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Micrometastatic Disease and Isolated Tumor Cells as a Predictor for Additional Breast Cancer Axillary Metastatic Burden

Amy Cyr, MD¹, William E. Gillanders, MD¹, Rebecca L. Aft, MD^{1,2}, Timothy J. Eberlein, MD¹, Feng Gao, PhD³, and Julie A. Margenthaler, MD, FACS¹

Julie A. Margenthaler: margenthalerj@wudosis.wustl.edu

¹Department of Surgery, Washington University School of Medicine, St. Louis, MO

²Department of Surgery, John Cochran Veterans Hospital, St. Louis, MO

³Division of Biostatistics, Washington University School of Medicine, St. Louis, MO

Abstract

Background—Our study aims were to investigate breast cancer patients with micrometastases or isolated tumor cells (ITCs) in sentinel lymph nodes (SLNs) to determine the rate of non-SLN metastasis and axillary recurrences, and to compare actual non-SLN metastasis rates with those predicted by the Memorial Sloan-Kettering Cancer Center (MSKCC) nomogram.

Methods—We identified 116 stage I to III breast cancer patients who underwent sentinel lymph node biopsy and had micrometastases or ITCs (<2-mm deposits). Patients underwent completion axillary lymph node dissection (ALND) (group 1) or had no further axillary surgery (group 2). $P < 0.05$ was considered statistically significant.

Results—Of 116 patients with micrometastases or ITCs in SLNs, 55 (47%) underwent completion ALND (group 1), and 61 (53%) had no further axillary surgery (group 2). The rate of non-SLN metastases in group 1 patients was 9 (16%) of 55, which was significantly less than that predicted by the MSKCC nomogram (median 30%, $P < 0.001$). Patient age, race, tumor histology, tumor grade, estrogen receptor/Her-2neu status, and lymphovascular invasion did not differ significantly between group 1 patients with positive non-SLNs and those with negative non-SLNs ($P > 0.05$ for each), but patients with positive non-SLNs had larger tumors ($P < 0.001$). No patient in group 1 experienced an axillary recurrence, while only one patient (1.6%) in group 2 experienced axillary recurrence.

Conclusions—The actual rate of positive non-SLNs for breast cancer patients with SLN micrometastases or ITCs who underwent completion ALND was significantly less than that predicted by the MSKCC nomogram. The rate of axillary recurrence is negligible, regardless of the extent of axillary staging.

Sentinel lymph node (SLN) biopsy (SLNB) has become the standard for axillary staging in patients with clinically node-negative breast cancer. Typically patients with metastatic disease found in a SLN undergo completion axillary lymph node dissection (ALND). Because pathologists can focus on a small number of SLNs rather than routinely evaluating the entire axillary contents, and because of the more widespread use of immunohistochemistry (IHC), micrometastases and isolated tumor cells (ITCs) are more frequently being identified.

The clinical significance and management of ITCs (<0.2 mm) and micrometastatic (0.2–2 mm) sentinel lymph node disease remains unclear. ITCs and micrometastases have been considered separate categories since the American Joint Commission on Cancer staging manual was updated in 2002.¹ Many studies show that micrometastatic disease may be associated with worse overall survival, disease-free survival, and/or a higher likelihood of distant recurrence compared to N0 disease, although other studies refute this.^{2–10} The data are less clear regarding the prognostic significance of ITCs.^{3,5,6} Current American Society of Clinical Oncology (ASCO) guidelines recommend completion ALND when SLNs have tumor deposits >0.2 mm, i.e., for micrometastatic disease, but not for ITCs.¹¹

