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Breast Reconstruction and Post Mastectomy Radiotherapy: A Primer for Members of a Multidisciplinary Team

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ABSTRACT

Background: Post-mastectomy radiation therapy (PMRT) is a key component in managing breast cancer with increased potential for locoregional recurrence. Breast reconstruction has evolved to include various techniques that can be categorized according to the type of reconstruction (implant-based versus autologous reconstruction), and the timing of reconstruction (one versus two-step techniques).

Methods/Results: This review article aims to provide a digestible summary of PMRT in the context of breast reconstruction by summarizing salient existing literature with a focus on considerations of the plastic surgeon. The main findings summarized in this review include the technique and timing of breast reconstruction, how breast reconstruction can affect radiation delivery, and the type of reconstruction. Within implant-based reconstruction, existing data on the location of the implant in the context of PMRT and PMRT delivery to the tissue expander versus permanent implant are reviewed. Each consideration may alter the probability of successful reconstruction and patient satisfaction.

Conclusion: It is essential for the multidisciplinary breast cancer team to have knowledge of the various reconstructive options, and to understand the safety and comparative effectiveness of staged reconstruction in the setting of PMRT. Additionally, one must consider that reconstructive procedures may have implications on the timely administration of PMRT. This review serves as a reference for members of the oncologic care team when discussing reconstructive options with patients who will receive PMRT as part of their treatment plan.

Introduction

Post-mastectomy radiation therapy (PMRT) is a key component in treating breast cancer patients at high risk for locoregional recurrence. As more patients undergoing mastectomy desire reconstruction, PMRT becomes an increasingly important consideration when deciding the type and timing of reconstruction. PMRT may cause multiple adverse effects that may influence patient satisfaction; therefore, careful

consideration must be given to the interplay between these two factors.

Breast reconstruction has become increasingly popular after the Women's Health and Cancer Rights Act of 1998 which mandated that insurance providers cover all post-mastectomy reconstructive and symmetrizing procedures. Breast reconstruction enhances aesthetic outcomes after mastectomy and has been consistently shown to improve patient quality of life and decrease psychosocial harms after mastectomy.¹ As different reconstructive techniques emerge, it is necessary for the entire oncologic team to understand the role of reconstructive surgery within the context of concurrent oncologic treatment.

When caring for reconstructive patients receiving PMRT, it is important to acknowledge that there is no well-defined, evidence-based algorithm for choosing the

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appropriate reconstructive plan. Often, these decisions are made based on surgeon preference and institutional bias. The interactions between PMRT and breast reconstruction play a crucial role in complication profiles and patient satisfaction. Therefore, it is critical for the entire oncologic team to have a thorough understanding of breast reconstruction in order to assist the patient in making individualized decisions regarding the optimal cancer and reconstructive care.

Methods

Search strategy

We performed a literature review utilizing PubMed to find articles about breast reconstruction utilizing either autologous or implant-based reconstruction. The articles selected for this review included retrospective chart reviews, descriptive studies, case reports, and cohort studies. Our timeframe included studies published between 2000-2020. We specifically focused on finding papers that analyzed timing of breast reconstruction after PMRT, impact of PMRT on implants, whether implant location affects PMRT, and the effects of PMRT on autologous reconstruction. We chose to include studies that we felt best addressed the most important considerations faced by plastic surgeons when approaching reconstruction after PMRT. Each of these considerations regarding breast reconstruction after PMRT was then summarized and reported in its own subsection in the 'results' section.

Results

Breast Reconstruction Techniques

Breast reconstruction can be performed with various techniques such as using the patient's own tissue to reconstruct the breast (autologous reconstruction), or with prosthetic implants. These procedures can be performed as single or two-stage reconstruction. In the two-stage reconstruction technique, a temporary tissue expander is initially placed at the time of mastectomy, and later replaced with a permanent implant or autologous tissue flap. Choosing the appropriate reconstructive technique and its timing are crucial considerations when evaluating a patient for breast reconstruction.

