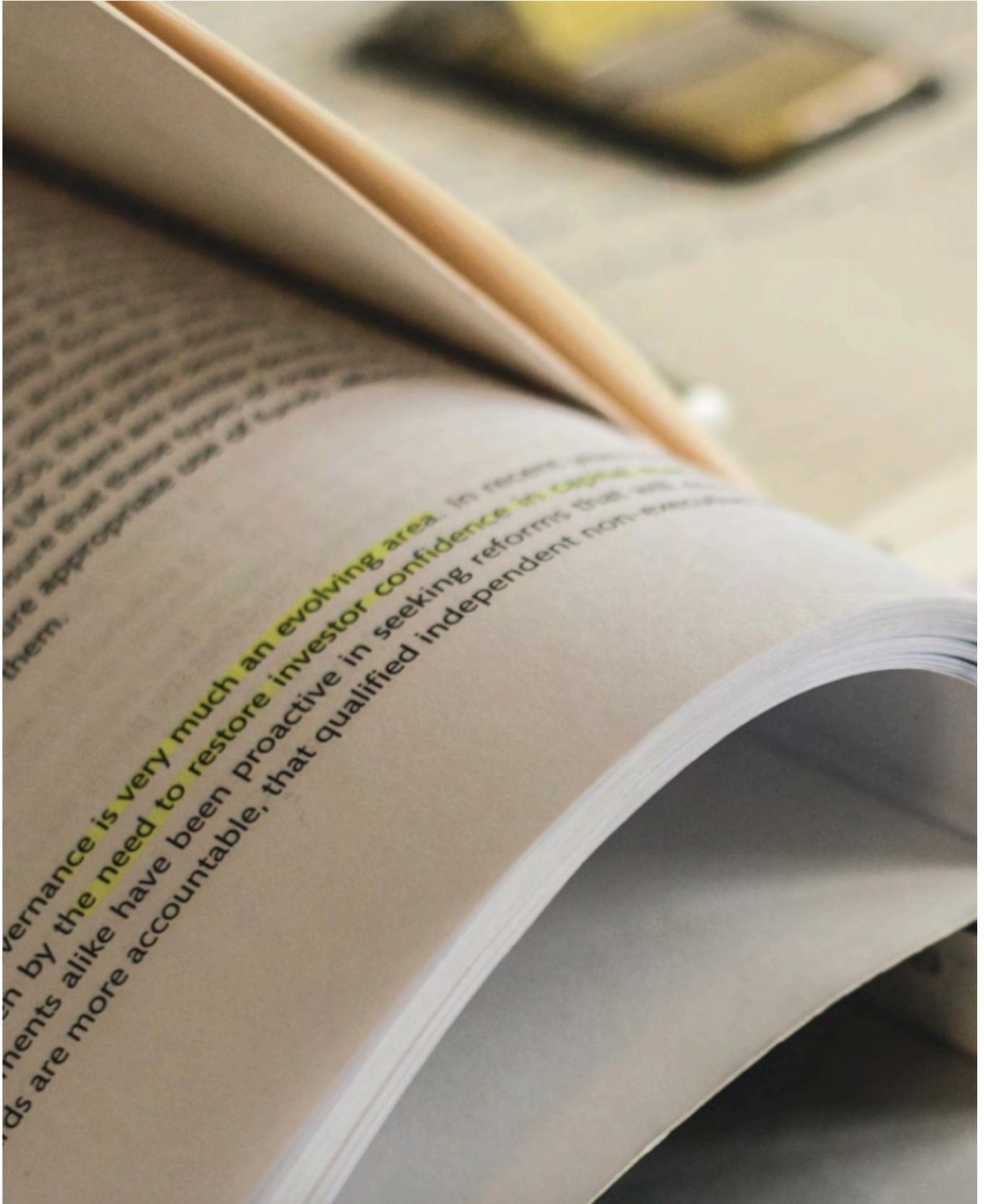


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Radiation Therapy and Immediate Breast Reconstruction

Novel Approaches and Evidence Base for Radiation Effects on the Reconstructed Breast

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KEYWORDS

- Postmastectomy radiotherapy • Implant • Autologous • Breast reconstruction • Complications
- Reconstruction failure

KEY POINTS

- Immediate breast reconstruction is directly affected by radiation therapy.
- Immediate breast reconstruction can be either autologous or implant based.
- Autologous breast reconstruction is the gold standard.
- Implant-based reconstruction has significantly higher failure and complication rates than autologous reconstruction.
- Complications can be mitigated by judicious timing of surgery and the use of adjuncts, such as acellular dermal matrices and fat grafting.

INTRODUCTION

The global trend for breast cancer is increasing. The number of breast cancer diagnoses has escalated.¹ In conjunction with this, there has been an expansion in the role of radiotherapy as an adjunct treatment. There are growing numbers of patients receiving radiotherapy, either following breast-conserving surgery or mastectomy to prevent locoregional recurrence. Hence, a greater number of patients approaching plastic surgeons requesting reconstruction following mastectomy

for residual or recurrent breast cancer would present with a history of previous irradiation.

The other increasing trend is the inclination toward immediate breast reconstruction (IBR) following mastectomy, despite the need for post-mastectomy radiotherapy (PMRT).^{2–7} There are several factors that contribute to this, including changes in legislation, such as the Women's Health and Cancer Rights Act of 1998 in the United States and the National Institute of Clinical Excellence's guidelines for breast cancer treatment and reconstruction in the United Kingdom in

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2002; increasing access to surgeons offering IBR; a younger cohort of patients who are keen to have IBR; sex of the plastic surgeon⁸; and finally, greater awareness of the availability of IBR through social media, publications, and advocacy groups.

As reconstructive surgeons, a previous history of radiotherapy to the residual breast or the potential need for PMRT directly impacts on our decision-making process for the type of breast reconstruction.⁹ The sequelae of PMRT on the reconstructed breast and the variety of algorithms and adjuncts that have been proposed to mitigate these effects are discussed in the following article.

POSTMASTECTOMY RADIOTHERAPY

Over the last decade, there has been mounting indications and a diminishing threshold for PMRT. The use of PMRT is widely accepted for patients with early invasive breast cancer who have had a mastectomy and are at a high risk of local recurrence, that is, those with 4 or more positive axillary lymph nodes or involved resection margins.^{10,11}

In 2014, a meta-analysis performed by the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) demonstrated that PMRT reduces locoregional recurrence, overall recurrence, and breast cancer mortality in patients with 1 to 3 positive lymph nodes.¹² However, the recurrence rates reported in this meta-analysis were higher than those reported in more contemporary series, most likely because most of the trials included in the meta-analysis were conducted in the 1970s and 1980s, that is, before the advances in systemic therapy. The subsequent trend in later series demonstrated lower locoregional recurrences.^{13–18} The factors responsible for this include smaller tumor sizes, fewer positive axillary lymph nodes, more complete axillary clearance, and more effective systemic regimes.¹⁹ Therefore, it remains controversial whether PMRT can be attributed in lowering locoregional recurrences in the intermediate-risk group of patients (patients with high-risk node-negative disease and 1 to 3 lymph nodes involved). Currently, we are awaiting the outcome of the UK Selective Use of Postoperative Radiotherapy After Mastectomy (SUPREMO) Trial to determine if radiotherapy is advocated for patients who have had a mastectomy for early invasive breast cancer and who are at an intermediate risk of local recurrence, taking into account modern systemic therapy and surgical techniques compared with the EBCTCG patient cohort.