Only approximately half of patients with macrometastases in the SLN will have positive non-SLNs, and that likelihood lessens as the amount of disease in the SLN decreases.^{5,12,13} Therefore, most patients undergoing subsequent ALND for ITCs or micrometastatic disease are unlikely to have any additional disease found in non-SLNs. In such patients, ALND serves as a means of staging patients, rather than providing therapeutic value. However, the importance of axillary staging is now under investigation as biologic tumor profiles are increasingly used to stratify women prognostically to various treatment algorithms.^{14–16} Women who are identified as being unlikely to have additional nodal disease or as unlikely to benefit from further axillary staging may ultimately be spared the morbidity of ALND. Memorial Sloan-Kettering Cancer Center (MSKCC) created a nomogram to predict the likelihood of finding metastases within non-SLNs.¹³ Although the nomogram takes into account the method by which SLN metastases are identified (routine hematoxylin and eosin [H&E], additional H&E levels, or IHC), it may not be reliable when the SLN has micrometastatic disease or ITCs only.¹⁷

Our study aims were to determine the rate of non-SLN metastases for patients with ITCs or with micrometastatic SLNs, to determine the rate of axillary recurrence in the absence of completion ALND, and to compare actual non-SLN metastasis rates with those predicted by the MSKCC nomogram in patients who proceed with completion ALND. A secondary aim was to determine whether the likelihood of positive non-SLNs or axillary recurrence differed between patients with ITCs versus micrometastases in their SLNs.

METHODS

Institutional review board approval was obtained before the commencement of this retrospective study. Clinical, demographic, and pathologic data from all breast cancer patients treated at our institution are prospectively recorded in a database. We reviewed this database and identified 1409 stage I to III breast cancer patients who underwent SLNB at our institution between January 1, 1998, and June 30, 2009; a total of 120 (9%) were identified with micrometastases (0.2–2-mm tumor deposits) or ITCs (<0.2 mm) within the SLN. Incomplete information existed for four of these patients, and they were excluded. Therefore, a total of 116 patients were included in the analysis. Data recorded included age at diagnosis, race, tumor size, histology, grade, estrogen receptor (ER) status, Her-2neu status, presence of lymphovascular invasion, and the use of neoadjuvant and/or adjuvant systemic therapy. For patients who did receive neoadjuvant systemic therapy, pretreatment clinical tumor size was used. Pathology reports were reviewed to determine the size of the SLN metastasis and, where available, the type of pathology used to identify the metastatic disease, i.e., routine H&E sections, frozen section, and/or IHC. All breast pathology at our institution is reviewed by a dedicated breast pathologist. However, the slides were not reviewed again for this study analysis. For patients who underwent subsequent completion ALND, the absence or presence of non-SLN disease was recorded, as well as the number of positive non-SLNs as applicable.

The likelihood of identifying positive non-SLNs was calculated for each patient by the MSKCC nomogram (<http://www.mskcc.org/mskcc/html/15938.cfm>). When inputting patient data into the nomogram, routine H&E for identification of SLN metastasis was presumed unless the pathology report stated otherwise. We were unable to compute the likelihood of having positive non-SLNs for 13 patients because of missing information, such as tumor size, or because the primary tumor lacked an invasive component. For several patients, pathology reports estimated tumor size as a range. For these patients, the nomogram was used to compute the likelihood of positive non-SLNs at both the lower and upper limits of the tumor size estimate, and a value halfway between the two nomogram estimates was used for the analysis.

Patients were divided according to whether they underwent completion ALND (group 1) or had no further axillary surgery (group 2). The rates of non-SLN metastases in group 1 patients were compared to that predicted by the MSKCC nomogram. Axillary recurrences were identified and recorded. Patients were followed by clinical examination and mammogram (in patients after lumpectomy); routine axillary imaging surveillance was not performed. All data were transferred to a single spreadsheet (Excel; Microsoft, Redmond, WA). Data were compared by χ^2 , Student's *t*-test, and Fisher's exact test, as appropriate. All statistical analyses were performed by SAS software (SAS Institutes, Cary, NC). A *P* value of <0.05 was taken to indicate significance, and all statistical tests were two-sided.

