry readings were recorded immediately at the completion of the reconstruction at hours 1, 2, 3, 4, 6, 12, and 24 | N/a | 24 h |
| Salgarello *et al*.[28] 2018 | Oximetry | Somanetics INVOS 5100C Cerebral/Somatic Oximeter (Covidien) | Postoperative | Measurements recorded continuously for 48 h starting in the post-anesthesia care unit | An rSO2 value of 30% or drop rate in rSO2 by 20% | 48 h |
| Carruthers *et al*.[29] 2019 | Oximetry | ViOptix | Intraoperative and postoperative | Probe applied intraoperatively to skin paddle and remained on until discharge, measurements recorded continuously | N/a | Until discharge with a mean of 3.4 days |

| | | | | | | |
|---|---|---|---|---|---|---|
| Tran *et al.*[30] 2021 | Oximetry | ViOptix | Intraoperative and postoperative | Probe placed on skin island intraoperatively after flap inset, remained and took continuous readings during the hospitalization | A decrease in tissue saturation readings of 20 points from the postoperative baseline | Until discharge (no mean length of stay provided) |
| Kumbasar *et al.*[31] 2021 | Oximetry | INVOS 700 cerebral oximetry monitoring system | Postoperative | Continuous monitoring began postoperatively in the post-anesthesia care unit and remained until discharge | A 10% decrease in oximetry levels, critical tissue oximetry measurements as a skeletal muscle oxygen saturation level below 65%, or a drop in StO2 level of more than 20% lasting for 20 minutes | 72 h |
| Koolen *et al.*[32] 2016 | Oximetry | ViOptix | Postoperative | Probe was placed onto the surface of the flap in the operating room at the conclusion of the procedure and left in place for 3 days | A rapid 20-point drop from baseline in 1 h or an absolute recording less than 30 percent | 72 h |

OR: operating room.

assessed were: 0.02 (95%CI 0.01-0.03) for congestion, 0.03 (95%CI 0.01-0.13) for necrosis, 0.03 (95%CI 0.02-0.03) for hematoma and 0.01 (95%CI 0.00-0.16) for infection. In studies using postoperative thermography, the pooled prevalence rates of the remaining flap complications assessed were: 0.03 (95%CI 0.00-0.29) for congestion, 0.04 (95%CI 0.00-0.36) for necrosis, 0.00 (95%CI 0.00-1.00) for hematoma and 0.04 (95%CI 0.00-0.56) for infection. The overall pooled prevalence of complications in studies using oximetry was 0.10 (95%CI 0.04-0.21) compared to 0.12 (95%CI 0.01-0.54) for those using thermography [Supplementary Digital 4]. Additional forest plots demonstrating the results of this meta-analysis are available in the supplemental materials section [Supplementary Digitals 5-10] [Table 3].

## DISCUSSION

This meta-analysis is the first study to extensively investigate the current state of literature comparing the use of thermography to oximetry following microsurgical breast reconstruction for flap monitoring. Oximetry has been described thoroughly in the literature and has significantly contributed to breast reconstruction outcomes by identifying threatened flaps before or in conjunction with physical examination findings[14]. Thermography for flap monitoring has also been documented, but until more recently, technological impediments limited its use[14]. In recent years, advances in smartphones and portable cameras have driven its resurgence[14,21]. However, a question remains regarding the usefulness of thermography compared to oximetry. The results of this systematic review show that limited high-level evidence exists regarding thermography as opposed to oximetry. The evidence that is available regarding each method indicates that the two modalities may have comparable outcomes. Therefore, additional investigation could show the utility of thermography as an adjunct or alternative to oximetry. Ultimately, evidence for the use of oximetry due to better salvage rate and lower overall complication rates may be stronger than that for thermography. However, both modalities have the potential to improve outcomes, especially given additional research and development.

