



Scan for Author
Video Interview

Variability in Reexcision Following Breast Conservation Surgery

Laurence E. McCahill, MD

Richard M. Single, PhD

Erin J. Aiello Bowles, MPH

Heather S. Feigelson, PhD, MPH

Ted A. James, MD

Tom Barney, BS

Jessica M. Engel, MSN

Adedayo A. Onitilo, MD, MSCR

THE CURRENT ENVIRONMENT OF health care reform in the United States calls for increasing physician and hospital accountability and transparency of health care outcomes.¹ Surgical outcomes are usually assessed by mortality because it is an unambiguous outcome. For operations associated with low mortality, identifying outcomes that reflect the quality of care is challenging.²⁻⁴

Breast-conserving therapy, or partial mastectomy, is one of the most commonly performed cancer operations in the United States. Current estimates suggest 60% to 75% of breast cancer cases undergo partial mastectomy as initial treatment.⁵ Operative mortality estimates for partial mastectomy are less than 1%; however, low mortality does not necessarily equate to high quality.⁴ Currently, there are no readily identifiable quality measures that allow for meaningful comparisons of breast cancer surgical outcomes among treating surgeons and hospitals.

Partial mastectomy is optimally performed by achieving adequate surgical margins during the initial surgical

Context Health care reform calls for increasing physician accountability and transparency of outcomes. Partial mastectomy is the most commonly performed procedure for invasive breast cancer and often requires reexcision. Variability in reexcision might be reflective of the quality of care.

Objective To assess hospital and surgeon-specific variation in reexcision rates following partial mastectomy.

Design, Setting, and Patients An observational study of breast surgery performed between 2003 and 2008 intended to evaluate variability in breast cancer surgical care outcomes and evaluate potential quality measures of breast cancer surgery. Women with invasive breast cancer undergoing partial mastectomy from 4 institutions were studied (1 university hospital [University of Vermont] and 3 large health plans [Kaiser Permanente Colorado, Group Health, and Marshfield Clinic]). Data were obtained from electronic medical records and chart abstraction of surgical, pathology, radiology, and outpatient records, including detailed surgical margin status. Logistic regression including surgeon-level random effects was used to identify predictors of reexcision.

Main Outcome Measure Incidence of reexcision.

Results A total of 2206 women with 2220 invasive breast cancers underwent partial mastectomy and 509 patients (22.9%; 95% CI, 21.2%-24.7%) underwent reexcision (454 patients [89.2%; 95% CI, 86.5%-91.9%] had 1 reexcision, 48 [9.4%; 95% CI, 6.9%-12.0%] had 2 reexcisions, and 7 [1.4%; 95% CI, 0.4%-2.4%] had 3 reexcisions). Among all patients undergoing initial partial mastectomy, total mastectomy was performed in 190 patients (8.5%; 95% CI, 7.2%-9.5%). Reexcision rates for margin status following initial surgery were 85.9% (95% CI, 82.0%-89.8%) for initial positive margins, 47.9% (95% CI, 42.0%-53.9%) for less than 1.0 mm margins, 20.2% (95% CI, 15.3%-25.0%) for 1.0 to 1.9 mm margins, and 6.3% (95% CI, 3.2%-9.3%) for 2.0 to 2.9 mm margins. For patients with negative margins, reexcision rates varied widely among surgeons (range, 0%-70%; $P = .003$) and institutions (range, 1.7%-20.9%; $P < .001$). Reexcision rates were not associated with surgeon procedure volume after adjusting for case mix ($P = .92$).

Conclusion Substantial surgeon and institutional variation were observed in reexcision following partial mastectomy in women with invasive breast cancer.

JAMA. 2012;307(5):467-475

www.jama.com

resection while maintaining maximum cosmetic appearance of the breast. Failure to achieve appropriate mar-

gins at the initial operation will require additional surgery with reexcision rate estimates ranging from

For editorial comment see p 509.

Author Video Interview available at www.jama.com.

