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Cosmetic outcomes following breast conservation surgery and radiation for multiple ipsilateral breast cancer: Data from the Alliance Z11102 Study

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Abstract

Background—The diagnosis of multiple ipsilateral breast cancer (MIBC) is increasing. Historically, the primary treatment for MIBC has been mastectomy due to concerns about in-breast recurrence risk and poor cosmetic outcome. The Alliance Z11102 study prospectively assessed cosmetic outcomes in women with MIBC treated with breast conserving therapy (BCT).

Methods—Z11102 was a multicenter trial enrolling women with 2 or 3 separate sites of biopsy proven malignancy separated by ≥ 2 cm within the same breast. Cosmetic outcome was a planned secondary end-point. Data were collected with a 4-point cosmesis survey (1=excellent, 4=poor)

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and the BREAST-Q (scored 0–100). All patients undergoing successful breast-conserving therapy were treated with whole breast radiation. Associations were assessed with chi-square or Fisher's exact tests as appropriate.

Results—Cosmetic outcome data for 216 eligible women who completed therapy are included in this analysis. Of the 136 patients who completed the survey 2 years postoperatively, 70.6% (N=96) felt the result was good or excellent while 3.7% (N=5) felt the result was poor. We found no significant differences in patient reported cosmetic outcomes when stratifying by patient age, number of lesions (2 or 3), number of incisions, number of lumpectomies or size of largest area of disease. Mean satisfaction score on the BREAST-Q was 77.2 six months following whole breast radiation and 73.7 three years following surgery.

Conclusions—BCT performed for MIBC results in good or excellent cosmesis for the majority of women. From a cosmetic perspective, BCT is a valid surgical approach to women with MIBC.

Keywords

multiple ipsilateral; multifocal; multicentric; breast cancer; breast conservation; cosmesis; radiation therapy

Background

For millennia, mastectomy represented the only known surgical approach to breast cancer. In the 1970s and 80s, large, prospective trials confirmed the feasibility and oncologic safety of breast conservation therapy (BCT) in appropriately selected early stage breast cancer patients.^{1–3} Studies were generally limited to women with unifocal disease. Women with multiple synchronous tumors in the same breast, multiple ipsilateral breast cancer (MIBC), are often denied breast conserving surgery based on data from retrospective studies performed in the 1980s and early 1990s reporting adverse outcomes. These studies reported local regional recurrence rates (LRR) between 23–44% in the MIBC patient population.^{4–6} Concern regarding poor cosmetic outcomes with larger or multiple lumpectomy cavities and larger volume of breast tissue resection in patients also prompted recommendation for mastectomy as larger excisions have been associated with poor cosmetic outcomes.^{7–9}

Over the last 30 years, wide scale implementation of screening mammography has led to breast cancer detection at earlier stages. Improvements in all aspects of multidisciplinary care (diagnostic imaging, margin assessment, CT planning for radiation, systemic therapy) have decreased both local and systemic recurrence. Simultaneously, the incidence of pre-operative diagnosis of previously occult MIBC has increased given more sensitive breast imaging modalities including magnetic resonance imaging (MRI), tomosynthesis, positive emission mammography (PEM) and ultrasound. Currently, between 13–60% of women with newly diagnosed breast cancer have MIBC.^{10–13} This wide range in incidence reflects varying definitions of MIBC, preoperative vs pathologic assessment and improvements in imaging. Pre-operative evaluation with MRI detects MIBC in 15–20% of patients.^{14–18} This translates to thousands of women each year obligated to mastectomy if this is the only treatment option presented. Mastectomy can have deleterious effects on patients. Several studies have demonstrated diminished body image, quality of life, coping, breast satisfaction

and self-esteem in patients undergoing mastectomy, with or without reconstruction, in comparison to women undergoing BCT.^{19–21} Therefore, safely eliminating unnecessary contraindications for BCT in women who desire it may improve both physical and emotional recovery.

