Review





The radiated breast and autologous reconstruction: benefits and alternatives

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Abstract

Despite advancements in research and technology, breast cancer remains the second leading cause of cancerrelated mortality affecting women worldwide. Radiation therapy is a widely recommended adjunct to surgery due to its significant role in reducing loco-regional recurrence. Its use, however, is not without consequences. Radiation triggers a series of pathophysiologic events leading to tissue injury; reactive oxygen species incites (1) vascular damage and chronic hypoxia; (2) an inflammatory response; and (3) activation of myofibroblasts to induce fibrosis. As a result, radiotherapy interferes with wound healing and negatively impacts the quality of the skin. These pathophysiologic consequences complicate the sequence of breast reconstruction and require surgeons to consider timing and the type of reconstruction (autologous vs. implant), with respect to radiotherapy to improve patient outcomes. In this article, we briefly review radiation-induced tissue effects and their impact on breast reconstruction. More specifically, we comment on the traditional use of autologous tissue, microsurgical technical pearls for irradiated fields, reconstructive timing paradigms, and lymphedema prevention. With continued progress, derivation, and innovation, plastic and reconstructive surgery has consistently advanced and revolutionized both medicine and surgery. This review considers the future implications of breast reconstruction and how it will impact patients, healthcare, and the field. While not an exhaustive review, we aim to provide a comprehensive discussion and insights. In summary, the authors discuss the possibilities of a paradigm shift in breast reconstruction, emphasizing the need for surgeons to have an armamentarium capable of all breast reconstruction options for the best possible patient outcomes.

Keywords: Breast reconstruction, autologous reconstruction, radiation, radiated field, radiotherapy



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INTRODUCTION

Despite advancements in research and technology, breast cancer remains the second leading cause of cancer-related mortality affecting women worldwide. About 1 in 8 women in the US are diagnosed during their lifetime^[1]. The primary goal for breast cancer management is eradication of cancer, prevention of metastasis, and reduction of local recurrence. Surgery, sometimes combined with radiotherapy, effectively manages localized cancer, whereas systemic therapy (i.e., hormonal therapy, chemotherapy, targeted therapy, combined therapy) controls for metastatic relapse. Over time, breast conservation therapy (BCT) and, more recently, oncoplastic surgery have evolved to the forefront of management. With recent emphasis on cosmetic outcomes, BCT combined with postoperative radiotherapy has emerged as the preferred standard of care for early-stage breast cancer (stage I and II), replacing highly invasive surgeries such as simple and modified radical mastectomy^[2].

Radiation therapy is a widely recommended adjunct to surgery due to its significant role in reducing locoregional recurrence^[3]. Radiation reduces the 10-year risk of local cancer recurrence by approximately 50% and the 15-year risk of mortality by approximately 20% when combined with breast-conserving therapy^[1]. It is indicated for large tumors (> 5 cm), chest wall invasion, involvement of the lymph nodes, patients with partial or incomplete resection, and relief of widespread metastasis in palliative patients^[1,4]. Furthermore, postmastectomy radiation therapy (PMRT) has been employed for decades in patients with locally advanced disease with a high risk of recurrence. Relative contraindications to radiation therapy include small tumors, absence of nodal involvement, age > 70 years old, and hormone receptor-positive (HR+) cancers that lack evidence for improved survival with radiotherapy.

Radiation is commonly delivered by standard external beams for whole breast and nodal irradiation, brachytherapy for internal radiation, or a combination of both^[5]. The conventional radiation dosage of 45-50 Gray (Gy) is applied to the breast, with a boost treatment of 10-16 Gy for the lumpectomy site^[6]. An additional 45-50 Gy dose, dependent on recurrence risk, is applied to the regional node. Administration may take about six weeks, while hypofractionation, or lower doses of smaller fractionations, is reserved for low-risk individuals.

