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Is Sentinel Lymph Node Biopsy Indicated at Completion Mastectomy for DCIS Following Attempted Breast Conservation?

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Abstract

Background—Sentinel lymph node biopsy (SLNB) is recommended when mastectomy is performed for ductal carcinoma in situ (DCIS). The role of SLNB for women with DCIS who undergo mastectomy following 1 attempts at breast-conserving surgery (BCS) is uncertain. We examined the upgrade rate and SLNB yield in women who converted to mastectomy after 1 attempts at BCS for DCIS.

Methods—All patients who underwent 1 attempts at BCS prior to conversion to mastectomy with SLNB for DCIS were identified. Margin status as the indication for mastectomy was confirmed. Comparisons were made between patients with/without upgrade on final pathology.

Results—From 2/2006–11/2012, 233 patients underwent completion mastectomy following 1 attempts at BCS for positive/close margins (median age, 50 years; range 34–84). Median number of BCS attempts was 1 (range 1–4). Overall, 20 (9%) patients were upgraded on final pathology; 15 (6%) stage I, 5 (3%) stage II (3 micrometastasis, 2 macrometastasis). In 2 of 5 cases with a positive SLN, invasive carcinoma was not identified in the mastectomy specimen. The only factor associated with any upgrade was the presence of micropapillary DCIS (80% versus 55%, with and without upgrade; $p = 0.03$).

Conclusion—In this cohort of patients with DCIS who converted to mastectomy for positive/close margins after 1 attempts at BCS, 18 (8%) would have required second-stage axillary surgery had a SLNB not been performed and in 2 (1%) patients the SLN provided the only evidence of invasion. These findings support the recommendation for SLNB at the time of completion mastectomy.

Keywords

sentinel lymph node biopsy; mastectomy; breast-conserving surgery; ductal carcinoma in situ

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INTRODUCTION

Ductal carcinoma in situ (DCIS) is a non-invasive breast lesion with no theoretic potential for metastatic spread.¹ However, when DCIS is diagnosed by core needle biopsy, there is an approximately 23% to 30% rate of upgrade to invasive carcinoma at the time of surgical excision², and recommendations for axillary staging differ based on the primary breast operation. For women managed with breast-conserving surgery (BCS), sentinel lymph node biopsy (SLNB) is not routinely recommended at the time of the index breast operation. If invasive carcinoma is detected on final pathology, the patient may then return for a second-stage SLNB for appropriate axillary staging. This algorithm avoids the morbidity of SLNB in the majority of patients undergoing BCS who will not be upgraded to invasive carcinoma.

In contrast, due to the limitations of axillary staging following mastectomy, SLNB is recommended for women with DCIS undergoing mastectomy, as outlined by the American Society of Clinical Oncology (ASCO) Clinical Practice Guidelines Update for SLNB.³ When SLNB is performed at the time of mastectomy for DCIS, rates of axillary metastasis are reported to range from 5 to 20%, supporting this recommendation.⁴⁻⁷

A subgroup of DCIS patients undergo initial BCS attempts and are subsequently converted to completion mastectomy secondary to inadequate margin clearance. Because a large proportion of the pathology was likely removed and evaluated in the lumpectomy specimen with findings of DCIS alone, this population of patients who undergo initial BCS and are converted to completion mastectomy may theoretically incur lower rates of upgrade to invasive carcinoma and axillary metastasis. There are no current data assessing the role of SLNB for this specific cohort of patients. We sought to examine the rate of upgrade to invasive carcinoma and the yield of SLNB in women who converted to mastectomy for DCIS following attempts at BCS for positive or close margins.

METHODS

Following Memorial Sloan Kettering Cancer Center institutional review board approval, a prospectively maintained institutional database was used to retrospectively identify patients with a diagnosis of DCIS on core needle biopsy who underwent mastectomy with SLNB between February 2006 and November 2012. Patients who converted to mastectomy due to positive or close margins following 1 attempts at BCS were selected. Margin status as the indication for mastectomy was confirmed for all patients. Patients with a diagnosis of invasive disease prior to mastectomy or those who underwent SLNB before completion mastectomy were excluded from the study.

Positive margins were defined as ink on tumor, and close margins were defined as tumor 2 mm from the inked margin. Patient, tumor, and treatment characteristics were abstracted from the medical record, including method of DCIS diagnosis (imaging or physical exam abnormality), number of BCS attempts prior to mastectomy (1, 2, or 3), final BCS margin status (positive or close), DCIS histology (micropapillary, papillary, cribriform, solid, mixed, or flat), DCIS estrogen and progesterone receptor status, DCIS nuclear grade (high, intermediate, low), final pathology on mastectomy (DCIS, invasive carcinoma), axillary

procedure(s), and axillary pathology results. Comparisons were made between patients with and without upgrade (defined as invasive carcinoma and/or a positive SLN on final pathology) using t-tests, Chi square tests, and Fisher's exact test as indicated. Patients with only isolated tumor cells in the SLN were considered node negative for the purposes of the upgrade results in this study; however, it is noted that two patients with nodal isolated tumor cells were managed with a completion axillary lymph node dissection (ALND).

