

Role of Sentinel Lymph Node Biopsy in Ductal Carcinoma-in-situ Treated by Mastectomy

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Background: Sentinel lymph node biopsy (SLNB) is a widely accepted alternative to axillary lymph node dissection in invasive breast cancer. Its role in ductal carcinoma-in-situ (DCIS) is unclear. The purpose of this study was to determine factors associated with the subsequent diagnosis of invasive disease and to determine the role of SLNB when performing a mastectomy for DCIS.

Methods: A retrospective study was conducted of all mastectomies performed on patients with a preoperative diagnosis of DCIS between 2000 and 2005 at a single tertiary-care institution.

Results: Ninety mastectomies for DCIS were included, 54 (60%) of which were performed with concurrent SLNB. Of 44 patients diagnosed preoperatively with DCIS by core biopsy only, 34 patients (63%) had a concurrent SLNB, while 10 patients (28%) were treated with mastectomy alone ($P < .01$). Overall, 30 patients (33%) had invasive disease, 22 of whom received concurrent SLNB. Seven SLNB patients (13%) had positive SLNs. On univariate analysis, multifocality ($P = .03$), multicentricity ($P = .01$), comedonecrosis ($P = .01$), and diagnosis by core biopsy ($P < .001$) were associated with invasive disease on pathology. On multivariate analysis, comedonecrosis ($P = .04$) and diagnosis by core biopsy ($P < .01$) were independent predictors for invasion. There was no statistically significant predictor for sentinel lymph node metastasis.

Conclusions: Approximately one-third of patients with DCIS treated with mastectomy at our institution later had invasive disease, and factors associated with invasion have been identified. On the basis of our results, routine SLNB is recommended in this patient population.

Key Words: Biopsy—DCIS—Mastectomy—Sentinel lymph node.

Ductal carcinoma-in-situ (DCIS) represents approximately 20% of breast cancers detected with mammographic screening¹ and is defined as neoplastic ductal epithelial cells without any evidence of invasion through the basement membrane of the duct. Despite the lesions being noninvasive, studies

have shown that up to 2% of DCIS lesions as diagnosed by routine pathologic techniques can be associated with axillary lymph node metastases.^{2,3} Given the low rate of axillary metastases and the estimated breast cancer specific mortality rate of 2%, axillary lymph node dissection (ALND) is not routinely indicated for DCIS.

Because DCIS lesions are increasingly detected by mammographic screening and diagnosed with percutaneous core biopsy, there exists an inherent underdetection rate of invasive disease as a result of sampling error. Some recent studies have found that 10% to 20% of lesions diagnosed as DCIS by

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core biopsy can harbor invasive disease at final pathology.^{4,5} If invasive disease is found after excision, axillary node assessment is indicated to help determine prognosis and guide adjuvant therapy.⁶ Currently, sentinel lymph node biopsy (SLNB) is the accepted alternative to an ALND for clinically node-negative patients⁷ with invasive breast cancers. Because of the lower morbidity associated with this procedure, it has also been considered by many surgeons in the management of patients with a preoperative diagnosis of DCIS. Studies that evaluated SLNB in patients with DCIS have reported rates of sentinel lymph node (SLN) involvement as high as 20%^{4,5,8-10} when the SLNs are assessed by intensive pathologic evaluation. Clearly, the difference between SLN-positive rate and the previously reported axillary metastases rate of 2% is important, and it has led to a reexamination of which patients with a preoperative diagnosis of DCIS should be offered a SLNB.

One of the factors influencing a surgeon's choice to offer SLNB to patients with DCIS is whether breast-conserving surgery or mastectomy will be used to excise the lesion. Factors that favor the decision of choosing a mastectomy include the presence of multicentric disease, a large tumor to breast size ratio, the inability to establish clear margins with breast-conserving surgery, a contraindication to breast irradiation, or simply patient preference. The use of SLNB at the time of a mastectomy for a lesion with a preoperative diagnosis of DCIS has been recommended^{4,5,10-15} because many indications for mastectomy in DCIS are also risk factors for invasive disease. In addition, SLNB is not technically feasible immediately after a mastectomy as a result of interruption of the lymphatic tracts; if marked invasive disease is found after a mastectomy, an axillary node dissection would be indicated for nodal staging, even though most of these patients will have node-negative disease.

