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Oncological Considerations for Breast Reconstruction

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1. Introduction

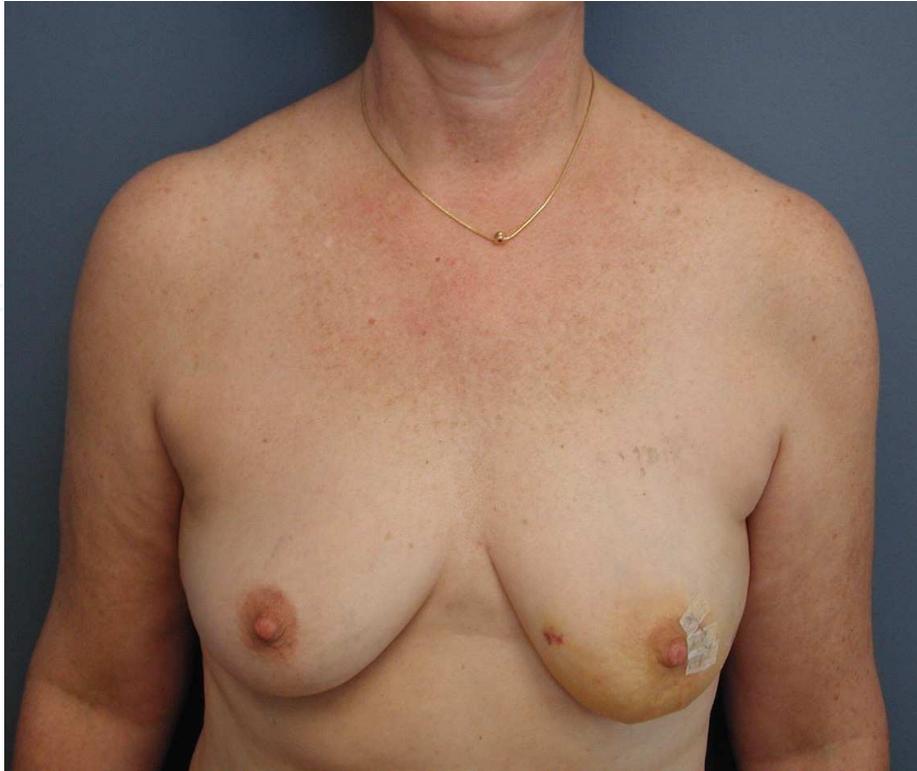
Fifteen percent of women treated for breast cancer with total mastectomy receive immediate or early breast reconstruction [1, 2]. The percentage is higher in young women and those treated in tertiary care medical centers. Immediate breast reconstruction (IBR) has several advantages [3, 4]. It can prevent some of the negative psychological and emotional sequelae seen with mastectomy. The aesthetic results of immediate reconstruction are superior to those seen after delayed reconstruction. IBR also reduces hospital costs by reducing the number of procedures and length of hospitalization. Immediate breast reconstruction has the potential to impact the treatment of breast cancer. It could affect the delivery of adjuvant therapy and the detection and treatment of recurrent disease. Chemotherapy and radiation therapy could also impact the complication rates of reconstruction. The oncological considerations of breast reconstruction are outlined in this chapter.