RESULTS

From February 2006 to November 2012, 233 breasts representing 231 patients met study criteria. Clinicopathologic features of the entire cohort are shown in Table 1. Median patient age was 50 years (range 34–84 years). The majority of cases (92%) had mixed DCIS histology, with cribriform, solid, and micropapillary components being described in 82%, 77.3%, and 56.7% of patients, respectively. The median number of attempts at BCS prior to mastectomy was 1 (range 1–4) (Table 2). Overall, 20 (8.6%; 95% confidence interval (CI) 5.3–13.0) patients were upgraded on final pathology, including 15 (6.4%) patients with stage I disease (pT1N0) and 5 (2.1%) patients with stage II disease due to the presence of axillary metastasis within the SLNB (3 micrometastasis and 2 macrometastasis). In 2 of 5 cases with a positive SLNB, invasive carcinoma was not identified on pathologic review of the mastectomy specimen (final pathology pTisN1 in 2 patients, and pT1N1 in 3 patients).

Among all clinical and pathologic variables examined, the only factor associated with any upgrade was the presence of a micropapillary component on DCIS histology (present in 80% of upgraded cases versus 54.5% of cases without an upgrade, $p = 0.03$, Table 3). Among patients with nodal metastases, all 5 patients had a micropapillary component on initial DCIS histology. There was no statistically significant difference in regard to BCS margin status at last excision (positive or close) prior to mastectomy among patients with and without an upgrade ($p = 0.58$).

Tumor and treatment characteristics of the 20 patients upgraded to invasive disease on final pathology are shown in Table 4. Although not statistically significant, invasive cancer was not identified in any case of low-grade DCIS or in any case where conversion to mastectomy occurred after 3 attempts at excision. Three of 5 cases with axillary metastasis identified on SLNB underwent completion ALND with no additional nodal disease identified.

DISCUSSION

While recommended by ASCO³ and the National Comprehensive Cancer Network¹², the use of SLNB for women with DCIS undergoing mastectomy remains variable.^{13,14} The primary indication of SLNB at the time of mastectomy for in-situ disease is to provide axillary staging in the event that invasive carcinoma is detected on final pathology. Although there are limited data showing the feasibility of SLNB following mastectomy, the identification rates are significantly lower¹⁵ and ALND remains the standard of care for axillary staging in patients with a preoperative diagnosis of DCIS found to have concomitant invasive disease after mastectomy. A meta-analysis by Brennan et al, which included 52 studies and 7350 cases of DCIS diagnosed by core needle biopsy, reported a 26% (95% CI 23–30%) overall

upgrade rate to invasive carcinoma at the time of surgical excision for all DCIS grades and sizes.² For the subset of patients who convert to mastectomy due to persistent close/positive margins after 1 attempts at BCT, the rates of upgrade to invasive carcinoma and/or the utility of SLNB in this setting remains uncertain. Here we report an overall upgrade to invasive carcinoma in the breast and/or axillary lymph nodes of 9% among a select cohort of DCIS patients who underwent initial attempts at BCS but converted to mastectomy for positive or close margins. Among this select patient population, 18 (8%) women were found to have invasive carcinoma in the breast and hence require axillary evaluation for complete staging, necessitating the decision for axillary surgery timing.

It is well established that the morbidity of SLNB is substantially less than ALND¹⁶, including a significantly reduced risk of upper extremity lymphedema, improved postoperative range of motion, and decreased sensory deficits. Given the improved safety profile, axillary staging with SLNB is preferred; highlighting the need to establish the risk of identifying invasive carcinoma when mastectomy is performed for DCIS, both in the primary setting and when patients fail prior attempts at conservation. Looking specifically at patients with larger lesion size, Tunon-de-Lara et al reported on a prospective multicenter study evaluating the rate of upgrade among women with core biopsy DCIS and extensive calcifications necessitating upfront mastectomy and report a higher rate of in-breast invasive carcinoma on final pathology of 39%.⁸ Others have reported that extensive calcifications and larger DCIS size are predictive of synchronous invasion.^{9–11} Our patient population represents a unique cohort in that, presumably, the majority of disease was removed at the time of initial lumpectomy with pathology yielding DCIS alone; however, given the extent of disease that mandated conversion to mastectomy, a 9% upgrade to invasive carcinoma remained. While there is also a risk of upgrade to invasive carcinoma when positive margins in DCIS are managed with re-excision, SLNB is not necessary when attempting BCS for DCIS because, with an intact breast, a SLNB remains feasible. Patients found to have invasive carcinoma on simple re-excision were excluded from this study, so we cannot comment on the upgrade rate in this setting or the yield of SLNB.

