The need to balance cosmesis in reconstruction with the oncologic needs of breast cancer patients is no more evident than in the discussion of radiotherapy (1). Radiotherapy is essential adjuvant therapy in the treatment of breast cancer, with the use of adjuvant radiotherapy widely shown to reduce local recurrence after both partial and total mastectomy and shown to prolong both disease-free and overall survival in patients with nodal disease (1-6). In the setting of breast reconstruction, the effects of radiotherapy are potentially two-fold, with consideration required of the impact of breast reconstruction on the administration of and the initiation of radiotherapy, as well as the effects of radiotherapy on operative complications and cosmetic outcome following immediate breast reconstruction. The current editorial piece aims to analyze this balance, contrasting both autologous and implant-based reconstruction. The literature is still evolving as to the relative role of autologous vs. alloplastic reconstruction in the setting of radiotherapy, and the more recent introduction of acellular dermal matrix and other compounds further complicate the evidence. Fat grafting and evolving techniques in breast reconstruction will herald new discussions on this front.

**Key Words:** Implant; reconstructive surgery; radiation; adjuvant therapy; breast reconstruction

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**Oncologic issues**

The impact of breast reconstruction on delaying the administration of radiotherapy has been explored in relatively few recent studies (7-11). This is surprising given the importance of the issue, with several significant studies demonstrating poorer oncologic outcomes with delays in radiotherapy (12-15). In fact, those studies which have addressed the issue have all been relatively low in numbers...
and based at single institutions. Each of these studies showed no delay in the initiation of adjuvant radiotherapy in patients undergoing immediate breast reconstruction. Breast reconstruction may also impact the delivery of radiotherapy, by means of distorting the chest wall anatomy and thus altering the design of the radiotherapy fields. This is in the setting of radiation fields which include the chest wall, internal mammary lymph nodes, supraclavicular lymph nodes and the apex of the axilla. Distorting the anatomy with a reconstructive flap or implant may diminish the radiation administered to these regions, or more commonly, may dictate the need for a wider radiation field (16-18).

The mode of action of radiotherapy involves the use of ionizing radiation, delivered by external beam radiation, to the chest wall and/or the surrounding lymph nodes. It is the mechanism of this effect, via direct disruption of protein and DNA molecules and the formation of free radicals and electrons causing molecular damage, that dictates both positive and negative outcomes (15). While these effects are directly toxic to malignant cells, radiation also damages healthy tissue. Direct tissue cellular damage with chromosomal alteration, microvascular occlusion with ischemia and inhibition of fibroblast action, are all implicated as mechanisms in tissue damage (19-22), leading to progressive loss of endothelial cells in the walls of microsculature and leading to characteristic blind ending capillaries and regional ischaemia. Structural changes to the skin include changes in epidermal and dermal keratinocytes and melanocytes, damage to skin appendages, skin thinning and fibrosis (19,21,22). These damaging tissue responses are associated with the increased incidence of operative complications, particularly those associated with healing.

Reconstructive outcomes

In the setting of implant reconstruction, adjuvant radiotherapy has been widely described as having an unacceptably high complication rate, particularly the complications of capsular contracture, and rupture of the implant envelope or fibrous capsule (23,24). This is particularly true for postoperative radiotherapy, but has been associated with preoperative radiotherapy as well. Where post-operative radiotherapy is predicted, such as those high-risk cancers that are large, multifocal or have lymph node involvement, implant reconstruction has been described widely as an ill-advised option. Many of the studies showing this were associated with older regimes and modes of administration of radiotherapy, and more recent techniques, such as helical tomographic radiotherapy, may improve outcomes in the setting of breast reconstruction (25).

While the same conclusions for autologous reconstruction have certainly been less rigid, there has been no consensus in the literature. In fact, our experience suggests that there are indeed complications in autologous reconstruction from radiotherapy, and that the effects of radiotherapy on implants in the setting of skin-sparing mastectomies may be less than previously suggested. The differences between autologous and implant reconstruction in this setting may thus be more comparable than previously suggested (1,23,26-28). Figures 1,2,3 highlight the effects of radiotherapy on autologous tissues alone, and highlight that these effects are not solely related to the alloplastic implant (Figures 1,2,3).

