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Breast-Conserving Surgery in Bilateral Breast Cancer

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Abstract

Background—Bilateral breast cancer (BBC) may present as synchronous(SBC) or metachronous breast cancer(MBC). Optimal surgical management of BBC patients is not well defined. Here we report on histopathology, treatment, and outcomes in BBC patients.

Methods—Upon IRB approval, we identified BBC patients diagnosed and treated for invasive breast cancer between 1999–2007. Retrospective chart review for demographics, histopathology, treatment, and outcomes was performed. Factors associated with BCS choice were collected. Contraindication to BCS was defined as any of the following one-breast findings: multicentric disease; tumor considered too large for BCS; patient without a nominal breast size for acceptable cosmetic results. McNemar's test for matched pairs(binary variables) or the paired t-test(continuous variables) was used to examine if a pathologic characteristic differed within a cancer pair. Kaplan-Meier methods estimated overall survival(OS).

Results—203 BBC patients(119 SBC,84 MBC) comprised our study group. Histopathologic characteristics of the first and second cancers diagnosed in both the SBC and MBC patients were very similar in histologic type and in molecular profiles. 57% of MBC patients underwent breast-conserving surgery at initial diagnosis versus 34% of patients with SBC. BCS contraindications were similar in both groups: 16(34%) of MBC and 28(36%) of SBC patients. Kaplan-Meier OS estimates at 5yrs/10yrs were 86%/78% for MBC, and 87%/77% for SBC patients, respectively.

Conclusions—OS was excellent for both MBC and SBC groups. Contraindications to breast-conserving surgery did not differ between groups. However, patients with SBC were less likely to undergo BCS compared to patients with MBC at time of initial diagnosis.

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Keywords

bilateral breast cancer; breast-conserving surgery

Introduction

Patients who are diagnosed with a primary breast cancer are at an increased risk of second primary breast cancers¹, i.e., synchronous (SBC) or metachronous breast cancer (MBC). Although there are various definitions of SBC, the most common definition of SBC is a contralateral breast cancer diagnosed within 90 days of the first tumor.² Patients with MBC are thought to develop a second primary over the course of follow-up, and usually defined as greater than 6 months from diagnosis of first tumor.³ Over the last 3 decades in MBC patients, the incidence of a second primary cancer in the contralateral breast has been reported in various studies as ranging from 1.4%–12.0%, with 6–15 years of follow-up.^{4–7}

The optimal surgical management of patients with BBC (bilateral breast cancer) is not well defined. For patients with BBC who undergo breast-conserving surgery (BCS), the follow-up and risk of locoregional recurrence of each primary cancer as well as the need for bilateral breast irradiation may all be factors in decision making. Similar outcomes have been reported with bilateral breast irradiation for BBC as for unilateral breast cancer.⁸

Here we report on the pathologic findings, treatment, and outcomes of patients with BBC. We also sought to identify factors associated with choice of BCS.

Methods

Institutional review board approval was obtained at Memorial Sloan Kettering Cancer Center. 203 BBC patients diagnosed and treated between 1999–2007 were identified from our prospectively maintained registered database of 10,629 patients reviewed during this time period. SBC was defined as an invasive BBC within 3 months of the initial diagnosis. The right-sided cancer was designated as “cancer 1” and the left-sided cancer was designated as “cancer 2” in the SBC group. MBC was defined as an invasive BBC diagnosed ≥ 6 months from the initial diagnosis. The initial cancer diagnosis was designated as “cancer 1” and the contralateral cancer was reported as “cancer 2” in the MBC group. Patients with a contralateral cancer diagnosed between 3 and 6 months after initial diagnosis were not included in this analysis to avoid misclassification between the two groups (n=4).

Retrospective chart review was performed to identify patient demographics, histopathology, and treatment information. Family history of breast cancer in a first- or second-degree relative, *BRCA* mutation testing, and contraindications for BCS were identified and recorded. Contraindication to BCS was defined as any of the following findings in one breast: multicentric disease; a tumor considered too large for BCS; or a patient with too small of a breast size for acceptable cosmetic results. We recorded instances in which the chart indicated patient choice as a primary reason for bilateral mastectomy in circumstances when the patient would have been a candidate for BCS or unilateral mastectomy.

Patient charts were reviewed for date of last follow-up and vital status. Location and date of recurrence were recorded for local/regional recurrence (index breast; contralateral breast; index axilla; or contralateral axilla) or distant metastasis. The locoregional and distant recurrences were calculated in each group.

