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ORIGINAL ARTICLE – BREAST ONCOLOGY

Real-World Application of Alliance ACOSOG Z11102: How Many Patients Can be Spared Mastectomy?

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ABSTRACT

Background. ACOSOG Z11102 demonstrated that breast-conserving surgery (BCS) with radiation is safe for multiple ipsilateral breast cancers (MIBCs), with re-excision and mastectomy conversion rates of 32.4% and 7.1%, respectively. Our objective was to evaluate the applicability of ACOSOG Z11102 in real-world practice.

Methods. A retrospective review of MIBC patients was performed to collect clinical and demographic information. Pathology was re-reviewed by two breast pathologists assessing distance between foci and presence of significant pathology in intervening tissue (incidental invasive carcinoma, ductal carcinoma in situ [DCIS], atypical ductal hyperplasia [ADH], atypical lobular hyperplasia [ALH], lobular carcinoma in situ [LCIS], and flat epithelial atypia [FEA]).

Results. Overall, 116 evaluable patients (70 mastectomy, 46 BCS) were included. The median age was 64 years (range 34–93), the median number of foci was 2 (range 1–3), and the median size of the largest focus was 1.7 cm (range 0.4–6.5). Most patients were cT1 (84, 72.4%) and cN0 (111, 95.7%). Of the 46 BCS patients, 23 (50%) needed re-excisions. Eleven of these 23 (47.8%) patients had successful re-excisions, while 12 (52.2%) underwent mastectomy. The successful BCS rate was 73.9%, with conversion to mastectomy in 26.1%. On review of intervening tissue, 26 (22.4%) patients had no pathologic findings, 57 (49.1%) had DCIS, 19 (16.4%) had ALH, 13 (11.2%) had ADH, 11 (9.5%) had LCIS, 6 (5.2%) had additional incidental invasive carcinoma, and 1 (0.9%) had FEA. Factoring in intervening findings and Z11102 criteria, 15/70 (21.4%) patients who underwent mastectomy could have been eligible for BCS.

Conclusions. Patient selection is critical when considering BCS for MIBC, as re-excision and mastectomy conversion rates may be higher in real-world practice.

Keywords Breast-conserving surgery · Mastectomy · Multiple ipsilateral breast cancer · Multifocal breast cancer · Multicentric breast cancer · Atypia

Breast cancer is the most common non-cutaneous malignancy among women in the United States, affecting one in eight women.[1] While most breast cancers are unifocal (UF), the incidence of multiple ipsilateral breast cancers (MIBCs) are on the rise as imaging techniques are improving.[2] The reported incidence varies between 6 and 75%, and the wide range is often attributed to the differing definitions of multifocality and multicentricity.[2,3] Magnetic resonance imaging (MRI) detects more MIBCs,[4–6] and it is known that preoperative MRI use increases the rate of mastectomies

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performed.[4] Not surprisingly, a 20% conversion to mastectomy rate was observed in a prospective series of 99 patients, after MRI detected multiple ipsilateral breast lesions.[6]

Since the early breast cancer surgery trials led by Fisher et al., which demonstrated equivalent overall survival (OS) for breast conservation (lumpectomy with adjuvant radiotherapy) compared with mastectomy, there has been a continued trend toward de-escalation.[7] Since that time, breast-conserving surgery (BCS) has been a mainstay of surgical therapy for UF breast cancer; however, the safety of BCS for patients with MIBC has been controversial. Historically, patients with MIBC were thought to carry a worse prognosis, and BCS has been advised against due to published local recurrence rates (LRRs) as high as 40% (23–40%).[8–10] Contemporary literature, comprised largely of retrospective studies, has shown nearly equivalent rates of local recurrence after BCS and mastectomy for the treatment of MIBC, which may be attributed to improved imaging and surgical techniques, optimized radiation therapy, and effective systemic therapy.[11–14] Alliance ACOSOG Z11102 was a prospective, single-arm trial of 204 patients investigating the LRR in women with MIBC following BCS and adjuvant radiation. The 5-year LRR was 3.1%, thus providing evidence that BCS is an oncologically safe option for patients with MIBC.[14] The secondary endpoints demonstrated a conversion to mastectomy rate of 7.1%, acceptable cosmetic outcomes, and radiation feasibility. Reported re-excision rates were 32.4%.[15] The aim of this study was to evaluate the applicability of the Z11102 trial in a real-world MIBC patient population, including determining margin positivity and conversion to mastectomy rates. Pathology was reviewed to determine if the intervening tissue between tumor foci contained abnormal findings that would typically be removed, to delineate true BCS potential.