Radiation induces the production of reactive oxygen species (ROS)^[7,8], ultimately leading to a cancer cell's destruction. However, surrounding healthy tissues are at risk for damage. Radiation triggers a series of pathophysiologic events leading to tissue injury; ROS cause (1) vascular damage and chronic hypoxia^[9]; (2) an inflammatory response^[10]; and (3) activation of myofibroblasts to induce fibrosis^[11]. As a result, radiation interferes with wound healing and negatively impacts the quality of the skin. Patients may present with skin breakdown, hair and gland loss, ischemia, and ulcer formation.

Fibrosis-related complications are categorized as acute or chronic. Acute radiodermatitis (i.e., erythema, edema, desquamation, and ulceration) occurs within three months of radiotherapy^[12]. Chronic radiation-induced fibrosis occurs 4-6 months post-radiotherapy and can be irreversible^[13]. Radiation-induced fibrosis complicates the sequence of breast reconstruction and forces surgeons to consider the timing of radiation and the type of reconstruction (autologous *vs.* implant) to improve patient outcome, as elaborated later^[14-16].

The types of breast reconstruction to consider include implant-based (direct-to-implant/immediate or delayed with tissue expanders) and autologous reconstruction. In contrast to the immediate approach (i.e., reconstruction at the time of mastectomy), the delayed approach may take months to years. Autologous breast reconstruction involves taking tissue from a donor site and transferring it to a recipient site.

Alternative options include postmastectomy flat closure, or an external prosthesis, which is non-invasive. The timing of breast reconstruction relative to radiation is discussed later in this article. Many studies have revealed that more complications (i.e., infection, capsular contracture) arise in irradiated patients than non-irradiated patients in both implant-based reconstruction^[17-20] and autologous breast reconstruction^[21,22].

Radiation effects on breast reconstruction

Complications of radiation to the reconstructed breast include capsular contracture, infection, reduced patient satisfaction, and adverse cosmetic outcomes. These complications may lead to loss of tissue expander or implant, and reconstructive failure requiring secondary breast reconstruction or revision. A systematic review reported a total complication rate of 48.7% and a revision surgery rate of 42.4% in implant reconstruction after radiotherapy^[23]. These rates were significantly higher than those who had implant reconstruction before radiotherapy (19.6% and 8.5%, respectively). Capsular contracture, the most common complication of radiation after implant reconstruction, affects nearly half of patients who have a history of radiation^[24-26]. It is important to note that capsular contracture behaves similarly to radiation-induced fibrosis.

Adverse cosmetic outcomes of radiation therapy in breast reconstruction have global, surface, and parenchymal effects^[27]. Globally, radiation therapy may result in edema or shrinkage. These global effects can cause asymmetry in the nipple-areolar complex, breast size, and breast shape. Surface effects include hyper- or hypopigmentation of the nipple-areolar complex, telangiectasia, and subcutaneous fibrosis. Like global effects, these effects may create asymmetry in breast shape, size, color, and texture. Parenchymal effects include fat necrosis, cysts, or radiation-induced malignancy such as angiosarcoma.

Early toxicity is associated with the duration of radiation, whereas late toxicity is associated with dose variation per fraction^[28]. Symptoms include fatigue, neuropathy, and pain in the chest, shoulders, and neck. The heart, lungs, liver, and spinal cord are organs at risk for damage^[5]. Proper surgical and radiotherapy planning is essential for minimizing symptoms and radiation dose to organs at risk. Figure 1 summarizes the literature reviewed and discussed in the previous commentary.

OBJECTIVE

In this article, we briefly review radiation-induced tissue effects and their impact on breast reconstruction. More specifically, we comment on the traditional use of autologous tissue, microsurgical technical pearls for irradiated fields, reconstructive timing paradigms, and lymphedema prevention. With continued progress, derivation, and innovation, plastic and reconstructive surgery has consistently advanced and revolutionized both medicine and surgery. This review considers the future implications of breast reconstruction and how it will impact patients, healthcare, and the field. While not an exhaustive review, we aim to provide a comprehensive discussion and insights on all breast reconstruction options.

