Original Investigation

Repeat Surgery After Breast Conservation for the Treatment of Stage 0 to II Breast Carcinoma

A Report From the National Cancer Data Base, 2004-2010

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IMPORTANCE Although complete excision of breast cancer is accepted as the best means to reduce local recurrence and thereby improve survival, there is currently no standard margin width for breast conservation surgery. As a result, significant variability exists in the number of additional operations or repeat surgeries patients undergo to establish tumor-negative margins.

OBJECTIVE To determine the patient, tumor, and facility factors that influence repeat surgery rates in US patients undergoing breast conservation surgery.

DESIGN, SETTING, AND PATIENTS Patients diagnosed as having breast cancer at a Commission on Cancer accredited center from January 1, 2004, through December 31, 2010, and identified via the National Cancer Data Base, a large observational database, were included in the analysis. A total of 316 114 patients with stage 0 to II breast cancer who underwent initial breast conservation surgery were studied. Patients who were neoadjuvantly treated or whose conditions were diagnosed by excisional biopsy were excluded.

MAIN OUTCOMES AND MEASURES Patient, tumor, and facility factors associated with repeat surgeries.

RESULTS A total of 241 597 patients (76.4%) underwent a single lumpectomy, whereas 74 517 (23.6%) underwent at least 1 additional operation, of whom 46 250 (62.1%) underwent a completion lumpectomy and 28 267 (37.9%) underwent a mastectomy. The proportion of patients undergoing repeat surgery decreased slightly during the study period from 25.4% to 22.7% ($P < .001$). Independent predictors of repeat surgeries were age, race, insurance status, comorbidities, histologic subtype, estrogen receptor status, pathologic tumor size, node status, tumor grade, facility type and location, and volume of breast cancer cases. Age was inversely associated with repeat surgery, decreasing from 38.5% in patients 18 to 29 years old to 16.5% in those older than 80 years ($P < .001$). In contrast, larger tumor size was linearly associated with a higher repeat surgery rate ($P < .001$). Repeat surgeries were most common at facilities located in the Northeast region (26.5%) compared with facilities in the Mountain region, where only 18.4% of patients underwent repeat surgery ($P < .001$). Academic or research facilities had a 26.0% repeat surgery rate compared with a rate of 22.4% at community facilities ($P < .001$).

CONCLUSIONS AND RELEVANCE Approximately one-fourth of all patients who undergo initial breast conservation surgery for breast cancer will have a subsequent operative intervention. The rate of repeat surgeries varies by patient, tumor, and facility factors and has decreased slightly during the past 6 years.

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In 1985, the National Adjuvant Bowel and Breast Project published the 5-year results of the B-06 randomized trial that found no difference in disease-free or overall survival between "segmental mastectomy" and total mastectomy for the treatment of invasive breast cancer.[1] In 2002, the 20-year results of this trial continued to reveal no difference in survival, yet substantial controversy remains regarding the definition of the phrase "free of tumor."[2] Until recently, no nationally or internationally accepted guidelines for an adequate margin width for invasive or noninvasive breast cancer have been available. This lack of a consensus has led to variable rates of reexcision and ranges in rates of 0% to 60%.[3] A study[4] of published data from 4 institutions found a 22% reexcision rate, and another Surveillance, Epidemiology and End Results survey study[5] found a 37% reexcision rate. With a conservative estimate of 60% of women with early-stage invasive and noninvasive breast cancer undergoing breast conservation in the United States and 20% requiring a second intervention to achieve an R0 resection, more than 20 000 women annually will require additional surgery to achieve margin-negative outcomes. The financial, psychological, and cosmetic effects of these repeat surgeries are significant and markedly increase the burden of breast cancer therapy.[6-8]

The National Cancer Data Base (NCDB) is a large observational database of Commission on Cancer (CoC) accredited cancer centers and is estimated to contain data on more than 70% of patients treated for cancer in the United States.[9] In this study, we examined patients who underwent initial breast conservation surgery (BCS) and what proportion of these patients underwent a subsequent completion partial mastectomy or mastectomy. We analyzed the patient, tumor, and facility factors associated with these repeat surgeries. The findings from this study seek to establish trends for repeat surgery across the United States and illustrate why adoption of consensus guidelines and subsequent outcomes analysis of the guidelines are needed to decrease repeat surgery rates.

Methods

This study was in compliance with the privacy requirements of the Health Insurance Portability and Accountability Act of 1996 as reported in the Standards for Privacy of Individually Identifiable Health Information (final rule, 45 CFR §160 and §164). No patient, physician, or hospital identifiers were examined in this study, no protected health information was reviewed, and the analysis was retrospective. Institutional review board approval and informed consent were not required for this study.