Thus, despite the ongoing debate on which patients with a preoperative diagnosis of DCIS should be offered a SLNB, many have agreed that SLNB should be performed in the subgroup that was treated with mastectomy.^{4,5,10-15} However, few data exist on the surgical outcomes of patients who underwent concurrent SLNB with mastectomy for DCIS. The objective of this study was to report our experience in combining mastectomy and SLNB in this selected patient population. We examined the rate of invasive disease found in patients with a preoperative diagnosis of DCIS treated with mastectomy, identified factors predictive for the diagnosis of invasive disease, and examined the value of concurrent SLNB in preventing a subsequent axillary dissection.

PATIENTS AND METHODS

Patient Selection

Ethics approval was obtained by the institutional review board of the University Health Network. A comprehensive search of the University Health Network operating room record database was performed from the years 2000 to 2005. The search criteria included all mastectomies, with or without nodal procedure, with or without immediate reconstruction. A total of 618 cases were identified. We then reviewed all the pre- and postoperative notes, core biopsy results, and surgical pathology reports to identify those with a preoperative diagnosis of DCIS. Patients with previous ipsilateral invasive disease were excluded. A total of 90 mastectomies were included in our study.

Sentinel Lymph Node Biopsy

SLNB was performed according to previously described methods.¹⁶ Depending on the surgeons' preference, sentinel nodes were mapped either by radioactive technetium-99m sulphuris colloid (Tc99) and/or Lymphazurin (isosulfan) blue dye. The technique of Tc99 or Lymphazurin blue dye injections varied throughout the study duration. Most patients who had undergone a previous excisional biopsy were injected with Tc99 around the cavity along with Lymphazurin blue dye, as well as intradermal Tc99 injection in the scar. Patients who had undergone a previous core biopsy and planned mastectomy were generally mapped with intradermal periareolar blue dye alone, or with peritumoral Tc99 with or without blue dye. The unfiltered Tc99 (40 mBq in 8 mL) was injected in four aliquots 2 to 36 hours before the surgery. For blue dye, 5 mL of 1% Lymphazurin blue was injected in four aliquots 5 minutes before the incision was made. Sentinel nodes were identified with the aid of a handheld gamma probe or by their blue appearance. All radioactive nodes were removed until the background radioactivity was less than 10% of the hottest node. All palpable and blue nodes were also removed.

Pathology

All preoperative biopsy findings (including the results of biopsies performed at other institutions) and surgical specimens were formally reviewed by one of the three breast pathologists at our institution to ensure accuracy of the diagnosis. Intraoperative frozen sections were not routinely performed. For patients

with a preoperative diagnosis of DCIS, sentinel lymph nodes were divided into two blocks, with one 5- μ m-thick hematoxylin and eosin-stained section per block. If the findings were equivocal or suspicious, further workup was performed as previously described.¹⁶ Each sentinel lymph node was bisected along its longitudinal axis to yield tissues slices 2 to 3 mm thick, and the slices were submitted in to for histologic examination. Five serial sections, each 3 to 5 μ m thick, were taken from each tissue slice of the sentinel lymph node. Sections 1, 3, and 5 were stained with hematoxylin and eosin, and sections 2 and 4 were immunohistochemically stained with CAM 5.2 (Becton-Dickinson, San Jose, CA) for low-molecular-weight cytokeratin. Multicentricity was defined as foci of tumor in more than one quadrant. Multifocality was defined as the presence of two or more foci of tumor confined to the same quadrant. Nodal status of patients was determined according to the American Joint Committee on Cancer 2002 tumor, node, metastasis system of pathologic classification of regional lymph nodes.

Statistical Analyses

SPSS software (SPSS, Chicago, IL) was used for data analysis. Statistical comparison of variables was performed by the χ^2 test, Fischer's exact test, and Student's two-tailed t-test. Standard univariate analyses were performed, and the most significant variables were further examined by multivariate analysis (binomial logistic regression). These variables also underwent collinear analysis. *P* values less than .05 were considered to be significant, and standard 95% confidence intervals (95% CI) are given.

