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Critical Review

Oncoplastic breast surgery in the setting of breast-conserving therapy: A systematic review

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Abstract

Breast-conserving therapy (BCT), or breast-conserving surgery with adjuvant radiation therapy, has become a standard treatment alternative to mastectomy for women with early-stage breast cancer after many long-term studies have reported comparable rates of overall survival and local control. Oncoplastic breast surgery in the setting of BCT consists of various techniques that allow for an excision with a wider margin and a simultaneous enhancement of cosmetic sequelae, making it an ideal breast cancer surgery. Because of the parenchymal rearrangement that is routinely involved in oncoplastic techniques, however, the targeted tissue can be relocated, thus posing a challenge to localize the tumor bed for radiation planning. The goals of this systematic review are to address the challenges, outcomes, and cosmesis of oncoplastic breast surgery in the setting of BCT.

Introduction

Breast-conserving surgery (BCS), or partial mastectomy with adjuvant radiation therapy (ART), has become a standard treatment alternative to mastectomy for women with early-stage breast cancer after many long-term studies have reported comparable rates of overall survival and local control.[1-6] In BCS, the removal of the tumor leaves a postsurgical deformity, or cavity, which can have a major effect on cosmesis. As surgical techniques advanced in the early 1990s, Audretsch introduced "oncoplastic breast surgery," an integration of plastic surgery techniques with BCS to reduce cosmetic defect following partial mastectomy.[7]

Oncoplastic breast surgery consists of various techniques that allow for an excision with a wider margin and a simultaneous enhancement of cosmetic sequelae, making it an ideal breast cancer surgery.[7,8] A 2008 audit of a specialist breast practice reported that breast reconstruction and oncoplastic operations accounted for 28% of all

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breast-cancer related procedures, indicating a rising utilization of oncoplastic breast surgery.[9] The surgical techniques used in oncoplastic breast surgery in the setting of breast conservation can be largely divided in 2 categories: volume displacement (VD) and volume replacement (VR).[8] Appropriate technique is chosen based on patient and tumor characteristics because the outcomes of the surgery may depend on the type of technique.

Adjuvant therapy, however, is ideally not affected by the surgical technique. Breast-conserving therapy (BCT), which consists of BCS followed by whole breast irradiation (WBI), has been long established as a standard alternative to mastectomy.[1,2,10] A total dose of 45 to 50 Gy in 25 daily fractions of 1.8 to 2 Gy over 5 weeks and a total of 10 to 16 Gy in 5 to 8 fractions are the conventional delivery schedules for WBI and boost irradiation, respectively.[10] Hypofractionated WBI, which consists of higher fraction doses (>2 Gy) delivered in fewer fractions over a shorter treatment course, is an alternative treatment to the conventional WBI in the setting of BCT.[11] A total dose of 40 to 44 Gy in 13 to 16 fractions over 3 weeks is the conventional delivery schedule for hypofractionated WBI.[11] The tumor-bed boost can be administered after WBI to reduce local recurrence rates in the setting of BCT. The use of boost after WBI has been demonstrated in multiple randomized studies to decrease local recurrences.[12-14] Because younger women are at a greater risk of local recurrence, and women who undergo oncoplastic breast surgery tend to be of younger age, a boost would be of greater benefit to them in terms of local control.[2,12,13,15-24] In addition to the conventional BCT, considerable variations exist in delivering radiation therapy (RT) after oncoplastic breast surgery. Recently, the use of Accelerated Partial Breast Irradiation (APBI) has been demonstrated as a possible alternative to WBI for patients who meet the selection criteria.[24] By targeting specifically the tumor cavity within a shorter period, APBI offers potential benefits by decreasing radiation dose delivered to normal tissue outside of the target volume and increasing accessibility of treatment to patients.[24]

Because of the parenchymal rearrangement that is routinely involved in oncoplastic techniques, however, the targeted tissue can be relocated, posing a challenge to localize the tumor bed.[12,25] Moreover, the boost irradiation may diminish cosmesis, which would offset the principal goal of oncoplastic breast surgery to enhance posttreatment cosmesis. To determine the optimal type of RT after oncoplastic BCS, the specific delivery method including the dosage, fraction, and timing needs to be reported in detail.[26,27] This systematic review aims to address the outcomes of oncoplastic BCS with adjuvant breast RT by evaluating local control and cosmetic sequelae to optimize future treatment plans for patients with breast cancer.