Given the inherent risk of upgrade to invasive carcinoma at the time of excision for DCIS, a number of studies have evaluated the utility of SLNB in this population. A review by Ansari et al of 22 studies reporting on rates of sentinel lymph node positivity in women with DCIS found that 7.4% of patients with a preoperative diagnosis of DCIS had axillary metastasis on SLNB.¹⁷ As one would presume, studies with higher rates of in-breast upgrades to invasive carcinoma also report higher rates of SLNB positivity. The previously mentioned prospective trial of patients with extensive calcifications and a core needle biopsy diagnosis of DCIS managed with upfront mastectomy found positive sentinel lymph nodes (excluding isolated tumor cells) in 19 of 190 patients (10%), with 8 micrometastasis and 11 macrometastasis.⁸ Among 18 women in our study with in-breast invasive carcinoma, 3 (17%) had a positive SLNB.

In addition to providing axillary staging for women with known in-breast invasive carcinoma, a small proportion of patients with DCIS are found to harbor invasive carcinoma only in the lymph nodes. While uncommon, in this clinical scenario, the information from the SLNB impacts overall treatment plans. In the current cohort, 2 patients (1%) had DCIS

alone in the breast with a positive SLNB. This low rate is similar to that reported by others, ranging from 0.4% to 14%^{8,18-23}, with a meta-analysis of 11 studies reporting a 4% rate of sentinel lymph node metastasis among women with DCIS alone on final pathology.¹⁷ Because adjuvant therapy is not common for women with DCIS following mastectomy, evidence of axillary nodal metastasis provides the only indication for systemic therapy for this small group of patients.

SLNB, while less morbid than ALND, is associated with potential post-surgical risks of lymphedema and sensory changes.²⁴ Better risk stratification could allow subsets of women to avoid unnecessary axillary surgery. We found zero upgrades in women who had 3 attempts at BCS prior to mastectomy, likely an indication of the large volume of tissue previously excised and reviewed without invasion. We also found zero upgrades in patients with low-grade DCIS; however, in larger studies, pathologic features such as grade have failed to identify a cohort of DCIS patients not at risk for upgrade.^{2,25,26} Until additional risk stratification is available, given the clinically relevant upgrade identified in this cohort, SLNB remains relevant for patients with DCIS undergoing completion mastectomy. Importantly, patients who incurred an upgrade had very low volume axillary nodal disease, and zero patients had additional nodal metastasis on completion ALND. In this select patient population, SLNB alone may be sufficient for axillary staging and systemic therapy decision making.

This is a retrospective series with the associated limitations. However, this population represents a large cohort of women with identical surgical management of DCIS with upfront BCS alone followed by completion mastectomy and SLNB for the management of positive or close margins. Among this cohort of patients, 8% would have required second-stage axillary staging and were spared the associated morbidity. SLNB is safe and feasible when performed at the time of completion mastectomy and avoids the potential need for an ALND for nodal staging in those patients found with invasive carcinoma on final pathology. Additionally, 2 (1%) patients would have been under-staged without the SLNB results. The 9% overall rate of upgrade and the potential for SLNB to signal otherwise occult invasive disease support the recommendation for SLNB at the time of completion mastectomy.

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Synopsis

Here we examine the rate of upgrade and the yield of SLNB in women who converted to mastectomy for DCIS with positive/close margins. Our findings support the recommendation for SLNB at the time of completion mastectomy.

Table 1

Clinicopathologic features of the entire cohort (n = 233)

Median age (range), years	50 (34–84)
Primary means diagnosis DCIS	
Physical exam	43 (18.5%)
Imaging	189 (81.5%)
Missing	1
DCIS histology on lumpectomy *	
Micropapillary	132 (56.7%)
Papillary	51 (21.9%)
Cribriform	191 (82.0%)
Solid	180 (77.3%)
Mixed	214 (91.9%)
Flat	72 (30.9%)
DCIS ER status	
Positive	109 (88.6%)
Negative	14 (11.4%)
Missing	110
DCIS PR status	
Positive	79 (76.7%)
Negative	24 (23.3%)
Missing	130
DCIS nuclear grade	
High	102 (43.8%)
Intermediate	114 (48.9%)
Low	17 (7.3%)