In patients with positive axillary lymph nodes, PMRT is delivered to the chest wall, supraclavicular or axillary fossa (or both), and the internal mammary

lymph nodes. There remains some controversy as to whether irradiating the internal mammary lymph nodes reduces overall mortality.^{20–23}

Historically, PMRT was delivered in a standard regime of 50 Gy in 25 fractions. However, in 2013, the UK Standardization of Breast Radiotherapy (START) trials presented robust data with 10-year follow-up results, demonstrating that appropriately dosed hypofractionated radiotherapy, such as 40 Gy in 15 fractions, was as safe and effective as the historical regime but with less harm to normal tissues.²⁴ Most of the patients had breast conservation in these trials, and only a small proportion of patients had irradiation of the chest wall or regional lymph nodes. This finding might be the reason why some guidelines, such as the latest German guidelines for diagnosis treatment and follow-up of breast cancer, still favor the standard fractionation, but hypofractionation is a valid option for PMRT.²⁵

Radiotherapy involves the use of ionizing radiation, which is delivered by external beam radiation to the targeted tissues, be it the chest wall or lymph node basins. This radiation, in turn, causes damage to the cells by producing irreversible changes during DNA replication or cell division or during the processing of DNA damage by enzymatic repair processes.²⁶ This damage is indiscriminate and affects malignant as well as healthy cells within the field of irradiation.

Long-term damage to the tissues occurs via several mechanisms. Firstly, the cells that are the progeny of exposed cells but that are not themselves exposed may divide, express delayed gene mutations, and carry chromosomal aberrations. This effect is known as radiation-induced genomic instability and can cause prolonged disruption of tissue volume within the radiation field.²⁷ Furthermore, recognition and clearance of apoptotic cells after exposure to radiation produces both a persistent macrophage activation and an inflammatory-type response.²⁸ Finally, there are also cytokine-mediated multicellular interactions, which initiate and sustain the fibrogenic process.^{29,30}

Translated clinically, early effects of radiotherapy include erythema and desquamation, whereas delayed effects include radiation-induced fibrosis, telangiectasia, skin thinning, and pigmentation. All of these sequelae are associated with increased risk of delayed healing, surgical complications, and poor cosmesis.

BREAST RECONSTRUCTION

Breast reconstruction following mastectomy can be classified by timing or type. Breast reconstruction can either be performed simultaneously with

the mastectomy (immediate reconstruction) or deferred for months or years following mastectomy (delayed reconstruction). The two main modalities of breast reconstruction are implant based or autologous.

IBR has been acknowledged to be superior to delayed reconstruction for a multitude of reasons. Firstly, IBR has been shown to be beneficial toward patients' satisfaction, posture, health-related quality of life, psychosocial well-being, and body image following mastectomy.^{31–33} IBR also offers enhanced cosmesis compared with delayed reconstruction, as it allows preservation of the inframammary crease and provides a more natural appearance. From the oncological perspective, studies have shown that IBR is safe and does not increase the incidence of local recurrence or distant metastases when compared with mastectomy alone.^{34,35} Furthermore, the presence of a breast reconstruction does not affect the delivery of postreconstruction radiotherapy.³⁶ Finally, despite the setting of PMRT, early creation of a breast mound has been shown to be beneficial for health-related quality of life and patient satisfaction compared with mastectomy alone or delayed reconstruction.³⁷

IMPLANT RECONSTRUCTION

Implant-based breast reconstruction confers multiple benefits to patients, including shorter operative time, quicker recovery, surgery and scars confined to a single site, and lower costs. In some patients, there is no alternative option for breast reconstruction because of the paucity of donor sites.

However, in the context of PMRT, a systematic review by Berbers and colleagues³⁸ showed that the total complication rate and revision surgery for implant reconstruction is significantly higher when performed after radiotherapy (48.7% and 42.4%, respectively) than before radiotherapy (19.6% and 8.5%, respectively). Multiple studies have also established that implant reconstruction correlates with higher complication rates and higher failure rates compared with autologous reconstruction.^{39–41} The associated complications are capsular contracture, infection, poor aesthetic outcome, and reduced patient satisfaction, as elaborated later.

Reconstruction Failure

Chetta and colleagues³⁹ established that, in 4781 patients who have had breast reconstruction and radiotherapy, 29.4% of patients with implant reconstruction experienced reconstruction failure compared with 4.3% of patients with autologous

reconstruction. The complication rate for implant reconstruction in this study was 45.3% compared with 30.8% in autologous reconstruction. These figures translate to 2 and 11 times greater odds of complications and failure of reconstruction, respectively, with implant-based reconstruction in irradiated patients compared with autologous reconstruction. Similar figures were obtained in other studies.^{40–43}

The strongest predictor of reconstruction failure was the absence of total prosthesis coverage, either by means of the serratus muscle or acellular dermal matrices. Fowble and colleagues⁴⁴ demonstrated a 32.5% reconstruction failure rate in patients without total coverage compared with 9.0% in patients with coverage ($P = .0069$). For patients with total coverage, the other predictors of failure were location of the mastectomy scar in the inframammary fold (19% vs 0%, $P = .0189$) and shorter interval between radiotherapy to exchange of implant.

The timing of radiotherapy during the reconstruction process has a direct influence on the outcome of the reconstruction. The reconstruction failure rates are increased in patients who receive radiotherapy with a tissue expander before exchange for a permanent implant, compared with patients who receive radiotherapy with a permanent implant in situ.^{38,45,46}

A systematic review by Lam and colleagues⁴⁶ revealed that the reconstruction failure rate in immediate 2-stage implant reconstruction is significantly higher with postreconstruction radiotherapy, that is, 18.6% compared with 3.1% in controls ($P < .00001$). Radiotherapy particularly increased the failure rate when given after stage one, with the tissue expander in situ (29.7% vs 5.0% in controls, $P < .00001$) in contrast to stage 2, after insertion of a permanent implant (7.7% vs 1.5%, $P = .00003$). In a single series, Nava and colleagues⁴⁵ demonstrated a 40% failure rate in the cohort of patients who received radiotherapy before undergoing the exchange of tissue expander to implant. This finding is in comparison with a failure rate of 6.4% in patients who received radiotherapy after undergoing the exchange of tissue expander to implant and 2.3% in the control group ($P < .0001$).⁴⁵

To circumvent the high reconstruction failure rates, Cordeiro and colleagues⁴⁷ proposed an algorithm for irradiation in patients with 2-stage implant reconstruction. In this algorithm, patients undergo mastectomy, placement of a submuscular tissue expander, and tissue expansion throughout chemotherapy and then exchange for a permanent implant before commencement of radiotherapy. This algorithm led to a 9.1%

reconstruction failure in the irradiated group compared with a 0.5% failure rate in the nonirradiated group ($P < .01$). The investigators cited the main cause of reconstruction failure in their patient cohort as infection (41.4% in irradiated patients and 44.5% in nonirradiated patients). The other factors instigating failure were implant extrusion (27.6%), capsular contracture (27.6%), and recurrent seroma (3.4%). This study was carried out over a period of 13 years and, therefore, offered some longevity in the data. Nevertheless, the investigators also performed Kaplan-Meier analysis, which showed that, in the long-term, irradiated implants remain in situ at a rate of 88.8% at 5 years, 85.2% at 8 years, and 82.5% at 12 years. The implant loss rates were greater than for nonirradiated implants ($P < .01$), but there was no significant difference in long-term replacement rates compared with nonirradiated implants.