This meta-analysis showed that partial flap loss occurred at a frequency of 1% for patients monitored with thermography compared to 1% for those monitored with oximetry. Total flap loss was experienced by 0% for patients monitored with thermography compared to 0% for those monitored with oximetry. These results demonstrated that thermography has similar results to oximetry regarding partial and total flap loss. This emphasizes that both types of monitoring

**Table 3. Outcomes of thermography *vs.* oximetry monitoring**

| >Complication rates | Number of studies | Total | Prevalence [95%CI] | $I^2$ (%) |
|---|---|---|---|---|
| | | **Threatened flaps** | | |
| Overall | 14 | 206/3,289 | 0.06 [0.03, 0.11] | 91% |
| Thermography | 3 | 14/95 | 0.10 [0.02, 0.42] | 0% |
| Oximetry | 11 | 192/3,194 | 0.05 [0.03, 0.10] | 92% |
| | | **Partial flap loss** | | |
| Overall | 14 | 37/3,289 | 0.01 [0.00; 0.03] | 28% |
| Thermography | 3 | 9/95 | 0.01 [0.00, 0.73] | 0% |
| Oximetry | 11 | 28/3,194 | 0.01 [0.00, 0.02] | 100% |
| | | **Complete flap loss** | | |
| Overall | 14 | 15/3,289 | 0.00 [0.00; 0.01] | 0% |
| Thermography | 3 | 0/95 | 0.00 [0.00, 1.00] | 0% |
| Oximetry | 11 | 15/3,194 | 0.00 [0.00, 0.01] | 0% |
| | | **Necrosis** | | |
| Overall | 8 | 158/1,802 | 0.03 [0.01, 0.12] | 77% |
| Thermography | 3 | 10/95 | 0.04 [0.00, 0.36] | 60% |
| Oximetry | 5 | 148/1,707 | 0.03 [0.01, 0.13] | 78% |
| | | **Congestion** | | |
| Overall | 8 | 37/1,527 | 0.02 [0.01, 0.04] | 38% |
| Thermography | 2 | 3/63 | 0.03 [0.00, 0.29] | 0% |
| Oximetry | 6 | 34/1,464 | 0.02 [0.01, 0.04] | 25% |
| | | **Hematoma** | | |
| Overall | 9 | 62/2,427 | 0.03 [0.02, 0.03] | 0% |
| Thermography | 2 | 0/63 | 0.00 [0.00, 1.00] | 0% |
| Oximetry | 7 | 62/2,364 | 0.03 [0.02, 0.03] | 0% |
| | | **Infection** | | |
| Overall | 6 | 67/1,803 | 0.01 [0.00, 0.13] | 1% |
| Thermography | 2 | 5/63 | 0.04 [0.00, 0.56] | 0% |
| Oximetry | 4 | 62/1,740 | 0.01 [0.00, 0.16] | 0% |
| | | **Return to OR** | | |
| Overall | 10 | 179/2,504 | 0.05 [0.02, 0.09] | 87% |
| Thermography | 2 | 9/95 | 0.01 [0.00, 0.73] | 0% |
| Oximetry | 8 | 170/2,409 | 0.05 [0.03, 0.09] | 87% |
| | | **Rate of salvage** | | |
| Overall | 10 | 190/3,171 | 0.06 [0.03, 0.11] | 94% |
| Thermography | 2 | 14/62 | 0.23 [0.14, 0.35] | 12% |
| Oximetry | 8 | 176/3,109 | 0.12 [0.05, 0.33] | 94% |

OR: operating room.

may have their roles as efficacious monitoring tools to identify and prompt successful interventions in breast microvascular reconstruction. Compared to the existing literature, both sub-groups of studies included in this meta-analysis show better outcomes for partial and complete flap loss rates. Indeed, the literature reports partial flap loss in up to 9% of patients undergoing autologous breast reconstruction and complete flap loss in less than 5% of patients[1-10,33,34]. If not for the postoperative monitoring in each of our studies, it could be hypothesized that a larger proportion of patients who had partial flap failure would have progressed to total flap failure instead. Noninvasive, postoperative monitoring of breast flaps provides plastic surgeons a chance to identify threatened flaps before they show physical signs of distress and require additional therapy. As a result, flaps that may have otherwise been lost can be completely salvaged or only partially lost instead.

In the pooled patient population, skin necrosis was present in 4% of the patients monitored with thermography compared to 3% for those monitored with oximetry. Based on our results, oximetry seems to be marginally better suited for preventing this type of complication. A study by Olsen *et al.* showed a cumulative 14% complication rate for non-infectious surgical site complications in 1,799 of their patients who underwent autologous breast reconstruction[35]. This rate is higher than in either of the sub-groups presented in this study and demonstrates the potential benefits that both oximetry and thermography as postoperative monitoring tools may bring to patients undergoing autologous breast reconstruction. It is also important to note that Olsen *et al.* acknowledged a high possibility of under-reporting this type of complication within their cohort, further strengthening the evidence supporting the implementation of either of the monitoring tools presented in our paper[35].