More recent retrospective studies, performed in an era of earlier detection, improved therapies and multidisciplinary care teams, have demonstrated equivalent LRR in appropriately selected women with MIBC treated with BCT when compared to women treated for unifocal disease.^{22–26} Given the retrospective nature of these data, a prospective investigation of the oncologic safety of BCT for MIBC is imperative in order to facilitate preoperative counselling and improve shared decision making for women with MIBC. Given the link between cosmetic perception and psychological recovery²⁷, an analysis of patient-reported cosmetic outcomes in the MIBC population is also critical to understand best strategies for surgical management.

The Alliance Z11102 study is the first multicenter trial to prospectively assess the oncologic safety of BCT in women with MIBC. Data from Z11102 have demonstrated the feasibility of BCT in women with MIBC.²⁸ Each participant signed an IRB-approved, protocol-specific informed consent document in accordance with federal and institutional guidelines. The primary study endpoint, LRR, is awaiting maturation and has yet to be reported. Herein we report breast cosmesis, assessed by both patients and surgeons, a secondary endpoint of the study.

Methods

Z11102 was a single arm, prospective, multicenter trial which enrolled women with 2 or 3 sites of biopsy-proven malignancy separated by ≥ 2 cm within the same breast. Details of the inclusion and exclusion criteria have been previously reported.²⁸ Patients were registered between 11/2012 and 8/2016. Data were locked for analysis 2/2020.

All women were treated with breast-conserving surgery performed through a single or multiple incisions. Oncoplastic techniques for cavity closure and breast reconstruction were permitted. Patients who did not achieve negative margins after breast conservation were excluded from final data analysis. Patients who successfully completed BCT were treated with conventional whole breast radiation (180–200 cGy daily) including a cavity boost to all tumor sites (total dose of 60 Gy, hypofractionation not allowed). Radiation target delineation was performed according to the Radiation Therapy Oncology Group contouring consensus definitions as outlined in the initial study publication, limiting the volume of breast that received the full 60 Gy to 40%.²⁸

The primary endpoint of the study is local recurrence, assessment of which is awaiting sufficient follow-up. Cosmetic outcome was a planned secondary endpoint of the trial. Surgeon and patient perception of cosmesis were assessed 30 days postoperatively using the 4-point scoring system originally described by Winchester and Cox.²⁹ This system rates the breast appearance on a 4-point Likert scale: 1 (excellent--appearance nearly identical to the contralateral breast), 2 (good), 3 (fair) and 4 (poor--major functional and aesthetic sequelae

in the treated breast). This single item questionnaire has been previously used in multiple studies including in NSABP B-39.³⁰ Patients with a fair or poor score are considered to be a cosmetic “failure”. Patients were also administered the BCT module of the BREAST-Q³¹ postoperatively at the following time points: 30 days and 6, 12, 18, 24, 36, 48 and 60 months.

The BREAST-Q is a validated instrument for collection of patient-reported outcomes following various types of breast surgery. Patient reported data in the BREAST-Q are converted to a score between 0–100 with the higher scores representing more favorable outcomes.^{31–33} The Z11102 trial used the BCT module of the BREAST-Q to measure patient satisfaction, body image and quality of life. Of note, the BCT BREAST-Q assesses changes related to both surgery and radiation.^{31–32} Association of patient factors (age), tumor factors (grade, size) and surgical factors (number of incisions) with breast cosmesis and BREAST-Q scores were assessed with chi-square or Fisher’s exact tests as appropriate.

Data collection and statistical analyses were conducted by the Alliance Statistics and Data Center. Data were reviewed by the Alliance Statistics and Data Center and by the study chairperson as mandated by Alliance policies. The Alliance Data Safety Monitoring Board reviewed safety data for this trial at least twice a year.

Results

Of 270 women enrolled, 54 were excluded due to withdrawal, ineligibility or conversion to mastectomy. Ineligible patients were found to have too little distance (<2cm) between lesions on central radiology review or imaging outside the time range proscribed in the study requirements. The data presented in this study reflect 216 eligible patients with MIBC who completed breast-conserving therapy. Median follow up was 49 months (range 0.5–73.6). 65 patients were followed for at least 5 years.