2. Local recurrence after skin sparing and nipple sparing mastectomy

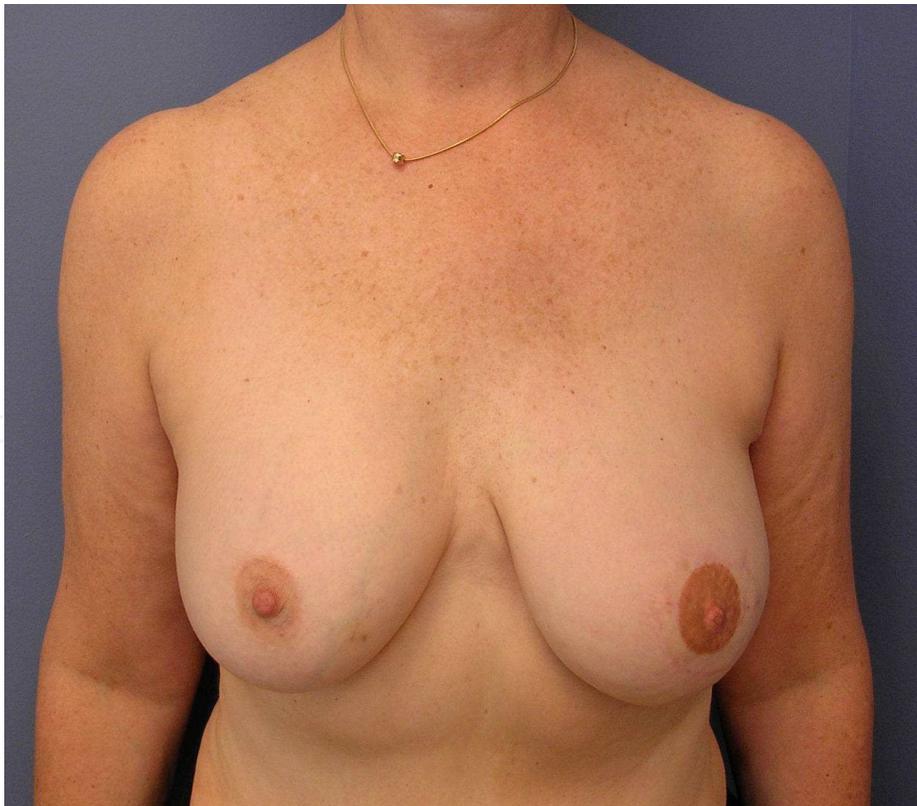
Women with breast cancer who undergo immediate breast reconstruction do not have a worse survival than those not undergoing breast reconstructions. A review of a large National Cancer Institute database of 51,702 breast cancer patients identified 8,645 (16.7%) who underwent immediate breast reconstruction [5]. Patients treated by mastectomy and IBR had a lower hazard of death (HR 0.62) compared to those treated by mastectomy alone ($p < 0.001$). The study was controlled for age, race, income, and tumor stage. Potential compounding factors like obesity, smoking, and underlying chronic disease were not accounted for.

Skin sparing mastectomy (SSM) has markedly improved the aesthetic results of immediate breast reconstruction (Figure 1). Preservation of the native skin envelope and the inframammary fold reduces the amount of tissue necessary for reconstruction [6]. Breast symmetry can often be achieved without operating on the contralateral breast and the periareolar incisions are inconspicuous in clothes.

There have been concerns that the skin, nipple and inframammary fold preservation reduce the effectiveness of total mastectomy. There is a large body of evidence that the local recurrences (LRs) after SSM are comparable to non-skin sparing mastectomy (Table 1) [7-9]. Care must be taken however, in patients with superficial cancers or diffuse DCIS to assure adequate surgical margins.



(a)



(b)

Fig. 1. (a) Preoperative photograph (b) Postoperative photograph after skin sparing mastectomy and TRAM flap reconstruction

<i>Author</i>	<i>Followup (Months)</i>	<i>SSM (N)</i>	<i>LR in SSM (%)</i>	<i>Non-SSM (N)</i>	<i>LR in Non-SSM (N)</i>
Newman [81]	50	437	6.2	437	7.4
Carlson [7]	41.3	187	4.8	84	9.5
Kroll [8]	72	114	7.0	40	7
Simmons [9]	15.6-32.4	77	3.9	154	3.2
Rivadeneira [82]	49	71	5.6	127	3.9
Medina-Franco [83]	73	176	4.5	-	-
Carlson [84]	64.6	565	5.5	-	-
Slavin [85]	44.8	51	3.9	-	-
Toth [86]	51.5	50	0	-	-
Spiegel [87]	117.6	221	4.5	-	-
Foster [88]	49.2	25	4.0	-	-

SSM skin sparing mastectomy

LR local recurrence

Non-SSM non skin sparing mastectomy

Table 1. Published series of local recurrence of breast cancer after skin sparing and non-skin sparing mastectomy

Nipple sparing mastectomy (NSM) is growing in popularity because of its perceived aesthetic benefits (Figure 2). Patient satisfaction with nipple-areolar reconstruction following SSM can be disappointing [10]. Data regarding the oncological safety of NSM is hampered by small sample size, varying indications and surgical techniques, and short follow-up (Table 2). There are limited oncological and reconstructive indications to perform NSM. Large tumors and those located in the central breast have an increased incidence of nipple involvement. Larger, more ptotic breasts are not good candidates for the procedure. Nipple elevation cannot be achieved without preservation of a dermoglandular pedicle which impacts the completeness of mastectomy. The ideal candidate for a NSM has small to moderate sized breasts with minimal ptosis.