METHODS

A comprehensive literature review was meticulously conducted using the PubMed database from 12/01/2023-12/15/2023 by three independent researchers. Systematic reviews, literature reviews, clinical research, randomized controlled trials, and case series published between January 1995 and December 2023 were included. This review included studies on breast cancer treatment, breast reconstruction, radiation or radiotherapy, various types of breast reconstruction (e.g., autologous, implant), patient satisfaction, clinical outcomes, microsurgical technical pearls for irradiated fields, reconstructive timing paradigms, and lymphedema. With a structured outline as a guide, we curated over 100 references relevant to our research inquiry. This flexible yet robust methodology ensured a comprehensive coverage of pertinent literature.

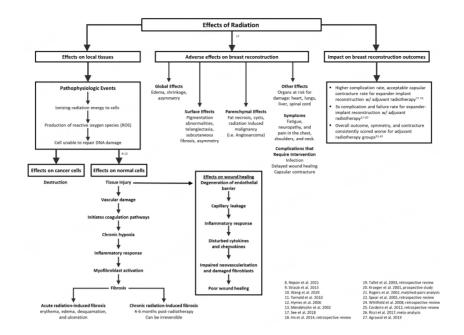


Figure 1. General overview of the literature on radiation and its effects on cancer treatment and wound healing.

DISCUSSION

Traditional use of autologous tissue in a previously irradiated breast

Breast reconstruction aims to rebuild the breast mound using several types of flaps. Local pedicled flaps are adjacent to the defect and remain attached to the original blood supply. Free flaps are donated vascularized tissues (abdomen, back, buttocks, or thigh) transferred to the breast blood supply^[29]. Discussing the different types of free flaps is beyond the scope of this article. However, these include transverse rectus abdominis muscle (TRAM), muscle-sparing free TRAM, deep inferior epigastric perforator (DIEP), superficial inferior epigastric artery (SIEA), profunda artery perforator (PAP), transverse upper gracilis (TUG), diagonal upper gracilis (DUG), vertical upper gracilis (VUG), latissimus dorsi flap, gluteal artery perforator (GAP) flaps, and others.

Autologous tissue is traditionally preferred for patients with previously irradiated breasts, as it enables the transfer of healthy tissue to the irradiated tissue^[23,24]. Radiation-induced complications in implant-based reconstruction consist of capsular contracture, infection, and mastectomy flap necrosis. Radiation-induced complications in autologous reconstruction involve volume loss, contracture, wound dehiscence, fat necrosis, and flap fibrosis^[30-31]. Compared to autologous tissue reconstruction, implant-based reconstruction has a greater risk of surgical-site infection and reconstructive failure^[32-34]. The optimal timing of autologous tissue transfer relative to radiation continues to be a subject of debate and will be discussed later in this article.

Autologous breast reconstruction in the irradiated field is associated with greater patient satisfaction and improved quality of life compared to implant-based reconstruction. Reported complications of autologous breast reconstruction following failed implant-based reconstruction include partial flap loss (3%), hematoma (3%), vascular compromise (1%), and total flap loss (1%)^[35,36]. Despite these complications, autologous breast reconstruction as a salvage technique for failed implant-based breast reconstruction has been found to have an acceptable complication risk profile and is associated with significantly improved patient satisfaction and quality of life.

While autologous breast reconstruction remains a favorable surgical approach for a previously irradiated field, there has been a growing interest in pre-pectoral breast reconstruction. With the advancement of microsurgical techniques, application of fat grafting principles, and monitoring of intraoperative flap perfusion, pre-pectoral breast reconstruction continues to be revisited and appreciated as it has shown promising outcomes^[37-39].