Methods

A comprehensive literature search of PubMed was performed using combinations of the following search terms: oncoplastic breast surgery, breast conserving surgery, breast cancer, RT, radiotherapy, volume displacement, volume replacement, breast tissue rearrangement, and breast reconstruction in articles published between January 1995 and January 2015. Trials eligible for this review included randomized control trials, cohort studies, and retrospective series. The titles and abstracts of the potentially relevant publications (n = 1194) were examined to include only English-language studies that report oncoplastic breast surgery followed by RT, and to eliminate studies that fall under the following exclusion criteria: (1) including only surgical techniques; (2) case reports or reviews; (3) participating number of patients <30; and (4) involving complete mastectomy. Qualified studies were then cross-referenced until the search strategy was exhausted. Among 109 articles that were initially identified for full review, 41 were selected for inclusion (Table 1). The remaining 68 articles were not included because of the use of tissue expander or implants, preoperative RT, techniques involving lipofilling, prior history of breast augmentation, and lack of cosmesis report and/or recurrence rate. The rates of satisfaction rating or local recurrence used in the analysis were calculated based on the number of patients with such events provided in each study. A generalized linear mixed model with a random effect on study was used to estimate the overall probabilities of events of interest. Estimated probabilities along with 95% confidence intervals (CIs) were reported. All statistical analyses were performed using SAS 9.4 (Cary, NC).

Results

Surgical techniques used in oncoplastic BCS

As mentioned previously, oncoplastic BCS can be largely divided in 2 types of surgical techniques: VD and VR. VD involves mobilizing local glandular flaps and redistributing them to the resection defect, resulting in a net loss of breast volume.[8] Using this principle of VD, reduction mammoplasty can be performed on patients with large breasts. On the other hand, VR relies on harvesting autologous tissue from a remote site and transferring the flap into the resection defect while preserving breast volume.[8] Women with small breasts or large tumor/breast ratio may not be suitable candidates for VD, because they do not have sufficient breast tissue to be redistributed to the resected region. For these women, VR may serve as an alternative by using tissue from a remote site to reconstruct the resection defect; however, should they require a complete mastectomy in the future,

Table 1 Patient demographics and tumor characteristics

Study	Patient no.	Mean age (range)	Tumor stage	Receptor status (%)	Chemotherapy (neoadjuvant/ adjuvant, %)	Mean tumor size (range, mm)	Mean specimen weight (range, g)	Positive margins (%)	Oncoplastic surgery
Nizet et al, 2015[60]	72	57 (36-78)	pTis (6%), pT1a-1b (10%), pT1c (38%), pT2-3 (40%) Nx (4.3%), N0 (69.4%), N1mi (4.3%), N1a (13.9%), N2a (5.7), N3a (0%)	ER-/PR- 17.9	12.5/—	18.7 (0-80)	110 (17-903)	0	VD (RM)
Roth et al, 2014[37]	134	—	pNx (10%), pN0 (88%), pN1mi (2%), pN1b (1%)	ER+/PR+ 79 ER+/PR- 9 ER-/PR+ 1.5 ER-/PR- 11 HER2 - 38	—/—	14 (3-35)	—	0	VD
Yang et al, 2011[42]	58	46	0 (17%), I (55%), IIa (17%), IIb (10%)	—	—/48	—	84 (29-140)	—	VD
Caruso et al, 2008[61]	61	45.3	pT1a (3%), pT1b (10%), pT1c (44%), pT2 (41%), pT4 (2%) N0 (68%), N1 (29%), N2 (3%)	ER+ 1.6 ER+/PR+ 79 ER-/PR- 23	—/—	—	—	0	RM
Ballester et al, 2009[43]	86	54 (29-75)	T0 (36%), T1 (17%), T2 (46%), T2 (1%)	—	16/—	33.6 (0-140)	150 (28-484)	4.7	VD (RM)
Rageth and Tausch, 2009[44]	134	—	—	—	—/—	—	—	—	VD
Maguire, 2013[45]	79	61.9 (34.9-76.9)	0 (9.2%), I (60.5%), IIA (17.1%), IIB (4.0%), III (9.2%) Tis (9.3%), T1(74.7%), T2 (16.0%) N0 (73.7%), N1 (16.7%), N2 (3.3%), N3 (6.7%)	—	10/28	—	—	0	VD (RM)
Lee et al, 2014[62]	213	45.7 (23-65)	0 (8.3%), I (45.4%), IIA (28.7%), IIB (11.1%), IIIA (5.1%), IIIB (0%), IIIC (0.5%), IV (0.9%)	—	77.5/—	—	148.4 (50-408)	—	VR
Gendy et al, 2003[63]	49	48 (34-69)	N0 (71%), N1 (27%), NA (2%)	— —	—/—	22 (7-50)	—	0	VR
Losken et al, 2004[64]	39	49 (28-73)	0 (5%), T1N0 (49%), T1N1 (5%), T2N0 (13%), T2N1 (13%), T3N0 (5%), T3N1 (5%), IV (5%)	ER+/PR+ 64 ER-/PR- 20 ER+/PR- 8 ER-/PR+ 8	12.8/—	26 (2-65)	—	0	VR
Massa et al, 2015[38]	32 ERT 16 IORT16	52 (37-78)* 62 (48-79)**	T1b - T2* Tis - T2**	—	—/—	—	—	0	RM* RM**
Silverstein et al, 2015[32]	311 Standard, 245; extreme, 66	—	—	—	—/—	23* 77**	142* 217**	3.7* 16.7**	RM* RM**
Egro et al, 2015[47]	117	53.6	0 (15.4%), 1 (41.9%), 2 (9.4%), 3 (12.0%), unknown (3.1%)	—	19/46	17	524.4	—	RM
Eaton et al, 2014[65]	86	53 (34-80)	Tis (13%), T1 (47%), T2 (30%), T3 (6%), T4 (3%) N0 (76%), N1 (21%), N2 (2%), N3 (1%)	ER+ 59 HER2+ 20	—/59	—	—	0	RM
Schrenk et al, 2006[66]	121	59.2 (33-78)	DCIS III (9%), T1a (2%), T1b (9%), T1c (28%), T2 (40%), T4a (1%) LNP (64.8%)	ER+ 77 PR+ 66 HER2+ 82	12/29	DCIS, 52.4 (15-100); invasive, 21.2 (0-140)	267.6 (39-1090)	0	RM
Goffman et al, 2005[48]	57	—	T1 (33%), T2 (35%), T3 (12%), T4 (9%)	—	—/67	—	—	—	RM
Chang et al, 2004[40]	37	52 (34-77)	—	—	—/—	(6-52)	653 (144-1924)	0	RM
Munhoz et al, 2006[49]	74	46.6 (29-69)	T1 (55%), T2 (45%)	—	—/29.7	—	610 (215-950)	0	RM
Clough et al, 2003[15]	101	53 (31-91)	T0N0 (6%), T1N0 (12%), T1N1 (3%), T2N0 (50%), T2N1 (20%), T3N0 (2%), T3N1 (4%), T4N0 (3%)	—	16.8/—	32 (10-70)	222 (20-1900)	5	TM
Losken et al, 2007[50]	63	47 (11-75)	0 (25%), I (38%), II (10%), III (11%), LNP (19%)	—	—/—	—	236 (18-922)	0	RM
McCulley and Macmillan, 2005[51]	50	53 (35-69)	NI (44%), NII (44%), NIII (12%)	—	—/46	28	269 (30-736)	0	TM
Nos et al, 1998[52]	50	53 (41-71)	T0N0 (12%), T1N0 (10%), N1N1 (2%), T2 N0 (42%), T2N1 (26%), T3N0 (2%), T3N1 (2%), T4N0 (4%)	—	20/10	32.5 (15-60)	266 (40-1450)	6	TM
Fitoussi et al, 2010[53]	540	52 (28-90)	0 (22.8%), I (23.3%), IIA (32.6%), IIB (15.6%), IIIA (3.1%), IIIB (1.7%), IIIC (0.2%), unidentified (0.7%)	—	17.2/—	29.1 (4-100)	187.7 (8-1700)	7.4	TM
Chakravorty et al, 2012[12]	146	59 (26-83)	T1 (46%), T2 (48%), T3 (6%) LNP (20%)	—	25/35	21 (1-98)	67 (11-1050)	0	TM
Caruso et al, 2011[67]	50	—	Stage 0 [Tis, N0, M0] (3.8%),	ER-/PR- 22	22/—	17	—	2	TM