RESULTS

On the basis of our study criteria, 90 patients were included onto our study. Forty-six patients were preoperatively diagnosed with DCIS by excisional biopsy, and 44 were diagnosed by core biopsy only. Eighteen patients presented with palpable lesions.

Predictors of Invasive Disease

The group of patients with a subsequent diagnosis of invasive disease, regardless of whether SLNB was performed, was compared with the group with in situ disease only. Of all patients, 30 (33%) had invasive disease, 6 of whom had microinvasive disease (≤ 1 mm), and 24 had macroinvasive disease (> 1 mm). One patient was diagnosed with lymphovascular

invasion, but no other definite invasive focus was identified; this patient was not considered to have invasive disease for the purposes of this analysis. Twenty-two patients (73%) with invasive disease found in the mastectomy specimen had received concurrent SLNB, whereas 32 (53%) of 60 patients with noninvasive disease had a SLNB. On univariate analysis, the average size of the DCIS, nuclear grade, presence of lobular cancerization, and the presence of calcifications were not statistically significantly different between the two groups.

Of the histological subtypes, micropapillary morphology was more common with the noninvasive specimens ($P = .02$, odds ratio [OR] .3, 95% CI 1.1–9). Four pathologic features were significantly associated with a subsequent diagnosis of invasion: multifocality (47% vs. 23%, $P = .03$, OR 2.9, 95% CI 1.1–7.3), multicentricity (23% vs. 5%, $P = .01$, OR 5.8, 95% CI 1.4–24), comedonecrosis (90% vs. 63%, $P = .01$, OR 5.2, 95% CI 1.4–19), and preoperative diagnosis by core biopsy only (77% vs. 35%, $P < .01$, OR 6.1, 95% CI 2.2–16). A subsequent multivariate analysis revealed that comedonecrosis and diagnosis by core biopsy remained statistically significantly associated with invasion of any extent (Tables 1 and 2).

Subgroup Analysis

By use of the four pathologic features identified by univariate analysis (Table 2), permutations were taken from all factors absent to all factors present to identify any differences in invasion rates. When the mastectomy specimen lacked multicentricity, multifocality, and comedonecrosis, and diagnosis was made by excision, a 9% invasion rate was still observed ($n = 11$). The largest subgroup with one factor present comprised those with comedonecrosis only ($n = 23$), where three patients (13%) had invasion. When two factors were present, the largest subgroup comprised those having comedonecrosis and diagnosis by core biopsy only ($n = 23$), where 10 patients (43%) had invasive disease. Finally, when all four factors were present, all five patients in this subgroup had consequent invasive disease found in their surgical specimen. A similar trend in increasing invasion rates were found when considering all other subgroups in increasing order of number of pathologic features present (data not shown).

Predictors of Sentinel Node Positivity

Fifty-four mastectomies (60%) were performed with concurrent SLNB (group 1), and 36 (40%)

TABLE 1. Invasion versus ductal carcinoma-in-situ (DCIS) only

Characteristic	Invasion	No invasion	P value	Odds ratio (95% CI)
Total number	30 (33%)	60 (67%)		
Age (y) ^a	53.2	53.8	.78	
SLNB (n)	22	32		
Positive SLNs	3 (14%)	4 (13%)		
Average DCIS size (cm) ^a	6.21	6.12	.92	
Average invasion size (cm)	.51	NA		
Nuclear grade ^b				
1	0	2	.91	
2	7	14		
3	23	44		
Multifocal	14 (47%)	14 (23%)	.03	2.9 (1.1–7.3)
Multicentric	7 (23%)	3 (5%)	.01	5.8 (1.4–24)
Solid	25 (83%)	42 (70%)	.21	2.1 (.7–6.5)
Cribiform	21 (70%)	52 (87%)	.09	0.4 (.1–1.1)
Papillary	5 (17%)	8 (13%)	.75	1.3 (.4–4.4)
Micropapillary	8 (27%)	31 (52%)	.02	0.3 (.1–.9)
Lobular cancerization	14 (47%)	17 (28%)	.10	2.2 (.9–5.5)
Calcifications	13 (43%)	29 (48%)	.82	0.8 (.3–2.0)
Microcalcifications	11 (37%)	18 (30%)	.63	1.4 (.5–3.4)
Comedonecrosis	27 (90%)	38 (63%)	.01	5.2 (1.4–19)
Diagnosis by excision	7 (23%)	39 (65%)	< .01	.2 (.1–.4)
Diagnosis by core biopsy only	23 (77%)	21 (35%)	< .01	6.1 (2.2–16)
Palpable lesion	5 (17%)	13 (22%)	.78	.7 (.2–2.3)

