Review

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Breast Reconstruction and Radiation Therapy

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Abstract

Purpose: The optimal approach to the integration of postmastectomy reconstruction and radiation therapy is not well-established. This review will summarize current literature pertaining to the most common types of reconstruction in the setting of postmastectomy radiation therapy (PMRT).

Data Sources: Literature from PubMed was reviewed from 2000 to 2016.

Study Selection: Studies were selected with relevance to "postmastectomy breast reconstruction," "breast reconstruction," and "breast reconstructive methods and PMRT." Surgical outcomes, patient satisfaction, and cost-effectiveness were examined.

Data Extraction: Data from publications was extracted, summarized, and converted to a table.

Results of Data Synthesis: Implant-based techniques are on the rise, in the setting of PMRT. Implant-based methods are more affordable in the short term and result in immediate breast-mound formation compared to autologous methods. When compared to implant-based reconstruction with PMRT, autologous reconstruction with PMRT results in better quality of life (QoL) and sensory recovery as well as fewer complications and failures. Among autologous flaps, deep inferior epigastric perforator flaps are considered superior to transverse rectus abdominal muscle (TRAM) pedicled flaps and may be more suitable for PMRT. Latissimus dorsi and muscle-sparing free TRAM flaps are also viable options. In delayed autologous, which may be advantageous for high-risk patients, the optimal timing to delay surgery after radiation therapy is unknown. Reconstruction with a 2-stage tissue expander-implant technique offers good to excellent cosmetic outcomes in the setting of PMRT, although there may be complications in this 2-stage process.

Conclusion: Surgical, cosmetic, quality of life, and life expectancy must be taken into account when selecting the way to integrate breast reconstruction and PMRT.

Keywords
breast reconstruction, implant reconstruction, autologous reconstruction, PMRT, quality of life

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Background

Vincent Czerny is credited with the first autologous breast reconstruction in 1895, which at the time consisted of transplantation of a lipoma from the patient's flank to the breast in order to fill a defect after excision of a fibroadenoma.[1,2] Since then, multiple methods of reconstruction, whether autologous or implant-based, have been introduced in order to rebuild the breast following its partial or complete removal. Autologous reconstruction typically involves tissue from the abdomen or back. Abdominal tissue–based reconstruction is most

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commonly accomplished with the pedicled transverse rectus abdominal muscle (TRAM) flap, the free TRAM flap, or the deep inferior epigastric perforator (DIEP) flap. When using tissues from the back, the latissimus dorsi (with or without an implant) is used when reconstructing the breast.[3]

Alternative to autologous reconstruction, prosthetic, or implant-based reconstruction involves silicone gel or saline inserts. If delayed reconstruction is required—as may be the preference when radiation is involved in the treatment of breast cancer—a 2-stage implantation can be performed. In this scenario, a fully inflated tissue expander is in place during radiation and later exchanged for a permanent implant (expander implant [EI] reconstruction). The timing and method of reconstruction can inform outcomes in terms of complications, cosmesis, patient satisfaction, and quality of life. This review will examine the current breast reconstruction literature to aid physicians and patients in their decision-making process in the setting of postmastectomy radiation therapy (PMRT). According to the Guidelines for Invasive Breast Cancer from the National Comprehensive Cancer Network, PMRT should be performed in cases of 4 or more positive lymph nodes and strongly considered in cases of 1 to 3 positive lymph nodes, positive margins or margins closer than 1 mm, or tumor > 5 cm in size. Currently, there is no level 1 evidence for indicating an optimal strategy for combining breast reconstruction and radiation therapy. It must be noted that the outcome of the methods of reconstruction may be biased due to different indications and restrictions and that this continues to be an ongoing and controversial discussion.

Methods

Literature from PubMed was reviewed from 2000 to 2016. A PubMed search was conducted using the terms "postmastectomy breast reconstruction," "breast reconstruction," and "breast reconstructive methods and PMRT." Studies reporting surgical outcomes, patient satisfaction, and cost-effectiveness published from 2000 to 2016 were included. Data were collected, organized, and summarized. The results are abridged in Table 1.