The Michigan Breast Reconstruction Outcomes Study demonstrated that patients undergoing reconstruction of any type, even without radiation, had a notable risk of 31.6% of a major complication such as hospitalization and/or reoperation within two years of surgery. Furthermore, this study demonstrated a higher rate of overall complications when reconstruction was performed in conjunction with PMRT.²

Patient Factors to Consider During Pre-Operative Planning

Need for PMRT is just one of the many considerations that play a role in selecting the appropriate type and timing of breast reconstruction.

This is a complex, collaborative discussion that must be made among the patient, plastic surgeon, and oncologists (radiation, medical, and surgical). Patient goals of reconstruction, prior abdominal wall/breast surgical history, anatomy including adequate donor/recipient vessels, and comorbidities (including tobacco use) are additional key patient factors to consider during the pre-operative planning period. Comorbidities that affect a patient's cardiac, pulmonary, and/or renal systems and physiologic ability to tolerate a longer, more complex autologous procedure are also important to recognize. All of these consideration and patient-specific factors should be discussed on an individualized basis to optimize reconstructive outcomes.

Breast Reconstruction Timing

Breast reconstruction can be performed at the time of mastectomy (immediate reconstruction), after mastectomy (delayed reconstruction), or with immediate placement of a tissue expander followed by definitive reconstruction at a later date (delayed-immediate reconstruction) (Table 1). Compared to delayed reconstruction, immediate breast reconstruction is associated with improved aesthetic results, enhanced ability to utilize the native mastectomy tissue envelope, and decreased overall cost.³ By reducing the number of required surgeries, the patient not only benefits from cost savings but also from the immediate psychological benefits associated with reconstruction which may decrease the number of patients resistant to undergo total mastectomy. Large, multicenter prospective studies have found no significant difference in patient reported outcomes in immediate versus delayed breast reconstruction at two-year follow up.^{3,4}

Over 70% of breast reconstructions in the USA are performed at the time of mastectomy in the immediate or delayed-immediate fashion.⁵ Despite this trend, there is a growing volume of literature that advocates for delayed reconstruction in certain patient groups receiving PMRT, as it is associated with fewer post-operative complications.⁶⁻¹² The Mastectomy Reconstruction Outcomes Consortium (MROC) compared immediate to delayed reconstruction and found that immediate or delayed-immediate reconstruction resulted in significantly higher failure rates compared to delayed reconstruction (6% vs. 1.3%). Furthermore, there were no significant differences in patient-reported outcomes between immediate and delayed reconstruction cohorts.⁶

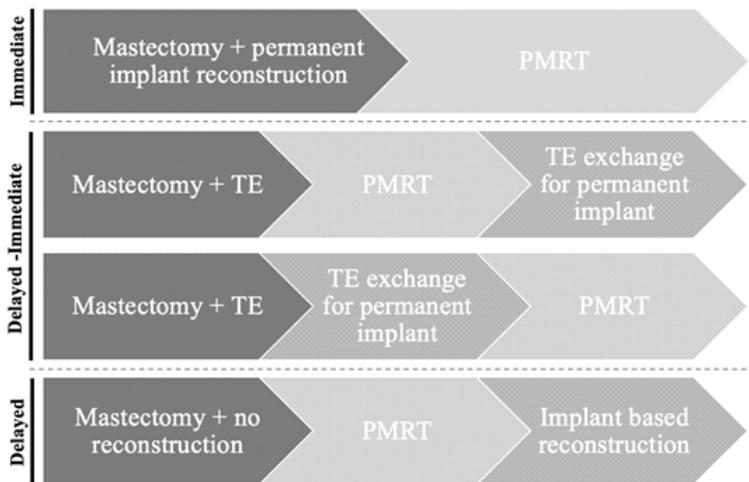
As the controversy surrounding reconstructive timing deepens, high quality evidence remains limited. Currently there are no randomized trials evaluating the impact of PMRT on reconstruction timing, complications, or cosmetic outcomes. Additionally, potential selection bias may exist as patients and/or surgeons can have strong personal preferences for either immediate, delayed, or delayed immediate reconstruction.(Figure 1)



Table 1. Advantages and disadvantages of variable timing of reconstruction.

