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Scientific Article

Interplay of Oncoplastic Reconstruction and Adjuvant Radiation Therapy in Breast Cancer

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Purpose: Oncoplastic breast surgery (OBS) combines breast cancer tumor removal with the cosmetic benefits of plastic surgery at the time of breast-conserving surgery. Potential advantages of OBS include wider surgical margins around the tumor bed, while the natural shape and appearance of the breast are maintained more than standard lumpectomy procedures. However, limited information is available regarding the potential effect on adjuvant radiation treatment planning.

Materials and Methods: Women with localized breast cancer undergoing lumpectomy with immediate OBS and adjuvant radiation therapy between 2014 and 2019 were reviewed. OBS was performed using volume displacement techniques and patients received whole-breast irradiation with 3-dimensional conformal radiation therapy.

Results: Volume of additional ipsilateral breast tissue removed during OBS ranged from 21 to 2086 cm^3 (median, 304 cm^3), 29% of patients had >500 cm^3 of tissue removed. Surgical margins were positive in 12.5% and were not affected by volume of breast tissue removed (445 vs 439 cm^3). Patients with surgical clips more often received a lumpectomy bed boost (75.9% vs 50.0%), boost volumes were on average 157 cm^3 with clips versus 205 cm^3 without clips. Mean V105 was comparable in patients with >500 cm^3 tissue removed and irradiated breast volume >1000 cm^3, while higher absolute volumes were found in patients with >26 cm posterior separation (58.0 cm^3 vs 102.7 cm^3; $P = .07$). No meaningful difference was observed in Dmax or radiation coverage (95% of the volume receiving 95% of the prescription dose) for patients with >26 cm posterior separation, >500 cm^3 of breast tissue removed, or irradiated breast volume >1000 cm^3.

Conclusions: Radiation dosimetry plans for patients undergoing oncoplastic surgery were acceptable and no significant radiation or surgical advantage was gained in patients with more tissue removed. Our study stresses the importance of clear communication between surgeons and radiation oncologists about sufficient marking of the lumpectomy cavity, using practices that minimize the need for re-excisions and minimize lumpectomy cavity disruption during rearrangement.

Introduction

Early stage breast cancer is now commonly treated with lumpectomy followed by adjuvant radiation as a form of breast-conserving therapy, whereas historically women received mastectomy with removal of the entire breast. This tissue preservation approach was a major step in maintaining breast appearance; however, advances in

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breast conservation have continued to improve. In conjunction with breast-conserving therapy, there has been wide acceptance and an increase in utilization of oncoplastic techniques for the treatment of breast cancer.[1] Oncoplastic techniques can be used in situations in which the resection alone would yield an unacceptable cosmetic outcome.[2] Increasingly, oncoplastic breast surgery (OBS) is being used to reshape the breast and fill defects in the tissue from the lumpectomy cavity, avoiding the creation of a significant breast deformity. This is often carried out with a reduction mammoplasty or mastopexy; a balancing procedure is often offered for the contralateral breast. Potential advantages of OBS include wider surgical margins around the cancer, achieved by removing large portions of the breast tissue, while the natural shape and appearance of the breast are maintained more than in standard breast resections.[3]

Approximately two-thirds of patients with early-stage breast cancer will undergo breast-conserving surgery as a component of their cancer care.[4] Radiation is frequently paired with breast-conserving surgery to reduce rates of local recurrence and provide equivalent oncologic outcomes to mastectomy.[5] In addition, radiation has been shown to improve survival compared with lumpectomy alone in randomized studies.[6]

Initially there was hesitation with OBS in patients requiring radiation due to concern for worse aesthetic outcomes, particularly due to evidence showing worsening cosmesis with increasing breast tissue resection volumes after standard lumpectomy followed by postoperative radiation.[7-9] Additionally, adoption of shorter hypofractionated radiation treatments raised the concern for theoretical increased fibrosis with higher daily dose of radiation. Furthermore, some oncoplastic techniques pose a challenge for target and delivery of adjuvant postoperative radiation. An OBS with significant volume displacement after lumpectomy can potentially relocate the primary tumor site and may impede identification of the tumor bed postoperatively. This challenging situation increases the difficulty in delineating an area for a tumor bed boost in patients who stand to benefit, potentially increasing concerns for higher recurrence rates, and excludes appropriately selected patients from partial breast irradiation.

On the upside, a reduction mammoplasty for women with large breasts may theoretically improve radiation set-up and minimize toxicity. We sought to review our practice and outcomes in patients undergoing OBS procedures followed by radiation.

Methods

Patient selection

After institutional review board approval, the medical records of patients with localized breast cancer undergoing lumpectomy with OBS and adjuvant radiation therapy between 2014 and 2019 were reviewed at a single institution. Patients included women over 18 years of age with localized breast cancer treated with whole-breast radiation. Patients with in situ disease or positive nodal status were included, but patients with synchronous bilateral tumors were excluded. A total of 92 patients were identified who underwent lumpectomy followed by immediate OBS.