RESULTS

Of 116 patients with micrometastatic SLN disease, 55 (47%) underwent completion ALND (group 1), and 61 (53%) had no further axillary surgery (group 2). Patients were not more likely to be in group 1 or group 2 according to the time period of the study. For group 1 patients, 30 patients were treated from 1998 to 2004 and 25 were treated from 2005 to 2009. For group 2 patients, 36 were treated from 1998 to 2004 and 25 were treated from 2005 to 2009. Thus, during years 1998 and 2004, 30 patients underwent ALND and 36 did not, and during years 2005 and 2009, 25 patients underwent ALND and 25 did not.

The median age of group 1 patients (51 years; range 32–79 years) was statistically significantly younger than the median age of group 2 patients (57 years; range 32–86 years). Group 1 patients were significantly more likely to have higher grade tumors ($P = 0.02$), and there was a trend toward larger tumor size, lobular versus ductal histology, and ER-negative status, but these latter variables did not reach statistical significance. The groups did not differ statistically significantly in terms of patient race, presence of lymphovascular invasion, or Her-2neu status. Patients in group 1 were more likely to have a mastectomy compared to patients in group 2 ($P = 0.0005$). There was a trend toward group 1 patients having increased numbers of SLNs removed compared to group 2 patients, but this did not reach statistical significance. In contrast, group 2 patients were more likely to have one or more non-SLNs removed compared to group 1 patients ($P = 0.003$). There were no differences between the groups with respect to the use of neoadjuvant systemic therapy or adjuvant endocrine therapy. There also were no differences between the groups with respect to the method of SLN metastasis detection (i.e., H&E vs. IHC; raw data not shown). Table 1 summarizes the characteristics of the two groups. The patients in group 1 were predicted by the MSKCC nomogram to have a median likelihood of having positive non-SLNs of 30% (range 3–81%). There was inadequate data to use the nomogram for six of these patients. The actual rate of positive non-SLNs in group 1 patients was 16%, which was significantly lower than that predicted by the MSKCC nomogram ($P < 0.001$). For group 2 patients, where the actual rate of positive non-SLNs is unknown, the MSKCC nomogram estimated the median likelihood of having positive non-SLNs at 17% (range 2%–63%). There was inadequate data to use the nomogram for seven patients in group 2.

Of the 55 women undergoing ALND, 9 were found to have positive non-SLNs (16%), and the median number of positive non-SLNs was 2 (range 1–5). All positive non-SLNs had macrometastatic disease except in one patient, who had only a 1-mm tumor deposit within the sole positive non-SLN found at ALND. This patient had a 1- to 2-mm tumor deposit within the SLN. The median age of patients having positive non-SLNs (49 years, range 38–65 years) was not statistically significantly different from those without non-SLN disease (51 years; range 38–79 years). Among those women in group 1, there was no difference between those who had positive non-SLNs and those who had negative non-SLNs with respect to race, tumor histology, ER status, Her-2neu status, tumor grade, and the presence or absence of lymphovascular invasion. Larger tumor size, however, was more common in women having positive non-SLNs ($P < 0.001$). Table 2 summarizes the characteristics of group 1 patients with and without non-SLN disease. Of the nine patients in group 1 with positive non-SLNs, the MSKCC nomogram was calculated for eight with sufficient data; the predicted median likelihood of finding positive non-SLNs was 36% (range 21%–81%). Of the 46 patients in group 1 with negative non-SLNs, the MSKCC nomogram was calculated for 41 with sufficient data; the predicted median likelihood of finding positive non-SLNs was 29% (range 3%–72%). This difference was not statistically significant.