Patient characteristics were summarized by whether a patient had MBC or SBC. Pathological characteristics were summarized for each cancer separately, and analyses compared each pair of cancers in patients with MBC and SBC separately. McNemar's test for matched pairs (binary variables) or the paired t-test (continuous variables) was used to examine if a pathologic characteristic differed within a pair of cancers. Overall survival (OS) was estimated using Kaplan-Meier methods. Among MBC patients, OS was calculated from the time of diagnosis of the second cancer. Statistical analysis was performed by SAS (SAS Institute, Cary, NC). *P*-values <0.05 were considered statistically significant.

Results

Our study group consisted of 203 BBC patients: 119 with SBC, 84 with MBC. Median age was 59 years (range, 36–88) for the SBC patients and 52 years (range, 31–80) for the MBC patients. 51 (43%) SBC patients had a family history of a first- or second-degree relative with breast cancer, and 35 (42%) MBC patients had a family history of breast cancer. Thirty-six (18%) of all patients underwent *BRCA* mutation testing. Of those tested, 9 patients (25%) tested positive for a *BRCA* mutation (5 in *BRCA1*, 4 in *BRCA2*). Six of 9 patients who were *BRCA* mutation carriers had bilateral mastectomies performed. Table 1 summarizes patient characteristics.

The median tumor size of the first cancer in MBC patients was 1.4cm (range, 0.1–7.0), and 0.8cm (range, 0.1 cm–6.0) for the second cancer ($p<0.0001$). The median tumor size in the SBC patients was 1.4cm (range, 0.1–9.0) and 1.3cm (0.2–6.5) ($p=0.51$).

Table 2 shows pathologic findings for the cancers in both groups. The histopathologic characteristics of the first and second cancers diagnosed in each of the SBC and MBC patients revealed that they were very similar, both in histologic type and in molecular profiles (estrogen receptor [ER], progesterone receptor [PR], and HER2). Table 3 shows the concordance within each group for cancer 1 and cancer 2 with respect to ER, PR, and HER2. The majority of patients in both groups had ER positive breast cancer. Invasive ductal carcinoma was the most common histologic type for both cancers in our patients, and within each group for cancer 1 and cancer 2 (Supplementary Table 1a and Supplementary Table 1b). The majority of BBC patients had negative axillary lymph nodes, absence of lymphovascular invasion, and unifocal tumors. We identified a small but significant difference in multifocality in the SBC group, with 35% and 21% of first and second cancers being multifocal ($p=0.01$).

Table 4 provides treatment information for our patients. The surgical treatment for SBC and MBC differed. Forty-eight (57%) of patients with MBC had BCS at initial diagnosis compared to 34% of patients with SBC. The majority of patients with SBC had a bilateral

mastectomy (78 patients); the other 38 patients had bilateral BCS, and 3 had a mastectomy performed on one side and BCS on the contralateral side.

Patients were more likely to undergo axillary SLNB than an ALND in both the MBC and SBC groups, and this is likely to reflect the period of time of our study, prior to SLNB becoming standard treatment.

Because more patients with MBC chose BCS with initial cancer diagnosis, they were also more likely to receive radiation therapy at diagnosis of their first cancer ($p=0.002$). Table 2 shows the number of patients who received radiation therapy following lumpectomy and mastectomy by MBC and SBC groups. Patients with MBC were more likely to receive chemotherapy during treatment for their first cancer ($p=0.0004$). There was no difference in hormonal treatment in either group. As expected, in SBC patients, we saw uniformity of adjuvant treatment in this group of patients.

Of 84 MBC patients, 48 (57%) had BCS at initial diagnosis and 40 (48%) had BCS for their second cancer ($p=0.07$). It is interesting to note that of the MBC patients who had undergone BCS at first cancer diagnosis, 18 (38%) had bilateral mastectomy at time of second diagnosis. It is unclear from chart review why those patients decided on bilateral mastectomy given they were disease free from the index cancer at the time of diagnosis of metachronous cancers.

We sought to identify whether there were contraindications to BCS in either group that would lead to the decision to proceed with mastectomy. Contraindications to unilateral BCS were similar in both groups: 16 (34%) of MBC and 28 (36%) of SBC, and not present in the majority of patients. Additionally, as mentioned previously, very few patients were tested for mutations in the *BRCA* genes. Of the 36 patients tested, only 9 had mutations, and 6 of these underwent bilateral mastectomy. We could not identify a contraindication to BCS in 43% of the patients who chose bilateral mastectomy for surgical treatment. On chart review, patient choice was quoted as a primary decision-making factor, but it is likely that there were other reasons possible beyond what we could discern from chart review.