METHODS

Patient Selection

A retrospective chart review of patients treated for MIBC between November 2010 and April 2023 at a tertiary cancer center was performed. All patients had preoperative mammography and ultrasound with percutaneous biopsy establishing their diagnosis. All included patients had a primary focus of invasive carcinoma and additional lesion(s) of either invasive disease or carcinoma in situ based on final pathology. Included patients had either cN0 or cN1 disease. Patients received either multiple lumpectomies or a mastectomy as their initial operations. Axillary surgery was performed via sentinel lymph node biopsy or axillary node dissection, at the discretion of the surgeon. Patients with histories of neoadjuvant systemic therapy, male sex, prior or concurrent contralateral disease, and/or known *BRCA* mutations were excluded from evaluation. Patients whose lumpectomy cavities may have ultimately abutted or connected and the intervening tissue could be evaluated were included, otherwise patients were excluded if the intervening tissue could not effectively be reviewed.

Data Collection and Pathologic Evaluation

The following characteristics were collected and analyzed: age at diagnosis, race, number and size of tumor foci, clinical stage (tumor and nodal status), preoperative MRI use, size of non-mass enhancement (NME), tumor biology, breast surgery, and axillary surgery type. We collected information on initial surgery, re-excision attempts, and definitive operations; the data collected were also used to calculate the margin positivity and conversion to mastectomy rates. Genetic testing information and results were also collected.

To determine the distance between tumor foci and whether the pathology of the intervening tissue would alter surgical management, the gross examination report and surgical specimen slides were re-reviewed by two subspecialized breast pathologists (BF and BT). The following were assessed: incidental microscopic foci of invasive carcinoma, ductal carcinoma in situ (DCIS), atypical ductal hyperplasia (ADH), atypical lobular hyperplasia (ALH), lobular carcinoma in situ (LCIS), and flat epithelial atypia (FEA). Using the criteria from ACOSOG Z11102, we determined the percentage of patients who could have received BCS, with consideration of the intervening tissue histopathology. For our study, ADH, ALH, LCIS, DCIS, and invasive carcinoma in the intervening tissue were considered significant pathologic findings that would have precluded BCS, because although ADH, ALH, and LCIS at the margin do not obligate re-excision, they would be localized for excision at the time of initial surgery if a preoperative biopsy revealed atypia. In contrast, despite conflicting data regarding association with invasive upgrade on excision, in this study FEA was not considered a lesion requiring excision or disallowing mastectomy if found in intervening tissue as it is generally not classified as a high-risk lesion.[16]

RESULTS

Patient and Tumor Characteristics

All patients diagnosed with MIBC between November 2010 and April 2023 were identified, with 151 meeting the inclusion criteria. Figure 1 depicts the patient selection process, with a final total of 116 patients. Patient demographics and clinicopathologic details are shown in Table 1. The median patient age was 64 years (range 34–93 years). A majority of patients (87.1%) were White, and the median number of foci was 2 (range 1–3), with an average distance