The median age was 61.5 years (SD 10.0). The majority of patients (n=208) had 2 foci of disease identified while 8 patients had 3 foci of disease (TABLE 1). Sixty patients underwent lumpectomies through a single incision while 143 had 2 incisions and 5 patients required 3 incisions for resection of all tumors. Data on number of incisions were missing for 8 patients. The surgeon performed routine closure in 178/216 (82.4%) patients. 26/216 (12%) had local tissue rearrangement while 4/216 (1.9%) had ipsilateral breast reshaping by a plastic surgeon and 3/216 (1.4%) had ipsilateral simultaneous breast reduction by a plastic surgeon. Data on type of closure was missing in 5/216 (2.3%) patients. Nineteen patients (8.8%) underwent synchronous contralateral symmetry procedures including 6 excisional biopsies, 5 mastopexies, 6 breast reductions and 2 that were not specified.

The median largest tumor size on final pathologic evaluation was 1.5 cm (range 0.1–6.5cm). 166/216 (76.9%) were node negative and 50/216 (23.1%) were node positive. Staging information is outlined in TABLE 2.

Cosmetic outcome data were collected from the 216 eligible women who completed surgery and radiation. Surgeon and patient scores are reported in TABLE 3. Thirty days post-operatively, the majority of patients (>86%) had a good or excellent cosmetic outcome when

assessed by both the surgeon and the patient. However, surgeons were more likely to rate cosmetic outcome good or excellent compared to patients: 95.2% versus 86.8% ($p=0.002$ by McNemar's test), respectively. In 17 patients, the surgeon assessed the outcome as good or excellent when the patient did not, but in only 3 cases the patient assessed the outcome as good or excellent when the surgeon did not.

Two years post operatively, 136 of 194 patients completed the survey. Of the surveyed patients, 70.6% at 2 years post operatively and 70.3% at 3 years felt the cosmetic result was good or excellent while 3.7% felt the result was poor at 2 years and 6.9% at 3 years. (TABLE 3) There were no significant differences in cosmetic assessment related to stage of disease.

Median satisfaction with breast on the BREAST- Q was 76.3 post-operatively with slight decrease to 73.7 by 3 years after surgery. The most common reports of adverse effects of radiation were noted in the 6 months post-operative survey with median score of 86.1 with improvement at later intervals to 92.4 at 24 months and 94.3 at 60 months. Physical well-being score on the BREAST-Q was low immediately after surgery with median score of 58.6. This increased to 80 at 6 months and continued to improve to scores between 70–80 from 12 and 60 months. (FIGURE 1)

We found no significant differences in patient reported cosmesis score or overall satisfaction in the BREAST- Q when stratifying by patient age, number of lesions (2 or 3), number of lumpectomies or size of largest area of disease immediately post operatively (TABLE 4) and at 3-year follow up (TABLE 5).

Discussion

This prospective multicenter study of women with MIBC treated with BCT including adjuvant radiation demonstrates good to excellent cosmetic outcome up to five years following treatment.

The increased understanding of the biologic underpinnings of breast cancer and improved systemic therapies has led to a departure from maximally invasive surgery as the only option for a curative approach. The National Surgical Adjuvant Breast and Bowel Project (NSABP) B-04 and B-06 trials in the United States and the work of Veronesi and colleagues in Europe demonstrated equivalency of survival in women undergoing less radical surgical procedures.^{1–2, 34} This led to de-escalation from radical mastectomy to simple mastectomy, and finally to breast conserving surgery. Indications for breast-conserving therapy have subsequently continued to evolve and expanded to patients with larger tumors that can be reconstructed with oncoplastic techniques leading to acceptable cosmetic outcomes.^{35–38} In parallel, the delivery of radiation has improved and targeted, curative systemic therapies have emerged. These developments have supported a safe decrease in the extent of breast surgery while simultaneously improving LRR.