Author Affiliations: Richard J. Lacks Cancer Center, Van Andel Research Institute, and Department of Surgery, Michigan State University, Grand Rapids (Dr McCahill); Departments of Mathematics and Statistics (Dr Single) and Surgery (Dr James), University of Vermont, Burlington; Group Health Research Institute, Seattle, Washington (Ms Aiello Bowles); Kaiser Permanente Colorado, Denver (Dr Feigelson); Van Andel Research Institute, Grand Rapids, Michigan (Mr Barney); Marshfield Clinic

Cancer Care at St Michaels, Stevens Point, and Marshfield Clinic Research Foundation, Marshfield, Wisconsin (Ms Engel); and Marshfield Clinic Hematology/Oncology Department, Weston Center, Weston, and Marshfield Clinic Research Foundation, Marshfield, Wisconsin (Dr Onitilo).

Corresponding Author: Laurence E. McCahill, MD, Richard J. Lacks Cancer Center, Saint Mary's Health Care, 250 Cherry St SE, Grand Rapids, MI 49503 (mccahill@trinity-health.org).

30% to 60%.⁶⁻⁹ These additional operations can produce considerable psychological, physical, and economic stress for patients and delay use of recommended adjuvant therapies. A high percentage (10%-36%) of women requiring reexcision undergo total mastectomy. Thus, the effect of reexcision on altering a patient's initial treatment of choice is significant.^{7,9-11}

Our previous work demonstrated reexcision rates following initial partial mastectomy ranging between 11% and 25% among surgeons at a single high-volume university-based breast center.³ We have expanded this analysis to include 3 additional geographically diverse health systems and their surgeons. We sought to measure variation in reexcision rates across hospitals and surgeons treating patients with similar clinical conditions. Furthermore, we explored whether patient demographic, clinical, and pathologic criteria were associated with an increased likelihood of reexcision following initial breast-conserving surgery for invasive breast cancer. The ability to define both predictors of reexcision and extent of variability should allow for full evaluation of the utility of reexcision as a meaningful measure of breast cancer surgery quality.

METHODS

We developed a Breast Cancer Surgical Outcomes (BRCASO) research consortium between the Cancer Research Network (CRN) and the University of Vermont. The CRN participating sites included Kaiser Permanente, Colorado; Group Health, western Washington state; and Marshfield Clinic, Wisconsin. The BRCASO cohort¹² includes women with breast cancer diagnosed between 2003 and 2008, and aged more than 18 years at diagnosis, whose initial breast cancer surgery was performed by a surgeon employed by a BRCASO study site, including any of the 3 participating CRN sites or Fletcher Allen Health Care Center, the sole hospital affiliated with the University of Vermont. We excluded men, patients with initial surgery performed by a surgeon

outside the health care system where the reexcision was performed, and patients with breast cancer never treated surgically. Institutional review board approval was attained from all participating sites, and information from study participants was obtained via waiver of written informed consent. We collected detailed data regarding clinical features of initial breast cancer diagnosis, as well as highly detailed data regarding initial and all subsequent breast cancer surgeries performed on all patients. For this analysis, we only included patients with a final diagnosis of invasive ductal carcinoma or invasive lobular carcinoma who underwent initial breast conservation, either partial mastectomy or open breast biopsy as their first operative procedure for the incident breast cancer.

Data Collection

Trained medical abstractors with experience in breast cancer abstraction completed data collection via an exhaustive review of surgical, pathology, radiology, and surgeon and medical/oncology clinical evaluations. The data collection instrument included clinical factors (age, previous history of breast cancer), demographic factors (insurance status, race/ethnicity as reported by study participants in the medical record), disease characteristics (preoperative nodal status, preoperative estimated tumor size), and treatment characteristics (initial surgical procedure type) at the time of initial surgical treatment decision making and at subsequent surgeries. Data collection at the participating CRN sites, including race/ethnicity data, partially relied on the CRN's primary source of data infrastructure, the Virtual Data Warehouse and the availability of electronic medical records.¹³ Data from the University of Vermont were entirely abstracted from medical records. The study focused on initial breast cancer surgery outcomes and did not evaluate utilization of radiation therapy, chemotherapy or hormonal therapy, or long-term outcomes such as local recurrence.