Additionally, this meta-analysis showed that the overall complication rate for flaps used in autologous breast reconstruction was 12% for patients monitored with thermography compared to 10% for those monitored with oximetry. Bennet *et al.*, in a study with a multicenter cohort of 706 patients who underwent autologous breast reconstruction, showed an overall complication rate of 46.7% with a re-operation rate of 27.6%[36]. On the other hand, Mehrara *et al.* showed an overall complication rate of 27.95% in 952 patients who underwent microvascular breast reconstruction[1]. Therefore, the results of this meta-analysis may show better outcomes in terms of overall complications than reported in the literature.

Furthermore, the results of this study showed that thermography prompted a return to the OR in 1% of the patients compared to 5% for oximetry. A study by Shammas *et al.* previously showed an overall return to the OR of 11% and, notably, a 27.8% return to the OR for their sub-patient population who underwent staged autologous procedures as compared to immediate microsurgical reconstruction[33]. It is interesting to note that while the take-back rate in our included studies was lower than in some of the literature, the outcomes were better than in most of the literature. While no causality can be determined, the monitoring could be hypothesized to have objectively and accurately identified flaps that required true intervention, leading to fewer take-backs but also more meaningful take-backs.

While there were no unified postoperative monitoring protocols across the studies, a trend was present. There was often an emphasis on either continuous or more frequent monitoring during the first 24 h postoperatively. This trend can be explained by Carruthers, 2019, who describe in their studies that nearly 96% of major complications of microsurgical breast reconstruction occur within those first 24 h following surgery[29]. These findings highlight the justifiable importance of more rigorous monitoring during this postoperative timeframe. Thus, while studies, such as that by Moderhak *et al.*, reported monitoring for up to 3 months in their cohort postoperatively, the focus of oximetry, thermography, or any postoperative monitoring method should prioritize this critical 24-hour time period regardless of surgeons' skills or center capabilities[37].

Of note, Phillips *et al.* described 19 patients who underwent 30 DIEAP flaps for breast reconstruction and monitored their patients using mobile smartphone thermography, demonstrating good outcomes[21]. Advances such as this are crucial to take into account, as cost efficiency is critical to medical practice. While some re-usable thermographic cameras can cost up to 20,000 USD, smartphone cameras are more affordable and can reduce the cost to as low as 200 USD[38]. Additionally, a study by Schoenbrunner *et al.* showed that oximetric monitoring raised the cost of postoperative flap monitoring by 2,000 USD per patient with devices costing 8,000-50,000 USD[39,40]. While this implies that the cost of both those types of monitoring is similar, the newer smartphone-based monitoring could become a compelling cost-efficient method. Continuing with the discussion of cost efficiency, another important factor to consider is the economic burden that results from flap complications and flap loss. Complications associated with autologous breast reconstruction are costly, with median costs for complications at 30 days found to be an additional $7,197 USD and at one year found to be an additional $10,644 USD[41]. Therefore, the price of monitoring flap perfusion may ultimately be more cost-effective for the sake of avoiding eventual flap complications and loss while certainly preventing additional psychological burden on patients.

### Limitations

While this is an original and pioneering study that aims to systematically review and compare the outcomes and complications of oximetric and thermographic flap monitoring for microvascular flap monitoring, it does have limitations. Given the specific type of outcome investigated and the paucity of experimental designs in this domain, it was not feasible to restrict study designs to only randomized controlled trials or case-control cohorts, resulting in high heterogenicity. The final patient population was thus retrieved largely from observational studies, which present biases inherent to their design (e.g., underreporting or information bias, and publication bias) and frequently incomplete data. This is a natural outcome when venturing into new territory and collecting data from multiple sources. Despite this limitation, our study represents a crucial first step in understanding the utility of thermography and oximetry for flap monitoring in microvascular breast reconstruction. Future research can build on our findings by comparing these monitoring techniques in a larger, more standardized patient cohort, with careful consideration of patient characteristics and comorbidities to enhance the rigor and precision of the comparison. Another significant limitation was the lack of consensus on what defines certain complications. For example, flap and skin necrosis were not reported in terms of area or percentage. Thus, some studies could have considered small defects while others may have chosen to only count larger areas of necrosis as a reportable complication. Furthermore, while postoperative monitoring can significantly impact outcomes, surgical experience, the volume of free flap performed in each institution, and variation in surgical technique can all have a major impact on complication rates. Lastly, it is important to note that a consensus on a unified cut-off indicating concern for a threatened flap when using oximetry or thermography should be established. Such a consensus could decrease heterogeneity within sub-groups and enable a more valid comparison of methods of breast flap monitoring.