The median interval between cancers in the MBC group was 2.5 years (range, 0.3–6.3). The median follow-up was 7.5 years (range, 0.1–12.6) for the MBC group, and 6.9 years (range, 0.1–13.4) for the SBC group. Locoregional recurrences occurred in 16 (19%) of the MBC patients (7 patients underwent BCS and 9 patients underwent mastectomy) and 6 (5%) of the SBC patients (1 patient underwent BCS and 5 patients underwent mastectomy). Distant metastases occurred in 12 (14%) of the MBC patients and 15 (13%) of the SBC patients. Kaplan Meier OS estimates at 5 and 10 years were 86% (95% confidence interval [CI], 0.76–0.92) and 78% (95% CI, 0.65–0.86) for MBC patients, and 87% (95% CI, 0.79–0.92) and 77% (95% CI, 0.66–0.84) for SBC patients, respectively. FIG 1(a) shows the OS for MBC, and FIG 1(b) for SBC patients.

A secondary analysis for OS was performed based on ER concordant tumors and discordant tumors of the cancer in both groups. There were 24 patients in the metachronous cancer group with discordant ER status, and the concordant cases had better OS ($p=.017$). There were 13 patients with discordant ER status in the synchronous group, and no significant

difference in OS was noted ($p=0.73$). Fig 1(c) shows OS for MBC, and Fig 1(d) shows OS for SBC patients by ER concordant and discordant cases.

Discussion

There is no general consensus on surgical treatment for patients with BBC. It has been suggested that therapy in BBC should resemble the treatment strategy in unilateral breast cancer.⁹ Within the group of patients with BBC, the MBC group and SBC group presented at different times, likely affecting choice of surgical treatment. The patients with SBC are faced with the diagnosis concurrently, and, as our data show, they are more likely to have similar surgical treatment for both breasts.

The MBCs are in fact more like unilateral breast cancers, as although all patients with primary breast cancer have a risk of developing contralateral breast cancer, that risk is low overall. The latest overview of the National Surgical Adjuvant Breast and Bowel Project (NSABP) B24 trial reported that with concurrent tamoxifen use, the risk of contralateral disease at 15 years follow-up was 7.3%¹⁰, again demonstrating that BBC is an uncommon event.

Additionally, our MBC data are consistent with prior published reports indicating that the first cancer is often more advanced and larger than the contralateral (second) cancer.¹¹ Our patients with MBC had significantly larger-size first tumors, and were more likely to receive chemotherapy for the first diagnosis. This likely reflects the more advanced nature of the first cancer compared to the second cancer in MBC patients. Also, after MBC patients are diagnosed with their first breast cancer, they may undergo enhanced screening in the future, contributing to detecting a metachronous cancer at a smaller size and/or stage.

Of the MBC patients who had BCS ($n=48$) at first cancer diagnosis, 18 (38%) had bilateral mastectomy at time of second diagnosis. It is unclear from chart review why those patients decided on bilateral mastectomy given they were disease free from the index cancer at the time of diagnosis of metachronous cancers, particularly as the metachronous tumors were smaller and multifocality did not significantly differ. Multiple reasons, including fear of having another diagnosis of breast cancer in the future, may have contributed to their decision.

SBC patients were less likely to have BCS overall, and 66% of SBC patients had a bilateral mastectomy at diagnosis. Very few SBC patients (3) had BCS surgery for one cancer and mastectomy for the other (contralateral) side. Contraindications to BCS did not differ between the MBC compared to the SBC group, i.e., 34% versus 36%. Overall, in our study group with BBC, 62% underwent bilateral mastectomy. This included all patients who underwent bilateral mastectomy as the definitive surgery, including those who had bilateral mastectomy for treatment of MBC and those thought to have a reason BCS could not be performed. Forty-four patients (35%) had a contraindication that BCS was not selected in one breast and thus did not account for the high percentage of bilateral mastectomy. However, our data are consistent with other published reports such as Kheirelseid et al that reported 64.7% of their BBC patients underwent bilateral mastectomy.⁶ It is a limitation to

our study and beyond the scope of this retrospective study to be able to fully identify all possible influential factors that are encompassed under surgical decision making, including patient choice. A further limitation of our study is that we did not have MRI data on all our patients, as this was not routinely used in the earlier years of our study period. Thus we do not know its effect in patients as a result.