Surgical margin status was recorded for the initial breast-conserving procedure and for any subsequent excisions. Margins were categorized as positive if there was tumor at the inked margin in the pathology report. Histologic tumor type at closest or any positive margin was categorized as either invasive cancer or ductal carcinoma in situ (DCIS), when DCIS co-existed with invasive cancer. For negative margins, the distance of the closest margin to the specimen edge was recorded in 1-mm increments. For purposes of analyses, when distinct margin distances were recorded for the invasive component as well as DCIS, the smaller of the 2 distances was used. The anatomic orientation of the closest or positive margin was recorded when indicated in the pathology report. Margins categorized as radial included those recorded as superior, inferior, lateral, or medial. Anterior and posterior margins were categorized as such.

We established volume criteria for surgeons based on average yearly case volume for all initial breast cancer operations identified in the BRCASO database. The upper and lower thresholds for the 4 volume categories were defined at the first and third quartiles of volume for all operations, with the middle threshold set closer to the mean in order to have more meaningful differences in case volume between categories 1 and 2. We defined low surgeon volume as less than 10 incident breast cancer operations annually, intermediate surgeon volume as 10 to less than 25 operations annually, high surgeon volume as 25 to less than 50 operations annually, and very high surgeon volume as 50 or more operations annually.

Statistical Analysis

Bivariate analyses relating reexcision and clinical covariates were performed by using Pearson χ^2 tests of independence for categorical variables and *t* tests for quantitative variables. The Cochran-Armitage trend test was used for ordinal variables. Variables that were significant in the univariate analyses, those identified from a stepwise logis-

tic regression model, and the variables of age and race/ethnicity were included in the multivariable random effects logistic regression model. Surgeons were entered as a random effect in the model and are nested within site, with no surgeon practicing in more than 1 site. This model was fit using maximum likelihood with adaptive quadrature.¹⁴ *P* values are reported for 2-sided tests and are not adjusted for multiple comparisons. Significance was defined by $P \leq .05$. Confidence intervals are reported at the 95% level. Analyses were performed by using the FREQ, LOGISTIC, and GLIMMIX procedures in SAS version 9.2 (SAS Institute).

Surgeon-Level Analyses

Results for the median odds ratio (OR) and the range of ORs (ROR) are reported to quantify variability among surgeons on a scale that is directly comparable with that used for other variables in the study (ie, ORs). The median OR and ROR are based on the random effects variance component (τ^2) from the logistic regression model. The median OR can be interpreted as the median value of the ratio of predicted odds of reexcision for 2 patients, randomly selected from different sites, with equivalent sets of covariates included in the reexcision model. In the model, the absolute difference between the log odds for 2 surgeons, with respect to reexcision, is a random variable following a half-normal distribution with variance $2\tau^2$. The median OR is given by $\exp[\sqrt{2} \times \tau \times \Phi^{-1}(0.75)]$, where Φ is the cumulative distribution function for the standard normal distribution and $\Phi^{-1}(0.75)$ is the 75th percentile of the distribution.¹⁵ The ROR is the ratio of the values at the 97.5th and 2.5th percentile of the distribution of ORs for individual surgeons. It represents a range of ORs because it is computed by exponentiation of the length of a 95% CI for the random effect variance component on the log-odds scale [$\text{ROR} = \exp(3.92 \times \tau)$], where 3.92 is $2 \times$ the 97.5th percentile of the standard normal distribu-

tion].¹⁶ The median OR and ROR provide measures of the outcome for a random effect that is directly comparable with the ORs used for fixed effects in the study.

RESULTS

Overall, there were 4580 patients with 4684 new breast cancers who underwent initial breast cancer surgery. We excluded 11 patients with known stage

Table 1. Demographic Variables Associated With Reexcision Following Initial Partial Mastectomy for Invasive Cancers in Patients With Initial Negative Margins