SLNB, sentinel lymph node biopsy; SLN, sentinel lymph node; 95% CI, 95% confidence interval. Data are presented as n (%) unless otherwise indicated.

^a By Student's t-test.

^b By Fisher's exact test.

TABLE 2. Multivariate analysis for predictors of invasion

Characteristic	Total	Invasion	Odds ratio	95% CI
Multifocal	28	14 (50%)	2.9	0.5–16.8
Multicentric	10	7 (70%)	2.6	0.8–9.0
Comedonecrosis	65	27 (42%)	4.6	1.6–13.3
Diagnosis by core biopsy only	44	23 (52%)	4.8	1.1–21.0

95% CI, 95% confidence interval.

without concurrent SLNB (group 2). Groups 1 and 2 had similar age (mean 52.8 and 55.0 years, respectively, $P = .40$), rates of multicentricity (13% vs. 8%, $P = .49$), multifocality (28% vs. 36%, $P = .49$), and average DCIS size (6.2 vs 6.0 cm, $P = .77$). Twenty patients from group 1 had a previous ipsilateral excision for the same DCIS lesion compared with 26 patients from group 2 (37% vs. 72%, $P = .001$). Twenty-two patients from group 1 (41%) and eight patients (22%) from group 2 had invasive disease at final pathology ($P = .12$) (Table 3).

There was a total of 54 successful sentinel node biopsies out of 55 attempted, giving a success rate of 98%. Twenty-four patients had their sentinel nodes assessed with blue dye only, 6 with Tc99 only, and 24 patients with both. Seven patients were found to have positive sentinel nodes: three had invasive disease, and four had no evidence of invasion even on subsequent pathology review of the primary tumor,

giving an overall SLN-positive rate of 14%. A comparison between these patients and those with SLN-negative disease did not reveal any pathologic factors that predicted positive sentinel nodes (Table 4).

Axillary Nodal Disease

Seven patients were found to have positive sentinel lymph nodes. Two (patients 1 and 2; Table 5) had gross metastases and invasive disease, and they proceeded to have completion ALND and adjuvant chemotherapy. After completion of ALND, disease of these two patients was staged as pN2 and pN1. Two patients (patients 4 and 5) had micrometastases (pN1mi) with no invasive component in their surgical specimens and had no further positive nodes at completion of ALND, but proceeded to undergo either adjuvant chemotherapy or radiotherapy, in both cases at the request of the patients. One patient

TABLE 3. Concurrent sentinel lymph node biopsy (SLNB) versus mastectomy only

Characteristic	Mastectomy		P value
	+ SLNB	only	
Total number	54 (60%)	36 (40%)	
Average age (y) ^a	52.8	55.0	.40
Average DCIS size (cm) ^a	6.2	6.0	.77
Total with invasion ^b	22 (41%)	8 (22%)	.01
T1mic	6 (11%)	0 (0%)	
T1a	11 (20%)	2 (6%)	
T1b	3 (6%)	5 (14%)	
T1c	2 (4%)	0 (0%)	
T2	0 (0%)	1 (3%)	
Multifocality	15 (28%)	13 (36%)	.49
Multicentricity	7 (13%)	3 (8%)	.51
Solid	44 (81%)	23 (64%)	.08
Cribriform	42 (78%)	31 (86%)	.41
Papillary	7 (13%)	6 (17%)	.76
Micropapillary	20 (37%)	19 (53%)	.19
Lobular cancerization	20 (37%)	11 (31%)	.65
Calcifications	26 (48%)	16 (44%)	.83
Microcalcifications	15 (28%)	14 (39%)	.36
Comedonecrosis	40 (74%)	25 (69%)	.81
Diagnosis by excision	20 (37%)	26 (72%)	< .01
Diagnosis by core biopsy only	34 (63%)	10 (28%)	< .01
Palpable lesion	11 (20%)	7 (19%)	1.0
SLNB method			
Blue dye	24	N/A	
Tc-sulfur	6	N/A	
Both	24	N/A	