Patients and tumor characteristics

Data was collected on patient characteristics, including age, race, and body mass index (BMI). Tumor characteristics were also recorded, including laterality, size, margin status, histology, grade, tumor markers, and nodal involvement. Documented treatment details included systemic therapy use, timing of surgery and radiation, extent of axillary dissection, volume of breast tissue removed bilaterally, radiation doses, and field size. Specific details to radiation planning included beam energy, breast volume, use of boost, boost volume, identification of clips in the target volume, posterior separation of breasts, hot spots, and quality of coverage of the target volumes. Margin status was determined postoperatively by pathologists, with positive margins having ink on tumor and close margins defined as <2 mm for invasive ductal carcinoma (IDC), invasive lobular carcinoma (ILC), and ductal carcinoma in situ (DCIS).

Radiation treatment

Patients were treated with external tangential beam radiation with 3-dimensional CT treatment planning. Simulation and treatment of all patients took place in the supine position on a breast board with arms overhead. Target volumes and organs at risk were contoured according to the Radiation Therapy Oncology Group (RTOG) guidelines.[10] Clinical and radiographic information were used to contour the lumpectomy bed, including mammographic images, surgical clips, lumpectomy scar, excision cavity volume, and seroma. The Varian Eclipse treatment planning system was used to obtain dosimetric variables. Breast volumes were reported in cubic centimeters (cm^3). Posterior separation was defined as the distance along the posterior border of the treatment tangents from the medial to lateral edge of the treated tissue. Field-in-field optimization was used to improve dose homogeneity and distribution. Hypofractionation was defined as >2 Gy per fraction (most commonly 40.05 Gy in 15 fractions) and conventional fractionation defined as ≤2 Gy per fraction (most commonly 50.00 Gy in 25 fractions). For hypofractionation plans, a maximum hotspot of 107% was used for dosimetric planning. Targeted boost radiation to the tumor bed was given at the discretion of the radiation oncologist, consisting of an additional 10 to 16 Gy with either photons or electrons delivered in 4 to 8 fractions. Boost volumes were determined based on preoperative imaging, seroma formation, and/or clips left by the surgeon. Patients were seen weekly during radiation treatment to assess toxicity, and follow-up was arranged within 3 months of treatment completion. Physician-reported skin toxicity was recorded according to the RTOG criteria.[11] Length of follow-up was calculated using the last day of radiation treatment and the date of the most recent follow-up visit.

Surgical technique

All patients underwent lumpectomy to remove the primary tumor by the breast surgical oncologist. Sentinel lymph node biopsy and/or axillary lymph node dissection was performed as indicated. OBS was performed by the plastic surgeon immediately after lumpectomy. Contralateral balancing procedures were performed in most patients. OBS was typically carried out through either volume displacement or volume replacement techniques. At this institution, reconstructive surgeons use predominately volume displacement techniques for breast reshaping, including mastopexies/reductions. These procedures rely on advancement, rotation, or transposition of a large area of breast to fill a small-to-moderate−sized defect.[12] Women with larger or ptotic breasts are often candidates for oncoplastic reduction and this technique is commonly used at our institution. Tissue density was assumed as 1 gm/cm^3 and amount of tissue removed was reported in cm^3, to remain consistent with recorded breast volume units (cm^3) included in radiation treatment plans.

Statistics

Frequencies, proportions and means were used to describe clinical characteristics of study participants. Differences between groups were compared using a *t* test for continuous variables or χ^2 test for categorical variables. All reported *P* values were 2-sided, and values less than .05 were considered statistically significant. Statistical analyses were conducted using IBM SPSS Statistics for Windows (v. 25.0).

Results

Patient characteristics and surgery outcomes

Median age was 56 years (range, 30-73) for patients undergoing OBS. Most patients had estrogen receptor (ER) positive tumors (74%), a low pathologic tumor stage (79% < pT2), pathologically negative nodes (76%), and grade 1 to 2 disease (77%). Percentage of patients included with BMI >30 was 58%. Patient characteristics are shown in Table 1. The volume of additional ipsilateral breast tissue removed during OBS ranged from 21 to 2086 cm^3 (median, 304 cm^3) and contralateral ranged from 6 to 1789 cm^3 (median, 325 cm^3). Twenty-nine percent of patients had >500 cm^3 of breast tissue removed from the ipsilateral breast.