Demographic Characteristics	Negative Margins Only (n = 1909)			P Value
	No. of Patients		Reexcision, % (95% CI)	
	Initial Breast Conservation	Reexcision		
Age at diagnosis, y				
<35	8	3	37.50 (3.95-71.05)	.005
35-44	131	21	16.03 (9.75-22.31)	
45-54	407	62	15.23 (11.74-18.72)	
55-64	546	78	14.29 (11.35-17.22)	
65-74	425	43	10.12 (7.25-12.98)	
≥75	392	35	8.93 (6.11-11.75)	
Race/ethnicity				
Non-Hispanic white	1501	186	12.39 (10.72-14.06)	.054
Black	35	4	11.43 (0.89-21.97)	
Asian	41	10	24.39 (11.25-37.54)	
Hispanic	34	8	23.53 (9.27-37.79)	
Unknown ^a	298	34	11.41 (7.80-15.02)	
BMI				
<18.5	15	6	40.00 (15.21-64.79)	.002
18.5-24.9	407	73	17.94 (14.21-21.66)	
25.0-29.9	497	71	14.29 (11.21-17.36)	
≥30.0	526	62	11.79 (9.03-14.54)	
Unknown	464			
Year of surgery				
2003	351	48	13.68 (10.08-17.27)	.22
2004	361	46	12.74 (9.30-16.18)	
2005	368	57	15.49 (11.79-19.19)	
2006	416	41	9.86 (6.99-12.72)	
2007	240	26	10.83 (6.90-14.77)	
2008	168	24	14.29 (8.99-19.58)	
Insurance type				
Commercial only	989	156	15.77 (13.5-18.05)	<.001
Medicaid only	29	4	13.79 (1.24-26.34)	
Medicare (any)	821	74	9.01 (07.05-10.97)	
Private pay	67	8	11.94 (4.18-19.70)	
Unknown	3			
Study site				
A	481	29	6.03 (3.90-8.16)	<.001
B	617	129	20.91 (17.70-24.12)	
C	634	81	12.78 (10.18-15.37)	
D	177	3	1.69 (0.00-3.60)	
Annual surgeon volume ^b				
0.0-9.9	418	70	16.75 (13.17-20.33)	<.001
10.0-24.9	815	112	13.74 (11.38-16.11)	
25.0-49.9	178	6	3.37 (0.72-6.02)	
≥50.0	498	54	10.84 (8.11-13.57)	

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).

^aPatients did not report race/ethnicity.

^bBased on average annual surgeries (cases per year averaged over several years of data).

IV cancer and 899 patients for whom final pathology demonstrated DCIS alone. We further excluded 79 patients with clinically suspected inflammatory breast cancer, 129 patients re-

ceiving neoadjuvant chemotherapy, 448 patients with preoperatively identified multifocal breast cancer, 278 patients with a history of previous breast cancer, and 12 patients with previous

breast or chest radiation, resulting in 2724 patients with new breast cancers considered clinically eligible for breast conservation. We then excluded 430 patients who underwent mastectomy as a first procedure, 25 patients operated on by surgeons with less than 10 total cases in the BRCASO data set, and 63 patients in which the margin status (positive or negative) was not able to be assessed.

After applying these exclusions, 2206 women with 2220 newly identified invasive breast cancers who underwent a breast-conserving first surgical procedure were included in the study. Overall, 509 patients (22.9%; 95% CI, 21.2%-24.7%) underwent additional surgery on the affected breast. Among these patients, 454 (89.2%; 95% CI, 86.5%-91.9%) underwent a single reexcision, 48 (9.4%; 95% CI, 6.9%-12.0%) underwent 2 reexcisions, and 7 (1.4%; 95% CI, 0.4%-2.4%) underwent 3 reexcisions. Among all patients undergoing initial breast conservation, a total mastectomy was subsequently performed in 190 patients (8.5%; 95% CI, 7.2%-9.5%).

The mean age for patients in this study was 62.16 years (95% CI, 61.63-62.69; range, 30-98 years) and 92.8% (95% CI, 91.6%-93.9%) of patients with reported race/ethnicity were non-Hispanic white. The mean invasive tumor size was 14.7 mm (95% CI, 14.3-15.1 mm) and 22.0% (95% CI, 18.9%-22.3%) of patients were node positive. There were 232 patients (10.5%; 95% CI, 9.2%-11.7%) with a final diagnosis of invasive lobular cancer, with the remainder diagnosed with invasive ductal carcinoma. TABLE 1 and TABLE 2 show demographic and clinical factors associated with reexcision rates in patients with initially negative pathological margins.