The NCDB, a joint program of the CoC of the American College of Surgeons and the American Cancer Society, is a prospectively collected, hospital-based data set. Using a deidentified, Health Insurance Portability and Accountability Act–compliant public utility file from the NCDB, we identified 316 114 patients with stage 0 to II breast cancer (≥18 years old) from January 1, 2004, through December 31, 2010, who underwent initial BCS. Patients who underwent neoadjuvant chemotherapy or endocrine therapy, as well as those whose diagnosis was obtained via excisional biopsy, were excluded. Only the first and last or definitive operations were recorded; operations that occurred between these operations are not recorded in the NCDB. The NCDB contains only the definitive margin status and does not contain the margin width.

Variables analyzed included age, race, insurance status, comorbidities, histologic subtype, estrogen receptor status, pathologic tumor size, node status, tumor grade, facility type and location, and volume of breast cancer cases. Patient race was coded as non-Hispanic white, black, Hispanic, Asian or Pacific Islander, Native American, and other or unknown. Insurance status was categorized as uninsured, private, managed care, Medicaid, Medicare, and Medicare with Supplement. Number of comorbidities was defined as 0, 1, or 2 or more. Tumor stage was categorized according to the *American Joint Committee on Cancer Staging Manual*, seventh edition, definition.[10] The histologic subtype of the tumor was categorized according to the *International Classification of Diseases for Oncology*.[11]

The NCDB defines facility type as community, comprehensive community, or academic/teaching facility. Community hospital cancer programs treat 100 to 500 newly diagnosed cancer cases each year, comprehensive community cancer programs treat 500 or more cases annually, and academic or research programs treat 500 or more cancer cases and participate in physician education and research. Facility location was categorized into regions according to the 2000 US Census as Northeast, Southeast, Atlantic, Great Lakes, South, Midwest, West, Mountain, and Pacific.[12] Volume of breast cancer cases was calculated at each of the 1416 facilities and further divided into 4 groups: fewer than 200 (small), 200 to 499 (medium), 500 to 1000 (large), and more than 1000 (very large).

Patient, tumor, and facility characteristics of individuals undergoing a single BCS were compared with those of patients undergoing a repeat surgery using the χ^2 test. Univariate and multivariable logistic regression models were used to determine predictors of repeat surgeries using odds ratios and 95% CIs. Odds ratios greater than 1 signified a higher likelihood of undergoing a repeat surgery. In the subgroup analysis, multivariable logistic regression models were executed separately for invasive and noninvasive cancer.

Trends in repeat surgery rates were investigated for noninvasive and invasive breast cancer cases and for patient age and tumor size. The Cochran-Armitage trend test was used to test for trends in binomial proportions of repeat surgery across the levels of year, age, and tumor size. The differences in repeat surgery rates by histologic subtype and regional variation were analyzed using the χ^2 test.

All statistical analyses were performed using SAS statistical software, version 9.2 (SAS Institute Inc). $P \leq .05$ was considered statistically significant; all statistical tests were 2-sided. The American College of Surgeons and the CoC have not verified and are not responsible for the analytic or statistical method used or the conclusions drawn from these data by the investigators.

Results

Patient, Tumor, and Facility Characteristics Associated With Repeat Surgeries

From January 1, 2004, through December 31, 2010, a total of 316 114 patients underwent initial BCS for an invasive breast cancer or ductal carcinoma in situ, of whom 241 597 (76.4%) underwent a single BCS and 74 517 (23.6%) underwent at least 1 additional operation. Of the 74 517 undergoing an additional operation, 46 250 (62.1%) underwent a completion lumpectomy and 28 267 (37.9%) underwent a mastectomy. In 2004, a total of 5282 (60.4%) of those undergoing at least 2 operations had completion BCS, which increased to 6669 (63.7%) in 2010, and 3459 (39.6%) underwent subsequent mastectomy in 2004 compared with 3806 (36.3%) in 2010. The proportion of patients undergoing repeat surgery decreased slightly during the study period from 25.4% to 22.7% ($P < .001$). **Table 1** lists patient demographic, tumor, and facility characteristics comparing patients undergoing a single BCS with those undergoing repeat surgery. The mean age was 59.8 years for patients undergoing a single BCS vs 57.1 years for patients undergoing repeat surgeries. A total of 237 470 patients (98.3%) undergoing single lumpectomy had only 0 to 1 comorbidity, reflecting the relative healthy cohort who developed breast carcinoma. Pathologic tumor size and histologic subtype were the 2 most notable patient factors associated with repeat surgeries, with significantly more large tumors and more ductal carcinoma in situ and invasive lobular carcinoma in the repeat surgery group. There was a significantly higher level of positive node status in the repeat surgery group (19 467 [26.2%] vs 41 029 [17.0%], $P < .001$). Academic or research facilities had a 26.0% repeat surgery rate compared with a rate of 22.4% at community facilities ($P < .001$). Regional variation in the rate of repeat surgeries and facility type was also significantly different, with a higher proportion of academic or research facilities in the repeat surgery group compared with the single BCS group (25 224 [34.3%] vs 71 748 [30.0%], $P < .001$).