3. Detection of local recurrence after breast reconstruction

The role of postreconstruction imaging after the treatment of breast cancer remains controversial. There is a paucity of data that addresses the issue and there no established guidelines [11]. The incidence of local recurrence of breast cancer is related to tumor stage. Most LRs after total mastectomy are in the skin and subcutaneous tissue and are readily detected by physical examination [12]. A flap or implant could potentially delay the discovery of chest wall recurrences.

Systemic relapse is not inevitable following local recurrence, especially after the treatment of DCIS [13, 14]. This argues that early detection of local recurrences may have a potential survival impact. All forms of mastectomy leave residual breast tissue. The differences are in terms of the microscopic breast tissue left behind in the skin and inframammary fold which are largely preserved after SSM. Torresan et al evaluated residual glandular tissue in the

skin flaps that would have been preserved after SSM [15]. They found that 60% contained residual glandular tissue and it correlated with skin flap thickness.



(a)



(b)

Fig. 2. (a) Preoperative photograph (b) Postoperative photograph after nipple sparing mastectomy and implant reconstruction

The completeness of mastectomy is important in the treatment of DCIS because most cases of recurrence represent unexcised residual disease. Several authors have reported LR of DCIS treated by SSM and IBR [13, 16, 17]. They found that the majority of LRs were invasive carcinomas. This suggests that postreconstruction mammography can have a role in the early detection of recurrences prior to the development of invasive carcinoma.

Physical examination of implant reconstruction is relatively easy. There is minimal soft tissue covering the implant except along the inframammary fold and in the axillary tail. Deep chest wall recurrences are extremely unlikely because the implants are placed in the

submuscular plane. Conventional mammographic evaluation has limited utility because the implants obscure soft tissue visualization. MRI, which has been used extensively to evaluate the integrity of silicone gel implants, may have a role in the selective surveillance after implant reconstruction [18-21].

Study	N	LR (%)	NAC Recurrence (%)	Follow-up (months)
Gerber [89]	60	6 (10)	1 (1)	101
Caruso [90]	50	6 (12)	1 (2)	66
Sacchini [91]	68	2 (2.9)	0 (0)	26.4
Voltura [92]	32	2 (6.3)	0 (0)	18
Benediktsson [93]	169	48 (28.4)	0 (0)	156
Kim [94]	152	3 (9.1)	2 (1.3)	60

Table 2. Local recurrences after nipple sparing mastectomy

The sensitivity of physical examination of autologous reconstruction is lower than that seen with implant reconstruction. Deep chest wall recurrences often avoid detection until symptoms develop. Autologous reconstruction causes less impairment of mammographic tissue visualization [22]. Benign mammographic findings after TRAM flap reconstruction include fat necrosis, lipid cysts, calcifications, lymph nodes, and epidermal inclusion cysts (Figure 3) [23]. Breast cancer recurrences in autologous tissue reconstruction are mammographically similar to that of primary tumors (Figure 4) [24, 25]. Proponents of surveillance mammography feel that screening breast cancer patients with autologous reconstructions can detect nonpalpable recurrences before clinical examination.

Helvie et al evaluated surveillance mammography in 113 patients after TRAM flap reconstruction [26]. Six patients underwent biopsy for suspicious mammographic findings and two local recurrences were detected. Two patients in the study group went on to develop recurrences that were detected by physical examination. There was one false-negative mammogram resulting in a sensitivity of 67% and specificity of 98% for surveillance mammography after TRAM flap reconstruction.

There is a paucity of data regarding the efficacy of MRI of the breast following autogenous breast reconstruction [27, 28]. Breast MRI has been shown to clearly delineate autogenous flaps from residual mammary adipose tissue. The absence of contrast medium uptake during breast MRI precludes recurrent carcinoma to a high probability. Fat necrosis in a TRAM flap will show early postoperative contrast enhancement but this resolves within six to twelve months. Rieber et al evaluated MRI of the breast in the follow-up of forty-one patients who had undergone autogenous tissue breast reconstruction [29]. MRI was able to distinguish flaps from surrounding residual breast tissue in all cases. It excluded disease recurrence in 4 patients with suspicious mammographic or sonographic findings. It returned false-positive findings in three cases.