Although it is beyond the scope of this review, it is important to highlight an emerging treatment for previously irradiated areas: the adjunctive use of fat grafting. It is believed that fat has a regenerative potential and is particularly useful in those who have previously undergone radiation^[39-40]. It is recognized as a tool that can reverse the aforementioned radiation-induced fibrotic skin changes^[41]. Despite surgical preference for free-flap-based autologous breast reconstruction, additional fat grafting in the setting of implant-based breast reconstruction has been found to achieve good reconstructive outcomes with improved skin quality^[42].

The pedicled latissimus dorsi flap is another great option for reconstruction, as it provides well-vascularized tissue to the radiated field^[43]. Offering soft tissue and even skin coverage to the defected area, it restores the form of the natural breast mound in conjunction with tissue expansion/implant. Indications for this option include high-risk patients with comorbidities who are not good candidates for free tissue transfer, or inadequate donor sites.

Despite a growing interest in pre-pectoral implant-based reconstruction, fat grafting, and pedicled latissimus dorsi flaps, autologous breast reconstruction remains a favorable surgical approach for a previously irradiated field due to its acceptable complication risk profile and improved patient satisfaction and quality of life.

Technical pearls for the challenging microsurgery case in a radiated field

The irradiated field presents a unique challenge for the reconstructive surgeon. The effect of radiation creates distorted tissue planes with non-ideal qualities: fibrosis and sclerosis secondary to chronic inflammation. Furthermore, vasculature may be compromised, resulting in hypoxia, which further leads to impaired wound healing. Therefore, standard reconstructive techniques may be insufficient and inadequate. Here, we present additional modalities and pearls that may be elicited for microsurgical reconstruction of an irradiated breast, aside from the essential practice of handling tissue and vessels with exceptional delicacy due to their increased fragility [Figure 2].

Supercharging, turbocharging, and vascular augmentation: hook up two instead of one

The concept of supercharging aims to enhance flap vascularity by anastomosing multiple arteries and/or veins. This concept, also dubbed turbocharging or venous super-drainage, is part of a broader concept called vascular augmentation that once arose from necessity in cases of compromised perfusion and from non-plastic surgery operations such as renal transplant^[44]. Supercharging utilizes a distant blood supply, whereas turbocharging uses one within the flap territory^[44]. The technique is theorized to prevent complications of poor perfusion by increasing vascularity and predictability of pedicles. Prior literature has mixed reviews on efficacy. Some studies have shown that venous supercharging helps prevent venous congestion and flap tip necrosis^[45], and that two-vein anastomosis shows a lower incidence of re-exploration and fat necrosis^[46]. Conversely, some data show more vascular complications with supercharging^[47], though it is unclear whether these adverse events are secondary to graft choice or the fact that anastomoses are not in normal tissue^[42].

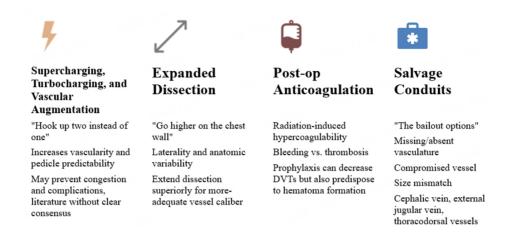


Figure 2. Technical pearls for the challenging microsurgery case in a radiated field.

Expanded dissection of recipient vessels: go higher on the chest wall

The internal mammary vessels, now widely accepted as the first-choice recipient vessels, have welldescribed anatomic variability^[48,49]. Bifurcation points may differ depending on laterality, and vessel crosssectional area decreases in the superior-inferior direction as the vessel travels along the sternal body. Furthermore, prior work has demonstrated the minimum necessary vessel caliber for certain flap sizes^[50]. For this reason, it may be necessary to extend the dissection of the recipient vessels more superiorly along the chest wall to expose larger mammary vessel recipients for anastomoses.