The majority of patients had a preoperatively established breast cancer diagnosis before the initial surgery, but for 109 patients (5.7%; 95% CI, 4.7%-6.8%) the initial procedure was an open surgical breast biopsy, which was associated with a marked increase in reexcision (45.0%; 95% CI, 35.6%-

Table 2. Clinical Variables Associated With Reexcision Following Initial Partial Mastectomy for Invasive Cancers in Patients With Initial Negative Margins

Clinical Characteristics	Negative Margins Only (n = 1909)			P Value
	No. of Patients		Reexcision, % (95% CI)	
	Initial Breast Conservation	Reexcision		
Tumor size, mm				.008
0.0-9.9	598	89	14.88 (12.03-17.74)	
10.0-19.9	905	88	9.72 (7.79-11.65)	
20.0-29.9	269	42	15.61 (11.28-19.95)	
30.0-39.9	89	12	13.48 (6.39-20.58)	
40.0-49.9	15	4	26.67 (4.29-49.05)	
≥50.0	8	2	25.00 (0.00-55.01)	
Unknown	25			
Malignant diagnosis established preoperatively				<.001
No	109	49	44.95 (35.62-54.29)	
Yes	1800	193	10.72 (9.29-12.15)	
Final pathological tumor type				.17
Invasive ductal carcinoma	1734	214	12.34 (10.79-13.89)	
Invasive lobular carcinoma	175	28	16.00 (10.57-21.43)	
Closest margin distance for negative margins, mm				<.001
0.0-0.9	267	128	47.94 (41.95-53.93)	
1.0-1.9	263	53	20.15 (15.30-25.00)	
2.0-2.9	240	15	6.25 (3.19-9.31)	
3.0-3.9	158	9	5.70 (2.08-9.31)	
4.0-4.9	137	2	1.46 (0.00-3.47)	
5.0-9.9	407	9	2.21 (0.78-3.64)	
≥10.0	32	0	0	
Unknown	405			
Closest margin direction				<.001
Anterior or posterior	702	65	9.26 (7.12-11.40)	
Multiple	180	11	6.11 (2.61-9.61)	
Radial	586	97	16.55 (13.54-19.56)	
Missing	441			
Lymph node status				.90
Negative	1450	188	12.97 (11.24-14.69)	
Positive	348	46	13.22 (9.66-16.78)	
Unknown	111			
ER/PR status				.16
ER and PR negative	254	39	15.35 (10.92-19.79)	
ER or PR positive	1641	200	12.19 (10.60-13.77)	
Unknown	14			
Lymphovascular invasion				.24
Yes	238	35	14.71 (10.21-19.21)	
No	1523	183	12.02 (10.38-13.65)	
Unknown	148			
Tumor grade				.64
High	457	53	11.60 (8.66-14.53)	
Low or medium	1425	177	12.42 (10.71-14.13)	
Missing	27			

Abbreviations: ER, estrogen receptor; PR, progesterone receptor.

54.3% vs 10.7%; 95% CI, 9.3%-12.2%; $P < .001$). Women younger than 35 years (reexcision rate of 37.5%; 95% CI, 4.0%-71.0%), with less than 18.5 body mass index (calculated as weight in kilograms divided by height in meters squared) (reexcision rate of 40.0%; 95% CI, 15.2%-64.8%), and initial margins of less than 1 mm (reexcision rate of 47.9%; 95% CI, 42.0%-53.9%) were all more likely to have reexcision based on univariable analysis. Reexcision rates for patients with initial negative margins varied by institution, from a low of 1.7% (95% CI, 0%-3.6%) at institution D compared with 20.9% (95% CI, 17.7%-24.1%) at institution B ($P < .001$). The anatomic direction of the closest involved margin also was associated with reexcision, with a demonstrated higher excision rate when the closest margin was a radial margin compared with anterior- or posterior-oriented closest margins. Reexcision rates for initial negative margins were associated with annual surgical volume on univariate analysis only.