The potential indications for postreconstruction imaging include patients with close surgical margins and patients with diffuse DCIS treated by SSM. Its routine use after autologous reconstruction after SSM for invasive carcinoma warrants further study. The low detection rate and specificity does not justify the routine use of MRI in the follow-up of patients

postreconstruction. MRI is most useful in patients with abnormal findings on physical examination or mammography and ultrasound. It is also helpful to delineate the extent of local disease recurrence.



Fig. 3. Mammographic appearance of fat necrosis in a TRAM flap reconstruction

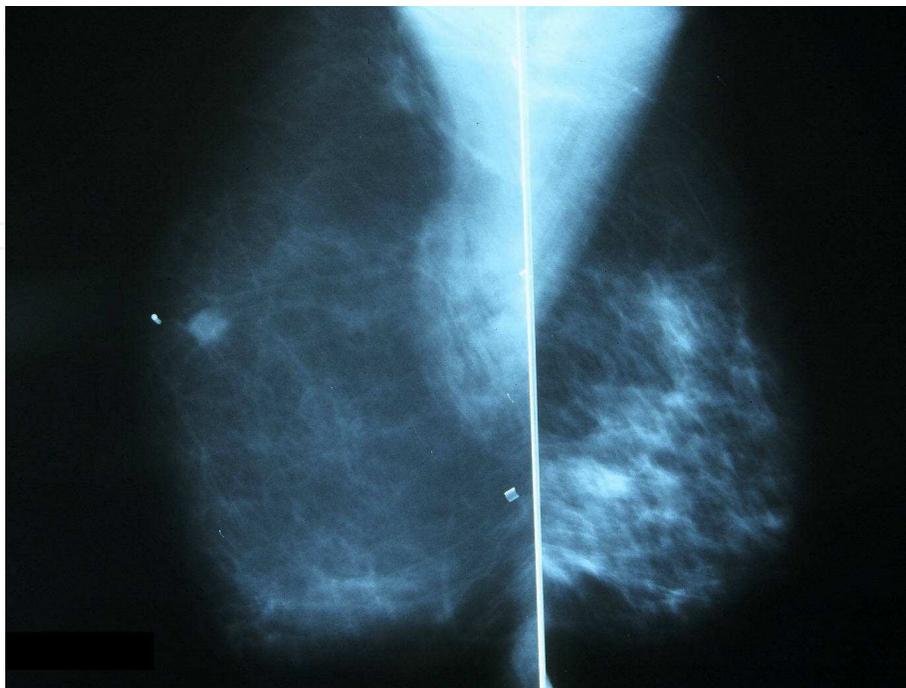


Fig. 4. Mammographic appearance of local recurrence in TRAM flap (L), opposite breast (R)

4. Breast reconstruction and adjuvant therapy

4.1 Chemotherapy

There are concerns that immediate breast reconstruction may delay the administration of adjuvant chemotherapy. A survey of 376 consultant breast surgeons in the United Kingdom and Ireland found that the majority (57%) preferred delayed reconstruction because of these concerns [30]. Breast reconstruction does have a high complication rate especially in patients who are obese, smoke tobacco, or have a history of chest wall irradiation. Alderman et al performed a multi-institutional study of complication rates after tissue expander or TRAM flap reconstruction [31]. They reported a 52% complication rate, with major complications occurring in 30% of patients.

It seems logical that the high complication rate of IBR could potentially delay the administration of adjuvant therapy. Studies comparing onset of chemotherapy after IBR and control group treated with mastectomy alone have failed to show significant differences [32-35]. Alderman et al performed a multi-institutional cohort study of 3643 breast cancer patients [35]. They found that IBR did not lead to an omission of adjuvant chemotherapy but was associated with a modest delay in initiating treatment. Wound complications after IBR must be treated aggressively to remove necrotic, potentially infected tissue. Patients with clean, open wounds can receive chemotherapy with minimal compromise in wound healing. These patients must be followed closely detect early signs of infection.