The effect of radiotherapy on operative outcome has been explored to a large extent, but not in any randomized control trials. For autologous reconstruction, there is conflicting data, with the timing of radiotherapy of importance. The complications that occur after autologous reconstruction in the previously irradiated chest are similar to those occurring in the setting of no radiation. However, given that the tissues have been afflicted with radiation damage, wound complications are more likely to be increased. Autologous reconstruction nevertheless, allows removal of some of the damaged tissue and the importation of donor healthy (non-irradiated) tissue.

The outcome of autologous reconstruction in the setting of previous (neoadjuvant) radiotherapy has been described in a large number of past studies (11,29-44), ranging from small, non-controlled studies, to large studies with over 100 cases that have been matched to a non-irradiated group. This diversity is echoed in their findings, with some of the larger studies demonstrating no significant difference in outcome and some showing significant increases in complication rates. The largest study was that of Williams et al. (1995), in which 118 patients with TRAM flap reconstruction after previous radiotherapy were compared to 572 patients without prior radiotherapy, with this study showing an increase in fat necrosis in patients with prior radiotherapy, but no increase in overall complications (35). Of the larger studies that assessed cosmetic outcome in the setting of previous radiotherapy, there were significantly poorer cosmetic scores (31,32). However, the overall incidence of these complications were not high, and as such autologous reconstruction is still considered safe after neoadjuvant radiotherapy. An additional consideration
of preoperative radiotherapy is that it may reduce the incidence of loco-regional recurrence and increase disease-free survival, thus reducing the incidence of local recurrence following reconstruction (1,45,46).

The outcomes following autologous reconstruction with subsequent adjuvant radiotherapy has been similarly explored widely, with variable results (34,41,42,47-55). Although most studies described extremely low flap loss rates, the incidence of tissue complications was generally greater than comparative groups, particularly that of fat necrosis. Several studies documented fat necrosis rates of greater than 20% (34,41,47,48). The largest study however, by Huang et al. (2006), did not demonstrate high complication rates, with a 0 flap loss and 8.5% incidence of fat necrosis, a figure comparable to those without adjuvant radiotherapy (51). Despite this, if radiotherapy is expected, delaying the reconstruction is the preferred mode of management because all too often the authors have witnessed the effect of post-reconstruction radiotherapy on well matched autologous reconstruction, resulting in

**Figure 1** Skin and flap contracture in a deep inferior epigastric artery (DIEA) perforator flap, in which postoperative radiotherapy was administered to the supero-medial pole of the breast. Marked skin changes, asymmetry, and nipple displacement are evident. Reproduced with permission from: Rozen WM, Ashton MW, Taylor GI. Defining the role for autologous breast reconstruction post-mastectomy: the social and oncological implications. Clin Breast Cancer 2008;8:134-42

**Figure 2** Skin and scar retraction in the setting of adjuvant radiotherapy following partial mastectomy. Reproduced with permission from: Rozen WM, Ashton MW, Taylor GI. Defining the role for autologous breast reconstruction post-mastectomy: the social and oncological implications. Clin Breast Cancer 2008;8:134-42

**Figure 3** Skin and nipple retraction in the setting of adjuvant radiotherapy following partial mastectomy. Reproduced with permission from: Rozen WM, Ashton MW, Taylor GI. Defining the role for autologous breast reconstruction post-mastectomy: the social and oncological implications. Clin Breast Cancer 2008;8:134-42
fibrosis, volume loss and displacement and elevation of the nipple and areolar complex (Figure 1).