Results

Postmastectomy Radiation Therapy With Autologous Versus Prosthetic Methods

When integrating postmastectomy reconstruction and radiation therapy, timing and method are considerations. Historically, high-risk patients—a population which includes those who have received or require radiation therapy—were discouraged from both immediate reconstruction and implant-based reconstructive procedures. However, recent data indicate that immediate implant-based reconstruction in the setting of PMRT is on the rise. According to Surveillance, Epidemiology, and End Results data from 2000 to 2010, including 5481 patients who underwent immediate reconstruction and required PMRT, the percentage of immediate implant-only procedures increased from 27% to 52%, and the percentage of immediate autologous reconstruction decreased from 56% to 32%. The regression analysis showed that the odds of immediate implant-based reconstruction over immediate autologous reconstruction increased each year by an odds ratio of 1.13 (95% confidence interval: 1.10-1.15).[4] A longitudinal study by Albornoz et al on 10,299 patients between 2001 and 2012 revealed that implant-based reconstruction within high-risk patients increased from 45 to 70.7 of 100 mastectomies ($P < .01$). The features defining high risk in this study included age more than 60 years old, body mass index ≥ 30, comorbidities based on Charlson scores[5] ≥ 1, smoking, stage 3 or 4 disease at time of mastectomy, and prior or PMRT. In high-risk patients, the rate of success, defined as tissue expander exchange to a permanent implant, or autologous procedures without vascular complications, was 88% for prosthetic and 95.5% for autologous reconstruction.[6] These findings reflect changing practice patterns in reconstruction in the setting of planned PMRT.

In a cost-effectiveness analysis model using payer perspective, using the BREAST -Q patient-reported outcome measure, delayed autologous and immediate implant techniques were compared against no reconstruction in patients requiring PMRT. A breast quality-adjusted life year value was considered 1 year or perfect breast health-related quality of life. The incremental cost-effectiveness ratios for immediate implant-based versus delayed autologous reconstruction was $57,906 and $102,509, respectively, with decreasing ratios with increasing life expectancy. It was concluded that despite slightly higher complication rates, for patients with advanced breast cancer who require PMRT, implant-based reconstruction use can be rationalized due to the low cost and health-related quality-of-life benefit due to early breast-mound restoration.[7] However, in a patient with greater life expectancy, autologous reconstruction costs are comparable to that of implant-based reconstruction and may be a superior option depending on patient risk factors.[7,8]

Various studies have attempted to assess the impact of PMRT on surgical outcomes following breast reconstruction. Postmastectomy radiation therapy, regardless of reconstructive method, has been found to have a detrimental effect on outcome with increased postoperative complications.[9] According to a systematic review of patients treated with PMRT with or without adjuvant chemotherapy from 2000 to 2015, there was a significantly higher weighted incidence of reoperation (37.0% vs 16.6%, $P < .0001$), total complications (41.3% vs 30.9%, $P < .0001$), and reconstructive failure (16.8% vs 1.6%, $P < .0001$) in implant-based reconstruction when compared to autologous.[10] Moreover, according to a retrospective meta-analysis of breast reconstruction and radiotherapy, results suggest that an autologous flap results in less morbidity when compared to implant-based reconstructions.[9] One single institution study comparing immediate latissimus dorsi flap versus tissue EI reconstruction after mastectomy followed by PMRT found a trend toward more wound complications requiring reoperation in the EI group, concluding that immediate reconstruction with

Table 1. Advantages and Disadvantages of Common Reconstruction Methods.

