

Incidence and Consequence of Close Margins in Patients with Ductal Carcinoma-In Situ Treated with Mastectomy: Is Further Therapy Warranted?

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ABSTRACT

Background. The impact of close margins in patients with ductal carcinoma-in situ (DCIS) treated with mastectomy is unclear; however, this finding may lead to a recommendation for postmastectomy radiotherapy (PMRT). We sought to determine the incidence and consequences of close margins in patients with DCIS treated with mastectomy.

Methods. The records of 810 patients with DCIS treated with mastectomy from 1996 through 2009 were reviewed. Clinical and pathologic factors were analyzed with respect to final margin status. Median follow-up was 6.3 years.

Results. Overall, 94 patients (11.7 %) had close margins (positive, $n = 5$; negative but ≤ 1 mm, $n = 54$; 1.1–2.9 mm, $n = 35$). Independent risk factors for close margins included multicentricity, pathologic lesion size ≥ 1.5 cm, and necrosis, but not age, use of skin-sparing mastectomy, or immediate reconstruction ($p > 0.05$). Seven patients received PMRT, and none had a locoregional recurrence (LRR). Among the remaining 803 patients, the 10-year LRR rate was 1 % (5.0 % for margins ≤ 1 mm, 3.6 % for margins 1.1–2.9 mm, and 0.7 % for margins ≥ 3 mm [$p < 0.001$]).

The 10-year rate of contralateral breast cancer was 6.4 %. On multivariate analysis, close margins was the only independent predictor of LRR ($p = 0.005$).

Conclusions. Close margins occur in a minority of patients undergoing mastectomy for DCIS and is the only independent risk factor for LRR. As the LRR rate in patients with close margins is low and less than the rate of contralateral breast cancer, PMRT is not warranted except for patients with multiple close/positive margins that cannot be surgically excised.

The incidence of ductal carcinoma-in situ (DCIS) has been steadily increasing with the widespread use of screening mammography, and now accounts for approximately 20–25 % of all breast malignancies.^{1,2} Though breast-conserving therapy, consisting of segmental excision of the cancer followed by radiotherapy, offers long-term survival outcomes equivalent to that with mastectomy alone and is an option for many patients, nearly one-third of patients with DCIS in the USA are treated with mastectomy.^{3–5} The local regional recurrence (LRR) rate for DCIS treated with mastectomy is not zero and is reported to be 0.8–3.3 %.^{6–10} Several studies have evaluated potential predictors of LRR after mastectomy for DCIS in an attempt to improve the already low rates of LRR.^{11–16} One of these potential predictors is margin status. There is a large body of literature regarding the relationship between margin status and risk of LRR in patients with DCIS who undergo breast-conserving therapy.^{1,17} However, there is controversy and a much smaller body of literature regarding the relationship

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between margin status and risk of LRR in patients with DCIS who undergo mastectomy. Furthermore, there is controversy regarding whether postmastectomy radiotherapy (PMRT) is required among patients with close and even positive margins after mastectomy for DCIS.

The purposes of this study were to determine the incidence of close margins in a large modern cohort of patients with DCIS treated with mastectomy at a single institution utilizing standardized intensive pathologic processing, to identify predictors of close or positive margins, to determine the impact of margin status on the incidence of LRR, and to assess the potential need for PMRT in patients with close or positive margins.

PATIENTS AND METHODS

After approval from the Institutional Review Board of the University of Texas MD Anderson Cancer Center, we used the MD Anderson Breast Cancer Management System database to identify patients with a diagnosis of pure DCIS who were treated with mastectomy from January 1996 through October 2009 and had a minimum follow-up time of 1 year. A total of 810 patients met these criteria. Demographic, diagnostic, clinical, pathologic, treatment, and follow-up variables were analyzed with respect to margin status at the time of mastectomy.