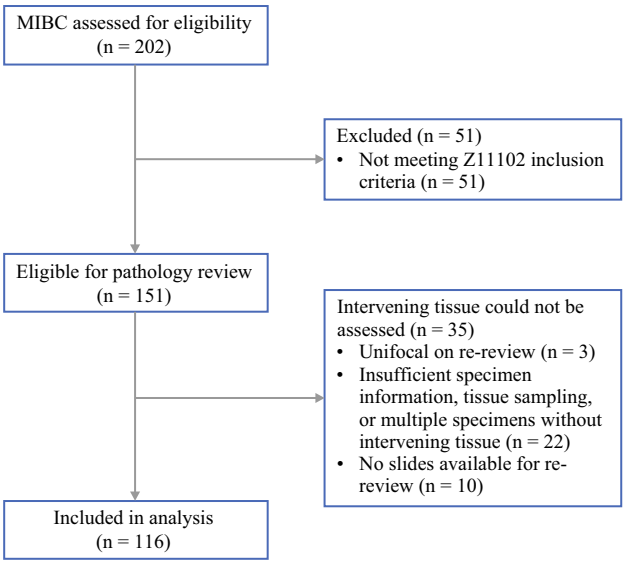

FIG. 1 CONSORT diagram for patient selection. *CONSORT* Consolidated Standards of Reporting Trials, *MIBC* multiple ipsilateral breast cancer

between foci of 2.26 cm (range 0.2–10.5 cm). The most common clinical stage was cT1 (84, 72.4%) and cN0 (111, 95.7%).

Most patients (82.8%) had preoperative MRI performed. Table 2 further characterizes preoperative MRI findings, size and number of lesions, and size of NME stratified by the final surgery received. Among patients who had an MRI, average NME was 4.8 cm and was larger among mastectomy patients (average 5.4 vs. 2.4 cm in BCS). Most patients (112, 96.6%) were hormone receptor-positive (HR+) and human epidermal growth factor receptor 2 (HER2)-negative (HER2−). Sentinel lymph node biopsy was the most common nodal procedure performed (93, 80.2%). In regard to genetic testing, 52/116 (44.8%) patients did not undergo testing before surgery, 58/116 (50%) had negative testing, and 6 patients were found to have pathogenic variants identified (2 ATM, 1 CHEK2, 1 PALB2, 1 PMS2, and 1 MSH6).

Breast Surgery Details

Of the 116 patients, 70 patients underwent mastectomy and 46 underwent BCS as their initial surgeries. Most patients (92, 79.3%) had a single surgery (69 mastectomy, 23 BCS). BCS patients experienced a re-excision rate of 50% (23/46 patients). Eleven patients (11/23, 47.8%) had successful re-excision attempts and maintained breast conservation. Twelve of 23 patients (52.2%) converted to mastectomy, with an overall conversion to mastectomy rate of 26.1% (12/46) [Fig. 2]. Within the mastectomy cohort, 6 patients had positive margins (initial surgery was mastectomy for all 6 patients)—3 were treated with post-mastectomy radiation therapy, 1 underwent nipple re-excision, and 2 had no further treatment. Finally, 33/70 (47.1%) patients underwent contralateral prophylactic mastectomy.

Re-excision attempts for BCS patients are further detailed in Fig. 3. Twenty BCS patients underwent one additional surgery: 10 had a single re-excision resulting in subsequent negative margins, and 10 were converted to mastectomy and that was their final surgery. One patient underwent three total surgical procedures: an initial lumpectomy, with two subsequent re-excisions to achieve negative margins. One patient underwent four total surgical procedures: three lumpectomy/re-excisions before converting to mastectomy. Finally, 1 patient underwent five total surgical procedures: four lumpectomy/re-excisions before converting to mastectomy. Before evaluation of the intervening tissue histopathology, 40/70 (54.1%) patients who underwent mastectomy would have been eligible for BCS based on the Z11102 criteria.

Pathology Findings

On review of the intervening tissue of all 116 patients, 26 (22.4%) had no pathologic findings, 57 (49.1%) had DCIS, 19 (16.4%) had ALH, 13 (11.2%) had ADH, 11 (9.5%) had LCIS, 6 (5.2%) had additional microscopic invasive carcinoma, and 1 (0.9%) had FEA (Fig. 4). Factoring in these intervening findings, 15/70 (21.4 %) patients who initially underwent mastectomy had either normal intervening tissue or intervening tissue with only FEA and could have been appropriate BCS candidates, while 55 had either ALH, ADH, LCIS, DCIS, or invasive carcinoma between the tumor foci. One of the 15 patients who would have been a mastectomy candidate based on pathology had a pathogenic variant in CHEK2, which does not preclude BCS. Of note, DCIS was present in 14/23 patients requiring re-excision for positive or close margins.