Postoperative anticoagulation

The radiation-induced chronic inflammation renders vessels hypercoagulable^[8], which raises concerns for flap failure. Jakobsson *et al.* found that hematoma was the most common reason for re-exploration after free flap, and that the use of a triple anti-thrombotic regimen was significantly associated with hematoma formation^[51]. The triple anti-thrombotic regimen referenced in the study consisted of preoperative low molecular weight heparin (LMWH), intraoperative heparin, and dextran. However, cessation of the regimen was associated with fewer hematomas and did not increase flap thromboembolic events^[51]. Postoperative immobility is often a concern in flap patients. The risk of postoperative anticoagulation has long been mitigated against bleeding and hematoma formation risk. Recent studies have found that post-op DVT prophylaxis significantly reduces DVT incidence^[45], and that heparin is more cost-effective than Lovenox^[52]. Furthermore, Lovenox dosing does not seem to reach adequate activated Factor Xa levels for prophylaxis in patients undergoing head/neck/breast free flap procedures^[53]. Other centers have implemented a 2-week prophylaxis protocol that lowers DVT but does not increase the incidence of hematoma^[54].

Salvage conduits: the bailout options

It is often said that the best postoperative results come with proper preoperative planning. As such, reconstructive microsurgeons must have backup options: a "plan B", which serves as a tactical remedy for unforeseen complications or situations. Imaging modalities such as ultrasound or contrast-enhanced CT can assist in the identification of suitable vascular conduits. The authors emphasize both preoperative planning and preparation. Deviations from the initial surgical plan must be discussed, and the team/operating room must have the necessary tools/equipment on hand. Salvage conduits may be necessary for various reasons, necessitating the use of a bailout option. This may be due to missing/absent vasculature, as prior literature has reported absent internal mammary veins^[55]. Moreover, the surgeon may encounter

inadequate/compromised vasculature. Size mismatches are sometimes present, as the left internal mammary vessel is known to be significantly smaller than the contralateral side^[56]. More commonly, the decision to utilize a salvage conduit arises from concerns of venous inadequacy, rather than compromised arterial quality^[57]. Several conduits exist for a bailout. The cephalic vein is a classically used option and can also be used to supercharge venous outflow^[58,59]. The external jugular vein has also been described^[52] and is mostly used due to size mismatch in a gluteal flap^[60]. Lastly, the contralateral internal mammary or thoracodorsal vessels are viable options to avoid a previously radiated chest field. These were the previous gold standard for microsurgical anastomosis, but the paradigm shifted when sentinel lymph node biopsy (SLNB) was favored over complete axillary lymph node dissection (ALND), making dissection and exposure of thoracodorsal vessels more extensive than deemed necessary.

In this review, we presented technical microsurgical pearls for breast reconstruction in irradiated fields, including the enhancement of flap vascularity, expanded dissection of recipient vessels, postoperative anticoagulation, and various salvage conduits. Understanding the challenges that radiation imposes can enhance preoperative planning, and familiarity with the aforementioned technical concepts can broaden the armamentarium of reconstructive surgeons, thus leading to optimal patient outcomes.

Delayed vs. immediate free flap reconstruction for the patient who will need radiation

Radiotherapy has clear survival rate benefits that warrant its inclusion when indicated^[61,62]. Furthermore, in the setting of PMRT, free flap reconstruction has been shown to have clear advantages over implant-based reconstruction^[32-34]. As a result, there is considerable debate about the timing and order of radiation therapy and free flap reconstruction to produce the best aesthetic outcome with minimal risk of complication.

There are three general approaches to timing free flap reconstruction: immediate, delayed-immediate, and delayed^[63,64]. The immediate approach entails free flap transfer and anastomosis directly following the mastectomy before closing the field. The flap must be able to tolerate post-procedure radiotherapy and avoid complications such as wound breakdown, flap necrosis, and/or flap failure. The delayed-immediate approach involves placing tissue expanders immediately after the mastectomy. Serial filling and expansion allow for shape and volume retention until the patient is able to receive the flap after radiation treatment to prevent damage from exposure^[65]. The delayed approach avoids reconstruction immediately after mastectomy, and instead occurs after radiation treatment^[63,65].