Group 1 was further subdivided by the amount of metastasis within the SLN, i.e., ITC or micrometastasis. Only women who clearly had less than micrometastatic disease were included in the ITC group. These pathology reports described “isolated cells,” measured the metastatic deposit as <0.2 mm, or staged the patient as N0(i+). Of the 55 patients in group 1, 41 (75%) had micrometastases within the SLN, and 5 of these had positive non-SLNs identified at completion ALND; this represents an overall rate of positive non-SLNs of 12%. Of the 55 patients in group 1, 14 had only ITCs in their SLNs, but 4 of these (29%) were found to have positive non-SLNs. Patient and tumor characteristics for this subgroup analysis are listed in Table 3. The median age of women with ITCs (52 years, range 38–82 years) was not statistically significantly different from the median age of women with micrometastatic disease (55 years; range 32–86 years). There was no difference between patients with ITCs versus micrometastases with respect to patient age, race, tumor histology, or ER status. Patients with ITCs were more likely to be associated with smaller tumor size and higher rates of Her-2neu amplification than patients with micrometastases ($P = 0.012$ and $P = 0.042$, respectively). Patients with micrometastases were more likely to have grade I tumors compared to patients with ITCs ($P = 0.002$), but a large percentage of patients with ITCs had unknown tumor grade. Patients with micrometastatic disease had significantly higher MSKCC nomogram predictions of having non-SLN metastases (29%, range 3%–81%, unable to compute for six patients) compared to patients with ITCs only (12%, range 2%–46%, unable to compute for seven patients) ($P < 0.001$).

The median follow-up for group 1 patients was 50 months (range 0–124 months). One patient developed an in-breast recurrence 2 years after undergoing neoadjuvant chemotherapy and breast-conserving therapy. She presented with a clinical T2 tumor measuring 3.3 cm by ultrasound. After neoadjuvant chemotherapy, her pathological tumor size was 2.5 cm, representing a marginal partial response. She had ITCs identified in one (of one) SLN on routine H&E and at ALND was found to have one additional positive node out of 11 removed. The size of the non-SLN metastasis was 9 mm. She ultimately developed lung metastases and is currently alive at 55 months’ total follow-up (31 months since her metastases were identified). There were no other known breast cancer-related events in group 1 patients.

Group 2 consisted of 61 patients who did not undergo any further axillary staging after their SLNB. Thirty-seven of these women had micrometastatic disease at SLNB, and 24 had ITCs only. The median follow-up for group 2 patients was 60 months (range 2–114 months).

There were no known locoregional or distant recurrences among the women with ITCs only. Of the 37 women with micro-metastatic disease, one died of distant metastases 7 years after her SLNB. One woman developed an in-breast recurrence 3 years after her SLNB. She then underwent a modified radical mastectomy and had no lymph node metastases identified. She was alive without further breast cancer-related events at 94 months' follow-up (58 months' follow-up since disease recurred). A third woman immediately developed locoregional recurrence while undergoing adjuvant chemotherapy. At her initial surgery, two SLNs and two non-SLNs were removed, and all were negative except for one SLN with a micrometastatic deposit. When she experienced recurrence, she underwent a modified radical mastectomy and had disease in 7 of 20 lymph nodes removed. Six months after her salvage surgery, she developed distant disease from which she ultimately died. She represents the only axillary recurrence in group 2. Therefore, the likelihood of axillary recurrence in the setting of micrometastatic SLN disease and in the absence of completion ALND was 1.6%. These outcomes are summarized in Fig. 1.

Eight patients in our cohort received neoadjuvant systemic therapy, either chemotherapy ($n = 6$) or endocrine ($n = 2$) therapy. Only one patient underwent SLNB before neoadjuvant therapy; seven underwent SLNB after neoadjuvant therapy. Of the eight patients who underwent neoadjuvant therapy, five underwent completion ALND after neoadjuvant therapy, and one underwent completion ALND before neoadjuvant therapy (included in group 1), while two had no further axillary surgery (included in group 2). Two of the neoadjuvant patients had ITCs found at SLNB, while the other six had micrometastases.

Four patients in our cohort had SLN disease without an identifiable invasive cancer in the breast (Tables 1, 3). To make certain that data from these four patients did not alter the statistical results, parallel analyses were performed with the exclusion of these patients (raw data not shown). The statistical significance did not change. For example, tumor size in Table 1 has a P value of 0.05 with the four patients included and 0.053 with the patients excluded; none of these patients is included in the Table 2 tumor size statistical analysis, and tumor size in Table 3 has a P value of 0.012 with the four patients included and 0.010 with the patients excluded. On the basis of these findings, the four patients were included in the overall final analysis, recognizing that the invasive component in the breast was not identified.