One indication for mastectomy that has persisted despite advances in the field is the case of MIBC. Retrospective studies in the era of modern therapies demonstrated acceptable LRR^{22–26} in women with MIBC undergoing BCT but surgeons remain reluctant due to the

lack of prospective trials demonstrating oncologic and cosmetic outcome data in women with multiple lesions requiring larger or multiple lumpectomy cavities. Additionally, data regarding the ability to safely administer a radiation boost to these larger or multiple cavities are lacking. Given increasing numbers of patients diagnosed pre-operatively with MIBC, understanding the LRR and cosmetic outcomes in women treated with BCT is critical to facilitate meaningful shared decision making conversations between patients and surgeons while ensuring best oncologic outcomes.

Studies in women with unifocal disease have demonstrated improved quality of life and patient satisfaction in women treated with BCT in comparison to those treated with mastectomy without reconstruction; patients undergoing immediate reconstruction report equivalent QOL and cosmetic satisfaction in comparison to BCT.^{39–40} Other studies have demonstrated decreased patient satisfaction following mastectomy in comparison to BCT even in patients undergoing implant based or autologous reconstruction^{21,37} For many women, the option of breast preservation is critical to well-being and psychologic recovery from breast cancer.

The patient-reported outcomes from the Z11102 trial are the first to prospectively assess satisfaction with breast appearance, physical well-being and adverse impact of radiation in women undergoing BCT for MIBC. Z11102 used both the 4 point breast cosmesis score as well as the BCT module of the BREAST-Q validated questionnaire. The COBALT Study by Volders et al⁴¹ investigated breast-specific factors that determined cosmetic outcome after BCT for unifocal disease. They found 70% of patients reported good or excellent cosmetic outcomes based on the 4-point scale 3 years following surgery. Our data in the MIBC population reveal a similar percentage with 70.3% reporting good or excellent results on the cosmesis survey 3 years postoperatively.

In the initial experience with the BREAST-Q BCT module, 200 women with a history of BCT were surveyed. Average time from surgery was 35.5 months. The median patient-reported score in the breast satisfaction domain was 68.⁴² The BREAST-Q data from the Z11102 trial demonstrate a mean breast satisfaction score of 73.7 three years following surgery and radiation. This result is consistent with data from the BCT cohort in a study by Flanagan et al.²¹ The Flanagan study compared BREAST-Q scores in the domains of breast satisfaction, psychosocial and sexual well-being after BCT to patient reported scores following mastectomy with implant based breast reconstruction. At 3 years post-surgery, the mean breast satisfaction score was 76 in the BCT group and 62 in the mastectomy with implant-based reconstruction cohort. This study concluded, as was demonstrated in Z11102, that breast satisfaction decreases over time following breast conserving surgery and radiation.²¹ Although the two populations may differ in important ways, it is notable that the breast satisfaction score after BCT for MIBC in Z11102 was higher than that seen after mastectomy with reconstruction in the Flanagan study.

For physical well-being, the present study reports a mean BREAST-Q score of 72.3 at 1 year post-operatively which is higher than the 67.9 reported 1 year post operatively in a population of patients undergoing BCT for unifocal disease studied by Krzos et al.⁴³ The Z11102 data on physical well-being are very similar to those presented by Vrouwe et al,

⁴⁴who studied 185 women who completed the BREAST-Q on average 38 months following partial mastectomy and radiation for unifocal disease. Vrouwe reported a mean physical well-being score of 73.5 points which is similar to the mean score of 77.7 in the Z11102 study. The data from Z11102 confirm acceptable outcomes in the domains of breast satisfaction and physical well in the majority of women with MIBC undergoing BCT. Importantly, the minority of patients (33/216, 15.3%) in Z11102 underwent oncoplastic reconstruction. Training and usage of oncoplastic techniques are increasing. This escalation of oncoplastic surgery will continue to improve cosmetic outcomes.

This study has limitations. Given the single arm design, patients accrued to the study had an underlying bias toward BCT rather than mastectomy. This may artificially inflate satisfaction with cosmetic outcome in a population desirous of breast preservation. The study is also limited by diminishing follow-up data. By year 3 post-surgery, 165 patients were evaluated in the clinic of whom 101 (61.2%) had completed the self-assessment cosmesis survey and over half had discontinued the BREAST-Q. Additionally, there was no control arm assessing BCT in patients with unifocal disease so comparisons are made to the available literature.