Demographic and clinical factors associated with reexcision for patients with initially positive margins are shown in TABLE 3 and TABLE 4. Reexcision was performed in 85.9% (95% CI, 82.0%-89.8%) of 311 patients with initial positive margins, with a slightly higher reexcision rate for DCIS at the margin (92.6%; 95% CI, 86.9%-98.3%) than for invasive cancer at the inked margin (83.5%; 95% CI, 78.7%-88.3%; $P = .04$). Other factors associated with a higher reexcision rate of positive margins included lobular breast cancer as a final diagnosis and the presence of lymphovascular invasion demonstrated on histology. Surgeon volume did not appear to be associated with the likelihood of reexcision, but institution was associated with reexcision of positive margins, with rates ranging from 73.7% to 93.5% ($P = .003$). Patients undergoing an initial breast-conserving procedure with an unknown malignant diagnosis were more likely to undergo a reexcision compared with patients who had a preoperatively established ma-

lignant diagnosis (96.8%; 95% CI, 92.5%-100.0% vs 83.1%; 95% CI, 78.4%-87.7%; $P = .005$).

In multivariable analysis of patients with initially negative margins (TABLE 5), tumor size, study site, and a known preoperative malignant diag-

nosis all remained significantly associated with reexcision. The Hosmer and Lemeshow goodness-of-fit test did not show significant lack of fit ($P = .88$) for the logistic regression model. The OR of reexcision for patients with negative margins at institution B was 6.16

Table 3. Demographic Variables Associated With Reexcision Following Initial Partial Mastectomy for Invasive Cancers in Patients With Initial Positive Margins

Demographic Characteristics	Positive Margins Only (n = 311)			P Value
	No. of Patients		Reexcision, % (95% CI)	
	Initial Breast Conservation	Reexcision		
Age at diagnosis, y				
<35	4	4	100.00 (100.00-100.00)	.20
35-44	30	25	83.33 (70.00-96.67)	
45-54	91	83	91.21 (85.39-97.03)	
55-64	80	66	82.50 (74.17-90.83)	
65-74	69	61	88.41 (80.85-95.96)	
≥75	37	28	75.68 (61.84-89.50)	
Race/ethnicity				
Non-Hispanic white	239	201	84.10 (79.46-88.74)	.44
Black	12	11	91.67 (76.03-100.00)	
Asian	7	7	100.00 (100.00-100.00)	
Hispanic	7	7	100.00 (100.00-100.00)	
Unknown ^a	46	41	89.13 (80.14-98.13)	
BMI				
<18.5	2	2	100.00 (100.00-100.00)	.07
18.5-24.9	85	79	92.94 (87.50-98.39)	
25.0-29.9	68	55	80.88 (71.54-90.23)	
≥30.0	92	74	80.43 (72.33-88.54)	
Unknown	64			
Year of surgery				
2003	67	56	83.58 (74.71-92.45)	.55
2004	55	47	85.45 (76.14-94.77)	
2005	61	57	93.44 (87.23-99.65)	
2006	50	41	82.00 (71.35-92.65)	
2007	33	28	84.85 (72.62-97.08)	
2008	41	36	87.80 (77.79-97.82)	
Insurance type				
Commercial only	191	168	87.96 (83.34-92.57)	.23
Medicaid only	9	7	77.78 (50.62-100.00)	
Medicare (any)	102	86	84.31 (77.26-91.37)	
Private pay	9	6	66.67 (35.87-97.47)	
Study site				
A	66	61	92.42 (86.04-98.81)	.003
B	134	106	79.10 (72.22-85.99)	
C	92	86	93.48 (88.43-98.52)	
D	19	14	73.68 (53.88-93.48)	
Annual surgeon volume ^b				
0.0-9.9	72	64	88.89 (81.63-96.15)	.52
10.0-24.9	148	125	84.46 (78.62-90.30)	
25.0-49.9	17	13	76.47 (56.31-96.63)	
≥50.0	74	65	87.84 (80.39-95.28)	

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).

^aPatients did not report race/ethnicity.

^bBased on average annual surgeries (cases per year averaged over several years of data).

(95% CI, 2.26-16.78) compared with study site A ($P < .001$). The broad CI partially reflects the wide variability in reexcision rates among surgeons at institution B.

We analyzed the association between individual surgeon and the likelihood of reexcision in our multivariable analysis. The FIGURE demonstrates reexcision rates for individual surgeons, which ranged between 0% and

70%. This Figure demonstrates both observed reexcision rates and those rates predicted by the statistical model for the 54 surgeons who had at least 10 procedures meeting the inclusion criteria for our study. The predicted reexcision rates account for both clinical variables as well as patterns of reexcision at the individual surgeon's study site.