DISCUSSION

SLNB has largely supplanted complete ALND for axillary staging in clinically node-negative breast cancer patients. Pathologic evaluation of a smaller number of nodes, combined with the use of IHC, has contributed to the identification of ITCs or micrometastatic disease within the SLN. Current ASCO guidelines recommend proceeding with completion ALND when tumor deposits of >0.2 mm are identified within the SLN.¹¹ Such micrometastatic disease may be of prognostic significance, and patients with micrometastatic SLN disease have up to a 20% likelihood of having positive non-SLNs.^{2-7, 12,18,19} The actual benefit of proceeding to completion ALND, however, remains controversial.

In one large study, Cox et al. reported on a series of 2381 patients who had either micrometastatic disease, defined as N1mic or N0(i+), or who had no metastatic disease identified at SLNB.³ Overall and disease-free survival were statistically significantly worse for patients with N1mic disease versus N0(i-) patients, but there was no statistically significant difference in overall or disease-free survival between N0(i+) and N0(i-) patients.³ Overall survival was statistically significantly less for N0(i+) patients who did not undergo ALND compared to N0(i+) patients who did, but there was only one axillary

recurrence among the N0(i+) patients who did not undergo ALND, and this was no higher than the rate of axillary recurrence among N0(i-) patients.³ In fact, reported rates of axillary recurrence in patients with macrometastatic SLN disease in the absence of completion ALND are very low, and ALND is therefore of questionable benefit in patients with even smaller metastatic deposits in the SLN.^{20–23} Additionally, adjuvant systemic therapy and/or radiotherapy is now given to a larger proportion of breast cancer patients, and the addition of such treatment, which improves disease-free survival in patients with micrometastatic SLN disease, may negate any potential benefit of completion ALND for these patients.^{4,6,20}

Older studies suggested a survival benefit with the locoregional control provided by ALND, and because the evidence regarding the benefit of completion ALND in the setting of ITCs or micrometastatic SLNB is mixed, a tool to predict additional axillary burden in these patients would be useful.^{24,25} The MSKCC nomogram is a widely used and validated tool to predict the likelihood of positive non-SLNs, but Alran et al. found it less reliable when applied to a population of patients with micrometastatic SLN disease.¹⁷ Like Van Zee et al., our study found that tumor size did statistically significantly predict non-SLN disease, while grade, histology, and ER status did not.¹³ Unlike Van Zee et al., however, we did not find the presence of lymphovascular invasion to be a statistically significant predictor of non-SLN metastases.¹³ We found that the nomogram overestimated the likelihood of finding positive non-SLNs among our patients with micrometastases and underestimated the likelihood of finding positive non-SLNs among our patients with ITCs.

The use of completion ALND did not affect axillary recurrence in our study. Of the 24 women with ITCs who did not undergo completion ALND, there were no known locoregional or distant recurrences. This is despite a 29% rate of non-SLN metastases among the women with ITCs who did undergo ALND. Thirty-seven patients with micrometastatic SLNs did not undergo completion ALND. Disease of one woman recurred within the breast, but no axillary disease at modified radical mastectomy was found. One patient died of distant disease years after her surgery but was not known to have any axillary recurrence. The only axillary recurrence observed in a patient not undergoing ALND occurred in a patient with micrometastatic SLN disease. Thus, our data seem to support the theory that omitting completion ALND for patients with micrometastatic SLN disease is not associated with a far higher likelihood of axillary recurrence.