Capsular Contracture

Capsular contracture is the most common complication following implant reconstruction and post-reconstruction radiotherapy. The capsular contracture rate quoted in the literature is variable because of the heterogeneity of the studies.

In the systematic review by Lam and colleagues,⁴⁶ the capsular contracture rates in irradiated tissue expanders and permanent implants were 8.9% and 7.9%, respectively. Cordeiro and colleagues⁴⁸ showed that the capsular contracture rate was lower when irradiating the tissue expander compared with the permanent implant. Baker grade III and IV capsular contractures were 15.9% and 1.22%, respectively, for tissue expanders compared with 44.6% and 6.3%, respectively, for permanent implants. This finding is attributed to the more aggressive capsulotomy performed at the time of exchange procedure. In patients with immediate 2-stage expander/implant reconstruction, Ho and colleagues⁴⁹ reported that 21.7% of patients who had PMRT developed capsular contracture compared with 10.0% without radiotherapy ($P < .008$). Spear and colleagues⁵⁰ demonstrated that 40.0% of patients who underwent nipple-sparing mastectomy and PMRT developed capsular contracture compared with 7.8% in those who had previously undergone breast-conserving surgery.

It is well established that the cause of capsular contracture is multifactorial. Salzberg and colleagues⁵¹ listed the risk factors as patient age, smoking, body mass index, oncologic breast, nipple-sparing mastectomy, incision site, implant size, implant surface characteristics, radiotherapy, and postoperative seroma/hematoma and/or

infection. Other factors that have been associated include choice of implant filler material, position of implant placement, texture of implant surface, and duration of implant.⁵² More recently, a local immune response triggered by silicone implants⁵³ and radiation-induced modification of the silicone have been implicated.⁵⁴

Capsular contracture is thought to be diminished with the utilization of acellular dermal matrix (ADM) in conjunction with implant or tissue expander reconstruction.^{51,55,56} Israeli and Feingold⁵⁷ advocated using ADM not only in primary implant reconstruction but also in revision cases combined with capsulectomy.⁵⁷ There has certainly been a paradigm shift of increased usage of ADM over the last decade since the initial report by Breuing and Warren⁵⁸ in 2005. Further to capsular contracture mitigation, ADM plays an important role in controlling the mastectomy pocket and prosthesis and providing coverage to the lower pole of the implant. Consequently, numerous ADMs have emerged in the market, be it human, porcine, or bovine derived.

Animal studies have demonstrated that capsule formation is minimized in the presence of ADM.^{59,60} In clinical studies, Leong and colleagues⁶¹ showed that breast capsules in the setting of ADM had significantly lower levels of inflammatory markers ($P < .01$), thereby supporting evidence that ADM may inhibit inflammatory and pro-fibrotic signaling characteristics of breast capsule development and decrease the risk of capsular contracture. Albeit slower, ADM has been shown to recellularize and revascularize even in the setting of radiotherapy^{62,63} and has been proven histologically to limit the elastosis and chronic inflammation seen in irradiated implants.⁶⁴

However, it is important to bear in mind that despite the utilization of ADM, irradiated patients still experience higher complications and reoperation than in nonradiated patients⁶⁵⁻⁶⁹ and there is a learning curve to overcome in the technique of inseting the ADM.^{68,70} Complications include infection, seroma, hematoma, skin necrosis, exposure of ADM, and implant loss.^{55,67,68}

In a long-term study of direct-to-implant and ADM-assisted breast reconstruction, Salzberg and colleagues⁵¹ reported a capsular contracture rate of 1.9% in irradiated breasts ($n = 104$), occurring within the first 2 years of reconstruction. The investigators observed that capsular contracture occurs early following ADM-assisted reconstructions, does not progress with time, and mitigates the occurrence of capsular contracture. Spear and colleagues⁷¹ demonstrated that timing of irradiation is also important in the setting of

ADM-assisted implant reconstruction. They revealed that tissue expanders with ADM irradiated after the first stage of IBR demonstrated higher rates of capsular contracture (grade III/IV), compared with the premastectomy radiotherapy cohort and the nonirradiated cohort (60.7% vs 41.2% vs 1.4%, $P < .0001$). The higher capsular contracture rates were corroborated by Moyer and colleagues⁶⁴ who reported a 33.3% capsular contracture rate.

The latest innovation in immediate breast reconstruction is the prepectoral placement of implants with either ADM or mesh. This technique was instigated because it was thought that elevation of the pectoralis major muscle caused some problems, such as animation deformities, chest tightness, pain, and muscle spasm.⁷² Sigalove and colleagues⁷³ described their rationale, indications, and preliminary outcome in 353 prepectoral implant reconstructions with ADM and stressed the importance of patient selection. Contraindications include patients and oncological factors. In their series, there was no incidence of capsular contractures, even in patients with a history of pre-reconstruction or postreconstruction radiotherapy ($n = 27$). However, their follow-up was 2 years, which is relatively short. Another nonrandomized prospective trial comparing the long-term outcomes for subpectoral and prepectoral breast reconstructions described no differences in terms of short- or long-term surgical complications or sexual well-being but did report a greater satisfaction with outcome in the prepectoral group ($P = .03$).⁷⁴ Becker and colleagues⁷⁵ published a series of 62 prepectoral breast reconstructions using either ADM or Vicryl mesh (Ethicon, Inc, Somerville, NJ, USA) with 2 cases of capsular contracture using the latter. Currently, one must be cautious in interpreting the outcome of prepectoral reconstruction with ADM, as long-term data are still unavailable.