Patients with locally advanced, Stage III breast cancer are generally treated with chemotherapy followed by total mastectomy and adjuvant radiation. The five-year survival is 50%-80%, and patients with a poor response to chemotherapy have an especially bad prognosis. It may be preferable to delay reconstruction until after mastectomy and adjuvant radiation in these patients. This avoids the potential problems with radiation delivery and the adverse effects of postmastectomy radiation therapy on immediate reconstruction. These issues will be discussed in detail later in the chapter.

Neo-adjuvant chemotherapy may impact the complication rate of immediate breast reconstruction and delay adjuvant radiation. Mitchem et al evaluated the impact of neo-adjuvant chemotherapy on tissue expander reconstruction [36]. Eleven (32%) of 34 expanders required removal with infection accounting for 82% of implant losses. Deutsch et al reported a 55% complication rate in 31 patients after immediate TRAM flap reconstruction who received neo-adjuvant chemotherapy [37]. Six percent had a delay in resumption of chemotherapy because of complications. Sultan et al found a 14% complication rate in 21 patients who received neo-adjuvant chemotherapy and underwent IBR [38]. The mean interval between surgery and resumption of chemotherapy was 19 days and there was no delay in any patients. Mehrara et al found that neo-adjuvant chemotherapy was an independent predictor of overall complications in free flap breast reconstruction [39]. Zweifel-Schlatter et al compared 47 patients undergoing immediate free flap breast reconstruction after neo-adjuvant chemotherapy with 52 patients who did not receive preoperative therapy and found no delay in beginning adjuvant therapy [40].

4.2 Radiation therapy

Postmastectomy radiotherapy (PMRT) is increasingly utilized in the adjuvant treatment of breast cancer. The current recommendations for PMRT include patients with 4 or more

positive axillary lymph nodes, locally advanced cancer, tumors 5 cm. or larger and positive margins. It is considered for medial quadrant tumors, tumors with lymphovascular invasion, and in patients with 1-3 metastatic lymph nodes. Two randomized trials have shown a survival benefit for post-mastectomy radiotherapy in patients with 1-3 metastatic lymph nodes [41, 42]. These studies were criticized because of high rate of regional failure in the non-irradiated group which was felt the result of inadequate axillary surgery and the use of non-anthracycline based chemotherapy. A survey of radiation oncologists found that only 58% would use PMRT in patients with 1-3 metastatic lymph nodes but 95% would recommend it for patients with 4 or more metastatic nodes [43].

There are technical problems related to irradiation of the reconstructed breast. Distortion of the chest wall anatomy means that radiotherapy portals need to be modified. The treatment is more difficult, particularly irradiating the internal mammary lymph nodes. This may result changing the depth of tangential fields resulting in increased volume of irradiated lung or heart. Motwani et al examined the effect of immediate autologous breast reconstruction on the technical delivery of PMRT [44]. Two radiation oncologists reviewed radiotherapy plans in 110 patients. These were compared to matched controls that had mastectomy alone. A scoring system was used that evaluated chest wall coverage, treatment of the internal mammary lymph node chain, minimization of lung exposure, and avoidance of the heart. They found that 52% of the immediate reconstruction patients had compromise of their radiotherapy plans compared to 7% of controls. If coverage of the internal mammary lymph nodes was eliminated, 23% of the IBR group had compromised plans. M.D. Anderson Cancer Center recommends deflating tissue expanders prior to the administration of PMRT to overcome potential dosimetry compromise [45]. Most institutions feel that the potential interference of breast implants with can overcome with alteration in treatment planning.

Radiation therapy has a negative impact on all forms of breast reconstruction. A meta-analysis of over 1,000 patients showed that patients undergoing PMRT and breast reconstruction were more likely to suffer morbidity compared to patients not receiving PMRT [46]. It also showed that autologous reconstruction was associated with less morbidity than implant reconstruction when PMRT was administered. There are three clinical scenarios that are encountered: immediate reconstruction in patients, who have received preoperative radiation, delayed reconstruction after PMRT, and immediate reconstruction in patients who will receive PMRT. Berry et al, reviewed 1037 cases of immediate breast reconstruction (expander 559 and autologous 478) [47]. Radiation whether administered preoperatively or postoperatively significantly increased the complication rate in expander reconstruction but had no significant impact on autologous reconstruction.