Preoperative Magnetic Resonance Imaging and Pathology Findings

Most patients underwent preoperative MRI (96/116, 82.8%). In BCS patients with positive margins requiring further surgeries, 17/23 (73.9%) cases had undergone preoperative MRI. All 6 mastectomy patients with positive margins had preoperative MRI performed. NME was reported in 39 (31 mastectomy, 8 BCS) of the 96 patients who had MRI (40.6%). Of all patients with positive margins, NME was reported in 6/23 (26.1%) BCS patients and 4/6 (66.7%) mastectomy patients.

On pathology re-review of the 31 mastectomy patients with NME on MRI, the intervening tissue of 19 patients (61.3%) contained DCIS, 5 (16.1%) had no pathologic findings, 4 (12.9%) had invasive carcinoma, 2 (6.5%) had

TABLE 1 Patient demographic and clinicopathologic characteristics

Variable	Mastectomy [$n = 70$]	BCS [$n = 46$]	Total [$N = 116$]
Age at diagnosis, years			
Median	61	66	64
Range	34–93	39–85	34–93
Race			
White	62 (88.5)	39 (84.8)	101 (87.1)
African American	5 (7.1)	6 (13)	11 (9.5)
Asian	3 (4.3)	0 (0)	3 (2.6)
Hispanic	0 (0)	1 (2.2)	1 (0.9)
Clinical T category			
cTis	5 (7.1)	1 (2.2)	6 (5.2)
cT1	45 (64.3)	39 (84.8)	84 (72.4)
cT2	18 (25.7)	6 (13)	24 (20.1)
cT3	2 (2.9)	0 (0)	2 (1.7)
Clinical N category			
cN0	66 (94.3)	45 (97.8)	111 (95.7)
cN1	4 (5.7)	1 (2.2)	5 (4.3)
Preoperative MRI			
Yes	59 (84.3)	37 (80.4)	96 (82.8)
No	11 (15.7)	9 (19.6)	20 (17.2)
Number of foci			
Median	2	2	2
Range	1–3	1–3	1–3
Size of foci, cm			
Median	2	1.25	1.7
Range	0.4–6.5	0.4–5	0.4–6.5
NME, cm			
Average	5.4	2.4	4.8
Range	0.4–15	0.7–5.5	0.4–15
Distance between foci, cm			
Average	2.9	1.4	2.26
Range	0.3–10.5	0.15–4.8	0.2–10.5
Tumor biology			
HR+/HER2−	68 (97.1)	44 (95.7)	112 (96.6)
HER2+ (any HR)	2 (2.2)	2 (4.3)	4 (3.4)
Axillary surgery			
SLNB	56 (80)	37 (80.4)	93 (80.2)
ALND	11 (15.7)	2 (4.3)	13 (11.2)
None	3 (4.3)	7 (15.2)	10 (8.6)

Data are expressed as *n* (%) unless otherwise specified

BCS breast-conserving surgery, *MRI* magnetic resonance imaging, *NME* non-mass enhancement, *HR* hormone receptor, *HER2* human epidermal growth factor 2, *SLNB* sentinel lymph node biopsy, *ALND* axillary lymph node dissection

TABLE 2 Imaging (MRI) characteristics, stratified by definitive surgery

Variable	BCS only [$n = 23$]	BCS with re-excision [$n = 11$]	BCS to mastectomy [$n = 12$]	Mastectomy [$n = 70$]
Preoperative MRI				
Yes	19 (82.6%)	9 (81.8%)	9 (75%)	59 (84.3%)
No	4 (17.4%)	2 (18.2%)	3 (25%)	11 (15.7%)
Size of lesions, cm				
Median	1.2	1.2	1.4	2
Range	0.4–5	0.6–2.4	0.4–3.7	0.4–6.5
Number of lesions				
Median	2	1	2	2
Range	1–3	1–3	1–3	1–3
NME, cm				
Average	2.75	1.6	3	5.4
Range	0.7–4.8	0.9–2.7	1.7–5.5	0.4–15

MRI magnetic resonance imaging, *BCS* breast-conserving surgery, *NME* non-mass enhancement