With the more widespread use of skin-sparing mastectomy (SSM) techniques, since the concept of preoperative plastic surgery planning together with SSM was first brought to the forefront by Toth et al. in 1991, an improvement in outcomes with implant reconstruction has developed (56,57). This involves the preservation of a native skin envelope with the removal of the breast, nipple-areolar complex, biopsy scars and skin overlying any superficial tumours, and the ideal SSM having a skin flap devoid of all breast tissue but having an adequate blood supply to prevent flap necrosis and delayed wound healing. It is believed that the preservation of the skin architecture and intact infra-mammary fold allows for immediate breast reconstruction, thereby reducing the number of reoperations and improving the cosmetic appearance of the breast, and diminish the need for tissue expansion and/or remodelling in the setting of radiotherapy. In many past studies, the expander/implant option was considered a poor option in post-mastectomy reconstruction, suggesting that tissue expansion was associated with a significantly higher complication rate (38,58-60). However, the field of implant-based reconstruction has undergone constant change, including the advent of dual chambers, anatomic and cohesive variations, texture modifications, and ever-evolving proprietary manipulation (Figure 4). As a result, implant-based reconstruction data are difficult to standardize between studies, or over any prolonged period of time. Similarly, size of implant, initial volume, final volume, and rapidity of expansion are tailored by individual surgeons to meet patient goals and expectations and can never be fully standardized. The development of skin-sparing and, more recently, nipple-sparing techniques also adds a distinct element to this variability.

We were recently involved in a study exploring the outcome of breast implants following conservative mastectomy and SSM, examining the complication and reoperation rates in patients who underwent delayed versus immediate reconstruction, as well as patients who did and did not undergo radiation therapy (28). In several hundred patients, we found the overall complication rate of our implant-based reconstruction to be 15%, with a reoperation rate of 10%. This is lower than many of the previously described studies. Not only were we able to conclude that implant-based reconstruction can be associated with a low complication rate, even in the setting of radiotherapy, but that immediate reconstruction is also associated with a statistically significant lower reoperation rate. Previous studies have concluded that radiation therapy is associated with an unacceptably high rate of capsular contracture and rupture of the implant envelope or capsule (1,22,61), with a study by Spear and Onweyu in 2000 comprising 40 consecutive patients undergoing staged expander/implant placement and radiotherapy, showing a capsular contracture rate of 21% in the irradiated group vs. 0% in the control group (62). Our findings did not echo these. While we found irradiated breasts having a statistically higher reoperation rate, overall complication rates were similar to non-irradiated breasts, and we postulate that with improvements in the targeting of radiotherapy in order to limit damage to surrounding tissue, improved surgical techniques, or better quality of implants, past conclusions may be overstated to current thinking.

In comparing implant and autologous reconstruction, the literature is varied, with some authors finding no
difference between autologous and implant reconstruction, both overall and in the setting of radiotherapy, with Rosen and colleagues finding that the complication rates were similar between TRAM and tissue expander/implant reconstruction for breast reconstruction (63), and this has been echoed in other series (64–66). In light of these findings, the studies described above have varied in their conclusions. Several conclude that delayed reconstruction results in fewer complications and better outcomes, and others suggest that immediate reconstruction is safe and has no adverse consequences over delaying reconstruction. A further compromise, the ‘delayed-immediate’ reconstruction has also been postulated, in which a two-stage approach comprises a tissue-expander in the first stage, and autologous reconstruction ensuing if radiation is subsequently not required (67). The group at greatest risk for requiring adjuvant radiotherapy, those with locally advanced or multifocal disease, larger tumors and/or nodal metastases, certainly warrant greater consideration of a delayed reconstruction. However, this group is not always easily determined preoperatively, as although preoperative ultrasound can predict nodal status, there is a low sensitivity for small macro-metastases and/or micrometastases (68). Similarly, both axillary node frozen section and imprint cytology have significant false-negative rates making intraoperative prediction also difficult, and thus it is only post-operatively that a complete management plan can be formulated (69,70). As such, a significant number of those not expected to require adjuvant radiotherapy will ultimately be found to require it, warranting consideration of planning a delayed reconstruction from the outset.

A range of techniques have been introduced to ‘protect’ implants from the deleterious effects of radiotherapy. While the addition of overlying autologous tissues is an established technique, particularly with the use of local perforator flaps but also more distant regional or free flaps, more recent techniques have also been introduced. Acellular dermal matrix as an implant cover can reduce infection and capsular contracture rates even in the setting of radiotherapy (71), however the evidence for this is not yet well established, with more studies certainly needed (72).