Many investigators have advocated the use of fat grafting to modify the effects of capsular contracture and to minimize complications following radiotherapy.^{76–78} Multiple studies have now established that fat grafting in breast reconstruction is oncologically safe.^{79–82} Reish and colleagues⁸³ established that patients who underwent nipple-sparing mastectomy and radiotherapy are more likely to have a secondary procedure for capsular contracture (12.5% vs 2.3%, $P < .001$) and fat grafting (13.6% vs 3.9%, $P < .001$) compared with those without radiotherapy. Furthermore, fat grafting has also been shown to play a role in reducing neuropathic pain following radiotherapy.⁸⁴ Choi and colleagues⁸⁵ demonstrated that fat retention after fat grafting

is volume and time dependent, that is, patients receiving higher volumes of injected fat had greater total volume retention, irrespective of prior irradiation or breast procedure. Nevertheless, it would be prudent to augment the volume of fat grafting by preparing the recipient site with releasing of the fibrous bands and/or external expansion.^{86,87}

Infection

Infection is a frequent cause of implant-based reconstruction failure with and without radiotherapy.⁴⁷ A large retrospective study ($n = 1952$) of immediate implant reconstructions by Reish and colleagues⁸⁸ showed that the incidence of infection is 5.1%. The predictors for infection were radiotherapy, chemotherapy, smoking, and mastectomy skin necrosis. In another study by Kearney and colleagues,⁸⁹ patients who received PMRT were more likely to experience tissue expander infection compared with patients who have not been irradiated (20.0% vs 2.6%, $P = .001$). Similar trends were demonstrated by other investigators.^{42,83}

A systematic review examining the impact of prophylactic antibiotics on surgical site infections and implant loss concluded that prolonged antibiotics did not significantly improve the outcome based on these parameters.⁹⁰ A single preoperative dose of antibiotics is equally effective as prolonged antibiotics in preventing surgical site infections in implant reconstruction.⁹¹

Furthermore, most surgical site infections in immediate breast reconstruction occur more than 30 days after the first- and second-stage procedures; the factors that significantly contribute to this are radiotherapy and body mass index.⁹²

Aesthetic Outcome

Nava and colleagues⁴⁵ reported that better aesthetic outcomes were achieved in patients who had their permanent implant irradiated, compared with those who had irradiation to the tissue expander. The outcome assessments were congruent between surgeons and patients. A similar outcome was reported by Cordeiro and colleagues.⁴⁸

In nipple-sparing mastectomies, radiotherapy did not result in significant nipple malposition⁸³ or nipple necrosis.^{42,50} However, one study presented a 55.6% incidence of high-riding nipples following radiotherapy.⁵⁰

In a systematic review, Berbers and colleagues³⁸ established that IBR with implants followed by radiotherapy yields a lower rate of revision surgery

compared with the corresponding autologous reconstruction patients (8.5% vs 23.6%).

Patient Satisfaction

There has been a significant expansion in implant-based breast reconstruction in the United States, that is, 203% since 2002.⁹³ Despite the potential complications mentioned earlier, the frequency of implant reconstruction in the setting of PMRT has also increased.⁶ Interestingly, patient satisfaction studies have revealed a mixed outcome. There are several large studies that have revealed high satisfaction among the patients and that most patients would choose implant reconstruction again.^{41,47,94} On the other hand, a systematic review of the literature showed that the satisfaction rate among patients and physicians were lowest in implant reconstruction after radiotherapy.³⁸ Another study substantiated the negative impact of radiotherapy on patients' quality of life and satisfaction.⁹³

Cost-effectiveness

It is difficult to determine the true cost-effectiveness of the various methods of reconstruction available. The methodology in these studies needs to be scrutinized, as there are many confounding factors in determining the choice of reconstruction for patients, including medical risk factors, patient choice, and the skill set of the surgeons. Taking into account the financial cost of the procedure and quality of life of patients after the reconstruction, one study found that implant reconstruction is not cost-effective when compared with pedicled and free autologous tissue reconstruction.⁹⁵ However, another study comparing the cost-effectiveness of single-staged versus staged prosthesis reconstruction found that direct-to-implant reconstruction is more cost-effective.⁹⁶

AUTOLOGOUS RECONSTRUCTION

Autologous breast reconstruction is regarded to be the gold standard of breast reconstruction by plastic surgeons. This method is preferred because the breast is reconstructed using the patients' own tissue, does not require maintenance surgery, will age naturally with patients, and adapt harmoniously with changes in the body habitus of patients. There are many donor sites that have been described, the most common being abdominal based.

To avoid any confusion or overlap with implant-based reconstruction, the subsequent text is based on autologous reconstruction without prostheses adjuncts. Prereconstruction radiotherapy

refers to patients who had PMRT before reconstruction or previous breast-conserving surgery and radiotherapy subsequently requiring mastectomy. Postreconstruction radiotherapy refers to patients who underwent IBR and then PMRT.

Overall Complications

Systematic reviews of the literature by Schaverien and colleagues⁹⁷ and Berbers and colleagues³⁸ have established no significant difference in overall complications when comparing autologous reconstructions that undergo radiation exposure and reconstructions without radiation. When comparing the different types of free flap reconstructions with and without PMRT, Chang and colleagues⁹⁸ found no significant difference in the early or late complications across the range of flaps. A comparison between prereconstruction and postreconstruction radiation of autologous flap reconstructions by Kelley and colleagues⁹⁹ demonstrated no significant difference in the total flap loss, wound healing, infection, seroma, hematoma, and fat necrosis.

In bilateral breast reconstruction after prior unilateral radiation, Fracol and colleagues¹⁰⁰ ascertained that the previously irradiated side is more likely to have an intraoperative vascular complication and the need for arterial anastomosis revision but no difference in the other postoperative complications as mentioned earlier. A similar observation has been reported by Fosnot and colleagues.¹⁰¹

El-Sabawi and colleagues⁴⁰ similarly found that autologous reconstructions have a lower incidence of total complications in comparison with implant-based reconstruction. However, autologous reconstruction also had significantly increased incidence of wound-related complications, hematoma, and seroma.

Fat Necrosis

Fat necrosis is of great interest in irradiated autologous reconstruction. In a systematic review, Khansa and colleagues¹⁰² established the rate of fat necrosis among patients with no history of irradiation was 8.7%, which is significantly lower than in patients who had prereconstruction (11.0%, $P = .022$) and postreconstruction irradiation (22.3%, $P = .001$). Schaverien and colleagues⁹⁷ corroborated that the mean prevalence of fat necrosis in immediate autologous reconstruction with postreconstruction radiotherapy was 22.0% to 23.8%, compared with approximately 14.9% in those with prereconstruction radiotherapy and delayed reconstruction, although this difference was not significantly different. However, Berbers

and colleagues³⁸ found that there was more fibrosis in autologous reconstruction with postreconstruction radiotherapy (36.0%) compared with prereconstruction radiotherapy (2.7%). Nevertheless, these meta-analyses were performed on retrospective studies, which were nonrandomized and heterogenous in their outcome parameters.

Clarke-Pearson and colleagues¹⁰³ performed a comparative study of immediate bilateral deep inferior epigastric perforator flap reconstructions, with unilateral PMRT, thereby allowing direct comparison between irradiated and nonirradiated flaps ($n = 11$). The investigators did not find clinically significant fat necrosis in any of the flaps; however, the numbers in their study were too small for statistical significance. In a prospective study by Taghizadeh and colleagues,¹⁰⁴ postreconstruction radiation did not cause any significant fat necrosis, the need for surgical removal of fat necrosis, or volume-enhancement revision surgery.