Surgical specimens were evaluated per routine MD Anderson standards. The mastectomy specimens were inked in different colors to identify each face of the specimen and then sectioned into 5-mm to 1-cm slices. The pathologist examined the slices grossly to identify suspicious areas and noted their proximity to margins. The slices were then radiographed, and the radiologist reviewed the films to determine the extent of any radiographic abnormalities and their proximity to margins, frozen section analysis was performed if indicated, and additional tissue was excised as needed. Final margin width was determined by examination of permanent paraffin-embedded sections. The number of permanent sections evaluated by the pathologist was based on the gross evaluation and the radiologic extent of the abnormality. Margin status was assigned to one of three groups according to the proximity of carcinoma to the inked surface of the specimen: positive, ≤ 1 , 1.1–2.9, and ≥ 3 mm.

Seven patients received PMRT. Six patients were treated with 50 Gy in 25 fractions to the chest wall followed by either a 10-Gy boost to the tumor bed (three patients) or a 16-Gy boost to the tumor bed (three patients). One patient was treated with 46 Gy to the chest wall followed by a 20-Gy boost to the tumor bed.

The χ^2 test was used to compare margin-status groups with respect to categorical variables. The Kruskal–Wallis

test was used to compare margin-status groups with respect to continuous variables. Variables with significant p values in the univariate analysis were utilized in multivariate logistic regression models, and odds ratios with 95 % confidence intervals [CIs] were generated. Kaplan–Meier product-limit methods were utilized to calculate two primary outcomes of interest, LRR and development of contralateral breast cancer. The differences in these outcomes were compared between the different variables with the log-rank test. All reported p values are two-sided, and $p < 0.05$ was considered statistically significant. Analyses were performed by Stata/IC, release 11.1 (StataCorp, College Station, TX), and Statistica, release 9.0 (StatSoft Inc., Tulsa, OK).

RESULTS

Patient Characteristics

A total of 810 patients with DCIS treated with mastectomy were identified. The median follow-up time was 6.32 years. Demographic and pathologic characteristics are summarized in Table 1. Just over half of the patients were aged >50 years, and nearly two-thirds were postmenopausal. The majority of patients (66 %) underwent immediate reconstruction, with 88 % of those patients undergoing a skin-sparing mastectomy. Estrogen receptor status was known in just over half of the patients, and one-quarter of the patients received adjuvant tamoxifen.

Postmastectomy Radiotherapy

Seven patients received PMRT. All seven were <50 years old and had multicentric or multifocal grade II or III DCIS. Four of these patients had positive margins. Of the remaining three patients, one had margins <2 mm in two locations, one had margins ≤ 1 mm in two locations, and the final patient was a 28-year-old woman with grade III DCIS with a margin <1 mm in only one location. No patient who received PMRT experienced a LRR.

Margin Status and Predictors of Close Margins

Intraoperative analysis identified initial margin <3 mm in 14.3 % ($n = 116$ patients). Intraoperative reexcision was performed on each of these patients and resulted in a change in margin status of at least one margin from <3 to ≥ 3 mm in 89 % ($n = 103$ patients). Nine patients (1.1 %) returned to the operating room for a second procedure to clear margins <3 mm. After mastectomy, 34 % of the margins <3 mm were superficial and 16 % were deep. After reexcision was performed 26 % of the margins <3 mm were superficial and 38 % were deep.

TABLE 1 Demographic and pathologic characteristics in patients with ductal carcinoma-in situ treated with mastectomy ($n = 810$)

Characteristics	n (%)
Race	
White	600 (74.1)
African American	85 (10.5)
Hispanic	66 (8.2)
Asian/Pacific Islander	46 (5.7)
Other	13 (1.6)
Age	
≤ 50 years	356 (44.0)
> 50 years	454 (56.0)
Median (range)	52 (20–88)
Menopausal status ^a	
Premenopausal	279 (34.5)
Postmenopausal	529 (65.5)
Bilateral breast cancer at diagnosis	
Yes	100 (12.4)
No	710 (87.6)
Initial presentation ^b	
Clinical	188 (23.3)
Radiological	618 (76.7)
Largest recorded mammographic dimension, cm, median (range) ^c	3.5 (0.3–20)
Skin-sparing mastectomy	
Yes	469 (57.9)
No	341 (42.1)
Immediate breast reconstruction	
Yes	534 (65.9)
No	276 (34.1)
Contralateral prophylactic mastectomy	
Yes	133 (16.4)
No	677 (83.6)
Largest recorded pathologic lesion size, cm, median (range) ^d	2.2 (0.02–19)
Nuclear grade ^e	
I or II	351 (43.9)
III	448 (56.1)
Multicentric ^f	
Yes	247 (38.8)
No	389 (61.2)
Multifocal ^g	
Yes	238 (38.7)
No	377 (61.3)
Comedo ^h	
Yes	252 (32.5)
No	523 (67.5)
Necrosis	
Yes	384 (47.4)
No	426 (52.6)