The overall surgeon level variance component was significant ($P = .003$).

The observed median OR of 1.59 (95% CI, 1.36-2.64) corresponds with the median value of the relative odds of reexcision between 2 randomly chosen surgeons from different sites. This indicates a relatively large individual surgeon effect, because half the ORs between 2 randomly chosen surgeons will be larger than 1.59. The range of ORs from the lower to the upper 2.5th percentile of the distribution is 6.8, indicating substantial heterogeneity among surgeons in reexcision.

Table 4. Clinical Variables Associated With Reexcision Following Initial Partial Mastectomy for Invasive Cancers in Patients With Initial Positive Margins

Clinical Characteristics	Positive Margins Only (n = 311)			P Value
	No. of Patients		Reexcision, % (95% CI)	
	Initial Breast Conservation	Reexcision		
Tumor size, mm				.78
0.0-9.9	72	61	84.72 (76.41-93.03)	
10.0-19.9	120	100	83.33 (76.67-90.00)	
20.0-29.9	65	56	86.15 (77.76-94.55)	
30.0-39.9	25	23	92.00 (81.37-100.00)	
40.0-49.9	13	12	92.31 (77.82-100.00)	
≥50	14	13	92.86 (79.37-100.00)	
Unknown	2			
Malignant diagnosis established preoperatively				.005
No	63	61	96.83 (92.50-100.00)	
Yes	248	206	83.06 (78.40-87.73)	
Final pathological tumor type				.003
Invasive ductal carcinoma	254	211	83.07 (78.46-87.68)	
Invasive lobular carcinoma	57	56	98.25 (94.84-100.00)	
Margin status				.04
Positive for DCIS only	81	75	92.59 (86.89-98.30)	
Positive for invasive	230	192	83.48 (78.68-88.28)	
Positive margin direction				.64
Anterior or posterior	48	42	87.50 (78.14-96.86)	
Multiple	8	6	75.00 (44.99-100.00)	
Radial	80	69	86.25 (78.70-93.80)	
Unknown	175			
Lymph node status				.46
Negative	215	185	86.05 (81.41-90.68)	
Positive	84	75	89.29 (82.67-95.90)	
Unknown	12			
ER/PR status				.82
ER and PR negative	32	27	84.38 (71.79-96.96)	
ER or PR positive	276	237	85.87 (81.76-89.98)	
Unknown	3			
Lymphovascular invasion				.04
Yes	70	65	92.86 (86.82-98.89)	
No	218	180	82.57 (77.53-87.60)	
Unknown	23			
Tumor grade				.57
High	67	56	83.58 (74.71-92.45)	
Low or medium	241	208	86.31 (81.97-90.65)	
Unknown	3			

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

COMMENT

Despite the significant physical, psychological, and financial effect of partial mastectomy reexcisions on patients, there remains a lack of standardization regarding its application among surgeons performing breast cancer surgery. Our results demonstrate an overall reexcision rate of 22.9% that is lower than previous studies demonstrating reexcision rates of 36% to 50%.^{7,11} Morrow et al⁹ reported a reexcision rate following initial breast-conserving therapy of 37.9% in a similarly large series of 1459 patients, with 26.0% undergoing partial breast reexcision alone and 11.9% ultimately undergoing mastectomy. Our lower reexcision rate may be partially explained by our more extensive exclusion criteria, which were specifically chosen to select for patients considered most eligible for breast conservation. We excluded a significant number of women with preoperatively established multifocal breast cancer, a relative but not absolute contraindication for breast-conserving therapy.