Surgical margins were positive in 12.5% (n = 10) of patients with residual disease at the time of lumpectomy. Patients with pure IDC were less likely to have a positive margin (3.8% of IDC, 11.4% of DCIS or mixed DCIS/IDC, and 40% of ILC or mixed ILC/IDC; *P* = .016). Only 3 of these 10 patients with a positive margin underwent re-excision, and with a median follow-up of 71.2 months (range, 15.2 − 91.9), there were no local recurrences within this group. An additional 31.3% of patients had close margins <2 mm. Histology for patients with either a positive or close margin was 26.9% of IDC, 45.5% of DCIS or mixed DCIS/IDC, and 80.0% of ILC or mixed ILC/IDC (*P* = .014). Lymphovascular space invasion (LVSI) and high tumor grades were not associated with positive margins. The mean volume removed was not significantly different between patients with a negative or positive margin (439 vs 445 cm^3, respectively; *P* = .96). Most patients started adjuvant radiation within 8 weeks from surgery or adjuvant receipt of chemotherapy (92.3%). Only 6 patients (6.5%) developed an infection requiring aspiration or antibiotics. Extremity lymphedema developed in 16.7% of patients and breast lymphedema in 24.4%.

Effect on radiation treatment

Irradiated breast volumes ranged from 303 to 2750 cm^3 (median, 1268 cm^3). Patients more frequently received hypofractionation (70 of 92, 76%) versus conventional fractionation (22 of 92, 24%), particularly among patients with negative nodes (62 of 70, 88.6%) compared with node-positive patients (8 of 22, 36.4%; *P* < .01). Radiation boost dose was delivered to 74% of oncoplastic patients; this included 9 of 10 patients who had a positive surgical margin. Among patients not receiving a boost, one had node-positive disease and 7 had positive or close margins <2 mm, which are typically indications for tumor bed boost due to higher risk of recurrence. Patients with clips to define the cavity were more likely to receive a boost (75.9% vs 50.0%). In patients without clips, boost volume was usually delivered to the quadrant involved, often with review of contours by the breast surgeon(s). The presence of clips did not significantly change the boost volume (mean 157 cm^3 vs 205 cm^3). Mean volume of the boost was similar for patients with less or more than 500 cm^3 removed (200 cm^3 vs 221 cm^3). The median

Table 1 Characteristics for lumpectomy patients undergoing oncoplastic reconstruction

	Oncoplastic patients	
Variable	No.	Percentage
Total patients	92	100
Pathologic T stage		
pT0	12	13
pTis	12	13
pT1	49	53
pT2	17	19
pT3	2	2
Pathologic N stage		
pN0	70	76
pN1	17	19
pN2	4	4
pN3	1	1
Histology		
DCIS	11	12
IDC	38	41
ILC	8	9
IDC and DCIS	33	36
IDC and ILC	2	2
Grade		
1	18	19
2	53	58
3	21	23
LVSI	12	13
Positive margin	10	11
Axillary staging		
None	6	6
SLNB	77	84
ALND	9	10
ER positive	68	74
Her2 positive	12	13
Chemotherapy	53	58
Neoadjuvant	24	26
Adjuvant	22	24
Both	7	8
Hormone therapy	64	70
Left breast	61	66
BMI >30	53	58
Radiation fractionation		
Conventional fractionation	22	24
Hypofractionation	70	76

V105% and Dmax for oncoplastic patients was 56 cm^3 (range, 0-578 cm^3) and 107% (range, 105-109%), respectively.

Women with remaining breast volume >1000 cm^3 on CT simulation imaging included 80.6% of the cohort, and 50.0% of all patients had posterior separation >26 cm. Patients with larger posterior separation (>26 cm) were likely to have plans with photon energies of 15MV or higher (61.1% vs 38.9%; P = .04). Mean breast volume irradiated was higher in patients with larger amount of tissue removed (>500 cm^3) at time of reduction, 1555 cm^3 versus 1317 cm^3 (P = .067). There was a small, but significant difference in mean Dmax for larger posterior separation (107.1% vs 106.5%; P = .01), but not for patients with >500 cm^3 tissue removed or breast volume >1000 cm^3. Mean V105 was comparable in patients with >500 cm^3 tissue removed and breast volume >1000 cm^3, whereas higher absolute volumes were found in patients with larger posterior separation (58.0 cm^3 vs 102.7 cm^3; P = .066). There was no compromise in coverage, defined as 95% of the volume receiving 95% of the prescription dose, for patients with >500 cm^3 tissue removed, breast volume >1000 cm^3, or posterior separation >26 cm. Grade ≥2 skin toxicity at the end of radiation treatment occurred in 18.1% of patients.