DCIS, ductal carcinoma-in-situ. Data are presented as n (%) unless otherwise indicated.

^a By Student's t-test.

^b By Fisher's exact test.

TABLE 4. Predictors for sentinel lymph node (SLN) positivity

Characteristic	SLN		P value
	Positive	Negative	
Total number	7	47	
Age (y)	47.30	53.6	.13
Total with invasion	3	19	1.00
Average DCIS size (cm)	8	6	.24
Nuclear grade (n)			
0	0	0	1.00
1	0	0	
2	1	10	
3	6	37	
Multifocal	3 (43%)	12 (26%)	.38
Multicentric	2 (29%)	5 (11%)	.22
Solid	6 (86%)	38 (81%)	1.00
Cribriform	5 (71%)	37 (79%)	1.00
Papillary	1 (14%)	6 (13%)	1.00
Micropapillary	4 (57%)	16 (34%)	.40
Lobular cancerization	2 (29%)	18 (38%)	.70
Calcification	3 (43%)	23 (49%)	1.00
Microcalcification	2 (29%)	13 (28%)	1.00
Comedonecrosis	6 (86%)	34 (72%)	.66
Excisional biopsy	2 (29%)	18 (38%)	.70
Core biopsy only	5 (71%)	29 (62%)	.70
Palpable lesion	1 (14%)	10 (21%)	1.00

DCIS, ductal carcinoma-in-situ. Data are presented as n (%) unless otherwise indicated.

(patient 3) had isolated tumor cells (ITC) (pN0(i+)) in her lone positive SLN along with invasive disease, but no positive nodes at completion of ALND; she proceeded to undergo adjuvant chemotherapy. The remaining two patients (patients 6 and 7) had no invasive disease; they did not proceed to have a completion ALND and had only ITC (pN0(i+)) in their SLNs. They did not receive any adjuvant therapy, and they were followed clinically with no recurrence to date (Table 5).

DISCUSSION

The role of SLNB in DCIS is far from clear. Routine axillary node sampling is generally not recommended because the axillary metastasis rate is only 2% by ALND and conventional hematoxylin and eosin staining.^{3,17,18} However, there is an inherent risk of invasive disease in patients with a preoperative diagnosis of DCIS that is based on core biopsy alone as a result of undersampling of the primary tumor. Cox et al.⁵ reported on 224 patients with a biopsy diagnosis of DCIS, and 10% were upstaged to infiltrating ductal carcinoma at the time of definitive therapy.⁵ Yen et al.⁴ discovered a 20% rate of invasion at final pathology in a series of 398 patients with an initial diagnosis of DCIS, and a 39% rate of invasion for the 159 patients treated by mastectomy. This group identified several clinicopathologic predictors of invasive cancer, including age < 55 years, diagnosis by core needle biopsy, mammographic DCIS size > 4 cm, and nuclear grade 3 DCIS. In our study, in which only mastectomy patients are included, 33% of DCIS had invasive disease on final pathology.