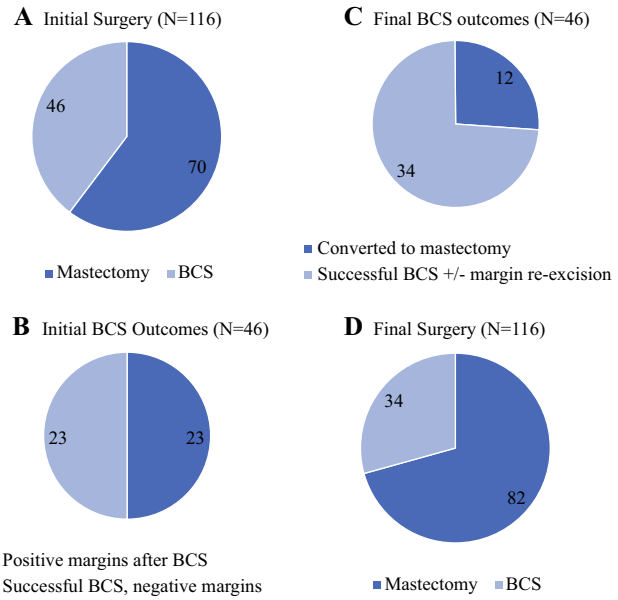

FIG. 2 Percentage of patients who underwent BCS or mastectomy at **A** initial surgery; **B** initial BCS outcomes with a positive margin rate of 50%; **C** final BCS outcomes including 12 patients (26%) who were converted to mastectomy; and **D** final surgery type. *BCS* breast-conserving surgery

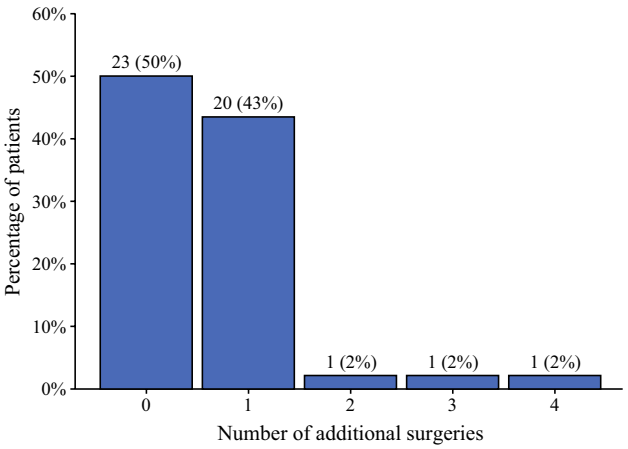

FIG. 3 Number of additional surgeries needed to achieve negative margins in the BCS cohort only. *BCS* breast-conserving surgery

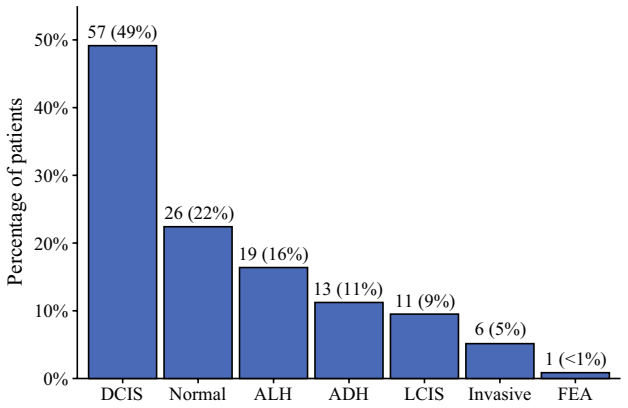

FIG. 4 Breakdown of observed intervening tissue findings from pathology re-review. The number of pathologies exceeds the total *N*, as some patients have more than one pathology. *DCIS* ductal carcinoma in situ, *ALH* atypical lobular hyperplasia, *ADH* atypical ductal hyperplasia, *LCIS* lobular carcinoma in situ, *FEA* flat epithelial atypia

ALH, and 1 (3.2%) had ADH. On pathology re-review of 8 BCS patients with NME on MRI, there were 7 (87.5%) cases of DCIS and 1 (12.5%) ALH.