We compared patient, tumor, and facility factors between the repeat surgery patients who had completion BCS vs completion mastectomy. Patients whose final operation was mastectomy had a higher percentage of invasive lobular carcinoma; 10 210 (36.1%) of the mastectomy patients were younger than 50 years compared with 11 722 (25.3%) in the completion lumpectomy group. Patients who underwent completion mastectomy had larger tumors; 14 815 (56.4%) of the tumors were less than 2 cm compared with 29 960 (70.4%) of the tumors in the patients undergoing completion lumpectomy.

Univariate and Multivariable Analysis of Factors Related to Repeat Surgeries

Univariate and multivariable analysis of the cohort revealed that younger patient age, black and Asian or Pacific Islander race, managed care insurance, Medicare and Medicaid, fewer comorbidities, invasive lobular carcinoma and mixed histologic subtypes, positive estrogen receptor status, larger tumor size, positive node status, higher tumor grade, academic or research facilities, and larger volume of breast cancer cases were all significantly associated with a greater likelihood of repeat surgery (**Table 2**). Significant variation was found in the repeat surgery rates depending on the patient's location in the country (**Figure 1**). Facilities in the Mountain region were 36.0% less likely to perform repeat surgery (odds ratio, 0.64; 95% CI, 0.61-0.68) compared with facilities in the Northeast.

Repeat Surgery by Invasive and Noninvasive Cancer Status

A total of 253 052 patients (80.1%) had invasive cancer. There was a slightly higher proportion of repeat surgery in the noninvasive group compared with the invasive group (59 218 [23.4%] vs 14 490 [24.6%]). Although the factors associated with repeat surgeries in patients with invasive cancers were similar to those in Table 2 for the entire cohort of patients, insurance status, comorbidities, and volume of breast cancer cases were not significant predictors of repeat surgery in the patients with noninvasive cancer.

Trends in Repeat Surgery

The repeat surgery rate for noninvasive and invasive cancer significantly decreased from 2004 to 2010 from 25.9% to 23.4% for noninvasive disease and 25.3% to 22.5% for invasive disease, respectively. Age was inversely related to repeat surgery rates. For patients 18 to 29 years old, the repeat surgery rate was 38.5% compared with 16.5% for those older than 80 years (**Figure 2**A). Tumor size also revealed a significant linear trend, with increasing tumor size associated with a higher repeat surgery rate (Figure 2B). For tumors smaller than 1.5 cm, the repeat surgery rate was 20.8% compared with a repeat surgery rate of 48.2% for tumors larger than 5 cm. On multivariate regression analysis, patients with tumors 2 to 5 cm were 23.0% more likely to undergo repeat surgeries than patients with tumors smaller than 2 cm. Histologic subtypes differed significantly by repeat surgery rates, with the lowest rate of 22.2% in the invasive ductal carcinoma group and the highest rate of 30.8% in the invasive lobular carcinoma group. When repeat surgery rates were stratified by institution, most institutions were within a range of 14% to 30%, with a bell-shaped distribution (**Figure 3**).

Discussion

In this study of approximately 316 000 patients who underwent initial BCS for treatment of a noninvasive or invasive breast tumor, nearly one-fourth underwent an additional operation. This is the largest study to examine repeat surgeries in patients undergoing initial BCS for stage 0 to II disease and one of only a few studies[4,5] that examined rates across different institutions. McCahill et al[4] examined reexcision rates at an academic health center and 3 health care plans and reported a 22% reexcision rate, with 39.9% of the 1459 patients who were surveyed through the National Cancer Institute's Surveillance, Epidemiology and End Results registries undergoing reexcision.[5] A study[13] from Canada reported a 26% reexcision rate among 489 patients from 26 hospitals. Additional studies[3,14-19] from multiple and single institutions have found

Table 1. Patient, Tumor, and Facility Characteristics of Patients Undergoing a Single Lumpectomy Compared With Those Undergoing a Repeat Surgery