It has been proposed that the diagnosis of two primary breast cancers may be the accumulation of genetic predisposition or possibly two independent sporadic events.¹² *BRCA1* and *BRCA2* mutation carriers have an annual risk of 2%–6% of developing a second primary breast cancer.¹³ In December 2013, the U.S. Preventive Services Task Force recommended risk assessment, genetic counseling, and genetic testing for *BRCA*-related cancer in those patients who may have an increased likelihood of a *BRCA* mutation. In addition to other factors, this included those patients with bilateral breast cancer.¹⁴ In our study, very few patients were tested for the *BRCA* genes, and only 9 patients had a mutation identified, of whom 6 had bilateral mastectomy. It is likely that a fewer-than-expected number of BBC patients underwent *BRCA* mutation testing because our patients were diagnosed during an earlier time period when routine gene testing was not often offered to patients with BBC.

We noted that BBC patients had similar pathologic tumor characteristics of first and second cancers. This finding was also seen in a study by Baker et al where there was no significant difference between the first and second primary tumor in the study's SBC and MBC patients in terms of histologic features and hormonal status.¹³ A more recent study by Huo et al¹⁵ found that in the majority of cases, concordance in histological and biological parameters was noted between first and second cancers.

Similarly, a recent report using SEER data found that among patients within SBC or MBC, pathologic tumor characteristics of the first and second cancer were likely to be the same. Discordant ER receptor status was found in 10% of SBC patients and 14–15 % of MBC patients. However, the report noted that a discordance in ER of each cancer was an independent prognostic factor in each group.¹⁶

In our study, the subset of patients who had discordant tumors comprised 13 patients in the SBC group and 24 patients in the MBC group (Table 3). An additional analysis did show that patients with a discordant ER receptor in the metachronous group had worse OS. This was not noted in the synchronous group, but our analysis was limited by the few patients with discordant cancers in the SBC group.

Sandberg et al also noted discordant ER adversely affected prognosis in SBC but not MBC. Interestingly, they noted MBC tumors that were concordant for ER positive receptors had similar outcomes to concordant ER negative tumors, thus raising the possibility of endocrine therapy resistance.¹⁷

A limitation to studies on analysis of concordance is the inherent possibility of misclassification of hormone receptors that can occur between primary and secondary cancers.¹⁸ It is a strength of our study that, being a single-institution study, the pathologic assessment was consistent for our patients.

Finally, it is important to note that the prognosis of metachronous BBC is difficult to assess because it is conditional on the age of the patient and the survival of the patient after the first cancer diagnosis.¹⁹ As reported by Diaz et al in a retrospective study of 120 cases of BBC, there was no difference in OS between patients with SBC and the second diagnosis of MBC.⁴ This was similar to the findings in our study where OS was similar in the MBC and SBC groups. Some studies show a trend toward decreased OS and local control for patients with SBC, and compared with either MBC or unilateral breast cancer,⁵ while other studies, such as a study by Nichol et al, showed that in a matched analysis, breast cancer-specific survival was equivalent in SBC patients and unilateral breast cancer patients.²⁰ As recognized in other studies, analyzing OS in MBC and SBC patients together is biased as the MBC patients have a survival advantage because they have lived long enough to develop the contralateral breast cancer.²¹

Further limitations to our study include the small group of patients identified over a few decades, where treatments may have varied. However, the small numbers of patients with BBC noted are consistent with published data. In a recent report by Londero et al,²² a review of the published literature reveals the prevalence of MBC and SBC is low, at 3% and 7%, respectively.

In conclusion, in patients with BBC, presenting with SBC led to a greater similarity in surgical treatment choice for both breasts, with the majority of patients choosing bilateral mastectomy. In patients with MBC, the majority of patients chose BCS at time of initial diagnosis. Contraindications to BCS did not differ between the groups. In our study, although OS was similar in the MBC and SBC groups, in MBC, patients with discordant ER receptor status had an overall worse prognosis.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Synopsis

Bilateral breast cancer is rare, and the choice of breast-conserving surgery is not well studied. In our study, patients with synchronous breast cancer were more likely to undergo bilateral mastectomy compared to patients with metachronous breast cancer.

Fig 1.