DISCUSSION

In this single-institution cohort of 116 patients with slides available for re-review, 70.7% underwent mastectomy and 29.3% underwent BCS as their final surgery. Margin positivity and conversion to mastectomy rates in the BCS cohort

were 50% and 26.1%, respectively. Fifteen patients (21.4%) who underwent mastectomy could have undergone BCS based on evaluation of the intervening tissue and applying criteria from ACOSOG Z11102.

The 26.1% conversion to mastectomy rate in this study is much higher than the 7.1% reported in Z11102. There are several possible explanations for this finding. Surgeons and investigators may be more motivated to achieve breast conservation in a clinical trial setting compared with real-world practice, especially when feasibility is a secondary endpoint. Patients who enrolled in Z11102 were likely highly motivated to undergo BCS, as most patients with positive margins chose BCS for their initial re-excision surgery,[15] whereas in our patient population, the percentage of patients choosing BCS or mastectomy for initial re-excision were equal. Patient preference, emotion and future testing anxiety, and physician counseling also influence surgical decision making.[17] In the real-world, the combination of having multiple tumors and positive surgical margins may influence patients to opt for a more definitive surgical procedure, for peace of mind, as opposed to continued breast conservation attempts.

The findings of ACOSOG Z11102 and the current study are significant as mastectomy may be overtreatment for some MIBC patients. Quality of life (QoL) considerations need to be taken into account when discussing mastectomy compared with BCS. Patients with MIBC are often younger and more likely to be premenopausal.[2] It has been observed that young patients are more likely to choose bilateral mastectomies for unilateral breast cancer and more likely to undergo breast reconstruction.[18] In our study, 47.1% of patients who chose mastectomy for their initial operations also opted for contralateral prophylactic mastectomy. However, literature supports that patient satisfaction is higher with BCS compared with bilateral mastectomies.[19–21] Flanagan et al. studied QoL measures via the BREAST-Q in 3233 women who underwent BCS or mastectomy with implant reconstruction. Breast satisfaction decreased over time whereas sexual and psychosocial well-being improved over time, regardless of surgical therapy. The receipt of radiation was found to be detrimental across all domains for both cohorts of patients.[20] Similarly, in a recent prospective cohort study of 292 patients, Vemuru et al. found that QoL measures (breast satisfaction, psychosocial and sexual well-being via the BREAST-Q survey) were higher among patients who received BCS compared with those who received mastectomy (with and without reconstruction), although mastectomy patients also had higher rates of neoadjuvant and adjuvant chemotherapy, which may have impacted these results.[21] These findings further emphasize the importance of patient counseling at initial surgical consultations.

Additional surgeries can result in significant patient dissatisfaction. The margin positivity rate of 50% within the BCS population in this study is high compared with the 32.4% reported in the trial, which may be due to variations in surgical practice or techniques. At our institution, intraoperative margin assessment was performed by all surgeons until mid-2022, however since then, some of our surgeons have adopted cavity shave margins. While our margin re-excision rates have remained relatively stable with the change in practice, techniques of margin assessment can directly influence margin positivity rates. Cavity shave margins have been shown to reduce re-excision rates by nearly 50%;[22] however, implementation of this strategy is variable. In a single-institution study of 55 surgeons, authors found that only 18% of their surgeons performed routine cavity shaves after publication of the SHAVE trial.[22,23] Some institutions prefer intraoperative frozen section(s) for assessment of margins, which allows for immediate re-excision of positive or close margins. In a retrospective single-institution study of 3201 patients undergoing BCS, 60% underwent successful intraoperative re-excision of margins, with a 1.2% reoperation rate for positive margins.[24] In another retrospective review of 157 patients undergoing bracketed excisions of MIBC, a 21% margin positivity rate was reported after intraoperative margin-directed re-excision of 33 cases (33/157, 21%), emphasizing the impact of margin assessment techniques on subsequent margin positivity rates.[25]