Procedure	Immediate Autologous	Delayed Autologous	Immediate Implant	Expander Implant
Advantages	Immediate breast mound in place More cost-effective in long-term Generally, safe with fewer complications and reconstructive failures than implant-based, in the setting of PMRT Results in less morbidity than implant-based reconstruction Higher QoL scores than Expander-implant Better cosmetic results compared to implant methods with PMRT Better skin sensation recovery after PMRT Single procedure	Allows more time for uncomfortable patients or high-risk patients who may be advised to wait for reconstruction More cost-effective in long-term Possibly better results if performed $\leq$12 months from the date of PMRT Same surgical, cosmetic, and QoL advantages as immediate autologous Less wound contracture, volume loss, fat necrosis, and revision surgeries compared to immediate autologous	Immediate breast mound in place Most cost-effective in the short-term Best aesthetic outcome if radiotherapy is not involved Single procedure	Good to excellent aesthetic results when PMRT is required Allows more time for patients to choose between an implant replacement or autologous reconstruction Ability to revise any asymmetries or radiation effects at time of TE removal
Disadvantages	Initially, more expensive Scarring across donor site Lack of final pathology report at time of surgery Complications: PMRT can result in wound contracture, volume loss, and fat necrosis (especially with chemotherapy)	Initially, more expensive Timing between PMRT and reconstruction is inconclusive Delayed cosmetic results Two procedures Complications: PMRT can result in wound contracture, volume loss, and fat necrosis	Relatively higher risk of complications compared to autologous Lack of final pathology report at time of surgery Complications: Capsular contracture is most common with PMRT Other complications include infection, implant exposure, and would breakdown Lymph node dissection associated with increased risk of implant loss	Relatively higher risk of complications compared to autologous and immediate implant Tissue Expander complications more likely to occur in smokers and those with radiation therapy Two procedures Complications: Infection, skin breakdown, capsular contracture, and implant loss possible with PMRT Long-term expander use is associated with rupture Lymph node dissection associated with increased risk of implant loss

Abbreviations: PMRT, postmastectomy radiation therapy; TE, tissue expander

a latissimus dorsi flap is a viable option for patients undergoing PMRT.[11] In the subset of patients who have received premastectomy whole breast radiation therapy, studies show a significant increase in the risk of complications associated with the use of expander implant-based reconstruction, and it is recommended that these patients strongly consider autologous reconstruction.[12,13]

Patient satisfaction in terms of cosmesis is an important consideration. When looking at both autologous and implant-based reconstruction with or without PMRT, PMRT decreases patient satisfaction in both methods.[14] In a pilot study on return of sensation to breast tissue, implants provided better static and moving sensation than did DIEP flaps. In the setting of PMRT, however, DIEP flap skin had better sensation recovery than did skin over implants.[15] In another survey of women undergoing reconstruction after mastectomy, adjusted satisfaction scores were 4.7 of 5 in those undergoing autologous reconstruction without radiation, 4.4 in those undergoing autologous

reconstruction with radiation, 4.1 in those undergoing EI reconstruction without radiation, and 2.8 in those undergoing EI reconstruction with radiation. It was concluded that the use of autologous reconstruction may mitigate the deleterious impact of PMRT on cosmetic outcomes.[16]

Immediate Autologous Reconstruction

There are mixed recommendations with regard to immediate autologous reconstruction when PMRT is required.[17] Concerns about wound healing, skin integrity, fat necrosis, and tissue vascularity all impact treatment sequencing decisions, and practice standards can vary between institutions. Moreover, adjuvant chemotherapy has been reported as an independent predictor of fat necrosis following PMRT of free abdominal flap reconstruction, although the effect of the timing of the chemotherapy is unknown.[17-19] Some series, one of which includes 183 immediate free TRAM flap reconstruction procedures followed by PMRT, report that PMRT after immediate reconstruction is safe, not associated with delays in adjuvant therapy, and well tolerated with comparable cosmetic outcome to those not requiring PMRT.[20] In a meta-analysis of observational studies, there were no significant differences in complication rates or need for revision surgery when comparing immediate autologous breast reconstruction with and without postoperative radiotherapy.[21]