Timing of Reconstruction
<p><i>Immediate: Reconstruction at time of mastectomy</i></p> <p>Advantages:</p> <ul style="list-style-type: none"> -Obtaining a symmetric reconstruction is more obtainable with immediate reconstruction vs delayed -Decreased overall cost via reduction in number of procedures -No difference in rates of locoregional recurrence or ability to detect/diagnose recurrence -Patients can immediately experience the psychological benefits of reconstruction and have been found to have superior post-operative QOL as compared to those waiting for delayed reconstruction after their mastectomy. <p>Disadvantages:</p> <ul style="list-style-type: none"> -Higher failure rate compared to delayed -Greater length of hospital-stay compared to mastectomy alone
<p><i>Delayed: No reconstruction at time of mastectomy with reconstruction at later date</i></p> <p>Advantages:</p> <ul style="list-style-type: none"> -Fewer post-operative complications in patients receiving PMRT -Provides patient time to consider reconstructive options <p>Disadvantages:</p> <ul style="list-style-type: none"> -May augment psychosocial harm or decrease patient quality of life following mastectomy -Increased number of surgeries required -Fibrotic tissue may be difficult to operate on
<p><i>Delayed-Immediate: Tissue expander placed at mastectomy, definitive reconstruction at later date</i></p> <p>Advantages:</p> <ul style="list-style-type: none"> -Avoids radiation of definitive reconstruction -Provides patient time to consider reconstructive options -Can increase size of overall reconstruction <p>Disadvantages:</p> <ul style="list-style-type: none"> -Propensity for surgical complications -Increased number of surgeries required -Fibrotic tissue may be difficult to operate on

Timing of Reconstruction and PMRT: Implant-Based Reconstruction



Timing of Reconstruction and PMRT: Autologous Reconstruction

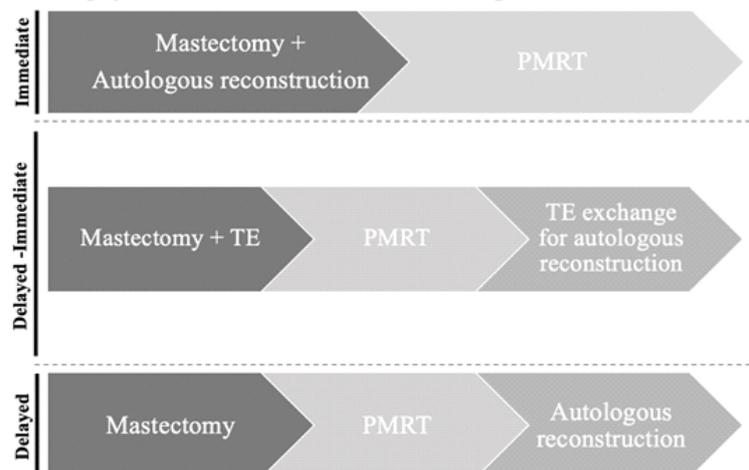


Figure 1. Timing of implant based reconstruction and autologous reconstruction as it relates to post mastectomy radiation.



The Effect of Breast Reconstruction on Radiation Therapy

In addition to the shared concerns of many plastic surgeons regarding the outcomes of reconstruction as they relate to the timing of PMRT, there is also the possibility that reconstruction can negatively impact the timing and quality of PMRT. Kahila *et al.* demonstrated that patients who underwent PMRT after immediate reconstruction had no compromise in the quality of PMRT administered.¹³ Furthermore, there was no significant difference in target volume coverage or mean lung/heart dosages between reconstructed and non-reconstructed patients.

An additional concern shared by plastic surgeons and radiation oncologists is the risk of post-operative complications and their ability to delay PMRT. Shammas *et al.* performed a review of the National Cancer Database to identify women undergoing mastectomy with immediate reconstruction and time to PMRT.¹⁴ A delay in radiation therapy was defined as PMRT initiation 12 weeks or more after mastectomy. Patients who underwent immediate breast reconstruction had an increased time to initiating radiation therapy (154 days versus 132 days, $p < 0.001$), and were more likely to have a delay in initiating PMRT (OR: 1.25). However, despite this delay, there was no significant reduction in survival supporting the collective assertion that immediate reconstruction is well tolerated and does not negatively influence overall survival, even in cases when PMRT is delayed.