(a) Overall survival for the MBC patients. For the MBC patients, follow-up begins at the time of diagnosis of the second cancer. (b) Overall survival for the SBC patients. (c) Overall survival for metachronous breast cancer. (d) Overall survival for synchronous breast cancer patients by estrogen receptor concordant and discordant cases.

Note: Yellow lines in Fig. 1a and 1b are 95% confidence limits for the Kaplan-Meier estimates.

Note: Concordance comparison was performed only on patients where ER status was known for both cancers. There were 4 patients in MBC and 2 patients in SBC, with one of the two cancers of unknown ER status that were excluded from the analysis.

MBC, metachronous breast cancer; SBC, synchronous breast cancer

Table 1
Patient characteristics

Characteristic	MBC (n = 84)	SBC (n = 119)	Total (n = 203)
Median age at diagnosis of first cancer (range)	52 years (31–80)	59 years (36–88)	
Family history of breast cancer			
None	49/84 (58%)	68/119 (57%)	117/203 (58%)
First degree	22/84 (26%)	35/119 (29%)	57/203 (28%)
Second degree	13/84 (15%)	16/119 (13%)	29/203 (14%)
BRCA mutation status			
Negative *	18/23 (78%)	9/13 (69%)	27/36 (75%)
BRCA1+ *	2/23 (9%)	3/13 (23%)	5/36 (14%)
BRCA2+ *	3/23 (13%)	1/13 (8%)	4/36 (11%)
Unknown	61	106	167

* Percentage among those tested

MBC, metachronous breast cancer; SBC, synchronous breast cancer

Table 2

Pathologic characteristics

Characteristic	MBC (n = 84)			SBC (n = 119)		
	Cancer 1	Cancer 2	p-value	Cancer 1 (Right)	Cancer 2 (Left)	p-value
Tumor median size (range)	1.4 cm (0.1–7 cm) n = 79	0.8 cm (0.1–6 cm) n = 81	<0.0001	1.4 cm (0.1–9 cm) n = 117	1.3 cm (0.2–6.5 cm) n = 71	0.51
Stage at diagnosis *						
I	37/67 (55%)	43/67 (64%)	0.95	57/98 (58%)	48/91 (53%)	0.45
II	18/67 (27%)	19/67 (28%)		29/98 (30%)	32/91 (35%)	
III	12/67 (18%)	5/67 (7%)		12/98 (12%)	11/91 (12%)	
IV	0/67 (0%)	0/67 (0%)		0/98 (0%)	0/91 (0%)	
Unknown	17	17		21	28	
Histology *						
Invasive ductal	70/84 (83%)	71/84 (85%)	0.44	88/119 (74%)	97/119 (82%)	0.40
Invasive lobular	11/84 (13%)	8/84 (10%)		26/119 (22%)	17/119 (14%)	
Mixed invasive	2/84 (2%)	2/84 (2%)		4/119 (3%)	2/119 (2%)	
Other invasive	1/84 (1%)	3/84 (3%)		1/119 (1%)	3/119 (3%)	
Multifocality *						
No	56/75 (75%)	63/81 (78%)	0.68	77/119 (65%)	94/119 (79%)	0.01
Yes	19/75 (25%)	18/81 (22%)		42/119 (35%)	25/119 (21%)	
Unknown	9	3		0	0	
Axillary lymph node positive						
Yes	29/84 (35%)	31/84 (37%)	0.72	45/119 (38%)	44/119 (37%)	0.88
No	55/84 (65%)	53/84 (63%)		74/119 (62%)	75/119 (63%)	
LVI *						
Yes	19/77 (25%)	19/83 (23%)	0.82	28/119 (24%)	28/119 (24%)	1
No	58/77 (75%)	64/83 (77%)		91/119 (76%)	91/119 (76%)	
Unknown	7	1		0	0	

Characteristic	MBC (n = 84)			SBC (n = 119)		
	Cancer 1	Cancer 2	p-value	Cancer 1 (Right)	Cancer 2 (Left)	p-value
ER*						
Positive	53/82 (65%)	55/82 (67%)	0.68	99/118 (84%)	98/118 (83%)	0.78
Negative	29/82 (35%)	27/82 (33%)		19/118 (16%)	20/118 (17%)	
Unknown	2	2		1	1	
PR*						
Positive	46/82 (56%)	38/81 (47%)	0.14	80/118 (68%)	76/118 (64%)	0.51
Negative	36/82 (44%)	43/81 (53%)		38/118 (32%)	42/118 (36%)	
Unknown	2	3		1	1	
HER2neu*						
Positive	7/73 (10%)	8/82 (10%)	1	7/117 (6%)	12/118	0.20
Equivocal	7/73 (10%)	1/82 (1%)		5/117 (4%)	(11%)2/118 (2%)	
Negative	59/73 (81%)	73/82 (89%)		105/117 (90%)	104/118 (88%)	
Unknown	11	2		2	1	