Timing

Sacotte and colleagues¹⁰⁵ examined the long-term complications of patients undergoing IBR and PMRT and found that the greatest risk for major complications occur within the first year after commencement of PMRT and decreases significantly with time. The investigators also established that there is no significant difference in major complications in patients undergoing implant-based versus autologous reconstruction (47.3% vs 30.4%, $P = .168$). Another study showed no significant difference in major complications between patients who had autologous reconstruction within 12 months and greater than 12 months after radiation.¹⁰⁶

Infection

Several studies have confirmed that a previously irradiated field confers an increased risk of infection following breast reconstruction.^{100,107} However, Kelley and colleagues⁹⁹ showed no significant difference in infection rates in autologous reconstruction before and after exposure to radiotherapy.

Reconstruction Failure

Systematic reviews by Berbers and colleagues³⁸ and Kelley and colleagues⁹⁹ confirmed that there was no significant difference in reconstruction failure if it was performed before or after radiotherapy.

Revision Surgery

Schaverien and colleagues⁹⁷ found that, despite the lack of difference in overall complications in the prereconstruction and postreconstruction

radiotherapy cohorts, there was more revision surgery in the latter group. However, in comparison with the control/no radiotherapy cohort, there was no difference in the rate of revision surgery, suggesting that the immediate reconstruction has greater influence on revision surgery than the radiotherapy. Similarly, Chang and colleagues⁹⁸ found a lower incidence of revisions in autologous reconstructions that underwent radiation compared with autologous reconstructions that have been performed as a delayed procedure after previous radiation exposure.

In contrast, although Berbers and colleagues³⁸ agreed that although there is more fibrosis in the postreconstruction radiotherapy group compared with the prereconstruction radiotherapy group, there was no statistical difference in revision surgery.

Aesthetic Outcome

A systematic review of the literature showed that most of the studies reported no significant difference in the aesthetic outcome between the IBR and delayed reconstruction group.⁹⁷ In another study by Crisera and colleagues,¹⁰⁸ the overall cosmetic score was not statistically different for patients not treated with irradiation from that who had received radiation preoperatively. The investigators noted some degree of shrinkage in 30% of patients, but only 10% required volume augmentation with implants. This figure is less than the 28% quoted in the literature.¹⁰⁹

Patient Satisfaction

Pusic and colleagues¹¹⁰ reported that patients who underwent autologous reconstruction were more satisfied with their breasts and had greater psychosocial and sexual well-being compared with those who had implant reconstructions at 1 year. Furthermore, Billig and colleagues¹¹¹ found that IBR and PMRT is safe and, from the patients' perspective, the breast aesthetics and quality of life were not compromised by flap exposure to radiotherapy. Berbers and colleagues³⁸ reported that patients' satisfaction is not affected regardless of whether they undergo IBR and PMRT or delayed reconstruction.

SUMMARY

In the context of PMRT, autologous breast reconstruction has lower complication rates compared with implant-based reconstruction. Despite this, implant-based reconstruction continues to be performed; but complications can be avoided with judicious timing and adjuncts, such as ADM and fat grafting.

REFERENCES

1. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. *CA Cancer J Clin* 2013;63(1):11–30.
2. Razdan SN, Cordeiro PG, Albornoz CR, et al. National breast reconstruction utilization in the setting of postmastectomy radiotherapy. *J Reconstr Microsurg* 2017;33(5):312–7.
3. Leff DR, Bottle A, Mayer E, et al. Trends in immediate postmastectomy breast reconstruction in the United Kingdom. *Plast Reconstr Surg Glob Open* 2015;3(9):e507.
4. Albornoz CR, Cordeiro PG, Pusic AL, et al. Diminishing relative contraindications for immediate breast reconstruction: a multicenter study. *J Am Coll Surg* 2014;219(4):788–95.
5. Frasier LL, Holden S, Holden T, et al. Temporal trends in postmastectomy radiation therapy and breast reconstruction associated with changes in National Comprehensive Cancer Network Guidelines. *JAMA Oncol* 2016;2(1):95–101.
6. Agarwal S, Kidwell KM, Farberg A, et al. Immediate reconstruction of the radiated breast: recent trends contrary to traditional standards. *Ann Surg Oncol* 2015;22(8):2551–9.
7. Lang JE, Summers DE, Cui H, et al. Trends in postmastectomy reconstruction: a SEER database analysis. *J Surg Oncol* 2013;108(3):163–8.
8. Iskandar ME, Dayan E, Lucido D, et al. Factors influencing incidence and type of postmastectomy breast reconstruction in an urban multidisciplinary cancer center. *Plast Reconstr Surg* 2015;135(2):270e–6e.
9. Weenk M, Wunschel P, Heine E, et al. Factors influencing the decision to pursue immediate breast reconstruction after mastectomy for breast cancer. *Gland Surg* 2017;6(1):43–8.
10. Gradishar WJ, Anderson BO, Balassanian R, et al. Invasive breast cancer version 1.2016, NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw* 2016;14(3):324–54.
11. Early and locally advanced breast cancer: diagnosis and treatment. Clinical guideline [CG80], National Institute for Health and Care Excellence, United Kingdom. 2009. Available at: <https://www.nice.org.uk/guidance/cg80>.
12. EBCTCG (Early Breast Cancer Trialists' Collaborative Group), McGale P, Taylor C, Correa C, et al. Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials. *Lancet* 2014;383(9935):2127–35.
13. Harris EER, Freilich J, Lin H-Y, et al. The impact of the size of nodal metastases on recurrence risk in breast cancer patients with 1–3 positive axillary nodes after mastectomy. *Int J Radiat Oncol Biol Phys* 2013;85(3):609–14.
14. Botteri E, Gentilini O, Rotmensz N, et al. Mastectomy without radiotherapy: outcome analysis after 10 years of follow-up in a single institution. *Breast Cancer Res Treat* 2012;134(3):1221–8.
15. Sharma R, Bedrosian I, Lucci A, et al. Present-day locoregional control in patients with t1 or t2 breast cancer with 0 and 1 to 3 positive lymph nodes after mastectomy without radiotherapy. *Ann Surg Oncol* 2010;17(11):2899–908.
16. Tendulkar RD, Rehman S, Shukla ME, et al. Impact of postmastectomy radiation on locoregional recurrence in breast cancer patients with 1–3 positive lymph nodes treated with modern systemic therapy. *Int J Radiat Oncol Biol Phys* 2012;83(5):e577–81.
17. McBride A, Allen P, Woodward W, et al. Locoregional recurrence risk for patients with T1, 2 breast cancer with 1–3 positive lymph nodes treated with mastectomy and systemic treatment. *Int J Radiat Oncol Biol Phys* 2014;89(2):392–8.
18. Lu C, Xu H, Chen X, et al. Irradiation after surgery for breast cancer patients with primary tumours and one to three positive axillary lymph nodes: yes or no? *Curr Oncol* 2013;20(6):e585–92.
19. Recht A, Comen EA, Fine RE, et al. Postmastectomy radiotherapy: an American Society of Clinical Oncology, American Society for Radiation Oncology, and Society of Surgical Oncology focused guideline update. *Ann Surg Oncol* 2017;24(1):38–51.
20. Whelan TJ, Olivetto IA, Parulekar WR, et al. Regional nodal irradiation in early-stage breast cancer. *N Engl J Med* 2015;373(4):307–16.
21. Poortmans PM, Collette S, Kirkove C, et al. Internal mammary and medial supraclavicular irradiation in breast cancer. *N Engl J Med* 2015;373(4):317–27.
22. Hennequin C, Bossard N, Servagi-Vernat S, et al. Ten-year survival results of a randomized trial of irradiation of internal mammary nodes after mastectomy. *Int J Radiat Oncol Biol Phys* 2013;86(5):860–6.
23. Thorsen LBJ, Offersen BV, Danø H, et al. DBCG-IMN: a population-based cohort study on the effect of internal mammary node irradiation in early node-positive breast cancer. *J Clin Oncol* 2016;34(4):314–20.
24. Haviland JS, Owen JR, Dewar JA, et al. The UK Standardisation of Breast Radiotherapy (START) trials of radiotherapy hypofractionation for treatment of early breast cancer: 10-year follow-up results of two randomised controlled trials. *Lancet Oncol* 2013;14(11):1086–94.
25. Kreienberg R, Kopp I, Albert U, et al. Interdisciplinary S3 guidelines for the diagnosis, treatment and follow-up care of breast cancer. 1st updated version 2008. 2nd edition. Germering/Munich: W. Zuckschwerdt Verlag, 2008.