Types of Breast Reconstruction: Implant Based Reconstruction

Currently, implant-based reconstruction (IBR) is the most common form of breast reconstruction in the United States, accounting for 82% of all reconstructions.⁵ Implants can be placed in the prepectoral plane or the subpectoral plane, either at the time of mastectomy or in a delayed fashion after tissue expander placement. Immediate, direct IBR rates at the time of mastectomy have increased by over 200% in the past 10 years.¹⁵ The decision for single or two-stage IBR depends on a variety of factors including viability of mastectomy flaps, final implant size, potential for PMRT, and surgeon preference. Patients who receive PMRT with IBR have increased rates of corrective surgery and overall poorer aesthetic outcomes when compared to autologous reconstruction.⁶ Up to 47.5% of immediate IBR patients may require revision after undergoing radiation therapy.¹⁶

Impact of Radiation on the Location of Implant Placement

Subpectoral implants have been historically favored in the setting of PMRT as it was thought that the overlying pectoralis muscle protects the implant from mastectomy flap loss, superior pole implant

rippling, and capsular contracture. However, this approach can be associated with animation deformities of the implant, increased pain, and muscle spasms.^{17,18}

Pre-pectoral IBR has been shown to result in less pain, improved aesthetic outcomes by mitigating animation deformities, and shorter operative time.¹⁹ However, concerns regarding the safety of PMRT in the setting of pre-pectoral implant placement exist. These include the potential for capsular contracture and the radiation oncologist's ability to properly provide radiation to the chest wall. As pre-pectoral IBR increases in popularity, preliminary studies have demonstrated favorable capsular contracture rates which are comparable to subpectoral IBR.^{20,21} Future prospective studies with larger sample sizes and longer follow-up periods are needed to better address the optimal plane for implant placement.

Impact of PMRT on Tissue Expander vs Permanent Implant in Two-Stage Reconstruction

In the United States, two-stage IBR is the most common method for IBR constituting 67% of breast reconstructions in 2019.⁵ For patients who will require PMRT, a common concern shared by plastic surgeons surrounds the timing of PMRT in relation to the final implant placement. Accordingly, there is no clear consensus indicating whether superior outcomes are obtained by applying radiation to the tissue expander or the permanent implant.

Cordeiro *et al.* demonstrated the acceptability of radiating the permanent implant with regard to aesthetic outcomes and patient satisfaction and was among the first studies to describe standardized radiation timing after immediate two-stage implant reconstruction.²² Expansion began 10-14 days after placement with exchange to permanent implant four weeks after the completion of chemotherapy. Radiation began one month after implant placement. Sixty-eight percent of radiated patients developed significant capsular contracture compared to 40% of non-radiated patients. Sixty-seven percent of the radiated patients were satisfied with their reconstructions compared to 88% of the non-radiated patients. Ten years later, the same group analyzed 2,133 two-stage implant reconstructions. Grade IV capsular contracture was present in 6.9% of radiated and .5% of non-radiated implants.²³

In contrast, some surgeons prefer to radiate the tissue expander and later replace it with a permanent implant, typically 3-6 months after the completion of PMRT. This process has several theoretical advantages: it allows the surgeon to inflate or deflate the device in the event of potential compromise of the mastectomy skin flap and it allows the surgeon to perform capsulectomies after the deleterious effects of radiation are apparent. Cordeiro *et al.* analyzed surgical and patient-reported outcomes from 94 and 210 women who had PMRT to their tissue expander



and implant, respectively. These experimental cohorts were compared to a control group of 1,486 women who had two-stage implant reconstruction without PMRT.²⁴ Both cohorts had tissue expanders placed at the time of mastectomy and expansion was started within 10-14 days and completed by 6 weeks. Tissue expanders were exchanged approximately six months after completion of PMRT. The authors demonstrated higher odds of reconstructive failure when PMRT was applied to the tissue expander (32% vs. 16.4%). Furthermore, Grade III and IV capsular contracture was significantly lower in the tissue expander group than the implant radiation group. Aesthetic outcomes were significantly poorer in radiated patients; however, there was no significant difference in aesthetic outcomes whether PMRT was administered to the expander or implant. While patients who did not receive PMRT were significantly more satisfied with their reconstruction, there was no difference in patient satisfaction scores between the tissue expander and implant groups.