Deep inferior epigastric perforator flaps may be optimal for patients who are undergoing PMRT following reconstruction. The DIEP flap procedure consists of the transfer of abdominal skin and fat to the mastectomy area, with dissected deep inferior epigastric arteries to supply the reconstructed breast. A study including 670 DIEP, 293 muscle-sparing free TRAM, 683 pedicled TRAM, and 144 free TRAM flap cases with an average follow-up of 5.5 years demonstrated that complete flap loss did not differ by flap type. However, partial flap loss was higher in the pedicled TRAM compared to DIEP (8.9% vs 4%, $P = .002$). Fat necrosis was higher in the pedicled TRAM compared to DIEP and muscle-sparing free TRAM flaps (25.3% vs 16.3% vs 15%, $P < .001$), and hernias were highest in the pedicled TRAM compared to DIEP and muscle-sparing TRAM flaps (6.7% vs 1.9% vs 4.8%, $P < .001$). Physical well-being scores favored the DIEP flap compared to the pedicled TRAM (scores: 83.5 vs 76.2, $P < .001$).[22] While this study did not examine the role of radiation, the DIEP flap may be a preferred option in the setting of radiation, as it seems more resilient. This is evidenced by a study of 125 patients undergoing immediate bilateral DIEP flaps with unilateral PMRT, which revealed no incidence of clinically significant fat necrosis in either the irradiated or the nonirradiated DIEP flaps. Aesthetic outcomes were satisfactory among all patients.[23] Another group examined 156 immediate DIEP flaps and found no difference in terms of fat necrosis, surgery for removal of fat necrosis, volume enhancement surgery, wound healing delay, or flap lost when comparing the irradiated versus nonirradiated flaps.[24] One institution postulated that irradiated muscle sparing free TRAM flaps would experience less fat necrosis than irradiated DIEP flaps and therefore examined all immediate reconstruction with muscle sparing free TRAM and DIEP flaps over a 10-year period. They found that while irradiated flaps developed fat necrosis at a higher rate than nonirradiated flaps (22.5% vs 9.2%, $P = .009$), there was no difference in fat necrosis between the DIEP and muscle sparing free TRAM flaps.[18] Another review of 446 flaps (2 most common being the free TRAM and DIEP) found no significant differences in terms of early or late complications among different types of irradiated flaps. However, there was a lower incidence of ipsilateral revisions required in those with postoperative radiation exposure, suggesting immediate reconstruction is well-tolerated.[25]

Delayed Autologous Reconstruction

In a comparison between immediate and delayed autologous reconstruction, most studies show less complications, including wound contracture, volume loss, fat necrosis, and revision surgeries, for delayed autologous reconstruction.[26-28] Evidence suggests that patients having breast reconstruction before PMRT have a higher risk of late complications. Patients with PMRT preceding breast reconstruction may be at a slightly increased risk of early postoperative complications, although they may be mitigated with appropriate time after healing from radiation therapy.[10,26,27]

When undergoing delayed reconstruction after PMRT, the optimal time from PMRT to reconstruction is unknown. Intraoperative vascular complications and postoperative wound infections have been shown to be significantly more likely to occur in the setting of autologous free flap reconstruction after PMRT, and it is felt that the timing of reconstruction may play a role.[29] A study by Baumann et al demonstrated that patients who underwent reconstruction at a minimum of 12 months from completion of PMRT developed fewer complications, including microvascular thrombosis and total flap loss, than those who underwent delayed reconstruction within 12 months of completing therapy.[30] However, other studies reveal that patients who undergo autologous reconstruction within versus after 12 months following PMRT have no significant differences in complications.[31,32] Due to paucity of data, the optimal time from PMRT remains uncertain.