Our study has several limitations. First, it is a retrospective chart review that includes patients diagnosed over the past 10 years. The American Joint Committee on Cancer staging categories have changed within this time, as has our institution's protocol for SLN handling. IHC was routinely used for all negative H&E SLNs early in the study period, but now is used only for SLNBs where the primary tumor has a lobular histology. Pathology during the study period was read by a variety of pathologists, although all specialized in breast pathology. Retrospective studies may be prone to selection bias, and retrospectively, it is unclear why certain patients underwent ALND and others did not. More worrisome patient or tumor characteristics may have contributed to the decision to proceed to ALND in certain women, though only higher tumor grade was identified as statistically significant in our analysis. Finally, some of the women who did not undergo completion ALND may have been treated instead with axillary radiotherapy, but this information was not readily available.

Despite these limitations, the current study demonstrates that 16% of patients who have ITCs or micrometastases in the SLNs will have positive non-SLNs. However, the rate of axillary recurrence seems to be negligible regardless of the extent of axillary surgical therapy. Longer-term data are needed to evaluate the prognostic importance of ITCs and micrometastases in SLNs and to evaluate the optimal therapy when micrometastatic disease

is found after SLNB. Several large, multi-institutional trials have been proposed or are underway to answer the question regarding the therapeutic necessity of completion ALND after a positive SLNB. The American College of Surgeons Oncology Group Study Z0011 randomized patients with a positive SLN to completion ALND versus no further axillary surgery to determine whether completion ALND was beneficial.²⁶ The study was suspended as a result of poor accrual, but results presented at the American Society of Clinical Oncology meeting in June 2010 indicated that completion ALND provided no statistically significant local control or survival benefit. The International Breast Cancer Study Group 23-01 trial is currently accruing patients to determine the prognostic significance of micrometastatic involvement of SLNs and the European Organization for Research and Treatment of Cancer is conducting the AMAROS (After Mapping of the Axilla: Radiotherapy or Surgery?) trial to compare the regional control of the axilla obtained by completion ALND versus axillary radiotherapy in patients with positive SLNs. These prospective data are needed so that guidelines may be developed to aid in the complex decision making that surrounds the diagnosis and treatment of ITCs and micro-metastatic SLN disease in women with breast cancer.

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FIG. 1.

Long-term follow-up for 116 patients with micrometastatic or isolated tumor cells (ITCs) in sentinel lymph nodes (SLNs) after sentinel lymph node biopsy (SLNB) who either underwent completion axillary lymph node dissection (ALND) or had no further axillary surgery. Four patients experiencing locoregional or distant recurrence are shown in relation to their original groups; all other patients are without evidence of disease progression at follow-up

TABLE 1

Patient and tumor characteristics for group 1 (ALND after SLNB) and group 2 (no further axillary surgery) patients

Variable	Group 1 (n = 55), n (%)	Group 2 (n = 61), n (%)	P value
Race			0.31
White	35 (64)	44 (72)	
African American	16 (29)	16 (26)	
Other	4 (7)	1 (2)	
Tumor size			0.05
TX	0	4 (7)	
T1	37 (67)	44 (72)	
T2	15 (27)	13 (21)	
T3	3 (5)	0	
Tumor histology			0.08
Ductal	42 (76)	49 (80)	
Lobular	10 (18)	4 (7)	
Other/mixed	3 (5)	8 (13)	
ER status			0.08
Positive	40 (73)	54 (89)	
Negative	11 (20)	5 (8)	
Unknown	4 (7)	2 (3)	
Her-2neu status			0.96
Amplified	11 (20)	11 (18)	
Non-amplified	38 (69)	43 (70)	
Unknown	6 (11)	7 (11)	
Tumor grade			0.02
I	14 (25)	24 (39)	
II	20 (36)	20 (33)	
III	19 (35)	9 (15)	
Unknown	2 (4)	8 (13)	
Lymphovascular invasion			0.38
Present	15 (27)	13 (21)	
Absent	33 (60)	44 (72)	
Unknown	7 (13)	4 (7)	
Surgical treatment of the breast			0.0005
Lumpectomy	29 (53)	51 (84)	
Mastectomy	26 (47)	10 (16)	
Neoadjuvant systemic therapy			
Yes	6 (11)	2 (3)	0.15
No	49 (89)	59 (97)	
Adjuvant endocrine therapy			0.16
Yes	24 (44)	41 (67)	