Characteristic	No. (%) of Patients		*P* Value
	Single Lumpectomy	Repeat Surgery	
Total No. of patients	241 597 (76.4)	74 517 (23.6)	
Age, y			
18-29	550 (0.2)	344 (0.5)	<.001
30-39	7113 (2.9)	3883 (5.2)	
40-49	43 952 (18.2)	17 705 (23.8)	
50-59	69 019 (28.6)	21 864 (29.3)	
60-69	67 179 (27.8)	18 312 (24.6)	
70-79	40 069 (16.6)	9695 (13.0)	
≥80	13 715 (5.7)	2714 (3.6)	
Race/ethnicity			
White	205 098 (84.9)	61 562 (82.6)	<.001
Black	22 448 (9.3)	8098 (10.9)	
Hispanic or Puerto Rican	3542 (1.5)	1110 (1.5)	
Asian or Pacific Islander	5974 (2.5)	2266 (3.0)	
Native American	493 (0.2)	142 (0.2)	
Other or unknown	4042 (1.7)	1339 (1.8)	
Insurance status			
Uninsured	3643 (1.5)	1220 (1.7)	<.001
Private	33 329 (14.1)	10 624 (14.5)	
Managed	112 574 (47.7)	38 314 (52.5)	
Medicaid	10 033 (4.3)	3660 (5.0)	
Medicare	17 221 (7.3)	4667 (6.4)	
Medicare with Supplementation	59 396 (25.2)	14 568 (19.9)	
No. of comorbidities			
0	212 565 (88.0)	65 534 (88.0)	.25
1	24 905 (10.3)	7768 (10.4)	
2	4127 (1.7)	1215 (1.6)	
Histologic subtype			
DCIS	44 342 (18.6)	14 490 (19.7)	<.001
IDC	168 393 (70.7)	48 179 (65.4)	
ILC	13 508 (5.7)	6021 (8.2)	
Mixed	10 920 (4.6)	4717 (6.4)	
Other	1013 (0.4)	301 (0.4)	
Estrogen receptor status			
Positive	199 141 (85.6)	61 274 (84.7)	<.001
Negative	33 179 (14.3)	10 929 (15.1)	
Equivocal	332 (0.1)	123 (0.2)	
Tumor size, cm			
<2	164 692 (73.4)	44 775 (65.1)	<.001
2-5	57 941 (25.8)	22 527 (32.7)	
>5	1670 (0.7)	1533 (2.2)	
Node status			
Negative	200 217 (83.0)	54 948 (73.8)	<.001
Positive	41 029 (17.0)	19 467 (26.2)	
Grade			
1	58 973 (24.4)	14 186 (19.0)	<.001
2	99 180 (41.1)	31 611 (42.4)	
3	66 199 (27.4)	23 060 (31.0)	
4	17 245 (7.1)	5660 (7.6)	

(continued)

Table 1. Patient, Tumor, and Facility Characteristics of Patients Undergoing a Single Lumpectomy Compared With Those Undergoing a Repeat Surgery (continued)

Characteristic	No. (%) of Patients		*P* Value
	Single Lumpectomy	Repeat Surgery	
Facility location			
Northeast	19 748 (8.2)	7130 (9.6)	<.001
Atlantic	39 026 (16.2)	12 796 (17.2)	
Southeast	51 949 (21.5)	16 151 (21.7)	
Great Lakes	46 437 (19.2)	15 149 (20.3)	
South	12 162 (5.0)	3092 (4.2)	
Midwest	18 315 (7.6)	6039 (8.1)	
West	14 241 (5.9)	3746 (5.0)	
Mountain	10 784 (4.5)	2424 (3.3)	
Pacific	28 935 (12.0)	7990 (10.7)	
Facility type			
Community cancer program	33 867 (14.2)	9483 (12.9)	<.001
Comprehensive community cancer program	133 374 (55.8)	38 865 (52.8)	
Academic or research	71 748 (30.0)	25 224 (34.3)	
Volume of breast cancer cases			
<200	57 663 (23.9)	16 960 (22.8)	<.001
200-499	95 966 (39.7)	28 569 (38.3)	
500-1000	66 556 (27.6)	20 425 (27.4)	
>1000	21 412 (8.9)	8563 (11.5)	

Abbreviations: DCIS, ductal carcinoma in situ; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma.