Overall, these seminal studies demonstrate that PMRT results in increased complications, regardless of whether the implant or tissue expander was radiated. Failure rates tend to be significantly higher when PMRT is applied to the tissue expander in two-stage reconstruction. However, when PMRT is applied to the tissue expander, this may result in less capsular contracture, likely due to the ability to perform capsulectomies and/or pocket adjustments at the time of the implant exchange procedure.

Types of Breast Reconstruction: Autologous Reconstruction

Autologous reconstruction describes the process of reconstructing the breast using the patient's own tissue, thereby obviating the need for implants. In 2019, autologous reconstruction represented approximately 14% of breast reconstruction procedures performed.⁵ In the United States, the Deep

Inferior Epigastric Flap (DIEP) from the abdomen comprises 54% of all autologous reconstructions. The type of autologous reconstruction is limited by the patient's body habitus, prior surgery, medical comorbidities, and patient preference. In general, the type and frequency of complications varies based on the type of flap utilized.

Autologous reconstruction has several distinct advantages when compared with implant-based reconstruction. In many patients, autologous reconstruction can overcome the need for the multiple surgeries required for implant replacement and capsular contracture correction by providing a life-long, durable reconstruction. Autologous reconstruction is associated with improved patient reported satisfaction, psychosocial well-being, and overall sexual well-being when compared with implant-based reconstruction.²⁵ Additionally, autologous reconstruction is associated with lower odds of surgical site infection and reconstructive failure in patients who undergo PMRT.^{26,27} Despite these advantages, autologous reconstruction is a larger, longer operation with the potential for additional scarring and/or injury to the area of flap harvest.

Timing for autologous reconstruction in patients requiring PMRT has a similar algorithm to that of implant reconstruction. Reconstruction can be performed at the time of mastectomy followed by PMRT, in a delayed-immediate fashion with irradiation of the tissue expander, or in a delayed fashion and performed after PMRT completion. Immediate reconstruction with autologous tissue can be advantageous as it is possible to perform the entire reconstruction at the time of mastectomy. However, if PMRT is required, there is the possibility that the radiation may cause unpredictable flap necrosis, discoloration, contracture, displacement, volume loss, or other complications that require additional revision procedures and/or hospitalizations.²⁸ To illustrate this,



Figure 2. Differential skin paddle designs and the impact of timing on autologous reconstruction.