TABLE 1 continued

Characteristics	n (%)
Estrogen receptor status ⁱ	
Positive	360 (76.6)
Negative	110 (23.4)
Adjuvant tamoxifen	
Yes	202 (24.9)
No	608 (75.1)
Adjuvant radiotherapy	
Yes	7 (0.9)
No	803 (99.1)

^a Two patients were perimenopausal

^b Not available for four patients

^c Not available for 423 patients

^d Not available for 182 patients

^e Not available for 11 patients

^f Not available for 174 patients

^g Not available for 195 patients

^h Not available for 35 patients

ⁱ Not available for 340 patients

Five patients (0.6 %) had positive final margins. Fifty-four patients (6.7 %) had final histologic margins that were not identified as positive but were ≤ 1 mm, 35 (4.3 %) had margins between 1.1 and 2.9 mm, and 716 (88.4 %) had margins ≥ 3 mm. Clinical and pathologic factors associated with margin status are shown in Table 2. On univariate analysis, patients were significantly more likely to have close margins if they were < 50 years old or premenopausal, underwent skin-sparing mastectomy or immediate breast reconstruction, had multicentric, multifocal, or comedo-type DCIS, had evidence of necrosis, or had large mammographic or pathologic lesion size. On multivariate analysis, the only independent predictors of margins < 3 mm were multicentricity, presence of necrosis, and largest recorded pathologic lesion size ≥ 1.5 cm (Table 3). Age and skin-sparing mastectomy were not identified as independent predictors of close margin status.

LRR and Contralateral Breast Cancer Development

Eight patients developed a LRR, seven patients developed invasive disease and one patient developed DCIS. Three of these eight patients had initial margins ≤ 1 mm, one patient had margins of 1.1–2.9 mm, and four patients had margins ≥ 3 mm. None of the patients who developed a LRR received PMRT. The median time to LRR was 2.8 years (range 1.3–10.9 years). The 10-year LRR rate among all patients who did not receive PMRT was 1.0 %. The 5- and 10-year LRR rates by margin status are shown

TABLE 2 Clinical and pathologic factors associated with close margins in patients with ductal carcinoma-in situ treated with mastectomy (*n* = 810)