wide variation in the reexcision rate from 0% to 60%, with a mean rate of 35%. In contrast, our study includes 1400 institutions from across the United States, and we are able to define an overall rate of repeat surgery of 23.6%, with identification of factors associated with increased or decreased rates of secondary breast surgery. The trend for repeat surgery has significantly decreased during the 6-year period from 25% to 22% to 23%, which may not be clinically significant but translates into a decrease of approximately 3000 cases per year. It is important to note the possibility that trends in the number of patients undergoing BCS and unilateral and bilateral mastectomy may have had a confounding effect on the incidence of repeat surgery. From January 1, 2004, through December 31, 2010, in the cohort of all patients undergoing breast cancer surgery at CoC hospitals, the BCS rate decreased 1.9%, the unilateral mastectomy rate decreased 3.2%, and the bilateral mastectomy rate increased 5.1%. Therefore, potentially, patients who were initially BCS candidates may have immediately undergone bilateral mastectomy, which may explain why the additional operation rate decreased over time. Subsequent surgical type did not significantly change during the study period, suggesting that patients who need a repeat surgery have continued to pursue BCS. However, we could only define the first and last or definitive surgery using the NCDB. We excluded those patients who underwent an excisional biopsy because this cohort would be expected to have a higher-than-average repeat surgery rate.[20] Patients who underwent neoadjuvant therapy were also excluded because of the variability in response to neoadjuvant therapy that could influence surgical choice.

The cohort in the NCDB affords the opportunity to see significant differences among patient, tumor, and facility groups. The findings of higher repeat surgery rates in patients who are younger, have large tumor sizes, and/or have a lobular histologic subtype have been repeatedly, although variably, documented previously.[4,17,18] O'Sullivan et al[21] from Fox Chase Cancer Center analyzed 2770 patients undergoing BCS during 25 years and identified younger age, lobular histologic subtype, and detection by physical examination as significant predictors of reexcision surgery. Investigators from the Henrietta Banting Breast Centre in Canada evaluated 1430 patients who underwent BCS and found that young age was the only variable predictive of positive margins and reexcision surgery.[22] Patient age was the most significant factor related to repeat surgeries in the current study. Reexcision after initial lumpectomy has been associated with increased use of bilateral mastectomy in younger patients[23] in the past decade, but our subsequent mastectomy rate decreased during the study period. Tumor histologic subtype was also an important factor in repeat surgery in this study; lobular carcinomas had higher repeat surgery rates then ductal carcinomas, but the repeat surgery rates in patients with noninvasive and invasive breast cancers were similar. A nomogram for predicting positive breast conservation margins has been published by physicians from the Netherlands.[24] Input variables for the nomogram include influential tumor factors identified in this study, such as tumor size, estrogen receptor status, and histologic subtype. Included in this nomogram are factors that cannot be attained in the NCDB inclusive of breast density, imaging characteristics, and the use of preoperative magnetic resonance imaging. Of interest, the use of patient age is not included in this nomogram but was influential in determining the output of repeat surgery in this study.

Table 2. Univariate and Multivariable Analysis of Patient, Tumor, and Facility Characteristics for Repeat Surgeries in Patients With Stage 0 to II Breast Cancer in the National Cancer Data Base From 2004 to 2010

Characteristic	Univariate		Multivariable	
	Odds Ratio (95% CI)	*P* Value	Odds Ratio (95% CI)	*P* Value
Age, y				
18-29	1 [Reference]		1 [Reference]	
30-39	0.87 (0.76-1.00)	.06	0.85 (0.73-0.98)	.03
40-49	0.64 (0.56-0.74)	<.001	0.68 (0.58-0.78)	<.001
50-59	0.51 (0.44-0.58)	<.001	0.54 (0.47-0.63)	<.001
60-69	0.44 (0.38-0.50)	<.001	0.47 (0.41-0.55)	<.001
70-79	0.39 (0.34-0.44)	<.001	0.42 (0.36-0.49)	<.001
≥80	0.32 (0.28-0.36)	<.001	0.34 (0.29-0.39)	<.001
Race/ethnicity				
White	1 [Reference]		1 [Reference]	
Black	1.20 (1.17-1.24)	<.001	1.05 (1.02-1.09)	.001
Hispanic or Puerto Rican	1.04 (0.98-1.12)	.21	0.97 (0.90-1.05)	.43
Asian or Pacific Islander	1.26 (1.20-1.33)	<.001	1.18 (1.12-1.25)	<.001
Native American	0.96 (0.80-1.16)	.66	1.03 (0.83-1.28)	.77
Other or unknown	1.10 (1.04-1.18)	.002	1.03 (0.96-1.10)	.48
Insurance status				
Uninsured	1 [Reference]		1 [Reference]	
Private	0.95 (0.89-1.02)	.16	1.08 (1.00-1.16)	.06
Managed	1.02 (0.95-1.09)	.63	1.13 (1.05-1.21)	.001
Medicaid	1.09 (1.01-1.17)	.03	1.10 (1.02-1.20)	.02
Medicare	0.81 (0.75-0.87)	<.001	1.13 (1.04-1.22)	.004
Medicare with Supplementation	0.73 (0.69-0.78)	<.001	1.09 (1.01-1.18)	.02
No. of comorbidities				
0	1 [Reference]		1 [Reference]	
1	1.01 (0.99-1.04)	.40	1.07 (1.04-1.11)	<.001
2	0.96 (0.90-1.02)	.17	1.03 (0.96-1.11)	.36
Histologic subtype				
DCIS	1 [Reference]		1 [Reference]	
IDC	0.88 (0.86-0.89)	<.001	0.82 (0.80-0.85)	<.001
ILC	1.36 (1.32-1.41)	<.001	1.35 (1.29-1.40)	<.001
Mixed	1.32 (1.27-1.38)	<.001	1.23 (1.18-1.29)	<.001
Other	0.91 (0.80-1.04)	.15	0.76 (0.66-0.88)	<.001
Estrogen receptor status				
Positive	1 [Reference]		1 [Reference]	
Negative	1.07 (1.05-1.10)	<.001	0.92 (0.89-0.95)	<.001
Equivocal	1.20 (0.98-1.48)	.08	1.08 (0.86-1.35)	.52
Tumor size, cm				
<2	1 [Reference]		1 [Reference]	
2-5	1.43 (1.40-1.46)	<.001	1.23 (1.21-1.26)	<.001
>5	3.38 (3.15-3.62)	<.001	3.40 (3.14-3.68)	<.001