Patient reported outcomes in the Z11102 study demonstrate that BCT is a cosmetically acceptable option for women with MIBC. As oncoplastic techniques are increasingly utilized, we anticipate that cosmetic outcomes and patient satisfaction following BCT in MIBC will continue to improve. The local recurrence data from the trial are eagerly awaited.

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Synopsis

Z11102 was a prospective, single arm trial assessing the role of breast conservation therapy (BCT) in women with multiple ipsilateral breast cancer (MIBC). Overall BCT in women with MIBC resulted in good or excellent cosmesis for the majority of women, similar to that seen in unifocal disease treated with BCT.

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FIGURE 1.
BCT BREAST Q

TABLE 1

Patient demographics and tumor characteristics

	Total (N=216)
Age at registration	
Mean (SD)	61.7 (10.3)
Median	61.5
Range	(40.0–87.0)
Number of malignant lesions identified pathologically	
2	208 (96.3%)
3	8 (3.7%)
Overall histologic type	
All DCIS	1 (0.5%)
All invasive ductal	125 (57.8%)
All invasive lobular	18 (8.3%)
DCIS/invasive ductal	46 (21.3%)
DCIS/invasive lobular	5 (2.3%)
Invasive ductal/lobular	20 (9.3%)
Other	1 (0.5%)
Histologic grade	
G1 (Low)	57 (26.4%)
G2 (Intermediate)	105 (48.6%)
G3 (High)	51 (23.6%)
GX (Grade cannot be assessed)	3 (1.4%)
ER Status	
ER positive	197 (91.2%)
ER negative	9 (4.2%)
Mixed	9 (4.2%)
Unknown	1 (0.5%)
PR Status	
PR positive	180 (83.3%)
PR negative	17 (7.9%)
Mixed	18 (8.3%)
Unknown	1 (0.5%)
HER2 results	
HER2 Positive	11 (5.1%)
HER2 Negative	187 (86.6%)
Mixed	12 (5.6%)
Not Done	6 (2.8%)
Clinical T Stage	
T1	130 (60.2%)
T2	86 (39.8%)
Clinical N Stage	

	Total (N=216)
N0	207 (95.8%)
N1+	9 (4.2%)
Pre-operative axillary lymph node sampling	
Yes	23 (10.6%)
No	193 (89.4%)
Axillary lymph node positive on percutaneous biopsy	
(N/A - pre-op ALN sampling not done)	193 (0.0%)
Yes	9 (39.1%)
No	13 (56.5%)
Equivocal (cellular atypia)	1 (4.2%)

TABLE 2

Surgical Pathology

Number of invasive or DCIS lesions identified		
0		1 (0.5%)
1		10 (4.6%)
2		189 (87.5%)
3		15 (6.9%)
4		1 (0.5%)
Largest invasive tumor size (cm)		
Mean (range)		1.7 (0.1–6.5)
Minimum microscopic distance between any two lesions (cm)		
Mean (range)		2.8 (0.0–9.0)
Pathologic N Stage		
N0		166 (76.9%)
N1		41 (19.0%)
N2		4 (1.9%)
N3		3 (1.4%)
NX		2 (0.9%)
Pathologic T Stage		
Missing		1
T0		1 (0.5%)
Tis		3 (1.4%)
T1		161 (74.9%)
T2		48 (22.3%)
T3		2 (0.9%)
Pathologic Overall Stage		
0		2 (0.9%)
IA		131 (61.5%)
IIA		59 (27.7%)
IIB		14 (6.6%)
IIIA		4 (1.9%)
IIIC		3 (1.4%)
Missing		3
Total number of operations performed to obtain negative margins		
1		161 (74.9%)
2		48 (22.3%)
3		5 (2.3%)
5		1 (0.5%)
Unknown/Missing		1