Factors	Margins positive or ≤ 1 mm, <i>n</i> (%)	Margins 1.1–2.9 mm, <i>n</i> (%)	Margins ≥ 3 mm, <i>n</i> (%)	<i>p</i> value, overall	<i>p</i> value, positive or ≤ 1 versus ≥ 1.1	<i>p</i> value, positive or ≤ 1 versus 1.1–2.9
All patients	59 (7.3)	35 (4.3)	716 (88.4)			
Race						
White	38 (64.4)	26 (74.3)	536 (74.9)			
African American	12 (20.3)	2 (5.7)	71 (9.9)			
Hispanic	7 (11.9)	3 (8.6)	56 (7.8)			
Asian/Pacific Islander	2 (3.4)	3 (8.6)	41 (5.7)			
Other	0 (0)	1 (2.8)	12 (1.7)	0.218	0.053	0.166
Age						
Median (range), years	45 (22–77)	50 (37–70)	53 (20–88)	<0.001 ^a	<0.001 ^a	0.008 ^a
≤ 50 years	44 (74.6)	19 (54.3)	293 (40.9)			
> 50 years	15 (25.4)	16 (45.7)	423 (59.1)			0.043
Menopausal status ^b						
Premenopausal	37 (63.8)	16 (45.7)	226 (31.6)			
Postmenopausal	21 (36.2)	19 (54.3)	489 (68.4)			0.088
Initial presentation ^c						
Clinical	16 (27.1)	9 (25.7)	163 (22.9)			
Radiological	43 (72.9)	26 (74.3)	549 (77.1)	0.719	0.474	0.882
Largest recorded mammographic lesion dimension, cm, median (range) ^d	6.0 (1.0–20)	5.0 (0.8–9.8)	3.0 (0.3–18)	<0.001 ^a	<0.001 ^a	0.212 ^a
Skin-sparing mastectomy						
Yes	42 (71.2)	27 (77.1)	400 (55.9)			
No	17 (28.8)	8 (22.9)	316 (44.1)	0.005	0.032	0.527
Immediate breast reconstruction						
Yes	51 (86.4)	28 (80.0)	455 (63.6)			
No	8 (13.6)	7 (20.0)	261 (36.4)			0.410
Contralateral prophylactic mastectomy						
Yes	15 (25.4)	4 (11.4)	114 (15.9)			
No	44 (74.6)	31 (88.6)	602 (84.1)	0.119	0.053	0.102
Largest recorded pathologic lesion size, cm, median (range) ^e	5.1 (0.2–19)	4.7 (1.5–17)	2.0 (0.02–18)	<0.001 ^a	<0.001 ^a	0.974 ^a
Nuclear grade ^f						
I or II	18 (30.5)	14 (40.0)	319 (45.3)			
III	41 (69.5)	21 (60.0)	386 (54.7)	0.081	0.031	0.345
Multicentric ^g						
Yes	33 (62.3)	18 (56.3)	196 (35.6)			
No	20 (37.7)	14 (43.8)	355 (64.4)	<0.001	<0.001	0.583

TABLE 2 continued

Factors	Margins positive or ≤ 1 mm, n (%)	Margins 1.1–2.9 mm, n (%)	Margins ≥ 3 mm, n (%)	p value, overall	p value, positive or ≤ 1 versus ≥ 1.1	p value, positive or ≤ 1 versus 1.1–2.9
Multifocal ^h						
Yes	27 (60.0)	18 (56.3)	193 (35.9)			
No	18 (40.0)	14 (43.7)	345 (64.1)	<0.001	0.002	0.742
Comedo ⁱ						
Yes	29 (50.9)	13 (38.2)	210 (30.7)			
No	28 (49.1)	21 (61.8)	474 (69.3)	<0.001	0.002	0.242
Necrosis						
Yes	42 (71.2)	27 (77.1)	315 (44.0)			
No	17 (28.8)	8 (22.9)	401 (56.0)	<0.001	<0.001	0.527
Estrogen receptor status ^j						
Yes	31 (75.6)	28 (93.3)	301 (75.4)			
No	10 (24.4)	2 (6.7)	98 (24.6)	0.082	0.876	0.049

^a Calculated by the Kruskal–Wallis test

^b Two patients were perimenopausal

^c Not available for four patients

^d Not available for 423 patients

^e Not available for 182 patients

^f Not available for 11 patients

^g Not available for 174 patients

^h Not available for 195 patients

ⁱ Not available for 35 patients

^j Not available for 340 patients

TABLE 3 Multivariate logistic regression model of clinical and pathologic factors associated with close margins in patients with ductal carcinoma-in situ treated with mastectomy ($n = 810$)

Variables	Odds ratio	95 % CI	<i>p</i> value
Age			
≤50 years	1.00 (reference)		
>50 years	0.68	0.33–1.41	0.297
Menopausal status			
Premenopausal	1.00 (reference)		
Postmenopausal	0.58	0.29–1.19	0.137
Largest recorded mammographic dimension			
<1.5 cm	1.00 (reference)		
≥1.5 cm	2.87	0.81–10.08	0.101
Largest recorded pathologic lesion size			
<1.5 cm	1.00 (reference)		
≥1.5 cm	5.11	1.94–13.4	0.001
Skin-sparing mastectomy			
Yes	1.10	0.56–2.14	0.787
No	1.00 (reference)		
Immediate breast reconstruction			
Yes	1.00 (reference)		
No	0.54	0.25–1.17	0.120
Multicentric			
Yes	5.44	1.23–24.04	0.026
No	1.00 (reference)		
Multifocal			
Yes	1.00 (reference)		
No	3.04	0.67–13.9	0.151
Comedo			
Yes	1.00 (reference)		
No	1.15	0.66–2.00	0.626
Necrosis			
Yes	2.51	1.36–4.63	0.003
No	1.00 (reference)		
Estrogen receptor status			
Positive	1.00 (reference)		
Negative	0.53	0.26–1.10	0.088