The presence of DCIS has also been associated with an increase in margin positivity rates.[26,27] In a prospective randomized controlled trial comparing seed localization with wire localization for non-palpable breast cancers in 305 patients, the authors found that the presence of mammographic microcalcifications, DCIS, high tumor grade, large tumor size, stereotactic localizations, and multifocality were all risk factors associated with an increased risk of margin positivity.[26] In our patient population, DCIS was present in intervening tissue in 14/23 (60.8%) patients needing re-excision surgeries, contributing to the overall margin positivity rate. In an older study by Kurtz et al. of 61 patients with MIBC, the authors reported a high recurrence rate (36%) for multifocal (MF) tumors compared with 11% for UF cancers treated with BCS. However, one of the major limitations of this study was the issue of margins being inadequate or indeterminate for MF tumors, contributing to the higher recurrence rate.[8] It is critical to carefully examine margins if multiple ipsilateral lumpectomies are attempted.

Our study is unique as the intervening tissue between tumor foci was re-examined by subspecialized breast pathologists. The histology of the intervening breast tissue between tumor foci can alter the potential for BCS. This information is not routinely reported in breast cancer pathology reports and can be valuable in the considerations for subsequent surgical management.

ALH and LCIS in the presence of a concurrent malignancy was considered a theoretical indication for excision

in the current study. If detected in a preoperative setting, the recommendation would be excision to rule out additional sites of malignancy. Similarly, the presence of ADH was also significant when deciding if the patient could have received BCS. If ADH had been detected in a preoperative setting, surgical excision would be recommended. There is also known interobserver variability with diagnosing ADH versus DCIS.[28] A large proportion of our patients (49%) had DCIS admixed with and between invasive tumor foci as determined from the pathological review, justifying excision. Lastly, there were six cases of incidental microscopic invasive carcinomas seen on pathology re-review, justifying excision. We acknowledge that atypia within the margins does not constitute a positive margin and would not necessitate re-excision; we are not advocating for re-excision based on these findings, only attempting to inform on the possible pathology findings between MIBCs to generate hypotheses on whether these are a part of the same process or truly two separate cancers and help determine the ability to reliably perform multiple lumpectomies in our patient population.

Factoring in the presence of ALH, ADH, DCIS, LCIS, and carcinoma in intervening tissue, and considering the Z11102 criteria, we found that 15/70 (21.4%) patients who initially underwent mastectomy had either normal intervening tissue or intervening tissue with only FEA and would have been appropriate candidates for BCS in our patient population.

The addition of radiation to BCS likely has a vital role in treating disease seen within intervening tissue. The role of radiation in treating microscopic invasive/in situ disease is well established;[29,30] however, there is a paucity of data regarding radiation effects on atypia within remaining breast tissue. In a retrospective analysis of 414 patients who received lumpectomy and adjuvant radiation, authors sought to determine the impact of atypia found in surgical margins. They compared women with atypical hyperplasia (ADH, ALH) at the surgical margins with women without atypia at the margins. No difference in in-breast tumor recurrence, OS, or distant metastasis-free survival was seen between the two groups,[31] suggesting there is either no impact of residual atypia or a therapeutic benefit from radiation. This highlights the need for further investigation of radiation's effect on breast atypia.

Radiation may be the primary reason that multiple ipsilateral lumpectomies are safe for MIBC. In addition to Z11102, multiple studies, mostly retrospective, have been published assessing the safety of BCS for MIBC.[8–12,32] More contemporary studies have shown no difference in LRR for MIBC and UF tumors treated with BCS.[11,12,32] In a large retrospective analysis of 476 MIBC patients treated with BCS, Gentilini et al. found an LRR of 5.1% at 5 years follow-up, comparable with the LRR for UF tumors. They found that tumor biology has more influence on recurrence and survival rates, specifically HR− and HER2+ tumors.[12] In another retrospective review of 906 patients (673 MF, 233 MC), Lynch et al. found that multifocal/multicentric (MF/MC) disease was not an independent risk factor for locoregional recurrence, regardless of the type of surgical therapy performed. An LRR rate of 1.95% was found in the MF group after BCS compared with 1.02% in the UF group. However, in this study, none of their MC patients received BCS.[32] Lastly, in a prospective analysis by Ozturk et al., the LRR and OS of MF/MC tumors and UF breast cancers was assessed. The study evaluated 1865 cancers: 1493 UF, 330 MF, and 42 MC. The authors found that tumor biology is the most important predictor of local recurrence. On univariate analysis, only histologic grade and molecular subtypes impacted LRR. Surgery type, focality, and lymph node positivity had no impact. On multivariate analysis, HER2+ and triple-negative pathology impacted the LRR. No differences in LRR were seen between MF/MC and UF tumors, regardless of the surgical therapy. These researchers also saw no difference in OS for MF, MC, and UF patients in their study.[11] In short, tumor biology is the most influential variable, and multifocality and multicentricity do not appear to have an impact on recurrence and survival rates. The collective data suggest that BCS can be considered a safe and feasible oncologic procedure for the treatment of MIBC.