Immediate Implant-Based Reconstruction

Immediate permanent implant-based reconstruction offers the advantage of having a breast within a day. Some patients will undergo radiation therapy after immediate permanent implant-based reconstruction. A study of 144 implants reported that radiation therapy does not seem to cause a significant effect on breast implants in terms of complication rate.[33] However, in a systematic review of complications in breast reconstruction with implants, radiation therapy was associated with higher rates complications relative to the absence of radiation.[34] In a retrospective review of 132 patients undergoing implant reconstructions and PMRT, there was a complication rate of 15%,

which included infections, implant exposure, and hematomas. The most common complication was capsular contracture.[35] When comparing immediate and 2-stage expander-implant approaches, immediate implant reconstructions with PMRT had a significantly higher need for revision and lower aesthetic outcome score than the 2-stage implant reconstructions, with placement of the implant after PMRT.[36] In the setting of PMRT, implant-based reconstruction continues to be associated with a higher incidence of major corrective surgery than autologous tissue-based reconstruction.[36]

Delayed Expander Implant Reconstruction

Some patients undergo delayed/2-stage implant-based reconstruction in the setting of PMRT. In this scenario, a tissue expander is placed at the time of mastectomy and inflated fully before delivering radiation therapy. One disadvantage of a tissue expander is its ability to rupture. In a small study of 25 cases, 5 tissue expanders ruptured at 1.5 years after initial insertion. At 3 years postinsertion, the rupture rate was 32.6% and at 5 years it was 55.1%.[37] Thus, long-term use of a tissue expander may be associated with rupture. It is recommended that permanent implantation occurs within approximately 1 year of the first stage of EI-based reconstruction.[37] The sequencing of EI exchange in the setting of PMRT does not seem to affect the overall complication or reconstruction failure rate. However, the timing of the exchange after PMRT may affect the presence or type of complication that occurs.[38] Some reports reveal that delayed/2-stage, implant-based reconstruction in patients receiving radiation therapy and adjuvant chemotherapy result in fewer complications than immediate replacement of the expander.[39] In a study on the timing of implant exchange with TE and PMRT, it was found that performing implant exchange earlier after PMRT (<4 months) resulted in a higher rate of infections, whereas later exchange (>4 months) resulted in a higher rate of capsular contracture, although not statistically significant.[38]

In one of the largest (2133 implants) prospective long-term outcome studies in women undergoing immediate EI reconstruction with PMRT, there was increased implant loss (9.1% vs 0.5%, $P < .01$) and capsular contracture (6.9 vs 0.5%, $P < .01$) in the group receiving PMRT versus no PMRT.[40] According to a meta-analysis by Lee et al, prosthetic reconstruction in previously irradiated breasts significantly increased risk of reconstruction failure compared to cases without radiation.[13]

In retrospective series of 94 patients with mastectomy, TE/implant reconstruction failure was 20% with the majority of patients with good cosmesis. The most common cause of failure was infection (37%), followed sequentially by skin breakdown (21%), extrusion of expander or implant (16%), fibrosis/eschar (10.5%), trauma (10.5%), and pain (5%).[41] When comparing immediate implant and tissue exchange/implant methods, there may be an increased risk of developing complications in those who receive PMRT with exchange/implant versus permanent implant. In a systematic review and pooled analysis, PMRT to permanent implants reduced the rate of reconstructive failure compared to TE (18.8% vs 14.7%, $P < .01$).[10]

Complications surrounding the use of a tissue expander may inform later complications with the permanent implant. According to a retrospective review of tissue expander-based breast reconstructions performed from 2007 to 2011, it was found that of 196 patients, those with tissue expander complications were 3 times more likely to have a complication after placement of a permanent implant and 9 times more likely to fail permanent implant reconstruction. It has been suggested that autologous reconstruction be considered in patients with tissue expander complications, as opposed to an implant exchange, particularly in patients who are smokers and those undergoing radiation therapy. Both tobacco use and radiation therapy have been found to be statistically significantly associated with sustaining complications after both phases of reconstruction.[42] Special consideration and care must be taken for these patients.

Conclusions

With growing evidence supporting the benefits of PMRT, the optimal integration of postmastectomy reconstruction with PMRT is of utmost importance. The risks and benefits of immediate versus delayed as well as autologous versus implant-based reconstruction must be considered for each individual patient. There is no level 1 evidence indicating an optimal strategy, and this complex decision process involves consideration of quality of life, surgical outcomes, history of radiation therapy, cosmetic outcomes, and life expectancy.

Authors' Note

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Declaration of Conflicting Interests

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