**Timing**

Essential to the use of either implant or autologous reconstruction is the timing of both radiotherapy and reconstruction. In some settings, there is a preference to immediate radiotherapy, but where the oncology of the tumour permits delay to administration of radiotherapy, some principles can improve the reconstructive outcome. In implant reconstruction, there is a substantial benefit to maximising tissue expansion prior to radiotherapy - by allowing an inserted tissue expander to reach full volume and preferably to swap to a definitive implant prior to radiotherapy, the deleterious effects of radiotherapy can be minimised, in terms of soft tissue contracture and tissue loss. This will clearly eliminate the need to expand irradiated tissues, an almost impossible feat.

Autologous tissue transfer is advantageous in the irradiated situation, as the transfer of any non-irradiated tissue (whether locoregional or free tissue transplantation) into an irradiated bed will ‘revascularise’ that tissue and reduce the deleterious effects of the radiotherapy in the region - fibrosis, contracture and wound breakdown. If autologous tissue alone is planned for reconstruction, use of a tissue expander to hold the soft tissue envelope out to stretch and reaching a desired volume, can maximise the amount of available regional tissue, and minimise the amount of tissue needing transfer. Irradiation while fully expanded, but prior to free tissue transfer, can maximise these benefits, while maintaining the importation of non-irradiated tissue in a transferred flap.

**Modern techniques**

A range of techniques have been introduced to ‘protect’ implants from the deleterious effects of radiotherapy. While the addition of overlying autologous tissues is an established technique, particularly with the use of local perforator flaps but also more distant regional or free flaps, more recent techniques have also been introduced. Acellular dermal matrix as an implant cover can reduce infection and capsular contracture rates even in the setting of radiotherapy (71), however the evidence for this is not yet well established, with more studies certainly needed (72).

Fat grafting is another evolving technique in breast reconstruction that will herald new discussions on this front. Fat grafting has been successfully used to augment the reconstructed breast in the setting of both autologous and implant reconstruction (73–77), as well as being successfully used in the setting of primary breast reconstruction by fat grafting alone (78). In the setting of radiotherapy, there is discussion in the literature that the importation of tissue that becomes well-vascularised through grafting, particularly adipose-derived stem cells, can ‘revascularise’ the irradiated bed and reduce radiotherapy-related complications (77,79).
The use of fat grafting in the breast to achieve these ends has been described for both pre-radiotherapy and post-radiotherapy scenarios with benefit (76,80). Phulin et al. (2009) used fat grafting in irradiated head and neck tissues, and found an improvement in the quality of skin radiation damage after fat injection (79). They postulated that clinical improvement could be induced by an increase in vascularization and a revitalization of interstitial tissues, through an enhancement of angiogenesis via the secretion of growth factor and extracellular matrices. The adipose tissue is a potent source of multipotent stem cells, such as mesenchymal stem cells, and their intrinsic ability to secrete growth factors, in particular, angiogenic and antiapoptotic factors has been widely described (77,79).

As such, the literature is still evolving as to the relative role of autologous vs. alloplastic reconstruction in the setting of radiotherapy, and the more recent introduction of acellular dermal matrix and other compounds further complicate the evidence. Fat grafting and evolving techniques in breast reconstruction will herald new discussions on this front. What is clear is that breast reconstruction plays a highly important role in the management of patients with breast cancer, from a psycho-social and sexual stand-point, and that immediate breast reconstruction does not impair the oncologic safety of breast cancer management, with no increase in local recurrence rates, and no delays in the initiation of adjuvant chemotherapy or radiotherapy. Both neoadjuvant and adjuvant radiotherapy can increase the incidence of post-operative complications, with greater effects in the setting of postoperative radiotherapy, and if adjuvant radiotherapy can be predicted, a delayed reconstruction should be considered. However, a comparison of implant reconstruction to autologous techniques is not clear-cut.

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