(*continued on next page*)

Table 1 (*continued*)

Study	Patient no.	Mean age (range)	Tumor stage	Receptor status (%)	Chemotherapy (neoadjuvant/ adjuvant, %)	Mean tumor size (range, mm)	Mean specimen weight (range, g)	Positive margins (%)	Oncoplastic surgery
			stage I [T1, N0, M0] (40.3%), stage II A [T1, N1, M0] (9.6%), stage II A [T2, N0, M0] (15.3%), stage II B [T2, N1, M0] (25%), stage III A [T1, N2, M0] (3.8%), stage III B [T4, N0, M0] (1.9%)	≥1 hormonal receptor, 82					
Meretoja et al, 2010[54]	68	57 (37-80)	—	—	—/67	22 (3-100)	—	0	VD (20) RM (48)
Rietjens et al, 2007[68]	148	50 (31-71)	pTis (7%), pT1a-1b (10%), pT1c (41%), pT2-3 (40%) NX (8%), N0 (41%), N1mi (5%), N1a (30%), N2a (9%), N3a (7%)	ER+/PR+ 72 ER-/PR- 24	0/60	15.4	198 (20-2100)	4.7	RM
Grubnik et al, 2013[55]	251	56.3 (28-80)	Tis (10%), T1a (2%), T1b (19%), T1c (36)%, T2 (29%), T3 (1%), T4(3%)	ER+ 77 PR+ 60 HER2+ 30 ER-/PR-/ HER2- 12	25.5/32	48 (0-85)	237 (17-1316)	0	TM
Bogusevicius et al, 2014[56]	60	55.8 (33-84)	IIIA (61.7%), IIIB (23.3%), IIIC (15%) T0N2 (1.6%), T1N2 (8.4%), T2N2 (31.7%), T3N1 (16.7%), T3N2 (3.3%), T4N0 (3.3%), T4N1 (13.3%), T4N2 (6.7%), any TN3 (15%)	ER+ 30 PR+ 30 HER2+ 3.3	70/—	23.9	—	0	VR (33) RM (14) VD (13)
Down et al, 2013[69]	37	57 (35-86)	—	—/—	—/—	—	231.1	0	VD (18) VR (19)
Kronowitz et al, 2006[29]	50	—	—	—	—/—	—	—	0	VD (14) RM (33) VR (3)
Tenofsky et al, 2014[57]	58	60.9 (35-85)	—	—	—/—	11.0 (0-50.0)	—	0	VR (43) VD (5) RM (14)
Hamdi, 2013[70]	119	48 (31-69)	—	—	—/—	—	—	0	VD (26) VR (93)
Veiga et al, 2011[41]	45	52 (33-72)	—	—	0/—	—	—	—	RM (11) VR (34)
Munhoz et al, 2011[58]	106	48.6 (29-68)	—	—	—/30.1	—	342 (87-910)	1.8	RM
Bamford et al, 2015[71]	68	52 (36-77)	—	ER+ 63.2 PR+ 22.1 HER2+ 11.8	22.1/—	(3-85)	436.7 (123-1330)	0	TM
Khafagy et al, 2012[46]	30	51.86 (30-70)	LNP (56.7%)	ER+ 53.3 PR+ 50 HER2+ 63.3	—/20	22 (10-42)	—	—	VD
Chang et al, 2012[72]	79	53.6	0 (18%), I (14%), II (41%), III (22%), and IV (2%); phyllodes (2%)	ER+ 66 PR+ 52 HER2+ 20	47/15	DCIS: 28 (0.5-170) IDC: 24 (2-89) Lobular carcinoma: 35 (16-80) Phyllodes: 57 (37-76)	—	0	RM
Munhoz et al, 2009[73]	218	49 (23-71)	—	—	—/39.9	22.9 (5-39)	362 (89-880)	0	VD (16.0%) VR (24.2%) RM (48.2%)
Munhoz et al, 2006[59]	39	—	T1 (51%), T2 (49%)	—	—/28.2	—	590 (200-910)	0	RM
Munhoz et al, 2006[74]	34	—	T1 (65%), T2 (35%)	—	—/35.2	—	310 (215-550)	0	VR

ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; LNP, lymph nodal positivity; N, nodal status; NR, not reported; PR, progesterone receptor; RM, reduction mammoplasty; T, tumor size; VD, volume displacement; VR, volume replacement.

* patients who received ERT

** patients who received IORT

reconstruction with autologous tissue will not be an option.[28,29] Because of potential donor site morbidity associated with VR[30,31] and restrictions on possible future surgeries,[28,29] VD is a preferred method when patients meet the criteria. Among the studies included in our review, 37 involved the use of VD, whereas only 11 involved VR.

Comparison of local recurrences and cosmetic outcomes between VD and VR

A total of 4170 patients were included in 41 studies. The range of patients' mean age in 41 studies was 45 to 62 years. The range of average tumor size was 11 to 77 mm (extreme oncoplasty was performed on a mean tumor

size of 77 mm in Silverstein et al[32]) and the range of average specimen weight was 84 to 653 g. Nodal status was reported in 17 studies. The majority of the patients had nodal status of N0 in 13 studies (range, 68-88%), and only 8 studies reported nodal positivity, 4 of which reported N3 (range, 1-15%). The surgical techniques involved 2 methods: VD (n = 37) and VR (n = 11). Reduction mammoplasty (n = 23) and therapeutic mammoplasty (n = 8) were categorized under VD (Table 1).

Of the 37 studies that implemented VD, 34 reported follow-up data. The mean follow-up in these studies was 39 months (range, 1-262 months). The local recurrence rate was reported in 35 studies (range, 0%-10%). The distant recurrence rate was reported in 23 studies (range, 0%-38.3%) and the mortality rate was reported in 19 studies (range, 0%-23%). Patient-rated cosmesis was reported in 17 studies and professional rating on cosmesis was reported in 18 studies. In the 17 studies that included patient cosmesis, 70% to 100% of patients reported excellent/good satisfaction. In the 18 studies that involved professional rating, excellent/good satisfaction was reported 57% to 96% of the time. The type of RT was identified in all studies (35 studies used WBI and 2 studies used APBI), although the dose-fractionation was reported in only 16 studies, with daily fractions over 5 weeks that ranged of from a total of 45 to 52 Gy. The use of boost RT was reported in 17 studies. The dose for boost RT with a range of 10 to 15 Gy was reported in 13 studies, whereas the fractionation schedule was reported only in 3 studies (Table 2).

Of the 11 studies that used VR, the mean follow-up, reported in 10 studies, was 40 months (range, 3 to 120 months). The local recurrence rate was reported in 10 studies (range, 0%-10%). The distant recurrence rate was reported in 2 studies (range, 10.3%-38.3%), and the mortality rate was reported in 2 studies (range, 5.1%-23.3%). Patient rating on cosmesis was reported in 6 studies and professional rating on cosmesis was also reported in 6 studies. Excellent/good cosmesis rating by the patients ranged from 82.3% to 92.3%, which was higher than that reported by professionals (33% to 87.2%). The type of RT was identified in all studies (all 11 studies used WBI), although the dose-fractionation was reported in only 5 studies, with daily fractions over 5 weeks ranging from a total of 45 to 52 Gy. The use of boost RT was reported in 3 studies, all of which reported a range of 10 to 15 Gy without specified fractionation schedule (Table 3).