## CONCLUSION

Ultimately, this meta-analysis concludes that while oximetry monitoring currently has strong evidence for improving flap outcomes trends, the current data indicate that further studies may show that more updated, modern thermography is at least comparable to oximetry in achieving ideal patient outcomes. As of this systematic review, oximetry seems to be marginally superior to thermography and thus poses whether it would be valuable to put more resources into investigating thermographic monitoring techniques for microsurgical breast reconstruction. However, while outcomes themselves would not warrant further investigation, the emergent low-cost thermographic devices have the potential to improve cost-efficiency. Finally, this study highlights the importance of flap monitoring following microsurgical reconstruction of the breast and also encourages further cost analysis comparing thermography and oximetry.

## DECLARATIONS

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this manuscript.

### Authors' contributions

Initiating and designing the study and drafting the protocol: Foppian JA, Hernandez Alvarez A, Weidman A, Valentine L

Involved in the study design, optimizing the literature search, and resolving conflicts for the paper's inclusion: Foppian JA, Hernandez Alvarez A, Weidman A, Stearns S, Valentine L

Overseeing all aspects of study design and SR writing: Lin SJ

### Availability of data and materials

All relevant information for this systematic review is either part of the manuscript, figures, tables and digital supplemental content. Any additional information can be found on the PROSPERO protocol for this paper. If any further information is required or unclear, the reader is more than welcome to contact the corresponding author for clarification.

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### Conflicts of interests

All authors declared that there are no conflicts of interest.

### Ethical approval and consent to participate

Not applicable.

### Consent for publications

Not applicable.



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In the first paragraph: include the title and type (e.g., Original Article, Review Article, Case Report, *etc.*) of the manuscript, a brief on the background of the study, the question the author sought out to answer and why;
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|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
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Methods should contain sufficient details to allow others to fully replicate the study. New methods and protocols should be described in detail while well-established methods can be briefly described or appropriately cited. Experimental participants selected, the drugs and chemicals used, the statistical methods taken, and the computer software used should be identified precisely. Statistical terms, abbreviations, and all symbols used should be defined clearly. Protocol documents for clinical trials, observational studies, and other non-laboratory investigations may be uploaded as supplementary materials.

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This section contains the findings of the study. Results of statistical analysis should also be included either as text or as tables or figures if appropriate. Authors should emphasize and summarize only the most important observations. Data on all primary and secondary outcomes identified in the section Methods should also be provided. Extra or supplementary materials and technical details can be placed in supplementary documents.

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This section should discuss the implications of the findings in context of existing research and highlight limitations of the study. Future research directions may also be mentioned.

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It should state clearly the main conclusions and include the explanation of their relevance or importance to the field.

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| Organization as author | Diabetes Prevention Program Research Group. Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. *Hypertension* 2002;40:679-86. [PMID: 12411462] |
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| Journal articles not in English | Zhang X, Xiong H, Ji TY, Zhang YH, Wang Y. Case report of anti-N-methyl-D-aspartate receptor encephalitis in child. *J Appl Clin Pediatr* 2012;27:1903-7. (in Chinese) |
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| Book chapters | Meltzer PS, Kallioniemi A, Trent JM. Chromosome alterations in human solid tumors. In: Vogelstein B, Kinzler KW, editors. The genetic basis of human cancer. New York: McGraw-Hill; 2002. pp. 93-113. |
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| Conference paper | Christensen S, Oppacher F. An analysis of Koza's computational effort statistic for genetic programming. In: Foster JA, Lutton E, Miller J, Ryan C, Tettamanzi AG, editors. Genetic programming. EuroGP 2002: Proceedings of the 5th European Conference on Genetic Programming; 2002 Apr 3-5; Kinsdale, Ireland. Berlin: Springer; 2002. pp. 182-91. |
| Unpublished material | Tian D, Araki H, Stahl E, Bergelson J, Kreitman M. Signature of balancing selection in Arabidopsis. *Proc Natl Acad Sci U S A*. Forthcoming 2002. |

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#### 9.1.1 Initial manuscript check

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# OAE Publishing Inc.

## Brief Introduction

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245 E Main Street Ste 107, Alhambra
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