(continued)

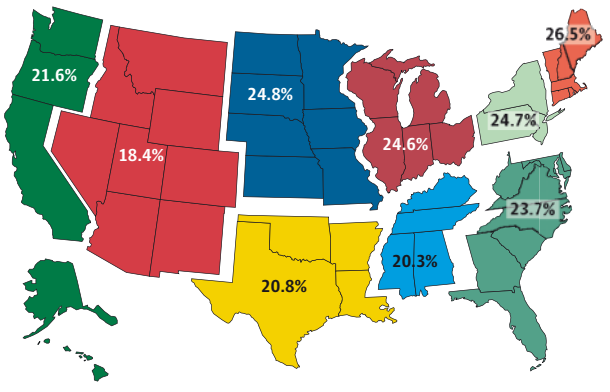
We found variance according to type of institution; academic centers were 19% more likely to perform a repeat surgery then community centers. This finding is in contrast to the findings from the Netherlands group, which reported no difference in reexcision rates between community and academic hospitals.[24] Closer pathologic examination of margins, patient preference, or input from the multidisciplinary team may play a role in the higher repeat surgery rate at the academic institutions. Volume of breast cancer cases was minimally associated with repeat surgery rates unless high-volume institutions were examined, which were 16% more likely to perform repeat surgeries then the low-volume institutions. These high-volume institutions are more likely to be academic facilities, and their repeat surgery rates may reflect patient referral patterns. Significant variance was found among different regions of the country. In the Mountain region, 2424 patients (3.3%) underwent repeat surgeries compared with 16 151 patients (21.7%) in the Southeast. In the study by McCahill

Table 2. Univariate and Multivariable Analysis of Patient, Tumor, and Facility Characteristics for Repeat Surgeries in Patients With Stage 0 to II Breast Cancer in the National Cancer Data Base From 2004 to 2010 (continued)

Characteristic	Univariate		Multivariable	
	Odds Ratio (95% CI)	*P* Value	Odds Ratio (95% CI)	*P* Value
Node status positive	1.73 (1.70-1.76)	<.001	1.58 (1.55-1.62)	<.001
Grade				
1	1 [Reference]		1 [Reference]	
2	1.33 (1.30-1.36)	<.001	1.20 (1.17-1.23)	<.001
3	1.45 (1.41-1.48)	<.001	1.24 (1.21-1.28)	<.001
4	1.36 (1.32-1.41)	<.001	1.29 (1.23-1.34)	<.001
Facility location				
Northeast	1 [Reference]		1 [Reference]	
Atlantic	0.91 (0.88-0.94)	<.001	0.88 (0.84-0.91)	<.001
Southeast	0.86 (0.83-0.89)	<.001	0.87 (0.84-0.91)	<.001
Great Lakes	0.90 (0.87-0.93)	<.001	0.94 (0.91-0.97)	<.001
South	0.70 (0.67-0.74)	<.001	0.73 (0.70-0.78)	<.001
Midwest	0.91 (0.88-0.95)	<.001	0.95 (0.91-1.00)	.03
West	0.73 (0.70-0.76)	<.001	0.76 (0.73-0.80)	<.001
Mountain	0.62 (0.59-0.66)	<.001	0.64 (0.60-0.67)	<.001
Pacific	0.77 (0.74-0.79)	<.001	0.76 (0.73-0.79)	<.001
Facility type				
Community cancer program	1 [Reference]		1 [Reference]	
Comprehensive community cancer program	1.04 (1.02-1.07)	.002	1.07 (1.03-1.10)	<.001
Academic or research	1.26 (1.22-1.29)	<.001	1.20 (1.16-1.25)	<.001
Volume of breast cancer cases				
<200	1 [Reference]		1 [Reference]	
200-499	1.01 (0.99-1.03)	.27	0.95 (0.92-0.98)	<.001
500-1000	1.04 (1.02-1.07)	<.001	0.94 (0.91-0.97)	<.001
>1000	1.36 (1.32-1.40)	<.001	1.17 (1.13-1.22)	<.001

Abbreviations: DCIS, ductal carcinoma in situ; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma.