Of these three, only the immediate approach always results in flap exposure to radiation. Due to early studies demonstrating the increased risk of complication, revisions, and flap failure, consensus favored the delayed or delayed-immediate approach^[21,22,66]Of these two approaches, the delayed-immediate approach was preferred due to its compromise between the aesthetic favorability of the immediate approach and the avoidance of exposure to radiation^[67,68]. Furthermore, the approach also offers time for the patient to consider treatment options. This flexibility in the reconstructive approach, as well as favorable patient outcomes, are the reasons for its preferred choice over the other reconstructive options.

However, current literature has contested the assertion that an immediate approach is inferior. Advances in radiotherapy including optimized beam angles, dosages, and three-dimensional planning for administration have resulted in reduced chest wall damage^[69]. Thus, while radiotherapy still damages the reconstructed breast, this damage has been lessened and may be more tolerable than in earlier studies. Supporting evidence includes multiple systematic reviews and meta-analyses, which found that immediate reconstruction has similar results to delayed and delayed-immediate^[70-72]. Heiman *et al.* found in their meta-analysis that the immediate approach offered superior clinical outcomes and flap survival to the other

approaches^[72]. Prospective trials and retrospective reviews also match these assertions, with results that suggest patient quality of life and aesthetic perception are similar between immediate and delayed, and that immediate reconstruction in the setting of PMRT does not appear to affect patient outcomes^[73,74].

This shift in interest and results favoring the immediate approach in research have new clinical implications for the debate between immediate and delayed reconstruction. Timing for the delayed-immediate approach avoids flap exposure to radiation while retaining the aesthetic outcomes of the immediate approach. The delayed-immediate approach is also applicable to high-risk patients at risk of flap complications. However, recent research suggests that immediate reconstruction is a reliable option in low-risk patients and can be offered as a treatment alternative. Figure 3 provides a preferred algorithm by the senior author for radiation considerations in the breast cancer patient. When consulting patients on reconstruction, an immediate approach may be a valid option for patients, particularly if their radiotherapy will be administered over a small area or at a low dosage that the flap can tolerate^[67,75,76]. However, this shift should be tempered by prior studies that have demonstrated an increased risk of complications with flap radiation exposure, including flap contracture, volume loss, and fat necrosis^[74,77]. As a result, based on existing literature, surgical planning should consider offering delayed-immediate reconstruction as an option for patients with PMRT.

Autologous reconstruction with lymph node transfer to prevent lymphedema in the radiated breast

With the aforementioned effects of radiation on tissue quality and the resultant vascular compromise, coupled with the effects of surgical dissection, breast reconstruction patients are prone to lymphedema, especially after ALND^[78]. An estimated 3%-8% of patients develop lymphedema even after just SLNB alone, with other known risks such as neoadjuvant/adjuvant chemoradiation (CRT) and obesity^[79]. The management of lymphedema is outside the scope of this special topic; however, it sometimes requires surgical techniques. Technological advances such as microscopes, and evolutionary techniques of lymphovenous bypass (LVB) and lymphovenous anastomosis (LVA) have demonstrated efficacy in reducing sequelae of lymphedema^[80]. However, equally important as treating lymphedema is preventing it. Vascularized lymph node transfer (VLNT) includes the microsurgical transplant of lymph nodes and an associated vascular pedicle from a donor to a recipient site. Lymph node transfer is believed to stimulate lymphangiogenesis, thereby improving lymphatic drainage of the recipient region and consequently reducing lymphedema^[81]. The procedure can be useful for both treating and preventing lymphedema. It is typically reserved for more advanced cases and poor candidates for LVA/LVB^[82], but can also be considered at the time of the index surgery.