Patient selection is important when evaluating a patient for breast conservation, especially one with MIBC. First, it is obviously important to consider the patient's anatomy, such as breast size and location of lesions, when evaluating the ability to achieve satisfactory cosmesis after multiple lumpectomies. Furthermore, the use of preoperative MRI may play an important role in patient selection. MRI was an important factor influencing LRR in Z11102. In an exploratory analysis, patients without preoperative MRI had a higher 5-year LR rate compared with those who underwent preoperative MRI (22.6% vs. 1.7%).[14] Imaging findings such as extent of calcifications and NME are also important considerations.[26,33] A retrospective review was performed of 554 patients who received preoperative MRIs and subsequent BCS over a 10-year period. The primary goal was to identify predictors of positive surgical margins after BCS on preoperative MRI. Patients with NME, larger tumor size, and lobular pathology were associated with positive margins after breast conservation, prompting the authors to recommend preoperative MRI in the setting of multiple tumors to predict patients at risk for positive margins.[33] While our sample size may be too small to draw definitive conclusions, some observations can be made. Since most patients with positive margins in this study (BCS: 17/23, 73.9%; mastectomy: 6/6, 100%) had preoperative MRI, a relationship between positive margins and NME can be observed. In our study, 34.5% (10/29) of all patients (6/23 BCS; 4/6 mastectomy) with positive margins had NME reported on MRI.

Additionally, atypia was also frequently seen in cases with NME on MRI. Combining both cohorts (mastectomy and BCS), atypia and or malignancy was seen in 87.2% (34/39) of patients with NME, demonstrating the possible implications of NME and highlighting an area of future study.

Our study has several important limitations. The retrospective nature precluded us from understanding patient wishes and preferences when making surgical decisions, which could have influenced mastectomy and mastectomy conversion rates. We also could not assess how imaging findings may have influenced the surgeons' recommendations. Our smaller sample size of 46 BCS patients could have also contributed to our observed higher margin positivity and mastectomy conversion percentages. In constructing the study cohort, some of the intervening tissue for breast conservation patients with multiple lumpectomy specimens could be evaluated because the cavities eventually connected, but this was not true for all patients. Additionally, there were other cases where intervening tissue and foci distance could not be determined due to unavailable pathology slides, incomplete grossing information, inadequate tissue sampling, and/or having separate lumpectomy specimens. All of this could have introduced bias and lead to an inaccurate estimate of intervening tissue pathologies. Additionally, our findings may not be generalizable across all tumor subtypes as most of our cohort was HR+, with a small subset that was HER2. Neoadjuvant chemotherapy recipients were excluded, following Z11102 exclusion criteria, which represents another patient population for future studies.

CONCLUSION

Obligatory mastectomy may be overtreatment for some patients with MIBC. The evolving literature suggests that multifocality and multicentricity do not appear to impact LRR and OS.[2,11–14,32] ACOSOG Z11102 demonstrated that multiple lumpectomies are safe and feasible from an oncologic standpoint, with good cosmetic outcomes after adjuvant radiotherapy.[14,15] The impact of ACOSOG Z11102 is significant and allows more patients to avoid the burden of mastectomy; however, patient selection including possible MRI evaluation is critical for successful BCS as re-excision and mastectomy conversion rates may be higher in real-world practice than the clinical trial setting.

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