Discussion

This study compared the differences in patients undergoing lumpectomy and radiation with OBS. Previous studies have sought to evaluate the relationship between volume of specimens removed and margin status in OBS compared with standard lumpectomy. Kaur et al was able to show that oncoplastic surgery results in larger excision volumes, and as a result, patients were more likely to have more margin-free procedures.[3] Our results are inconsistent with these prior reports. When examining only oncoplastic patients in our population, excision volumes were relatively similar in patients with positive and negative margins. There is a misconception that larger volumes of breast tissue removed during oncoplastic reduction minimizes surgical margin positivity. The location of additional tissue removal is often chosen based on rearrangement for ideal cosmesis and preserved sensation, rather than to add margin to the lumpectomy bed. As seen in this study, volume removed during OBS did not correlate with more margin-free procedures, and margin positivity rates were relatively high, especially in patients with pure DCIS and ILC. Routine cavity shave margins of the primary tumor became a standard of care based on randomized data during the course of this study.[13] In the setting of OBS, it can be difficult to take the patient back for re-excision of positive margins due to the rearrangement of the breast tissue and tumor bed, which can lead to disorientation of cavity margins. Our results suggest that routine cavity shave margins or intraoperative frozen section review should be considered standard in patients planned for oncoplastic reduction. This ensures the tissue removed for reduction is contributing to the goal of improving margin width, and subsequent re-excisions if needed could then be performed with localization of the tumor bed before rearrangement. Removal of additional margin in patients with DCIS and ILC may be of special interest.

Surgical clip placement at the time of lumpectomy was shown to be critical for tumor bed delineation by the radiation oncologist. Patients with clips were more likely to receive a tumor bed boost with radiation therapy, which remains important for local disease control in appropriately selected patients.[14-16] Not all patients with discernible clips received a boost. Patients with tissue rearrangement that displace the clips across several quadrants of the breast makes it challenging to deliver a targeted boost. Minimizing the extent of rearrangement of the tissue in the tumor bed will further aid in radiation boost planning, as patients with clips spanning multiple quadrants have higher risk of cosmetic toxicity with a boost treatment.[14] When performing oncoplastic breast surgery, plastic surgeons may fill the tumor bed with tissue to remove dead space in order to prevent deformation caused by adjuvant whole-breast irradiation. However, this method inherently disrupts the tumor bed and impairs adequate delineation for the radiation oncologist. Increased communication between plastic surgery and radiation oncology can reduce this disruption to improve localization and targetability of the tumor bed.

Accurate tumor bed localization is particularly important when considering partial breast irradiation (PBI). PBI is an advanced radiation therapy technique that delivers higher dose per fraction over a shorter period only to the tumor bed. Recent studies suggest cosmetic advantages and noninferior local control with external beam PBI in early-stage breast cancers, which has increased recent utilization of these techniques.[17,18] In addition to reducing treatment to surrounding normal breast and skin tissue, PBI also limits dose to critical structures such as the heart and lungs. Furthermore, regimens with only 5 fractions of radiation can increase access to radiation and reduce financial toxicity. Appropriate candidates for PBI should be discussed preoperatively, focusing on preservation of the tumor bed and adequate localization with clip placement, allowing patients the benefit of partial breast treatment.

Radiation dosimetry details for patients undergoing oncoplastic surgery were acceptable and no significant dosimetric advantage was gained in patients with more tissue removal. Dosimetric coverage and hotspots are often related to the distance along the posterior edge of the radiation beam, and hence the size of thoracic cavity, rather than the volume of the breast, is typically the main driving factor. This most likely explains our dosimetric findings. The optimum breast target constraint is unknown, whether to control for maximum point dose or a volumetric constraint (ie, V105, V107), but attempts to minimize these parameters should be undertaken as they likely result in superior cosmesis.[19-22] Our study stresses the importance of clear communication between surgeons and radiation oncologists about sufficient marking of the lumpectomy cavity, using practices that minimize the need for re-excisions, and minimizing lumpectomy cavity disruption during rearrangement.

The retrospective design from a single institution represents the main limitation of this study, limiting the ability to draw definitive conclusions. The quality of any retrospective paper is dependent on the accuracy and completeness of the medical record. Larger prospective studies with longer follow-up are needed that collect quality-of-life outcomes. In addition, photographic assessment of early and late cosmetic effects by blinded viewers would provide valuable results. Clinical assessment for edema, breast shrinkage, pigmentation changes, and palpable induration would also provide more context.

Conclusion

Our results show radiation treatment plans for oncoplastic surgery patients were acceptable and no significant advantage was gained in patients with more tissue removal. Our study highlights the importance of clear communication between surgeons and radiation oncologists to minimize tumor bed disruption during OBS. Surgical margins remain an issue for improvement. Our study suggests that routine shave margins should be taken at the time of lumpectomy in OBS patients to reduce the risk of positive or close margins and that special surgical considerations may be needed in patients with pure DCIS and ILC. Future study should aim to collect quality-of-life outcomes among patients undergoing oncoplastic breast surgery and adjuvant radiation therapy.

Disclosures

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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