Chest wall irradiation after expander / implant reconstructions results in an increase incidence of capsular contraction and implant exposure. Because of this, many authors feel that implant reconstruction is contraindicated when postmastectomy radiation is planned. Krueger et al performed a prospective evaluation of tissue expander reconstruction in 81 patients, including 19 patients who received radiation [48]. Patients receiving radiation had a two fold increase in complications ($p=0.006$) and a four fold increase in reconstruction failure ($p=0.005$). The addition of autologous tissue such as the latissimus flap may reduce the risk of complications seen with the use of implants in the setting of radiation [49].

Radiation also has a deleterious effect on TRAM flap reconstruction as evidenced by increased incidence of fibrosis, fat necrosis, and revisional surgery [50-52]. There is an unpredictable volume, contour, and symmetry loss that is seen with pedicled TRAM flaps, free TRAM flaps, and DIEP flaps. Tran et al reviewed the M.D. Anderson Cancer Center experience of TRAM flap irradiation [52]. The review included 41 TRAM flaps (free TRAM 32, pedicled TRAM 9). Ten patients (24%) required an additional flap to correct radiation induced contracture. Nine patients (22%) maintained normal breast volume and palpable fat necrosis was noted in 34% of flaps. The paper by Rogers and Allen has demonstrated similar deleterious effects of radiation on DIEP flap reconstruction [51]. They reported a 23.3% incidence of fat necrosis in the radiated group vs. 0% incidence in the control group. Radiation fibrosis was seen in 56.7% of cases with 5 (16.7%) requiring surgical revision.

5. The treatment of local recurrence after breast reconstruction

Surgical options following LR after breast reconstruction depend on the location and number of metastatic deposits and previous treatment. Imaging of the reconstructed breast and body scans are necessary to delineate the extent of tumor involvement (Figure 4). Isolated local recurrences can be treated with removal of as much reconstructed tissue as necessary to achieve negative margins. Adjuvant chest wall radiation is usually administered (Figure 5).

In cases of implant reconstruction, it may be necessary to remove a portion of the implant capsule necessitating implant removal in some cases [53]. Howard et al reviewed 16 cases of LR after TRAM flap reconstruction [54]. Eight recurrences occurred in the skin and were detected on physical examination. Eight recurrences occurred in the chest wall and were symptomatic, being detected on physical examination or diagnostic imaging. Twelve were felt amenable to surgical resection and three required removal of the entire TRAM flap.

6. Oncological considerations in partial mastectomy reconstruction

Oncoplastic surgery combines the principles of oncologic surgery (breast conserving therapy) and plastic surgery (breast reconstruction). It has the potential for better tumor free margins and enhancement of the cosmetic outcome [55]. Reconstruction can be performed via parenchymal rearrangement or volume replacement with local or distant flaps [56, 57].

Studies suggest these techniques are associated with low local recurrence but the long term oncological safety of these procedures is not clearly defined [58]. Young patients, especially those with diffuse high grade DCIS; do not appear to be good candidates because of the increase in margin involvement and LR. Follow-up mammographic evaluation does not appear to be significantly impacted by onco-plastic reconstruction.

6.1 Sentinel lymph node biopsy and breast reconstruction

Sentinel lymph node biopsy has replaced axillary dissection as the standard of care for axillary node sampling. The sensitivity of intraoperative pathological SLN analysis is 68%-91% [59-61]. It is related to the size of the metastatic deposits which is related to tumor size. False negative intraoperative diagnoses of sentinel lymph node metastases present unique problems in breast cancer patients after immediate breast reconstruction. The standard of

care for patients with tumor positive SLNs is a completion axillary lymph node dissection. This procedure can be technically demanding if a latissimus dorsi flap reconstruction has been performed or the thoracodorsal vessels have been used for microvascular reconstruction [62]. Fortunately, the internal mammary vessels have become the vessels of choice for microsurgical breast reconstruction. They are easier to access and permit early postoperative arm mobilization without risk of injury to the flap vascular pedicle. Vessel location facilitates placement and the latissimus dorsi muscle blood supply is preserved if salvage surgery is necessary. Internal mammary lymph nodes can sometimes be encountered at the time of vessel dissection [63]. Involvement of these lymph nodes has prognostic significance and should be biopsied when they are discovered.