26. McMillan TJ, Tobi S, Mateos S, et al. The use of DNA double-strand break quantification in radiotherapy. *Int J Radiat Oncol Biol Phys* 2001;49(2):373–7.
27. Gorgojo L, Little JB. Expression of lethal mutations in progeny of irradiated mammalian cells. *Int J Radiat Biol* 1989;55(4):619–30.
28. Lorimore SA, Coates PJ, Scobie GE, et al. Inflammatory-type responses after exposure to ionizing radiation in vivo: a mechanism for radiation-induced bystander effects? *Oncogene* 2001;20(48):7085–95.
29. Dickson J, Magee B, Stewart A, et al. Relationship between residual radiation-induced DNA double-strand breaks in cultured fibroblasts and late radiation reactions: a comparison of training and validation cohorts of breast cancer patients. *Radiother Oncol* 2002;62(3):321–6.
30. Herskind C, Johansen J, Bentzen SM, et al. Fibroblast differentiation in subcutaneous fibrosis after postmastectomy radiotherapy. *Acta Oncol* 2000;39(3):383–8.
31. Atisha D, Alderman AK, Lowery JC, et al. Prospective analysis of long-term psychosocial outcomes in breast reconstruction: two-year postoperative results from the Michigan Breast Reconstruction Outcomes Study. *Ann Surg* 2008;247(6):1019–28.
32. Chao L-F, Patel KM, Chen S-C, et al. Monitoring patient-centered outcomes through the progression of breast reconstruction: a multicentered prospective longitudinal evaluation. *Breast Cancer Res Treat* 2014;146(2):299–308.
33. Ciesla S, Polom K. The effect of immediate breast reconstruction with Becker-25 prosthesis on the preservation of proper body posture in patients after mastectomy. *Eur J Surg Oncol* 2010;36(7):625–31.
34. Gieni M, Avram R, Dickson L, et al. Local breast cancer recurrence after mastectomy and immediate breast reconstruction for invasive cancer: a meta-analysis. *Breast* 2012;21(3):230–6.
35. Huang C-J, Hou M-F, Lin S-D, et al. Comparison of local recurrence and distant metastases between breast cancer patients after postmastectomy radiotherapy with and without immediate TRAM flap reconstruction. *Plast Reconstr Surg* 2006;118(5):1079–86 [discussion: 1087–8].
36. Strålman K, Mollerup CL, Kristoffersen US, et al. Long-term outcome after mastectomy with immediate breast reconstruction. *Acta Oncol* 2008;47(4):704–8.
37. Razdan SN, Cordeiro PG, Albornoz CR, et al. Cost-effectiveness analysis of breast reconstruction options in the setting of postmastectomy radiotherapy using the BREAST-Q. *Plast Reconstr Surg* 2016;137(3):510e–7e.
38. Berbers J, van Baardwijk A, Houben R, et al. “Reconstruction: before or after postmastectomy radiotherapy?” A systematic review of the literature. *Eur J Cancer* 2014;50(16):2752–62.
39. Chetta MD, Aliu O, Zhong L, et al. Reconstruction of the irradiated breast: a National Claims-Based Assessment of Postoperative Morbidity. *Plast Reconstr Surg* 2017;139(4):783–92.
40. El-Sabawi B, Sosin M, Carey JN, et al. Breast reconstruction and adjuvant therapy: a systematic review of surgical outcomes. *J Surg Oncol* 2015;112(5):458–64.
41. Eriksson M, Anveden L, Celebioglu F, et al. Radiotherapy in implant-based immediate breast reconstruction: risk factors, surgical outcomes, and patient-reported outcome measures in a large Swedish multicenter cohort. *Breast Cancer Res Treat* 2013;142(3):591–601.
42. Sbitany H, Wang F, Peled AW, et al. Immediate implant-based breast reconstruction following total skin-sparing mastectomy: defining the risk of preoperative and postoperative radiation therapy for surgical outcomes. *Plast Reconstr Surg* 2014;134(3):396–404.
43. Momoh AO, Ahmed R, Kelley BP, et al. A systematic review of complications of implant-based breast reconstruction with preconstruction and postreconstruction radiotherapy. *Ann Surg Oncol* 2014;21(1):118–24.
44. Fowble B, Park C, Wang F, et al. Rates of reconstruction failure in patients undergoing immediate reconstruction with tissue expanders and/or implants and postmastectomy radiation therapy. *Int J Radiat Oncol Biol Phys* 2015;92(3):634–41.
45. Nava MB, Pennati AE, Lozza L, et al. Outcome of different timings of radiotherapy in implant-based breast reconstructions. *Plast Reconstr Surg* 2011;128(2):353–9.
46. Lam TC, Hsieh F, Boyages J. The effects of postmastectomy adjuvant radiotherapy on immediate two-stage prosthetic breast reconstruction: a systematic review. *Plast Reconstr Surg* 2013;132(3):511–8.
47. Cordeiro PG, Albornoz CR, McCormick B, et al. The impact of postmastectomy radiotherapy on two-stage implant breast reconstruction: an analysis of long-term surgical outcomes, aesthetic results, and satisfaction over 13 years. *Plast Reconstr Surg* 2014;134(4):588–95.
48. Cordeiro PG, Albornoz CR, McCormick B, et al. What is the optimum timing of postmastectomy radiotherapy in two-stage prosthetic reconstruction: radiation to the tissue expander or permanent implant? *Plast Reconstr Surg* 2015;135(6):1509–17.
49. Ho AL, Bovill ES, Macadam SA, et al. Postmastectomy radiation therapy after immediate two-stage tissue expander/implant breast reconstruction: a University of British Columbia perspective. *Plast Reconstr Surg* 2014;134(1):1e–10e.