Various techniques exist, and there are several options for nodal harvest. Some of the most commonly used basins for VLNT include the supraclavicular^[82], submental^[83], lateral thoracic^[84], inguinal^[85] (which can be taken at the time of DIEP harvest, i.e., a single operation)^[86], and the omentum^[87] (which can also be taken at the harvest of DIEP or msTRAM)^[86,88]. Although options for successive or combined operations are feasible, combined operations may have better results^[89] and also demonstrate better postoperative patient-reported quality of life (QOL)^[90]. Recently, the omental lymph node transfer has gained popularity, as current research continually demonstrates that it is a safe and feasible procedure without the additional risk of donor site lymphedema^[91].

Regardless of the nodal basin used, clinical judgment and provider discretion are paramount. Donor site morbidity such as scar location or lymphedema risk must be accounted for, and further studies are warranted to determine the long-term outcomes of such flaps and lymph node transfers^[92,93].

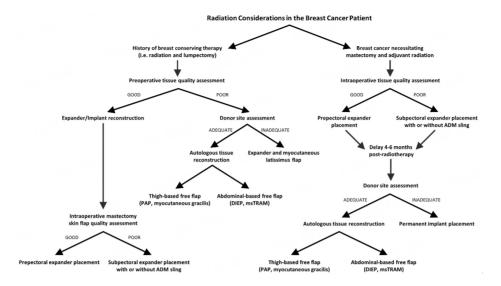


Figure 3. Radiation considerations in the breast cancer patient. ADM: acellular dermal matrix; PAP: profunda artery perforator; DIEP: deep inferior epigastric perforator; msTRAM: muscle-sparing transverse rectus abdominis myocutaneous.

A recent study in Japan compared conservative management versus combined-modality LVA and compression therapy for lymphedema in early breast cancer^[94]. The single-center retrospective analysis found that surgical lymphovenous anastomosis and compression therapy were more efficacious than conservative treatment alone, citing reductions in limb circumference and cellulitis incidence^[94]. Newer literature advocates for multidisciplinary approaches combining surgical modalities and medical therapies. Ciudad *et al.* present a multi-national algorithm for breast cancer-related lymphedema^[95]. The authors employed the breast cancer-related lymphedema multidisciplinary approach (B-LYMA) and found that the addition of suction-assisted lipectomy to LVA significantly reduced limb circumference, compared to LVA, VLNT, and combined DIEP flap and VLNT^[95].

In this review, we discuss the management of breast cancer-related lymphedema, including lymphovenous bypass and vascularized lymph node transfer. While each method has its own advantages and limitations, newer research calls for multidisciplinary and multimodal algorithmic treatment aimed at both prevention and treatment.

SUMMARY

Despite a growing interest in pre-pectoral implant-based reconstruction, fat grafting, and pedicled latissimus dorsi flaps, autologous breast reconstruction remains a favorable surgical approach for a previously irradiated field due to its acceptable complication risk profile and improved patient satisfaction and quality of life. In this review, we presented technical microsurgical pearls for radiated breasts, including the enhancement of flap vascularity, expanded dissection of recipient vessels, postoperative anticoagulation, and various salvage conduits. Furthermore, we propose an algorithm that describes the multiple approaches to timing free flap reconstruction for the previously irradiated patient. Lastly, we reviewed the prevention of lymphedema through several surgical techniques including LVB, LVA, and VLNT. When caring for the previously irradiated patient, we must consider all levels of care in which a paradigm shift in breast reconstruction may occur. This could mean a change in microsurgical techniques, reconstructive timing, preoperative optimization, and postoperative care.

FUTURE DIRECTIONS

Since its emergence from the core principles of general surgery, plastic and reconstructive surgery has consistently advanced and revolutionized both medicine and surgery. Microsurgery and even supermicrosurgery have evolved alongside medical and surgical technology, allowing practitioners and researchers to explore new frontiers. With each advancement, we must consider the future implications and how it will impact patients, healthcare, and the field. Here, the authors comment on potential future directions.