Use of WBI after oncoplastic BCS

WBI along with tumor-bed boost irradiation has been long established as a standard adjuvant therapy for BCS.[12-14,33] The delivery schedule for WBI involves whole breast radiation to a total dose 45 to 50 Gy in 25 daily fractions of 1.8 to 2 Gy over 5 weeks, and was delivered to suitable patients (range, 62.7%-100%) in studies that provided adjuvant RT schedules. Patient refusal of recommended treatment was the main reason that adjuvant RT was not delivered in up to 37.3% in some studies. Hypofractionated WBI, which consists of higher fraction doses (>2 Gy) delivered in fewer fractions over a shorter treatment course, is an alternative treatment to the conventional WBI in the setting of BCT.[11] Although not all studies reported their fractionation scheme, those that reported it used the conventional scheme of a total dose of 40 to 44 Gy in 13 to 16 fractions over 3 weeks.

A total of 23 studies were identified that included data on local recurrences for patients who underwent oncoplastic BCS with WBI. Two studies were excluded from this analysis because of discrepancies between total number of patients and the number of patients receiving RT, as well as not providing information about local recurrence rates. As a result, only 21 studies were included in this analysis. The overall estimated probability of local recurrence when whole breast radiation was delivered after oncoplastic breast surgery was 0.015 (95% CI, 0.008-0.03).

Professional ratings regarding cosmesis were reported in 10 studies in patients who underwent oncoplastic BCS followed by WBI. The rating scales varied across studies, and cosmesis ratings >60%, 50%, and 66% were considered as satisfactory in 5-, 4-, and 3-point rating scale, respectively. The overall estimated probability of satisfaction based on professional ratings was 0.877 (95% CI, 0.784-0.934). Eight studies included data regarding patient rating of cosmesis. The overall estimated probability of satisfaction based on patient ratings was 0.913 (95% CI, 0.815-0.962).

Use of local boost RT after oncoplastic BCS

For early-stage breast cancer, local recurrences occur most commonly around the tumor bed.[34] The use of boost after whole breast radiation has been demonstrated in multiple randomized studies to decrease local recurrence[12-14,33]; therefore, it is reasonable to extrapolate that a local recurrence in the setting of oncoplastic BCS would be able to be minimized by administering the tumor-bed boost RT after WBI. However, because of the parenchymal rearrangement that is routinely involved in oncoplastic techniques, possible tissue relocation poses a challenge to localize the tumor bed for administration of boost radiation.[12,25] Moreover, the additional radiation exposure from the boost RT may potentially exacerbate cosmetic defect, which would offset the principal goal of oncoplastic BCS to enhance posttreatment cosmesis.[26,27]

The use of boost RT was reported in 15 studies, most of which used the conventional delivery schedule of a total of 10 to 16 Gy in 5 to 8 fractions. Three studies with