(a)



(b)

Fig. 5. (a) Photograph tissue expander reconstruction of the right breast immediately after completing radiation (b) Appearance 12 months after completing radiation

A few studies have suggested SLN biopsy prior to mastectomy and IBR to avoid potential complications seen with PMRT [64-66]. This could facilitate decision making regarding immediate breast reconstruction and avoid a second operation in cases of FNG SLN biopsies. McGuire et al found that SLN biopsy before mastectomy and IBR changed the operative strategy in 62% of patients [67].

7. Contralateral prophylactic mastectomy

More women are choosing to have a contralateral prophylactic mastectomy (CPM) at the time of treatment of their unilateral breast cancer. Tuttle et al used SEER data to evaluate the treatment of unilateral breast cancer from 1998-2003 [68]. They found the rate of CPM in women undergoing total mastectomy more than doubled in the six year period. The use of CPM is associated with younger patient age, a family history of breast cancer, the use of immediate breast reconstruction, the use of breast MRI at the time of diagnosis, non-invasive histology, and prior attempts at breast conservation [68-73].

Contralateral prophylactic mastectomy at the time of total mastectomy and IBR has two main advantages: it reduces the risk of developing a new cancer and it facilitates breast reconstruction. Women with unilateral breast cancer have an increased risk of developing a second cancer in the contralateral breast. The annual incidence of new breast cancer has been reported to be 0.7% - 1.8% [74-76]. Adjuvant hormonal therapy has been shown to reduce this risk. Despite the high incidence of cancer development, most patients will not experience a survival benefit from a CPM. The risk of systemic metastases from the index cancer exceeds the risk of contralateral cancers, which tend to be lower in stage. Younger women with stage I and II estrogen receptor negative cancer have been shown to benefit from CPM [70].

The Society of Surgical Oncology updated their position statement on prophylactic mastectomy in 2007 [77]. It detailed potential indications in patients with current or previous diagnosis of breast cancer to include:

- Patients at high risk of contralateral breast cancer (BRCA mutation, strong family history)
- Patients with mammographically dense breasts or those with diffuse indeterminate microcalcifications
- Patients with unilateral breast cancer treated by total mastectomy and IBR who desire improved symmetry or have a desire for bilateral reconstruction

A CPM and bilateral reconstruction is especially useful in cases of implant based reconstruction (Figure 6). The contralateral breast frequently requires remedial surgery to achieve symmetry with an implant reconstructed breast. Clough et al found that the cosmetic outcome of unilateral implant reconstruction deteriorated with time [78]. They attributed this asymmetry largely to ptosis of the native breast seen with aging. Bilateral reconstruction would prevent this asymmetry development.

The majority of women are satisfied with their decision to undergo CPM [79]. The most common reasons for regret appear to be poor cosmetic outcome and a diminished sense of sexuality [80].



(a)



(b)

Fig. 6. (a) Photograph after left TRAM flap reconstruction (b) Appearance 12 months after completing radiation.

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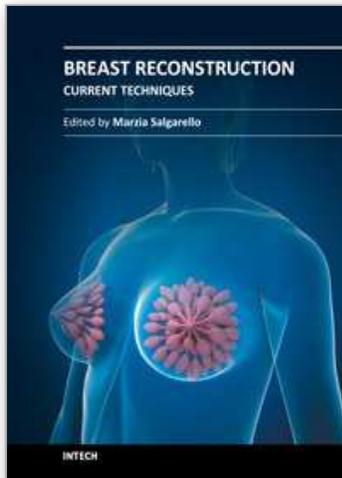
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Breast reconstruction is a fascinating and complex field which combines reconstructive and aesthetic principles in the search for the best results possible. The goal of breast reconstruction is to restore the appearance of the breast and to improve a woman's psychological health after cancer treatment. Successful breast reconstruction requires a clear understanding of reconstructive operative techniques and a thorough knowledge of breast aesthetic principles. Edited by Marzia Salgarello, and including contributions from respected reconstructive breast plastic surgeons from around the world, this book focuses on the main current techniques in breast reconstruction and also gives some insight into specific topics. The text consists of five sections, of which the first focuses on the oncologic aspect of breast reconstruction. Section two covers prosthetic breast reconstruction, section three is dedicated to autogenous breast reconstruction, and section four analyzes breast reconstruction with a fat graft. Finally, section five covers the current approaches to breast reshaping after conservative treatment.

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