in Table 4. Predictors of LRR are identified in Table 5. On univariate analysis, the only predictors of LRR were margin status, multicentricity, and multifocality. On multivariate analysis, the only independent predictor of LRR was margin <3 mm (hazard ratio 8.4, 95 % CI 1.9–37, $p = 0.005$). Of the eight patients with a LRR, five were treated with chest wall resection, and three had no further surgical management because they had evidence of metastasis at the time of recurrence.

Among the 546 patients who did not undergo contralateral prophylactic mastectomy, have bilateral breast cancer at the time of diagnosis, or have a history of contralateral breast cancer, 30 patients developed contralateral breast cancer during follow-up. Twelve of these patients (40 %) developed DCIS, and 18 (60 %) developed invasive

cancer. This represents a 10-year contralateral breast cancer incidence of 6.4 % (Table 4).

DISCUSSION

To our knowledge, this is the largest contemporary study evaluating the incidence and consequences of close margins in patients with DCIS treated with mastectomy. Margins were evaluated utilizing standardized intraoperative extensive specimen evaluation with radiographic correlation. Close final margins occurred in 94 of the 810 patients (11.7 %). We found that margin status was the only independent predictor of LRR and on multivariate analysis, the only independent predictors of close margins were pathologic size ≥ 1.5 cm, multicentricity, and

TABLE 4 Rates of locoregional recurrence (LRR) and contralateral breast cancer development by margin status in patients with ductal carcinoma-in situ treated with mastectomy ($n = 810$)

LRR	Margins positive or ≤ 1 mm (%)	Margins 1.1–2.9 mm (%)	Margins ≥ 3 mm (%)	p value, overall ^a	p value, positive or ≤ 1 versus ≥ 1.1 ^a	p value, positive or ≤ 1 versus 1.1–2.9 ^a
5-year LRR rate, entire series	4.5	3.5	0.7	<0.001	<0.001	0.574
10-year LRR rate, entire series	4.5	3.5	0.7	<0.001	<0.001	0.574
5-year LRR rate, patients who did not receive radiotherapy ($n = 803$)	5.0	3.6	0.7	<0.001	<0.001	0.531
10-year LRR rate, patients who did not receive radiotherapy ($n = 803$)	5.0	3.6	0.7	<0.001	<0.001	0.531
10-year rate of development of contralateral breast cancer ($n = 546$) ^b	6.8	0	6.7	0.529	0.934	0.248

^a Calculated by the Kaplan–Meier method. Differences were compared by the log-rank test

^b Excludes patients who had contralateral prophylactic mastectomy, bilateral breast cancer at diagnosis, or history of contralateral breast cancer

necrosis. Several margin definitions were investigated to provide some clarity for the definition of a ‘close margin’ and to ensure that our findings would be as widely applicable to many clinical practices. Though we did observe an increase in the LRR rate as margins became narrower, in all subgroups of patients with close margins this rate was less than the rate of contralateral breast cancer development even when patients did not receive PMRT.

Many smaller studies have attempted to identify predictors of LRR with varied results. Carlson et al.¹¹ studied 223 patients treated with mastectomy for DCIS and identified high grade and margins <1 mm, but not young age, large tumor size, or necrosis, as predictors of LRR. Godat et al.¹³ studied 83 patients treated with mastectomy for DCIS and reported only one LRR (LRR rate 1.1 %), in a patient with multifocal comedo necrosis and a deep margin <5 mm. Kelley et al.¹⁴ studied 496 patients treated with mastectomy for DCIS and reported 11 LRR, all among patients who had a Van Nuys Prognostic Index score of 10–12 with multifocal disease and evidence of comedo-type necrosis.