50. Spear SL, Shuck J, Hannan L, et al. Evaluating long-term outcomes following nipple-sparing mastectomy and reconstruction in the irradiated breast. *Plast Reconstr Surg* 2014;133(5):605e–14e.
51. Salzberg CA, Ashikari AY, Berry C, et al. Acellular dermal matrix-assisted direct-to-implant breast reconstruction and capsular contracture: a 13-year experience. *Plast Reconstr Surg* 2016;138(2):329–37.
52. Siggelkow W, Faridi A, Spiritus K, et al. Histological analysis of silicone breast implant capsules and correlation with capsular contracture. *Biomaterials* 2003;24(6):1101–9.
53. Wolfram D, Rabensteiner E, Grundtman C, et al. T regulatory cells and TH17 cells in peri-silicone implant capsular fibrosis. *Plast Reconstr Surg* 2012;129(2):327e–37e.
54. Ribuffo D, Torto Lo F, Giannitelli SM, et al. The effect of post-mastectomy radiation therapy on breast implants: unveiling biomaterial alterations with potential implications on capsular contracture. *Mater Sci Eng C Mater Biol Appl* 2015;57:338–43.
55. Ho G, Nguyen TJ, Shahabi A, et al. A systematic review and meta-analysis of complications associated with acellular dermal matrix-assisted breast reconstruction. *Ann Plast Surg* 2012;68(4):346–56.
56. Vardanian AJ, Clayton JL, Roostaeian J, et al. Comparison of implant-based immediate breast reconstruction with and without acellular dermal matrix. *Plast Reconstr Surg* 2011;128(5):403e–10e.
57. Israeli R, Feingold RS. Acellular dermal matrix in breast reconstruction in the setting of radiotherapy. *Aesthet Surg J* 2011;31(7 Suppl):51S–64S.
58. Breuing KH, Warren SM. Immediate bilateral breast reconstruction with implants and inferolateral AlloDerm slings. *Ann Plast Surg* 2005;55(3):232–9.
59. Uzunismail A, Duman A, Perk C, et al. The effects of acellular dermal allograft (AlloDerm®) interface on silicone-related capsule formation—experimental study. *Eur J Plast Surg* 2008;31(4):179–85.
60. Stump A, Holton LH, Connor J, et al. The use of acellular dermal matrix to prevent capsule formation around implants in a primate model. *Plast Reconstr Surg* 2009;124(1):82–91.
61. Leong M, Basu CB, Hicks MJ. Further evidence that human acellular dermal matrix decreases inflammatory markers of capsule formation in implant-based breast reconstruction. *Aesthet Surg J* 2015;35(1):40–7.
62. Komorowska-Timek E, Oberg KC, Timek TA, et al. The effect of AlloDerm envelopes on periprosthetic capsule formation with and without radiation. *Plast Reconstr Surg* 2009;123(3):807–16.
63. Myckatyn TM, Cavallo JA, Sharma K, et al. The impact of chemotherapy and radiation therapy on the remodeling of acellular dermal matrices in staged, prosthetic breast reconstruction. *Plast Reconstr Surg* 2015;135(1):43e–57e.
64. Moyer HR, Pinell-White X, Losken A. The effect of radiation on acellular dermal matrix and capsule formation in breast reconstruction: clinical outcomes and histologic analysis. *Plast Reconstr Surg* 2014;133(2):214–21.
65. Nahabedian MY. Acellular dermal matrices in primary breast reconstruction: principles, concepts, and indications. *Plast Reconstr Surg* 2012;130(5 Suppl 2):44S–53S.
66. Pestana IA, Campbell DC, Bharti G, et al. Factors affecting complications in radiated breast reconstruction. *Ann Plast Surg* 2013;70(5):542–5.
67. Salzberg CA, Ashikari AY, Koch RM, et al. An 8-year experience of direct-to-implant immediate breast reconstruction using human acellular dermal matrix (AlloDerm). *Plast Reconstr Surg* 2011;127(2):514–24.
68. Colwell AS, Damjanovic B, Zahedi B, et al. Retrospective review of 331 consecutive immediate single-stage implant reconstructions with acellular dermal matrix: indications, complications, trends, and costs. *Plast Reconstr Surg* 2011;128(6):1170–8.
69. Rawlani V, Buck DW, Johnson SA, et al. Tissue expander breast reconstruction using prehydrated human acellular dermis. *Ann Plast Surg* 2011;66(6):593–7.
70. Lardi AM, Ho-Asjoe M, Mohanna P-N, et al. Immediate breast reconstruction with acellular dermal matrix: factors affecting outcome. *J Plast Reconstr Aesthet Surg* 2014;67(8):1098–105.
71. Spear SL, Seruya M, Rao SS, et al. Two-stage prosthetic breast reconstruction using AlloDerm including outcomes of different timings of radiotherapy. *Plast Reconstr Surg* 2012;130(1):1–9.
72. Spear SL, Schwartz J, Dayan JH, et al. Outcome assessment of breast distortion following submuscular breast augmentation. *Aesthetic Plast Surg* 2009;33(1):44–8.
73. Sigalove S, Maxwell GP, Sigalove NM, et al. Prepectoral implant-based breast reconstruction: rationale, indications, and preliminary results. *Plast Reconstr Surg* 2017;139(2):287–94.
74. Bernini M, Calabrese C, Cecconi L, et al. Subcutaneous direct-to-implant breast reconstruction: surgical, functional, and aesthetic results after long-term follow-up. *Plast Reconstr Surg Glob Open* 2015;3(12):e574.
75. Becker H, Lind JG, Hopkins EG. Immediate implant-based prepectoral breast reconstruction using a vertical incision. *Plast Reconstr Surg Glob Open* 2015;3(6):e412.
76. Salgarello M, Visconti G, Barone-Adesi L. Fat grafting and breast reconstruction with implant: another