* Percentage of those tested

MBC, metachronous breast cancer; SBC, synchronous breast cancer; LVI, lymphovascular invasion; ER, estrogen receptor; PR, progesterone receptor

Table 3
Concordance of cancer 1 and cancer 2 in each group for ER, PR, and HER2

Metachronous ^a			Synchronous ^a		
	<i>Negative</i>	<i>Positive</i>		<i>Negative</i>	<i>Positive</i>
<i>ER Negative</i>	16 (20%)	13 (16%)	<i>ER Negative</i>	12 (10%)	6 (5%)
<i>ER Positive</i>	11 (14%)	40 (50%)	<i>ER Positive</i>	7 (6%)	92 (79%)
<i>Total</i>		80 (100%)	<i>Total</i>		117 (100%)
<i>PR Negative</i>	24 (30%)	11 (14%)	<i>PR Negative</i>	21 (18%)	16 (14%)
<i>PR Positive</i>	19 (24%)	25 (32%)	<i>PR Positive</i>	20 (17%)	60 (51%)
<i>Total</i>		79 (100%)	<i>Total</i>		117 (100%)
<i>HER2 Negative</i>	51 (81%)	5 (8%)	<i>HER2 Negative</i>	93 (84%)	10 (9%)
<i>HER2 Positive</i>	5 (8%)	2 (3%)	<i>HER2 Positive</i>	5 (5%)	2 (2%)
<i>Total</i>		63 (100%)	<i>Total</i>		110 (100%)

ER, estrogen receptor; PR, progesterone receptor

* Concordance comparison was only performed on patients in whom ER, PR, and HER2 was known for both cancers

Table 4**Treatment characteristics**

Treatment	MBC (n = 84)			SBC (n = 119)		
	Cancer 1	Cancer 2	p-value	Cancer 1 (Right)	Cancer 2 (Left)	p-value
Breast Surgery*						
Lumpectomy	48/84 (57%)	40/84 (48%)	0.074	40/119 (34%)	39/119 (33%)	0.564
Mastectomy	36/84 (43%)	43/84 (51%)		79/119 (66%)	80/119 (67%)	
ALND only	0/84 (0%)	1/84 (1%)		0/119 (0%)	0/119 (0%)	
Axillary surgery*			0.005			0.423
ALND	39/84 (46%)	24/84 (29%)		44/119 (37%)	39/119 (33%)	
SLNB	44/84 (52%)	59/84 (70%)		75/119 (63%)	77/119 (65%)	
None	1/84 (1%)	1/84 (1%)		0/119 (0%)	3/119 (3%)	
Radiation therapy*			0.002			0.166
Yes	59/80 (74%)	42/79 (53%)		64/111 (58%)	44/112 (39%)	
Post-lumpectomy	43	36		60	31	
Post-mastectomy	16	6		4	13	
No	21/80 (25%)	37/79 (47%)		47/111 (42%)	68/112 (61%)	
Post-lumpectomy	4	4		32	4	
Post-mastectomy	17	33		15	64	
Unknown	4	5		8	7	
Post-lumpectomy	1	1		4	3	
Post-mastectomy	3	4		4	4	
Chemotherapy*			0.0004			0.317
Yes	54/83 (65%)	31/81 (38%)		80/112 (71%)	81/112 (72%)	
No	29/83 (35%)	50/81 (62%)		32/112 (29%)	31/112 (28%)	
Unknown	1	3		7	7	
Hormone therapy*			0.683			0.157
Yes	43/83 (52%)	46/83 (55%)		89/110 (81%)	87/110 (79%)	

		MBC (n = 84)		SBC (n = 119)			
Treatment		Cancer 1	Cancer 2	p-value	Cancer 1 (Right)	Cancer 2 (Left)	p-value
No		39/83 (48%)	37/83 (45%)		21/110 (19%)	23/110 (21%)	
Unknown		1	1		9	9	

* Percentage of those tested

MBC, metachronous breast cancer; SBC, synchronous breast cancer; ALND, axillary lymph node dissection; SLNB, sentinel lymph node biopsy