Variable	Group 1 (<i>n</i> = 55), <i>n</i> (%)	Group 2 (<i>n</i> = 61), <i>n</i> (%)	<i>P</i> value
No	31 (56)	20 (33)	
Number of SLNs removed			0.053
1	19 (35)	26 (43)	
2	13 (24)	23 (37)	
3	20 (36)	11 (18)	
Unknown	3 (5)	1 (2)	
Number of non-SLNs removed			0.003
0	47 (86)	35 (57)	
1	3 (5)	17 (28)	
2	3 (5)	6 (10)	
3	2 (4)	3 (5)	

ALND Axillary lymph node dissection, *SLNB* sentinel lymph node biopsy, *TX* unknown primary tumor size, *ER* estrogen receptor, *SLNs* sentinel lymph nodes

TABLE 2

Patient and tumor characteristics in 55 patients undergoing ALND for ITCs or micrometastatic-positive SLNs, grouped according to those with positive non-SLNs and those with negative non-SLNs

Characteristic	Positive non-SLNs (<i>n</i> = 9), <i>n</i> (%)	Negative non-SLNs (<i>n</i> = 46), <i>n</i> (%)	<i>P</i> value
Race			0.40
White	7 (78)	28 (61)	
African American	1 (11)	15 (33)	
Other	1 (11)	3 (7)	
Tumor size			< 0.001
T1	3 (33)	34 (74)	
T2	3 (33)	12 (26)	
T3	3 (33)	0	
Tumor histology			0.28
Ductal	5 (56)	36 (78)	
Lobular	3 (33)	7 (15)	
Other/mixed	1 (11)	3 (7)	
ER status			0.99
Positive	7 (78)	33 (72)	
Negative	2 (22)	9 (20)	
Unknown	0	4 (9)	
Her-2neu status			0.53
Amplified	3 (33)	8 (17)	
Nonamplified	5 (56)	33 (72)	
Unknown	1 (11)	5 (11)	
Tumor grade			0.93
I	3 (33)	11 (24)	
II	3 (33)	17 (37)	
III	3 (33)	16 (35)	
Unknown	0	2 (4)	
Lymphovascular invasion			0.99
Present	3 (33)	13 (28)	
Absent	5 (56)	27 (59)	
Unknown	1 (11)	6 (13)	

ALND Axillary lymph node dissection, ITCs isolated tumor cells, SLN sentinel lymph node, ER estrogen receptor

TABLE 3

Patient and tumor characteristics for patients with ITCs versus micrometastatic disease in SLNs

Variable	ITCs (<i>n</i> = 38), <i>n</i> (%)	Micrometastases (<i>n</i> = 78), <i>n</i> (%)	<i>P</i> value
Race			0.580
White	28 (74)	51 (65)	
African American	8 (21)	24 (31)	
Other	2 (5)	3 (4)	
Tumor size			0.012
TX	4 (11)	0	
T1	23 (61)	58 (74)	
T2	9 (24)	19 (24)	
T3	2 (5)	1 (1)	
Tumor histology			0.130
Ductal	26 (68)	62 (79)	
Lobular	4 (11)	10 (13)	
Other/mixed	8 (21)	6 (8)	
ER status			0.090
Positive	29 (76)	64 (82)	
Negative	4 (11)	12 (15)	
Unknown	5 (13)	2 (3)	
Her-2neu status			0.042
Amplified	10 (26)	12 (15)	
Nonamplified	21 (55)	60 (77)	
Unknown	7 (18)	6 (8)	
Tumor grade			0.002
I	7 (18)	31 (40)	
II	14 (37)	26 (33)	
III	8 (21)	19 (24)	
Unknown	9 (24)	2 (3)	

ITC isolated tumor cells, *SLN* sentinel lymph node, *TX* unknown primary tumor size, *ER* estrogen receptor