Our current indications for mastectomy in patients with DCIS include large tumors, multicentric disease, contraindications to radiation (e.g., previous irradiation, scleroderma, pregnancy), unacceptable cosmesis with breast-conserving surgery, patient preference, or inability to achieve negative margins after lumpectomy. Many of these indications are also risk factors for having invasive disease at surgical pathology. Should invasive disease be discovered after a mastectomy, SLNB may not be accurate or feasible because lymphatic drainage had been interrupted. If proper nodal staging is to be carried out, this patient will be subjected a complete axillary node dissection, which is associated with higher morbidity rate, including increased paresthesia, arm weakness, pain and stiffness of the shoulder, and lymphedema.^{8,19,20} For these reasons, many have

TABLE 5. Characteristics of sentinel lymph node (SLN)-positive patients

Patient	Age (y)	DCIS size (cm)	Invasion size (cm)	Core biopsy only	Palpable mass	Positive SLNs	Positive non-SLNs	Nodal stage	Adjuvant therapy
1	46	2.7	0.25	Yes	No	1/1	4/12	pN2	AC/T/R/X
2	54	7.0	1.0	Yes	Yes	1/2	1/10	pN1	AC/R
3	41	10.0	0.8	Yes	No	1/4	0/11	pN0(i+)	AC/T/R/X
4	34	9.4	0	Yes	No	2/4	0/13	pN1mi	R
5	46	5.0	0	No	No	1/1	0/14	pN1mi	AC/X
6	57	12.5	0	Yes	No	1/6	0/0	pN0(i+)	None
7	53	9.2	0	No	No	5/9 ^a	0/0	pN0(i+)	None

DCIS, ductal carcinoma-in-situ; T, Taxol; R, radiation; X, tamoxifen; AC, Adriamycin-cyclophosphamide.

^a All five positive SLNs were isolated tumor cells only, and thus the patient was considered to have nodal stage pN0(i+) disease.

recommended concurrent SLNB in patients receiving mastectomies for preoperative diagnoses of DCIS, or should at least be offered as part of their initial surgical management.^{4,5,10-15} Other groups, however, have advocated sentinel node mapping on the basis of other pathological factors such as age, size, grade, diagnosis by core biopsy, and more.^{4,8,9,21-24} Our analysis showed that factors associated with finding invasive disease included comedonecrosis and diagnosis by core biopsy. In a subgroup analysis that used the four pathological features (Table 2) identified on univariate analysis, the absence of all four factors still demonstrated a 9% invasion rate. Although the number of patients is relatively small in each subgroup, the rate of invasion seemed to correlate with the number of factors present. Given this high rate of invasion, these data support the routine use of concurrent SLNB in all patients undergoing mastectomy for DCIS.

Studies examining the rate of sentinel nodal metastases in DCIS with microinvasion have reported the positive node rate of up to 18%.^{4,5,9,10,21,25} Pendas et al.²¹ examined 87 patients with DCIS, five of whom had positive sentinel lymph nodes (6%) by cytokeratin and immunohistochemical staining. Cox et al.⁵ discovered an 18% lymph node metastasis rate in a subgroup of patients with DCIS treated with mastectomy.⁵ Klauber-DeMore et al.¹⁰ examined 76 patients with high-risk DCIS, and 9 patients (12%) were discovered to have positive nodes, seven of which were metastases <2 mm. Factors that are considered to be high risk for SLN-positive disease included presence of palpable mass, mammographic mass, histology suspicious but not diagnostic for microinvasion, multicentric disease requiring mastectomy, or histologically high nuclear grade or non-high nuclear grade with necrosis.¹⁰ Yen et al.⁴ showed that the lone independent predictor of positive sentinel nodes in their series was an initially palpable tumor. Our positive sentinel node rate of 13% (7 patients of 54 receiving SLNB) is comparable to that

of other studies that used SLNB with patients with DCIS.^{4,5,10,21} However, our data did not demonstrate any pathological factor predictive of sentinel nodal metastases, including palpable mass. This may be due to our small sample size.

On the basis of our results, performing a concurrent SLNB with mastectomy in our patients with DCIS seemed to benefit at least 21 (39%) of 54 patients. Nineteen patients out of the 22 with invasive disease avoided a level I and II ALND by having negative sentinel nodes. A further two patients may have benefited as a result of the detection of micrometastatic nodal disease in the absence of definite invasion in the DCIS lesion, implying that there was some occult invasive disease in the primary tumor.