TABLE 3

Patient and surgeon reported outcomes

	5–30 days post- surgery (N=216)	6 months post-WBI (N=205)	12 months post-WBI (N=199)	18 months post-WBI (N=196)	24 months post-WBI (N=194)	36 months post-WBI (N=165)	48 months post-WBI (N=93)	60 months post-WBI (N=44)
Patient Breast Cosmesis Score								
Excellent	89 (51.7%)	49 (32.5%)	43 (30.1%)	46 (33.1%)	44 (32.4%)	37 (36.6%)	20 (38.5%)	4 (21.1%)
Good	60 (34.9%)	71 (47.0%)	64 (44.8%)	64 (46.0%)	52 (38.2%)	34 (33.7%)	17 (32.7%)	10 (52.6%)
Fair	21 (12.2%)	28 (18.5%)	30 (21.0%)	24 (17.3%)	35 (25.7%)	23 (22.8%)	13 (25.0%)	5 (26.3%)
Poor	2 (1.2%)	3 (2.0%)	6 (4.2%)	5 (3.6%)	5 (3.7%)	7 (6.9%)	2 (3.8%)	0 (0.0%)
Missing or Not Done	42	54	56	57	58	64	41	25
Surgeon Breast Cosmesis Score								
Excellent	104 (54.7%)							
Good	76 (40.0%)							
Fair	10 (5.3%)							
Poor	0 (0.0%)							
Missing or Not Done	26							
BreastQ Score: Satisfaction with Breast								
N	175	159	148	143	143	101	54	17
Mean (SD)	76.3 (18.2)	77.2 (19.0)	75.7 (17.5)	76.1 (18.9)	74.9 (17.2)	73.7 (20.1)	77.0 (17.5)	71.1 (12.7)
BreastQ Score: Adverse Effects of Radiation								
N	61	158	149	140	142	97	54	17
Mean (SD)	95.7 (13.3)	86.1 (16.8)	88.7 (15.5)	91.1 (14.6)	92.4 (11.9)	91.1 (13.1)	93.9 (11.6)	94.3 (10.1)
BreastQ Score: Physical Well-Being								
N	171	158	147	142	142	99	54	17
Mean (SD)	58.6 (23.1)	67.6 (28.2)	73.2 (27.4)	75.4 (27.9)	77.7 (25.5)	77.7 (27.0)	80.4 (25.5)	72.8 (30.7)

TABLE 4

Cosmetic results based on univariate analysis immediate post-surgery visit

	Patient Cosmesis Score		p-value
	Excellent/Good (1/2)	Fair/Poor (3/4)	
	N=149	N=23	
Patient Age			0.77
Median (range)	63 (40 – 87)	61 (43 – 75)	
Number of lesions (preop imaging)			0.24
2	144 (96.6%)	21 (91.3%)	
3	5 (3.4%)	2 (8.7%)	
Number of lesions (preop biopsy)			0.24
2	144 (96.6%)	21 (91.3%)	
3	5 (3.4%)	2 (8.7%)	
Size of largest lesion (path)			0.70
Median (range)	1.3 (0.1 – 5.0)	1.5 (0.5 – 6.5)	
Type of first surgery			0.097
Single lumpectomy	39 (26.2%)	8 (34.8%)	
Two lumpectomies	104 (69.8%)	12 (52.2%)	
Three lumpectomies	3 (2.0%)	1 (4.4%)	
Other	3 (2.0%)	2 (8.7%)	
Path Stage			0.63
0	1 (0.7%)	0	
IA	94 (64.0%)	15 (65.2%)	
IIA	37 (25.2%)	6 (26.1%)	
IIB	11 (7.5%)	1 (4.4%)	
IIIA	1 (0.7%)	1 (4.4%)	
IIIC	3 (2.0%)	0	
Type of closure			0.54
Routine	125 (84.5%)	18 (78.3%)	
Other	23 (15.5%)	5 (21.7%)	
Total number of operations of obtain clean margins			0.88
1	110 (74.3%)	18 (81.8%)	
2	34 (23.0%)	4 (18.2%)	
3	3 (2.0%)	0	
5	1 (0.7%)	0	
Missing/Unknown	1	1	
% of Breast Volume Receiving 60 Gy			0.73
1–20%	16 (14.0%)	3 (16.7%)	
21–20%	62 (54.4%)	12 (66.7%)	
41–50%	32 (28.1%)	3 (16.7%)	
>50% (contraindicated by protocol)	4 (3.5%)	0	
Missing/Unknown	35	5	