Our finding that close margins were an independent predictor of LRR agrees with previously published evidence that margin status is one of the strongest predictors of LRR. Carlson et al.¹¹ found a 10.5 % LRR rate among patient with margins <1 mm and suggested reexcision or PMRT for such patients. Rashtian et al. evaluated 574 patients with DCIS treated with mastectomy and identified 84 patients with margins <10 mm. After excluding four of these patients who were treated with PMRT, they found a 7.5 % LRR rate overall, a 16 % LRR rate for patients with margins ≤ 2 mm, and a 2 % LRR rate for patients with margins 2.1–10 mm. This high LRR rate among patients with margins <2 mm has led some practitioners to consider PMRT when margins are <2 mm or positive.¹⁸ Chadha et al. studied 207 patients treated with mastectomy for DCIS and reported that LRR occurred in two patients (0.9 %). Both LRRs occurred in patients with margins <1 mm, and there were no LRRs among patients with margins ≥ 1 mm.¹⁶

In 2012, Owen et al. from British Columbia reported on 637 patients treated with mastectomy for DCIS with a median follow-up time of 12 years. This represents the second largest published series of patients with DCIS treated with mastectomy. The authors found an overall 10-year LRR rate of 1 %.¹⁹ Although relatively high proportion of patients (4.9 %) had positive margins, only two of these patients developed a LRR and none of these patients received PMRT. The authors concluded that mastectomy provides excellent locoregional control for DCIS and that routine use of PMRT is not justified.¹⁹

The frequency of close margins varies in the literature as a result of differences in the patient populations

TABLE 5 Predictors of locoregional recurrence (LRR) in patients with ductal carcinoma-in situ treated with mastectomy (*n* = 810)

Characteristics	Patients with LRR, <i>n</i> (%)	Patients without LRR, <i>n</i> (%)	<i>p</i> value
All patients	8 (1.0)	802 (99.0)	
Race			
White	7 (87.5)	593 (74.0)	
African American	1 (12.5)	84 (10.5)	
Hispanic	0 (0)	66 (8.2)	
Asian/Pacific Islander	0 (0)	46 (5.7)	
Other	0 (0)	13 (1.6)	0.831
Age, years, median (range)	53 (20–88)	47.5 (41–62)	0.363
Menopausal status ^a			
Premenopausal	5 (62.5)	274 (34.2)	
Postmenopausal	3 (37.5)	526 (65.8)	0.096
Bilateral breast cancer at diagnosis			
Yes	1 (12.5)	99 (12.5)	
No	7 (87.5)	703 (87.6)	0.997
Initial presentation ^b			
Clinical	1 (12.5)	187 (23.5)	
Radiological	7 (87.5)	611 (76.5)	0.464
Largest recorded mammographic dimension, cm, median (range) ^c	2.5 (0.7–14)	3.5 (0.3–20)	0.816
Skin-sparing mastectomy			
Yes	7 (87.5)	462 (57.5)	
No	1 (12.5)	340 (42.5)	0.088
Immediate breast reconstruction			
Yes	7 (87.5)	527 (65.8)	
No	1 (12.5)	275 (34.3)	0.196
Contralateral prophylactic mastectomy			
Yes	1 (12.5)	132 (16.4)	
No	7 (87.5)	670 (83.6)	0.765
Largest recorded pathologic lesion size, cm, median (range) ^d	1.2 (0.5–8.0)	2.2 (0.02–19)	0.659
Nuclear grade ^e			
I or II	2 (25.0)	349 (44.1)	
III	6 (75.0)	442 (55.9)	0.278
Margin status			
≤1 mm	3 (37.5)	56 (7.0)	
1.1–2.9 mm	1 (12.5)	34 (4.2)	
≥3 mm	4 (50.0)	712 (88.8)	0.002
Multicentric ^f			
Yes	5 (100.0)	242 (38.4)	
No	0 (0)	389 (61.7)	0.005
Multifocal ^g			
Yes	5 (100.0)	233 (38.2)	
No	0 (0)	377 (61.8)	0.005
Comedo ^h			
Yes	2 (25.0)	250 (32.6)	
No	6 (75.0)	517 (67.4)	0.648
Necrosis			
Yes	6 (75.0)	378 (47.1)	
No	2 (25.0)	424 (52.9)	0.115