A number of studies oppose the routine use of SLNB for DCIS. Farkas et al.¹¹ reported no positive sentinel lymph nodes in 46 cases of DCIS treated by surgical resection and SLNB. They found that all patients with microinvasive disease on final pathology were excluded, and 20 patients were treated with mastectomy.¹¹ Kelly et al.³ reviewed 134 patients with a final histologic diagnosis of DCIS who received a level I or II axillary node dissection, SLNB, or both, and only 2% were found to have micrometastases. Total mastectomy was performed on 127 of these patients. Again, in this study, patients with any invasive cancer on final pathology were excluded. Although we agree that there is a very low incidence of metastases from DCIS, from a practical standpoint, the possibility of invasive disease undetected by analysis of preoperative core biopsy samples is important, and understaging by biopsy alone does exist. A concurrent SLNB, with its associated lower morbidity, may provide an additional means to reduce such a diagnostic challenge.

Interestingly, patients with positive sentinel nodes were found in the groups with both invasive disease and DCIS only. The two patients with gross nodal metastases (one with nodal stage pN2 and the other pN1) had invasion within their primary tumor, while

the two patients with micrometastatic disease (pN1mi) did not have invasion detected in their primary tumor. Three of the sentinel node–positive patients had only ITC (pN0(i+)) discovered in their lymph nodes. The management of a positive sentinel lymph node in the absence of invasion in the surgical specimen is currently an area of controversy. In our own practice, we tend not to advise any further axillary nodal procedure for patients with only ITC in SLNs in the absence of invasive disease. There is little, if any, evidence from clinical trials to suggest that survival would be altered by leaving ITC in the axilla²⁶; in fact, studies have been published suggesting that the presence of cytokeratin and immunohistochemically stained positive cells in the axilla do not affect the survival of patients with DCIS.^{27,28} However, a meta-analysis of 25 studies suggests that there was a 10% to 15% chance of nonsentinel lymph node metastases if these so-called low-volume metastases were found.²⁹ Another study of 102 patients with DCIS with negative axillary lymph nodes reexamined by keratin immunohistochemistry staining showed a 13% rate of micrometastases, but none of them correlated with recurrence over a 10- to 28-year period.³⁰ For micrometastatic disease, there may be a possibility of an occult invasive lesion missed on surgical pathology, and a completion ALND is offered to the patient after counseling about the risks and benefits of the procedure. Until further data are presented regarding the benefit of treating ITC or micrometastases, the decision to treat with chemotherapy, hormonal therapy, and radiation must be individualized. If gross metastases are found, a completion ALND would be indicated.

A limitation of this study was that the length of follow-up was short (median, 2 years). The nature of the disease is that it is relatively slow growing, and for an accurate assessment of recurrence rates, a large study would be required with longer follow-up. The clinical significance of micrometastases and ITC will likely require a follow-up period of 12 years or more.³⁰ The data presented in this study are from surgical pathology, and not from core or excisional biopsy pathology. If comedonecrosis was not present in the core biopsy sample but present in the final specimen, there may be limited information from which to counsel a patient on whether to offer a concurrent SLNB with mastectomy. An informative follow-up study would be to prospectively follow patients using our prognosticating factors of comedonecrosis and diagnosis of DCIS by core biopsy only, and to examine their outcomes after mastectomy and SLNB. The present study represents a

single-center experience, and despite being one of the few studies to date examining the role of sentinel lymph node biopsies in women with DCIS treated by mastectomy, the validity of our findings would be strengthened with a larger number of patients across different centers. Future work in this area may include a larger study with longer follow-up times and examination of recurrence rates with actuarial survival data among these patients. Second, it will be interesting when evidence is available regarding the prognostic indications for the significance of ITC and micrometastases in sentinel nodes. This will serve to continue the evolution of the staging and treatment of breast cancer, and to improve the quality of life and disease-free survival among patients.

Overall, 33% of patients were found to have invasive disease with a preoperative diagnosis of DCIS, with no specific subgroup of patients with an invasion rate of <9%. Our results also indicated that at least 39% of patients benefited from having a concurrent SLNB at the time of mastectomy. Thus, routine SLNB is recommended in this patient population, especially in those whose DCIS were diagnosed by core biopsy, and have evidence of comedonecrosis.

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