	Breast Q Overall Satisfaction Score				p-value
	<50 N=9	50–74 N=75	75–99 N=47	100 N=43	
Patient Age					0.55
Median (range)	63 (43 – 75)	65(43 – 87)	60 (40 – 81)	60 (43 – 79)	
Number of lesions (preop imaging)					0.65
2	9 (100%)	73 (97.3%)	45 (95.7%)	40 (93.0%)	
3	0	2 (2.7%)	2 (4.3%)	3 (7.0%)	
Number of lesions (preop biopsy)					0.65
2	9 (100%)	73 (97.3%)	45 (95.7%)	40 (93.0%)	
3	0	2 (2.7%)	2 (4.3%)	3 (7.0%)	
Size of largest lesion (path)					0.08
Median (range)	1.8 (0.7 – 3.0)	1.3 (0.1 – 6.5)	1.2 (0.3 – 4.5)	1.5 (0.7 – 3.5)	
Type of first surgery					0.35
Single lumpectomy	4 (44.4%)	17 (22.7%)	13 (27.7%)	14 (32.6%)	
Two lumpectomies	5 (55.6%)	54 (72.0%)	33 (70.2%)	26 (60.5%)	
Three lumpectomies	0	0	1 (2.1%)	2 (4.6%)	
Other	0	4 (5.3%)	0	1 (2.3%)	
Path Stage					0.31
0/I	6 (66.7%)	47 (62.7%)	33 (70.2%)	26 (61.9%)	
IIA	1 (11.1%)	22 (29.3%)	11 (23.4%)	11 (26.2%)	
IIB	0	5 (6.7%)	2 (4.3%)	4 (9.5%)	
IIIA	1 (11.1%)	1 (1.3%)	0	0	
IIIC	1 (11.1%)	0	1 (2.1%)	1 (2.4%)	
Type of closure					0.16
Routine	6 (66.7%)	64 (86.5%)	37 (78.7%)	39 (90.7%)	
Other	3 (33.3%)	10 (13.5%)	10 (21.3%)	4 (9.3%)	
Total number of operations of obtain clean margins					0.50
1	7 (77.8%)	53 (72.6%)	39 (83.0%)	33 (76.7%)	
2	2 (22.2%)	19 (26.0%)	7 (14.9%)	8 (18.6%)	
3	0	0	1 (2.1%)	2 (4.6%)	
5	0	1 (1.4%)	0	0	
Missing/Unknown	0	2	0	0	
% of Breast Volume Receiving 60 Gy					0.47
1–20%	1 (25.0%)	5 (8.6%)	8 (22.2%)	5 (14.3%)	
21–20%	3 (75.0%)	36 (62.1%)	16 (44.4%)	22 (62.9%)	
41–50%	0	16 (27.6%)	11 (30.6%)	7 (20.0%)	
>50% (contraindicated by protocol)	0	1 (1.7%)	1 (2.8%)	1 (2.9%)	
Missing/Unknown 22(%)	5	17	11	8	