* Note: A specimen can have more than one histology, therefore, these percentages add up to > 100%

DCIS, ductal carcinoma in situ; ER, estrogen receptor; PR, progesterone receptor

Table 2

Surgical procedures and pathology results of the entire cohort (n = 233)

No. attempts at BCS prior to mastectomy	
1	166 (71.2%)
2	55 (23.6%)
3	12 (5.2%)
Margin status of final BCS prior to mastectomy	
Close	107 (45.9%)
Positive	126 (54%)
Any upgrade to invasive carcinoma	20 (8.6%)
Final in-breast pathology	
DCIS	215 (92.3%)
Invasive carcinoma	18 (7.7%)
Axillary surgery	
SLNB alone	227 (97.4%)
SLNB and ALND *	6 (2.6)
Axillary pathology	
pN0	228 (97.9%)
pN1mic	3 (1.3%)
pN1	2 (0.9%)

* Indication for ALND was pN+ in 3 patients, failed SLNB in one patient, and pN0(i+) in 2 patients

DCIS, ductal carcinoma in situ; SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection

Table 3

Comparison of clinical and pathologic features of DCIS among women with and without an upgrade to invasive carcinoma

Characteristic	Final pathology		p-value
	DCIS (n = 213)	Invasive carcinoma (n = 20)	
Age, median (range), years	50 (34–84)	51 (34–78)	0.83
Primary means diagnosis			0.22
Physical exam finding	37 (17.5%)	6 (30.0%)	
Imaging	175 (82.5%)	14 (70.0%)	
Missing	1	0	
DCIS histology			
Micropapillary component	116 (54.5%)	16 (80.0%)	0.03
Other	97 (45.5%)	4 (20.0%)	
Solid component	164 (77.0%)	16 (80.0%)	1.00
Other	49 (23.0%)	4 (20.0%)	
Cribriform	174 (81.7%)	17 (85.0%)	1.00
Other	39 (18.3%)	3 (15.0%)	
Papillary	44 (20.7%)	7 (35.0%)	0.07
Other	169 (79.3%)	13 (65.0%)	
Flat	64 (30.0%)	8 (40.0%)	0.45
Other	149 (70.0%)	12 (60.0%)	
DCIS ER positive	92 (88.5%)	17 (89.5%)	1.00
Missing	109	1	
DCIS PR positive	66 (78.6%)	13 (68.4%)	0.35
Missing	129	1	
DCIS nuclear grade			0.05
High	97 (45.5%)	5 (25.0%)	
Intermediate	99 (46.5%)	15 (75.0%)	
Low	17 (8.0%)	0 (0.0%)	
Attempts at BCS prior to mastectomy			0.76
1	150 (70.4%)	16 (80.0%)	
2	51 (23.9%)	4 (20.0%)	
3	12 (5.6%)	0 (0.0%)	
Margin status of final BCS prior to mastectomy			0.58
Close	99 (46%)	8 (40%)	
Positive	114 (54%)	12 (60%)	

DCIS, ductal carcinoma in situ; ER, estrogen receptor; PR, progesterone receptor; BCS, breast-conserving surgery

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Table 4

Tumor and treatment characteristics of patients upgraded on final pathology

Feature	pT1N0 (n = 15)	pT1N1 (n = 3)	pTisN1 (n = 2)
Tumor size			
T1mi (≤ 1 mm)	4 (27%)	1 (33%)	
T1a (> 1 mm, ≤ 5 mm)	7 (47%)	2 (67%)	NA
T1b (> 5 mm, ≤ 10 mm)	2 (13%)	0	
T1c (> 10 mm, ≤ 20 mm)	2 (13%)	0	
ER status			
Positive	12 (80%)	3 (100%)	2 (100%)*
Negative	2 (13%)	0	0
Missing	1 (7%)	0	0
PR status			
Positive	10 (67%)	3 (100%)	1 (50%)*
Negative	4 (27%)	0	1 (50%)*
Missing	1 (7%)	0	0
HER2neu status			
Overexpressing	2 (15%)	1 (33%)	NA
Negative	11 (85%)	2 (67%)	
Missing	2	0	
Nodal tumor size			
		0	0
Micrometastasis	NA	1 (33%)	2 (100%)
Macrometastasis		2 (67%)	0
Adjuvant therapy			
Chemotherapy alone	1 (7%)	1 (33%)	0
Endocrine therapy alone	8 (53%)	0	2 (100%)
Both	3 (20%)	2 (67%)	0
No systemic therapy	3 (20%)	0	0

* ER/PR status for the pTisN1 cohort refers to the DCIS receptor status

ER, estrogen receptor; PR, progesterone receptor; DCIS, ductal carcinoma in situ; NA, not applicable