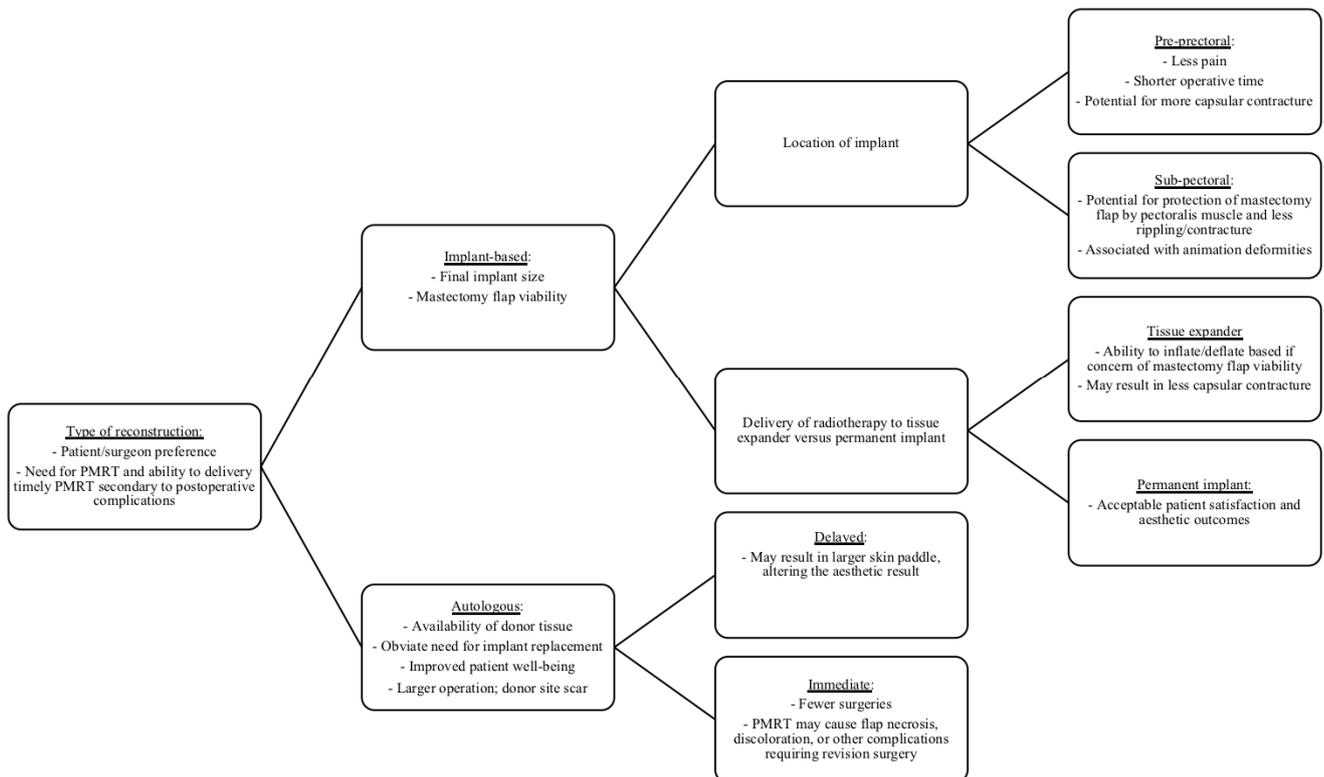


Figure 3. A summary of key findings for various considerations of available breast reconstructive methods.

Williams et al. compared the effects of radiation on immediate and delayed abdominal flaps and found that 31.6% of immediate flaps developed fibrosis with 0% in the delayed reconstruction group.²⁹ Fifty-two percent of immediate flaps experienced some deleterious post-radiation changes such as fat necrosis, volume loss, or contracture and 32% required revision surgery. These findings led the authors to recommend delaying autologous reconstruction until after radiation completion

The timing of reconstruction has the ability to change the final result of autologous reconstruction. If the mastectomy skin flap is able to be preserved as is the case in immediate reconstruction and delayed immediate reconstruction, the skin paddle of the flap can be tailored to be a small island that can later be used to create the nipple-areola complex. When performing a delayed reconstruction, the autologous flap is larger, as it must be used to reconstruct the entire breast mound. This difference in flap size results in different aesthetic results, although it has been shown that patients have high satisfaction ratings of aesthetic outcomes with both types of autologous reconstruction.³⁰ (Figure 2)

Discussion

Post-mastectomy radiation therapy is a necessary component of breast cancer care for an increasing number of patients as it has been shown to reduce rates of locoregional recurrence and improve overall survival.^{31,32,33} Unfortunately, there are deleterious

effects associated with PMRT that can negatively impact reconstructive outcomes. Currently, there is no high-level evidence that identifies an optimal treatment algorithm for combining PMRT and breast reconstruction and the vast majority of studies are retrospective, non-randomized, and include small patient samples. However, when many of these studies are analyzed, trends emerge. For example, in cases of autologous reconstruction, delaying definite reconstruction until after PMRT has been associated with better aesthetic outcomes and decreased need for revision surgery. With regard to implant reconstruction, decreased failure rates may sway providers towards providing radiation to the implant instead of the tissue expander. This review provides an overview of various reconstructive techniques and how they are impacted by PMRT. (Figure 3) With this information, oncologic care teams can help provide more comprehensive information to patients in order to optimize their satisfaction with their breast cancer treatment and reconstruction.

Conflict of Interest

Justin Broyles serves as a consultant for AHRQ and the medical advisory board for Healshape Inc.

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