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 adjuvant 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 postmastectomy 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 surgeon[8]; 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 diagnosism 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