TABLE 5

Cosmetic results based on univariate analysis 3 years post surgery visit

	Cosmesis Score		p-value
	Excellent/Good N=71	Fair/Poor N=30	
Patient Age			0.56
Median (range)	60 (40 – 82)	62 (43 – 87)	
Number of lesions (preop imaging)			0.55
2	68 (95.8%)	30 (100.0%)	
3	3 (4.2%)	0	
Number of lesions (preop biopsy)			0.55
2	68 (95.8%)	30 (100.0%)	
3	3 (4.2%)	0	
Size of largest lesion (path)			0.97
Median (range)	1.5 (0.1 – 4.5)	1.5 (0.2 – 2.8)	
Type of first surgery			0.39
Single lumpectomy	20 (28.2%)	9 (30.0%)	
Two lumpectomies	47 (66.2%)	19 (63.3%)	
Three lumpectomies	1 (1.4%)	2 (6.7%)	
Other	3 (4.2%)	0	
Path Stage			0.61
0	0	0	
IA	44 (62.9%)	23 (76.7%)	
IIA	22 (31.4%)	6 (20.0%)	
IIB	3 (4.3%)	1 (3.3%)	
IIIA	0	0	
IIIC	1 (1.4%)	0	
Type of closure			0.38
Routine	57 (80.3%)	25 (89.3%)	
Other	14 (19.7%)	3 (10.7%)	
Total number of operations of obtain clean margins			0.38
1	48 (69.6%)	19 (63.3%)	
2	20 (29.0%)	9 (30.0%)	
3	1 (1.4%)	1 (3.3%)	
5	0	1 (3.3%)	
Missing/Unknown	2	0	
% of Breast Volume Receiving 60 Gy			0.052
1–20%	14 (21.2%)	5 (18.5%)	
21–20%	37 (56.1%)	11 (40.7%)	
41–50%	15 (22.7%)	8 (29.6%)	
>50% (contraindicated by protocol)	0	3 (11.1%)	
Missing/Unknown	5	3	

	Breast Q Overall Satisfaction Score				p-value
	<50 N=3	50–74 N=48	75–99 N=23	100 N=25	
Patient Age					0.23
Median (range)	55 (52 – 55)	60.5 (43 – 87)	58 (41 – 78)	65 (43 – 78)	
Number of lesions (preop imaging)					0.16
2	3 (100%)	48 (100%)	21 (91.3%)	24 (96.0%)	
3	0	0	2 (8.7%)	1 (4.0%)	
Number of lesions (preop biopsy)					0.16
2	3 (100%)	48 (100%)	21 (91.3%)	24 (96.0%)	
3	0	0	2 (8.7%)	1 (4.0%)	
Size of largest lesion (path)					0.50
Median (range)	2.0 (1.0 – 2.5)	1.4 (0.2 – 4.5)	1.3 (0.1 – 4.2)	1.6 (0.2 – 2.9)	
Type of first surgery					0.82
Single lumpectomy	0	14 (29.2%)	7 (30.4%)	4 (16.0%)	
Two lumpectomies	3 (100%)	30 (62.5%)	16 (69.6%)	19 (76.0%)	
Three lumpectomies	0	2 (4.2%)	0	1 (4.0%)	
Other	0	2 (4.2%)	0	1 (4.0%)	
Path Stage					0.39
0/I	3 (100%)	34 (70.8%)	15 (65.2%)	13 (54.2%)	
IIA	0	12 (25.0%)	6 (26.1%)	10 (41.7%)	
IIB	0	2 (4.2%)	2 (8.7%)	0	
IIIA	0	0	0	0	
IIIC	0	0	0	1 (4.2%)	
Type of closure					0.55
Routine	3 (100%)	39 (84.8%)	17 (73.9%)	22 (88.0%)	
Other	0	7 (15.2%)	6 (26.1%)	3 (12.0%)	
Total number of operations of obtain clean margins					0.88
1	2 (66.7%)	30 (62.5%)	15 (71.4%)	20 (80.0%)	
2	1 (33.3%)	15 (31.2%)	6 (28.6%)	5 (20.0%)	
3	0	2 (4.2%)	0	0	
5	0	1 (2.1%)	0	0	
Missing/Unknown	0	0	2	0	
% of Breast Volume Receiving 60 Gy					0.016
1–20%	0	10 (23.3%)	1 (4.6%)	8 (34.8%)	
21–20%	2 (66.7%)	19 (44.2%)	12 (54.6%)	13 (56.5%)	
41–50%	0	13 (30.2%)	8 (36.4%)	1 (4.4%)	
>50% (contraindicated by protocol)	1 (33.3%)	1 (2.3%)	1 (4.6%)	1 (4.4%)	
Missing/Unknown	0	5	1	2	