Table 2 Outcomes of volume displacement and RT

Study	Patients receiving RT (%)	RT dose-fractionation (Gy)	Patients receiving boost RT (%)	Boost RT dose-fractionation (Gy)	Patient rating on cosmesis	Professional rating on cosmesis	Local recurrence (%)	Distant recurrence (%)	Mortality (%)	Mean follow-up (mo, range)
Nizet et al, 2015[60]	94.4	41.6 Gy in 13 fx (6)/42.4 Gy in 20 fx (1)/42.5 Gy in 16 fx (13)/45 Gy in 20 fx (43)/ 46 Gy in 23 fx (1), 3 Gy in 25 fx (50)	80.6	6.6 Gy in 1 fx	—	—	1.4	1.4	0	32 (19-51)
Roth et al, 2014[37]	100	PDR: 50.4 Gy (63 hourly pulses, 0.8 Gy single doses) HDR: 32 Gy (BID in 4 Gy fx)	—	—	—	—	0.7	2.2	2.2	40 (4-106)
Yang et al, 2011[42]	100	—	—	—	83% excellent/ good at 12 mo	83% excellent/ good at 12 mo	0	—	—	21
Caruso et al, 2008[61]	100	50	—	10	—	—	1.6	9.8	8.2	68 (36-120)
Ballester et al, 2009[43]	—	—	—	—	—	93% excellent/ good	2.3	3.5	—	20 (1-80)
Rageth and Tausch, 2009[44]	62.7	—	—	—	97% favorable/moderate (patient/professional unspecified)		—	—	—	—
Maguire, 2013[45]	100	Median, 46 (in 1.8-2.0 Gy fx)	0	0	88% excellent/good between 1-3 years postsurgery	—	0	0	—	35
Rietjens et al, 2007[68]	95.3	50	95.3	10	—	—	3	13	7.53	74 (10-108)
Down et al, 2013[69]	—	—	—	—	—	—	0	—	—	29.3
Hamdi, 2013[70]	—	—	—	—	—	—	1.7	—	—	48 (6-120)
Khafagy et al, 2012[46]	100	—	100	—	Excellent in 80%, good in 13.3%, acceptable in 6.7 , 0% poor	Excellent in 73.7%, good in 20%, acceptable in 6.6% , 0% poor	0	0	—	24
Massa et al, 2015[38]	100* 100**	4550 (in 1.8-2 Gy fx) 5* times/wk 18-21**	100* 0**	10-16 (in 5-8 Gy fx) over 1-1.5 wk* 0**	100% favorable (scores >6)* 100% favorable (score >6)**	—	0* 0**	12.5* 0**	0* 0**	62* 35**
Silverstein et al, 2015[32]	100* 100**	—	100* 100**	—	—	—	1.2* 1.5**	—	—	24* 24**
Egro et al, 2015[47]	100	—	—	—	—	Mean 63.4%	—	—	—	46.1
Eaton et al, 2014[65]	100	45 (range, 45-54) in 1.8 Gy fx	58.1	14.92 (range, 6.42-20) in 2.14 Gy fx	—	—	7.0	2.3	4.7	54 (1.2-214.8)
Schrenk et al, 2006[66]	92.6	—	92.6	—	80% excellent 20% good	Mean 8.7 (range, 5-10)	0	2.5	1.7	32 (11-106)
Goffman et al, 2005[48]	84.2	50.40	—	10	38% excellent, 34% very good, 22% good, 2% fair, 4% poor		3.5	7	3.5	19.2
Chang et al, 2004[40]	100	—	—	—	70% excellent	—	0	0	—	—
Munhoz et al, 2006[49]	100	Maximum 45-50 in daily fx	100	10	Good/very good in 81%, satisfactory in 16.2%, and poor in 2.7%		0	—	—	22 (6-69)
Clough et al, 2003[15]	87.1	—	5	—	—	88% acceptable at 2 y; 82% acceptable at 5 y	6.9 IBTR 2.0 CBTR	12.9	7.9	46 (7-168)
Losken et al, 2007[50]	73	—	—	—	95% acceptable at 6 mo; average, 4.2	—	2	—	0	39
McCulley and Macmillan, 2005[51]	92	—	—	—	—	96% excellent/ good/satisfactory 4% poor	0	0	0	13 (3-32)
Nos et al, 1998[52]	76	52 (range, 47-56) over 5 wk	6	—	92% satisfactory at 1 y	85% satisfactory at 1 y	6	14	10	48 (14-140)
Fitoussi et al, 2010[53]	—	—	7.4	10	—	90.3% satisfactory at 5 y	6.8	—	7.1	49 (6-262)
Chakravorty et al, 2012[12]	90	—	—	—	—	—	2.7	1.3	—	28 (6-81)
Caruso et al, 2011[67]	100	50	100	10	—	—	2	2	2	72.6 (32-168)
Meretoja et al, 2010[54]	—	—	—	—	84% acceptable (patient/professional unspecified)		0	4.4	1.5	26 (6-52)
Grubnik et al, 2013[55]	90.8	—	90.8	—	70% happy, 25% satisfied, 6% dissatisfied	96% acceptable (excellent/ good/fair)	2.4	1.2	3.2	50 (15-115)
Bogusevicius et al, 2014[56]	100	Maximum 50 (in 25 fx)	0	0	92.3% excellent/ good	87.2% excellent/ good	10	38.3	23.3	86
Kronowitz et al, 2006[29]	100	Minimum 50	100	10-15	—	57% excellent/ good (VD + RM)	2	—	—	29

Table 2 (*continued*)

Study	Patients receiving RT (%)	RT dose-fractionation (Gy)	Patients receiving boost RT (%)	Boost RT dose-fractionation (Gy)	Patient rating on cosmesis	Professional rating on cosmesis	Local recurrence (%)	Distant recurrence (%)	Mortality (%)	Mean follow-up (mo, range)
Tenofsky et al, 2014[57]	93.1	—	—	—	86.2% favorable	—	0	—	—	24.6 (2.9-44.7)
Veiga et al, 2011[41]	93.3	—	—	—	Mean 10 at 12 mo	Mean 9.25 at 12 mo	1	—	—	—
Munhoz et al, 2011[58]	100	Maximum 45-50 daily fx	100	10	92.4% very satisfied/satisfied	—	6.6	2.8	—	47 (12-108)
Bamford et al, 2015[71]	100	—	—	—	—	—	0	5.9	5.9	36 (1-62)
Chang et al, 2012[72]	94.9	—	—	—	—	—	2.3	2.3	1.3	39 (10-130)
Munhoz et al, 2009[73]	100	Daily fx dosing up to total 45-50	100	10	—	—	5.5	—	—	48 (10-108)
Munhoz et al, 2006[59]	100	Daily fx dosing up to total 45-50	100	10	—	Good/very good in 84.6%, satisfactory in 12.8%, poor in 2.5%	0	—	—	20 (5-79)