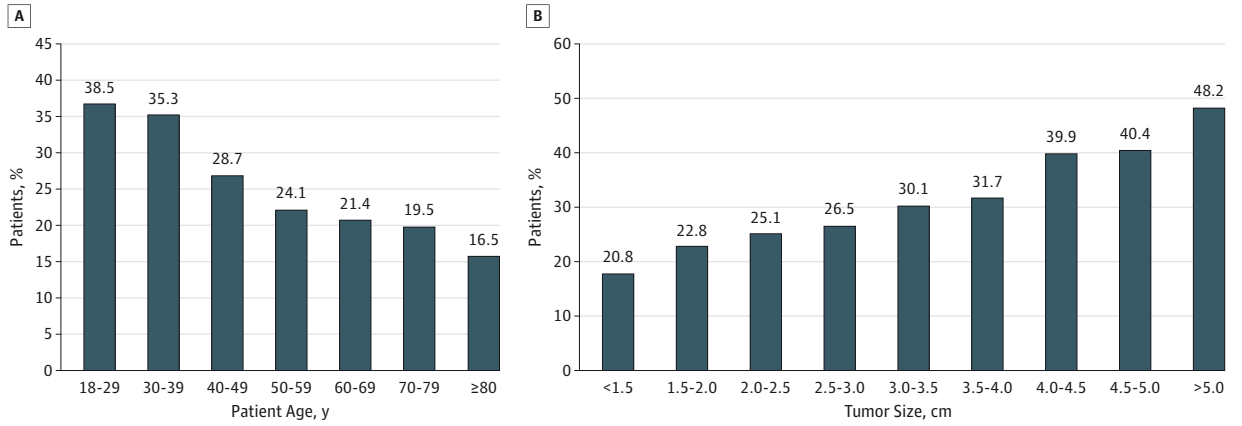
Figure 1. US Regional Variation in Repeat Surgery Rates in Patients With Stage 0 to II Breast Cancer in the National Cancer Data Base From 2004 to 2010 (*P*<.001)



et al,[4] location was one of few demographic factors to significantly correlate with reexcision.

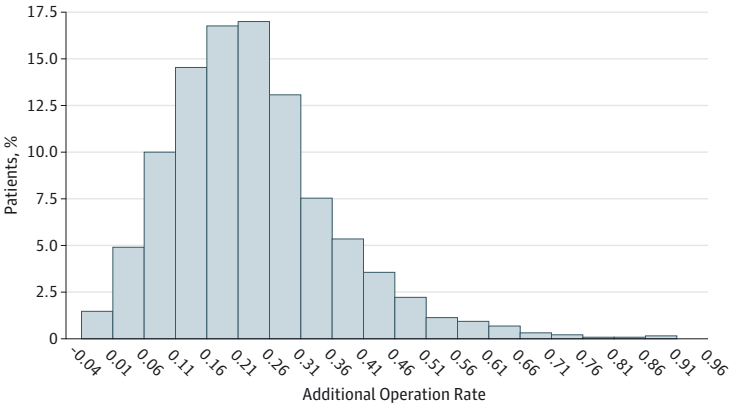
Physician interpretation of a negative margin varies significantly among differing oncologists. A survey of radiation oncologists revealed that 46% in North America required that there be "no tumor cells on the ink," whereas only 27% of European radiation oncologists concurred.[25] Two surveys of surgeons revealed that 11%[26] or 15%[27] would accept "any negative margin," whereas 28% and 78%, respectively, prefer 1 to 2 mm. At the root of the variability in repeat surgery rates for BCS is the lack of standardization of an acceptable margin width. The tumor margin width that will provide the lowest local recurrence rate has not been established in a randomized clinical trial setting. Of 6 randomized trials that compared breast conservation to mastectomy, including B-06, only 3 specified that margins had to be microscopically negative, but no specific width was determined.[1,28-30] In the other 3 trials, margins had to be only grossly negative,[31-33] and in 1 trial, 50% of margins were microscopically positive.[33,34] Nonetheless, all 6 trials had the equivalent survival of BCS to mastectomy. A 2010 meta-analysis did not reveal that any specific margin width for early-stage invasive breast cancer was associated with higher local recurrence, only that tumor at the inked margin was associated with greater risk of local recurrence.[35] In 2014, a follow-up meta-analysis[36] by this same group found that increasing the margin width does not affect local recurrence rates, indicating that there is no advantage in delineation of optimum margin width as long as the inked or transected margin is microscopically negative. A retrospective medical record review[37] published in 2013 reports that an institution-wide "no tumor on ink" policy has produced a 16% reexcision rate with a low local re-