- option for irradiated breast cancer patients. *Plast Reconstr Surg* 2012;129(2):317–29.
77. Ribuffo D, Atzeni M, Guerra M, et al. Treatment of irradiated expanders: protective lipofilling allows immediate prosthetic breast reconstruction in the setting of postoperative radiotherapy. *Aesthetic Plast Surg* 2013;37(6):1146–52.
 78. Serra-Renom JM, Muñoz-Olmo JL, Serra-Mestre JM. Fat grafting in postmastectomy breast reconstruction with expanders and prostheses in patients who have received radiotherapy: formation of new subcutaneous tissue. *Plast Reconstr Surg* 2010;125(1):12–8.
 79. Petit JY, Maisonneuve P, Rotmensz N, et al. Safety of lipofilling in patients with breast cancer. *Clin Plast Surg* 2015;42(3):339–44, viii.
 80. Kronowitz SJ, Mandujano CC, Liu J, et al. Lipofilling of the breast does not increase the risk of recurrence of breast cancer: a matched controlled study. *Plast Reconstr Surg* 2016;137(2):385–93.
 81. Wazir U, El Hage Chehade H, Headon H, et al. Oncological safety of lipofilling in patients with breast cancer: a meta-analysis and update on clinical practice. *Anticancer Res* 2016;36(9):4521–8.
 82. Silva-Vergara C, Fontdevila J, Descarrega J, et al. Oncological outcomes of lipofilling breast reconstruction: 195 consecutive cases and literature review. *J Plast Reconstr Aesthet Surg* 2016;69(4):475–81.
 83. Reish RG, Lin A, Phillips NA, et al. Breast reconstruction outcomes after nipple-sparing mastectomy and radiation therapy. *Plast Reconstr Surg* 2015;135(4):959–66.
 84. Caviggioli F, Maione L, Klinger F, et al. Autologous fat grafting reduces pain in irradiated breast: a review of our experience. *Stem Cells Int* 2016;2016:2527349.
 85. Choi M, Small K, Levovitz C, et al. The volumetric analysis of fat graft survival in breast reconstruction. *Plast Reconstr Surg* 2013;131(2):185–91.
 86. Khouri RK, Rigotti G, Cardoso E, et al. Tissue-engineered breast reconstruction with Brava-assisted fat grafting: a 7-year, 488-patient, multicenter experience. *Plast Reconstr Surg* 2015;135(3):643–58.
 87. Khouri RK, Smit JM, Cardoso E, et al. Percutaneous aponeurotomy and lipofilling: a regenerative alternative to flap reconstruction? *Plast Reconstr Surg* 2013;132(5):1280–90.
 88. Reish RG, Damjanovic B, Austen WG, et al. Infection following implant-based reconstruction in 1952 consecutive breast reconstructions: salvage rates and predictors of success. *Plast Reconstr Surg* 2013;131(6):1223–30.
 89. Kearney AM, Brown MS, Soltanian HT. Timing of radiation and outcomes in implant-based breast reconstruction. *J Plast Reconstr Aesthet Surg* 2015;68(12):1719–26.
 90. Wang F, Chin R, Piper M, et al. Do prolonged prophylactic antibiotics reduce the incidence of surgical-site infections in immediate prosthetic breast reconstruction? *Plast Reconstr Surg* 2016;138(6):1141–9.
 91. Townley WA, Baluch N, Bagher S, et al. A single pre-operative antibiotic dose is as effective as continued antibiotic prophylaxis in implant-based breast reconstruction: a matched cohort study. *J Plast Reconstr Aesthet Surg* 2015;68(5):673–8.
 92. Sinha I, Pusic AL, Wilkins EG, et al. Late surgical-site infection in immediate implant-based breast reconstruction. *Plast Reconstr Surg* 2017;139(1):20–8.
 93. Albornoz CR, Bach PB, Mehrara BJ, et al. A paradigm shift in U.S. breast reconstruction: increasing implant rates. *Plast Reconstr Surg* 2013;131(1):15–23.
 94. Brennan ME, Flitcroft K, Warriar S, et al. Immediate expander/implant breast reconstruction followed by post-mastectomy radiotherapy for breast cancer: aesthetic, surgical, satisfaction and quality of life outcomes in women with high-risk breast cancer. *Breast* 2016;30:59–65.
 95. Grover R, Padula WV, Van Vliet M, et al. Comparing five alternative methods of breast reconstruction surgery: a cost-effectiveness analysis. *Plast Reconstr Surg* 2013;132(5):709e–23e.
 96. Krishnan NM, Fischer JP, Basta MN, et al. Is single-stage prosthetic reconstruction cost effective? A cost-utility analysis for the use of direct-to-implant breast reconstruction relative to expander-implant reconstruction in postmastectomy patients. *Plast Reconstr Surg* 2016;138(3):537–47.
 97. Schaverien MV, Macmillan RD, McCulley SJ. Is immediate autologous breast reconstruction with postoperative radiotherapy good practice?: a systematic review of the literature. *J Plast Reconstr Aesthet Surg* 2013;66(12):1637–51.
 98. Chang EI, Liu TS, Festekjian JH, et al. Effects of radiation therapy for breast cancer based on type of free flap reconstruction. *Plast Reconstr Surg* 2013;131(1):1e–8e.
 99. Kelley BP, Ahmed R, Kidwell KM, et al. A systematic review of morbidity associated with autologous breast reconstruction before and after exposure to radiotherapy: are current practices ideal? *Ann Surg Oncol* 2014;21(5):1732–8.
 100. Fracol ME, Basta MN, Nelson JA, et al. Bilateral free flap breast reconstruction after unilateral radiation: comparing intraoperative vascular complications and postoperative outcomes in radiated versus nonradiated breasts. *Ann Plast Surg* 2016;76(3):311–4.
 101. Fosnot J, Fischer JP, Smartt JM, et al. Does previous chest wall irradiation increase vascular

- complications in free autologous breast reconstruction? *Plast Reconstr Surg* 2011;127(2):496–504.
102. Khansa I, Momoh AO, Patel PP, et al. Fat necrosis in autologous abdomen-based breast reconstruction: a systematic review. *Plast Reconstr Surg* 2013;131(3):443–52.
103. Clarke-Pearson EM, Chadha M, Dayan E, et al. Comparison of irradiated versus nonirradiated DIEP flaps in patients undergoing immediate bilateral DIEP reconstruction with unilateral postmastectomy radiation therapy (PMRT). *Ann Plast Surg* 2013;71(3):250–4.
104. Taghizadeh R, Moustaki M, Harris S, et al. Does post-mastectomy radiotherapy affect the outcome and prevalence of complications in immediate DIEP breast reconstruction? A prospective cohort study. *J Plast Reconstr Aesthet Surg* 2015;68(10):1379–85.
105. Sacotte R, Fine N, Kim JY, et al. Assessing long-term complications in patients undergoing immediate postmastectomy breast reconstruction and adjuvant radiation. *Pract Radiat Oncol* 2017;7(2):e91–7.
106. Mull AB, Qureshi AA, Zubovic E, et al. Impact of time interval between radiation and free autologous breast reconstruction. *J Reconstr Microsurg* 2017;33(2):130–6.
107. de Araujo TB, Jue Xu M, Susarla SM, et al. Impact of prior unilateral chest wall radiotherapy on outcomes in bilateral breast reconstruction. *Plast Reconstr Surg* 2016;138(4):575e–80e.
108. Crisera CA, Chang EI, Da Lio AL, et al. Immediate free flap reconstruction for advanced-stage breast cancer: is it safe? *Plast Reconstr Surg* 2011;128(1):32–41.
109. Tran NV, Chang DW, Gupta A, et al. Comparison of immediate and delayed free TRAM flap breast reconstruction in patients receiving postmastectomy radiation therapy. *Plast Reconstr Surg* 2001;108(1):78–82.
110. Pusic AL, Matros E, Fine N, et al. Patient-reported outcomes 1 year after immediate breast reconstruction: results of the mastectomy reconstruction outcomes consortium study. *J Clin Oncol* 2017;35(22):2499–506.
111. Billig J, Jagsi R, Qi J, et al. Should immediate autologous breast reconstruction be considered in women who require post-mastectomy radiation therapy? A prospective analysis of outcomes. *Plast Reconstr Surg* 2017;139(6):1279–88.