^a Two patients were perimenopausal

^b Not available for four patients

^c Not available for 423 patients

^d Not available for 181 patients

^e Not available for 11 patients

^f Not available for 174 patients

^g Not available for 195 patients

^h Not available for 35 patients

examined, the degree of intraoperative imaging and pathologic analysis of specimens, the extent of overall histologic sampling, and the way in which close margins are defined. We perform extensive intraoperative analysis of each mastectomy specimen, including specimen radiography and frozen section examination, if necessary, to assess the margins in real time. With this approach, while the patient is still under anesthesia, excision of additional tissue can be performed when necessary to clear or improve the margins. The question of whether PMRT should be used in patients treated with mastectomy for DCIS is further complicated by the finding that the closest margin is often deep or superficial. If the mastectomy included the fascia of the pectoralis major muscle, a close deep margin should be adequate given that DCIS is a noninvasive lesion. If the closest margin is superficial, typically skin excision and/or conversion from a skin sparing mastectomy to total mastectomy may be required in order to clear the margin. In a survey of 226 surgeons in the UK, 19 % responded that they would consider the use of PMRT for treatment of DCIS. More than two-thirds of these responders indicated that margin status was a factor in this decision, though they differed regarding the margin width that would indicate that PMRT should be considered, with some considering PMRT for margins <1 mm and others considering PMRT for margins <5 mm.²⁰

Aside from margin status, another possible predictor of LRR is the type of mastectomy performed, although we did not find an association between mastectomy type and LRR risk in our study. Carlson et al.¹¹ studied 223 patients treated with skin-sparing mastectomy for DCIS and reported a LRR rate of 4.2 %. Two-thirds of our patients underwent immediate breast reconstruction, 87 % of these patients underwent a skin-sparing mastectomy, and we did not observe a difference in LRR rate between patients who underwent skin-sparing mastectomy and those who underwent total mastectomy. One reason for this may be our use of extensive intraoperative analysis.

PMRT is often considered when the risk of LRR is above 10 %. The LRR rate in our series of 0.7 % for patients with margins ≥ 3 mm, 3.6 % for patients with margins 1.1–2.9, and 5 % for patients with margins ≤ 1 mm are all below this threshold. More important, the risk of LRR for patients with close margins was lower than the risk of development of contralateral breast cancer (6.4 %). The rate of contralateral breast cancer development is essentially the same as the rate reported by Meijnen et al.⁹ for patients with DCIS treated with mastectomy: 6.5 % over 8 years. Further, Kim et al.²¹ reported that 90 % of patients treated with mastectomy for DCIS who developed a LRR were successfully treated with excision and radiotherapy. On the basis of these data, we would not recommend routine PMRT for patients with margins

<3 mm. However, we did not specifically analyze patients with more than one margin < 3 mm or with positive margins as only very few patients in this series met these criteria, who might be expected to have a higher incidence of LRR. Of the seven patients in our series who received PMRT, six had either a positive or multiple close margins and none of these patients developed a LRR. For patients with a positive or multiple close margins, we would recommend reexcision when possible or consideration of PMRT if reexcision is not possible. PMRT would include radiation to the chest wall with a boost given to the area of the primary tumor.