BID, twice daily; fx, fraction; HDR, high dose rate; PDR, pulse dose rate; RT, radiation therapy.
* patients who received ERT
** patients who received IORT

boost RT and 3 studies without boost RT were used to estimate the professional cosmetic ratings. The overall estimated probability of satisfaction from professional cosmetic ratings was 0.849 (95% CI, 0.645-0.946) and 0.936 (95% CI, 0.03->0.999]) with boost and without boost, respectively. Three studies with boost RT and 2 studies without boost RT were used to estimate the patient generated cosmetic ratings. The estimated probability of satisfaction from patient cosmetic rating was 0.89 (95% CI, 0.596-0.979) and 0.84 (95% CI, 0.1-0.996) with and without the boost, respectively. These estimates were not conclusive for the purpose of direct comparison because the analysis was performed on a small number of studies that used different rating systems. The effects of boost RT, which appeared to increase patient rating on cosmesis but decrease professional rating, may be attributable to the limitations of the estimates. Although a similar comparison in local recurrence rates was attempted to be drawn between patients with and without boost, a meaningful comparison was not feasible because of the limitations in available data and inconsistencies in reporting of the follow-up period.

Use of APBI after oncoplastic BCS

APBI is typically delivered in 10 fractions over 5 days, twice daily, separated by at least 6 hours. A potential benefit derived from APBI is the decrease in the radiation dose delivered outside the targeted area because the treatment volume is the tumor cavity plus margin.[24] The accelerated fractionation scheme also allows for increasing accessibility of treatment to patients.[24] APBI may be performed using interstitial multicatheter brachytherapy, single-lumen balloon catheter brachytherapy, intracavitary multiple lumen catheter brachytherapy, 3-dimensional conformal external beam RT, or intraoperative RT (IORT).[35] A typical external beam APBI treatment plan will deliver 385 cGy twice daily for 5 days for a total dose of 3850 cGy. An APBI plan that uses multicatheter brachytherapy will typically deliver 340 cGy over 5 days, twice daily, for a total dose of 3400 cGy. Alternatively, APBI can be delivered in a single fraction to the lumpectomy cavity intraoperatively to a dose of 18 to 21 Gy. Among these distinct RT techniques, interstitial multicatheter brachytherapy is the longest used and investigated method of delivery.[36]

Two studies used APBI in lieu of WBI (Table 2) in patients who underwent oncoplastic BCS.[37,38] Roth et al investigated the feasibility and treatment results of interstitial multicatheter brachytherapy method after oncoplastic BCS.[37] The local recurrence was 0.7% upon applying a total pulse dose rate of 50.4 Gy or high dose rate of 32 Gy over 4 days, suggesting the potential feasibility of APBI using interstitial multicatheter brachytherapy method in considering alternatives to WBI in selected low-risk patients.[37] Massa et al investigated the use of IORT and conventionally fractionated external beam radiation after oncoplastic BCS.[38] All patients in Massa et al reported favorable judgments on the aesthetic outcome with a score of 6 or higher on a scale of 0 (worst) to 10 (best). This score included factors such as aesthetic global result, breast symmetry, areola-nipple symmetry, and scarring.[38] Although favorable cosmetic outcomes are achieved by the use of IORT in Massa et al, adjuvant APBI in the setting of oncoplastic rearrangement is still at experimental stage and its feasibility in lieu of WBI should be studied more in the future.

Table 3 Outcomes of volume replacement and radiation therapy

Study	Patients receiving ART (%)	ART dose-fractionation (Gy)	Patients receiving boost RT (%)	Boost RT dose-fractionation (Gy)	Patient rating on cosmesis	Professional rating on cosmesis	Local recurrence (%)	Distant recurrence (%)	Mortality (%)	Mean follow-up (mo, range)
Lee et al, 2014[62]	64.3	—	—	—	82.3% satisfaction (mean score, >4)	Mean 4.13	—	—	—	11.3 (4-23)
Gendy et al, 2003[63]	75.5	50 Gy in 25 fx over 5 wk	—	—	83.5% average satisfaction	3.8	4.1	—	—	53 (7-102)
Losken et al, 2004[64]	84.6	—	—	—	—	—	5.1	10.3	5.1	44 (3-78)
Bogusevicius et al, 2014[56]	100	Maximum 50 (in 25 fx)	0	0	92.3% excellent/good	87.2% excellent/good	10	38.3	23.3	86
Down et al, 2013[69]	—	—	—	—	—	—	0	—	—	29.3
Kronowitz et al, 2006[29]	100	Minimum 50	100	10-15	—	33% excellent/good (VR)	2	—	—	29
Tenofsky et al, 2014[57]	93.1	—	—	—	86.2% favorable	—	0	—	—	24.6 (2.9-44.7)
Hamdi, 2013[70]	—	—	—	—	—	—	1.7	—	—	48 (6-120)
Veiga et al, 2011[41]	93.3	—	—	—	Mean 10 at 12 mo	Mean 9.25 at 12 mo	1	—	—	—
Munhoz et al, 2009[73]	100	Daily fx dosing up to total 45-50	100	10	—	—	5.5	—	—	48 (10-108)
Munhoz et al, 2006[74]	100	Daily fx dosing up to total 45-50	100	10	Good or very good 88.2%, satisfactory in 8.8%, poor in 12.9%		0	—	—	23

ART, adjuvant radiation therapy. See Tables 1 and 2 for other abbreviations.