Figure 2. Additional Operation Rates in Patients With Stage 0 to II Breast Cancer in the National Cancer Data Base From 2004 to 2010 ($P<.001$)



A, Rates by age per decade. B, Rates by tumor size.

Figure 3. Distribution of Institutions' Repeat Surgery Rates in Patients With Stage 0 to II Breast Cancer in the National Cancer Data Base From 2004 to 2010



currence rate, indicating a precedence for adoption of this margin recommendation at the institutional level with favorable results. An article[38] published in 2010 from an international expert panel endorsed "tumor not touching ink" as an adequate margin. More recently, the Society of Surgical Oncology and the American Society for Radiation Oncology developed a consensus statement that delineates adoption of "no tumor on ink" as a standard for stage I and II invasive breast cancer.[39] Incorporation of the "no tumor on ink" standard for invasive breast cancer and a 2-mm margin for ductal carcinoma in situ, as supported by a systematic review in 2009,[40] will facilitate a decrease in the repeat surgery rate for patients with breast cancer.

Our study has several limitations. This is not a study of reexcisions but a study of repeat surgeries. We initially examined those patients undergoing lumpectomy and then determined how many underwent an additional operation. More than 92.0% of the patients had a negative margin, but the exact margin width is unknown. We are also limited on the data we can obtain from each facility. Preoperative imaging, localization techniques, use of frozen section, and shave margins are some facility and surgeon factors that are not collected by the NCDB but clearly influence the repeat surgery rates. Last, the NCDB file does not contain recurrence data, so we cannot correlate repeat surgery rates with local recurrence.

Conclusions

In this NCDB observation study, we found a wide range of repeat surgery rates across the country and how these rates vary across patient, tumor, and facility factors. These findings can be used by surgeons to better inform their patients regarding repeat surgery rates and how patient or tumor characteristics influence these rates. More important, these data can be used to further support the vitally important adoption of guidelines regarding reexcision after initial BCS. Standard definitions of adequate margins as set forth in the consensus guidelines by the Society of Surgical Oncology and the American Society for Radiation Oncology and the indications for reexcision will decrease the wide variation in repeat surgery rates and decrease costs and patient anxiety surrounding tumor-positive margins.

ARTICLE INFORMATION

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Study concept and design: Wilke.
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Drafting of the manuscript: Wilke, Czechura, Wang, Winchester, Yao.
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Invited Commentary

Breast Conservation Surgery and the Definition of Adequate Margins

More Is Not Better…It's Just More

Julie A. Margenthaler, MD; Aislinn Vaughan, MD

The definition of a sufficient margin after attempted breast conservation surgery for breast cancer has been a hotly debated topic for decades. Although there has been widespread acceptance that breast conservation surgery confers an equivalent survival outcome to mastectomy in prospective randomized trials,[1,2] there is a paradoxical reluctance to agree on what constitutes a negative margin and successful surgical excision. The study by Wilke et al[3] illustrates this finding; 23.6% of all patients in a large national database undergoing breast conservation surgery subsequently underwent lumpectomy or mastectomy. Furthermore, the percentage of reexcisions decreased only slightly from January 1, 2004, through December 31, 2010. The authors were unable to obtain exact pathologic margin width, but more than 92% of the patients had negative margins, indicating that a significant percentage of those undergoing additional operations had margins that were "negative at ink."

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The Society of Surgical Oncology and the American Society for Radiation Oncology developed a consensus statement,[4] supported by systematic review data, encouraging adoption of "no tumor on ink" as the standard definition of a negative margin for invasive stage I and II breast cancer. It is time to put our biases aside. We have robust evidence that additional operations for close, but negative, margins do not result in better outcomes. However, additional operations increase health care costs, misuse of resources, patient anxiety, and delay in adjuvant therapy. With more than 200 000 new invasive breast cancers diagnosed each year, a staggering number of women are undergoing procedures that are unnecessary and simply wasteful. Our hope is that the Society of Surgical Oncology and the American Society for Radiation Oncology guidelines will be rapidly adopted by surgeons. Data from the study by Wilke et al[3] will provide an excellent historical reference for future investigation of the success of this paradigm shift.

ARTICLE INFORMATION

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