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REFERENCES

1. Kuerer HM, Albarracin CT, Yang WT, et al. Ductal carcinoma in situ: state of the science and roadmap to advance the field. *J Clin Oncol*. 2009;27:279–88.
2. Jemal A, Siegel R, Ward E, et al. Cancer statistics, 2008. *CA Cancer J Clin*. 2008;58:71–96.
3. Burstein HJ, Polyak K, Wong JS, Lester SC, Kaelin CM. Ductal carcinoma in situ of the breast. *N Engl J Med*. 2004;350:1430–41.
4. Baxter NN, Virnig BA, Durham SB, Tuttle TM. Trends in the treatment of ductal carcinoma in situ of the breast. *J Natl Cancer Inst*. 2004;96:443–8.
5. Smith GL, Smith BD, Haffty BG. Rationalization and regionalization of treatment for ductal carcinoma in situ of the breast. *Int J Radiat Oncol Biol Phys*. 2006;65:1397–403.
6. Silverstein MJ, Barth A, Poller DN, et al. Ten-year results comparing mastectomy to excision and radiation therapy for ductal carcinoma in situ of the breast. *Eur J Cancer*. 1995;31A:1425–7.
7. Silverstein MJ, Lagios MD, Martino S, et al. Outcome after invasive local recurrence in patients with ductal carcinoma in situ of the breast. *J Clin Oncol*. 1998;16:1367–73.
8. Schouten van der Velden AP, van Vugt R, Van Dijk JA, Leer JW, Wobbes T. Local recurrences after different treatment strategies for ductal carcinoma in situ of the breast: a population-based study in the East Netherlands. *Int J Radiat Oncol Biol Phys*. 2007;69:703–10.
9. Meijnen P, Oldenburg HS, Peterse JL, Bartelink H, Rutgers EJ. Clinical outcome after selective treatment of patients diagnosed with ductal carcinoma in situ of the breast. *Ann Surg Oncol*. 2008;15:235–43.
10. Lee LA, Silverstein MJ, Chung CT, et al. Breast cancer-specific mortality after invasive local recurrence in patients with ductal carcinoma-in situ of the breast. *Am J Surg*. 2006;192:416–9.
11. Carlson GW, Page A, Johnson E, Nicholson K, Styblo TM, Wood WC. Local recurrence of ductal carcinoma in situ after skin-sparing mastectomy. *J Am Coll Surg*. 2007;204:1074–8.
12. Chan LW, Rabban J, Hwang ES, et al. Is radiation indicated in patients with ductal carcinoma in situ and close or positive mastectomy margins? *Int J Radiat Oncol Biol Phys*. 2011;80:25–30.

13. Godat LN, Horton JK, Shen P, Stewart JH, Wentworth S, Levine EA. Recurrence after mastectomy for ductal carcinoma in situ. *Am Surg*. 2009;75:592–5.
14. Kelley L, Silverstein M, Guerra L. Analyzing the risk of recurrence after mastectomy for DCIS: a new use for the USC/Van Nuys Prognostic Index. *Ann Surg Oncol*. 2011;18:459–62.
15. Childs SK, Chen YH, Duggan MM, et al. Impact of margin status on local recurrence after mastectomy for ductal carcinoma in situ. *Int J Radiat Oncol Biol Phys*. 2013;85:948–52.
16. Chadha M, Portenoy J, Boolbol SK, Gillego A, Harrison LB. Is there a role for postmastectomy radiation therapy in ductal carcinoma in situ? *Int J Surg Oncol*. 2012;2012:423520.
17. Lari SA, Kuerer HM. Biological markers in DCIS and risk of breast recurrence: a systematic review. *J Cancer*. 2011;2:232–61.
18. Rashtian A, Iganej S, Amy Liu IL, Natarajan S. Close or positive margins after mastectomy for DCIS: pattern of relapse and potential indications for radiotherapy. *Int J Radiat Oncol Biol Phys*. 2008;72:1016–20.
19. Owen D, Tyldesley S, Alexander C, et al. Outcomes in patients treated with mastectomy for ductal carcinoma in situ. *Int J Radiat Oncol Biol Phys*. 2012;85:129–34.
20. Mallon PT, McIntosh SA. Post mastectomy radiotherapy in breast cancer: a survey of current United Kingdom practice. *J BUON*. 2012;17:245–8.
21. Kim JH, Tavassoli F, Haffty BG. Chest wall relapse after mastectomy for ductal carcinoma in situ: a report of 10 cases with a review of the literature. *Cancer J*. 2006;12:92–101.