Equally as important to mitigating the effects of radiation is preventing them. However, preventing the adverse effects of radiation is not always feasible or possible, as radiotherapy cannot, and should not, be deferred when its benefits outweigh the risks. Predictive models that could analyze patient factors could serve as clinical decision support tools, enhancing multidisciplinary care, patient education, and shared decision-making. Healthcare professionals could utilize these models to predict, to a reasonable degree, the post-radiation course in any given patient. Understanding the potential risk factors and associated complication profiles could enable more accurate surgical planning and management. This, in turn, could enhance preparedness and overall outcomes. Radiation oncologists have stressed the need for radiation estimation since the 1980s, so as to better evaluate the pros, cons, and cost-effectiveness of radiotherapy^[96]. Palma *et al.* have described an algorithm for radiation complications, such as hypothyroidism after supraclavicular radiation in breast cancer^[97]. In Germany, a team of researchers have described an algorithm of predictive factors for radiotherapy complications in normal tissue with increasing age as a risk factor for telangiectasia and fibrosis^[98]. Smoking was also associated with an increased risk of telangiectasia^[99].

Personalized healthcare is becoming increasingly more common in modernized medicine. With an emphasis on improved patient outcomes and experience, treatment and management algorithms that are patient-centered and patient-specific are essential tools to achieve these outcomes. There exists a large body of literature outlining individualized breast cancer risk assessment^[99-101]. Other works attempt to create individualized breast cancer risk prediction models with the use of machine learning and artificial intelligence^[102,103]. Less research, however, focuses on complication or morbidity prediction. One study developed a protocol to investigate radiation-induced skin fibrosis resulting from breast cancer treatment, in an effort to derive an algorithm for personalized risk estimation^[104].

Adjuncts have also been employed to mitigate the effects of radiation. Intraoperatively, fat grafting, decellularized fat matrices, and/or acellular dermal matrix (ADM) have shown promise in reducing the negative effects of skin fibrosis. Adipose-derived stem cells have demonstrated a therapeutic effect in radiated fields, with the ability to amplify wound healing and alter genetic expression, modifying hypoxia and inflammation^[105,106]. Prophylactic lipofilling has been shown to be beneficial in mitigating radiation effects on tissue at both a qualitative and a quantitative level^[107,108]. Potential uses of hyperbaric oxygen and other pharmaceutical agents have also been utilized^[8]. ADM has shown promise in inhibiting capsular contracture in post-mastectomy radiotherapy^[109]. These findings were corroborated in a large Spanish multicenter analysis of 1,450 pre-pectoral breast reconstructions with ADM, reporting a low incidence of capsular contracture (2.1%)^[110]. Postoperative wound care with hydrogel and hydrocolloid dressings have also been used, citing the benefits of moist environments to prevent pain and accelerate wound healing^[111,112].

CONCLUSION

While certain dogma has prevailed due to important data in our literature, advances in radiation and multidisciplinary care have changed paradigms at certain institutions. With continued progress, derivation, and innovation, plastic surgery and microsurgery are rapidly evolving. While the authors are not suggesting that this is inevitable, plastic and reconstructive surgeons, along with patients and other healthcare providers, must consider the possibility of paradigm shifts in breast reconstruction. This could mean a change in microsurgical techniques, reconstructive timing, preoperative optimization, or postoperative care^[113,114]. Nonetheless, free tissue transfer will remain a vital reconstructive option not only for the breast, but also for extremities and other body regions. Reconstructive surgeons must have an armamentarium capable of these options for the best possible patient outcomes.

DECLARATIONS

Authors' contributions

Made substantial contributions to the conception and design of the article and performed literature review and interpretation: Ewing JN, Gala Z, Lemdani MS, Kovach III SJ, Azoury SC

Availability of data and materials

Not applicable.

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Conflicts of interest

Dr. Stephen Kovach is a consultant and speaker for Becton Dickinson, WL Gore and Company, Integra Life Sciences, Checkpoint Surgical, and Abvie Consulting. Dr. Said C. Azoury serves as a Youth Editorial Board member of the *Plastic and Aesthetic Research (PAR)* journal. All other listed 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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