Discussion

In this comprehensive literature review, the outcomes of oncoplastic BCS with adjuvant RT with and without boost were evaluated by assessing the local control and cosmetic sequelae. A total of 1194 potentially relevant publications were initially identified based on the previously discussed search criteria. After eliminating studies that did not meet secondary search criteria as detailed previously, 109 articles were initially identified. Of those, 41 were selected for this comprehensive review.

In patients who underwent oncoplastic BCS, the estimated probability of local recurrence when receiving conventionally fractionated whole breast radiation was 0.015 (95% CI, 0.008-0.03). Only 2 studies reported local recurrence rates in patients who underwent oncoplastic BCS followed by APBI, and none of the studies used hypofractionated whole breast radiation; as a result, a meaningful pooled probability estimate could not be calculated. Because of the lack of reports, a statistically significant conclusion regarding local control cannot be elucidated with respect to WBI compared with APBI. However, in an appropriately selected patient population who underwent oncoplastic BCS, APBI might represent an alternative treatment scheme in an investigational setting. There are significant challenges in accurately targeting the tumor bed for delivery of APBI after oncoplastic surgery, and in general, the use of oncoplastic BCS reduces the likelihood that APBI can be performed. Recently, a bioabsorbable 3-dimensional device with 6

permanent titanium clips (Biozorb, Focal Therapeutics, Aliso Viejo, CA) has been developed for use in oncoplastic reconstruction. Not only does this device allow for oncoplastic breast surgery, it also provides the radiation oncologist with specific landmarks for targeting of boost RT or APBI. Currently, a registry trial is under way to determine the cosmetic and local control benefits of the device.

Professional and patient satisfaction ratings were investigated with respect to WBI and APBI. In patients who underwent WBI, the overall estimated probability of satisfaction based on professional ratings was 0.877 (95% CI, 0.784-0.934). The overall estimated probability of satisfaction based on patient ratings was 0.913 (95% CI, 0.815-0.962). Patient-rated cosmesis in patients who underwent oncoplastic BCS followed by APBI was only available in the report by Massa et al. Of interest, all patients in Massa et al reported favorable judgments on the aesthetic outcome with a score of 6 or higher on a scale of 0 (worst) to 10 (best). Previous studies have reported unacceptable cosmetic outcomes related to the use of APBI in patients who did not undergo oncoplastic BCS.[39] The differences in these conclusions suggest that further data may need to be generated before definitive conclusions are drawn.

The effect of the boost on cosmesis was also reported by both professionals and patients. The overall estimated probability of satisfaction from professional cosmetic ratings was 0.849 (95% CI, 0.645-0.946) and 0.936 (95% CI, 0.03->0.999) with boost and without boost, respectively. The estimated probability of satisfaction from patient cosmetic rating was 0.89 (95% CI, 0.596-0.979) and 0.84 (95% CI, 0.1-0.996) with and without the boost, respectively.

This review is subject to the typical limitations of comprehensive reviews. Differences in reporting patterns of local recurrences as well as time frames of reporting these local recurrences make it difficult to make a statistically reliable comparison regarding local control with respect to each modality. In 2 studies, a local recurrence was reported without a given follow-up period.[40,41] Local recurrence rates without consistency in the follow-up period further raise the difficulty of making a comparison across studies and generating an assessment of the efficacy of different surgical methods and radiation treatments.

Furthermore, studies that reported cosmesis used methodologies that ranged from the Radiation Therapy Oncology Group Quality of Life Baseline Questionnaire, to pre- and postoperative photographs, and subjective assessments by patients and professional staff.[15,29,38,40-59] In addition, the scoring system in each methodology widely varied, such as 0% to 100% satisfaction, acceptable versus unacceptable, and excellent/good/satisfactory/poor.[15,29,38,40-59] The only standardization involved in methodology was the 5 parameters that were used in the cosmesis assessment: breast shape, symmetry, scars, nipple areola complex position and shape, and post-irradiation sequelae.[15,29,38,40-59] The differences in the methodology diminish the possibility of establishing a meaningful comparison across studies.

Oncoplastic BCS with adjuvant RT is an emerging area of clinical investigation, and future studies might benefit from adopting a more consistent and standardized reporting of data to better determine the optimal RT treatments for patients undergoing oncoplastic BCS. In addition, future prospective study should be designed to better understand the impact of oncoplastic surgery on radiation technique and local recurrence. Finally, because oncoplastic techniques may impact the type of radiation treatment the patient may ultimately receive, a preoperative referral to radiation oncology should be strongly considered. The radiation oncologist may request clips to better delineate the cavity, can comment on the clinical benefit of the boost in the individual patient, and can discuss the impact of the technique on fractionation scheme, to allow the patient to make an informed decision about the oncoplastic approach.

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