In our study, the incidence of initial positive margins following breast conservation was 14.0%, which compares favorably with a similar cohort of 489 patients with invasive breast cancer undergoing initial breast conservation at a Canadian cancer center in which 26% of patients had initial positive margins.¹⁰ Patients in that study had a preoperatively confirmed diagnosis of cancer in 69% of patients (vs 92.3% in our study, which likely contributed significantly to our lower initial positive mar-

gin rate). We identified 14.1% of patients with positive margins in our study who did not undergo any reexcision. This finding is notable given that positive margins (tumor at inked margin) have been correlated with a long-term increased risk of local recurrence and are therefore almost uniformly reexcised.¹⁷ A recent meta-analysis has suggested that the odds of local recurrence were 2.42 for women undergoing breast conservation with positive margins compared with negative margins.¹⁸

Surveys among surgeons have also indicated consensus on the intent to reexcise positive margins following breast conservation. Our study may indicate that surgeon intent and actual clinical practice patterns do not necessarily have full correlation. We examined some clinical factors associated with reexcision and identified that surgeons were less likely to reexcise positive margins for invasive ductal carcinoma compared with invasive lobular carcinoma (83.07 vs 98.25%, $P = .003$). This may be due to the concern that invasive lobular cancer is often considered to have less distinct borders and may contribute to the greater tendency of reexcision of positive margins involving invasive lobular carcinoma.

We also observed variation in the reexcision of positive margins among institutions, with rates ranging between 73.7% and 93.5% ($P = .003$). This may reflect institutional variation in surgeons' training, regional variation in interpretation of the required criteria for reexcision, or both. Specific pathological features (eg, extent of intraductal component), clinical characteristics (eg, volume of breast tissue, intent for adjuvant radiation therapy), and patient decision making roles that may have influenced the decision not to reexcise a positive margin were not determined in our study. We assume that some of the variation may be explained by differences in the perceived risk of residual tumor based on the extent of margin positivity (eg, focally positive margins vs extensive involvement). The overall low number of patients with posi-

tive margins not undergoing reexcision precluded multivariable analysis.

Controversy regarding the necessity of reexcision for patients with pathologically clear margins exists because there is no current consensus on the appropriate distance required for a clear margin to be deemed adequate.¹⁹⁻²¹ Although the goal of reexcision is to further reduce the risk of breast cancer recurrence and mortality, the true benefit of reexcision remains undetermined. Nearly half of reexcision specimens do not harbor residual cancer.^{6,11,22} In our study, we found that 47.9% of patients with clear but less than 1.0-mm margins underwent reexcision, and 20.2% of patients with margins between 1.0 and 1.9 mm underwent reexcision.

These reexcision rates are considerably lower than would be predicted based on 3 recent surveys of practice patterns for close margins.¹⁹⁻²¹ These surveys highlighted the inconsistency of reported practice patterns and physician interpretation of an acceptable margin distance. In the survey by Blair et al,²⁰ the majority of surgeons indicated more than 1-mm margins were required and a significant minority (30%) indicated a greater distance of 2-mm margins as acceptable. In the study by Azu et al,²¹ when surgeons were given a scenario of a patient with a small (0.8 cm) invasive cancer, 11.2% accepted tumor not touching ink, 42% accepted 1- to 2-mm margins, 27.9% accepted at least 5-mm margins, and 18.9% desired more than 10-mm margins. Our study indicates that surgeons' actual clinical practices differ dramatically from these survey results. Although the Azu et al²¹ survey study suggests a 5-mm margin is desired by 46% of surgeons, we identified 535 patients with 2.0- to 4.9-mm margins, only 26 (4.86%) of whom had reexcisions.

The effect of close but negative margins on local recurrence rates has not been conclusively determined and reexcision under these circumstances may or may not influence rates of recurrence.^{17,18} Some studies have shown

Table 5. Multivariable Analysis of Demographic and Clinical Variables Associated With Reexcision in Patients With Initial Negative Margins

Demographic and Clinical Characteristics	Negative Margins Only (n = 1909)	
	Odds Ratio (95% CI)	P Value
Age at diagnosis, y	0.99 (0.97-1.01)	.27
Race/ethnicity		
Non-Hispanic white	1 [Reference]	.71
Black	0.48 (0.16-1.45)	
Asian	0.92 (0.39-2.16)	
Hispanic	1.28 (0.47-3.54)	
Unknown ^a	0.91 (0.57-1.43)	
Insurance type		
Commercial only	2.15 (0.95-4.85)	.07
Medicaid only	3.42 (0.82-14.27)	
Medicare (any)	1.30 (0.52-3.27)	
Private pay	1 [Reference]	
Study site		
A	1 [Reference]	<.001
B	6.16 (2.26-16.78)	
C	2.79 (0.96-8.12)	
D	0.36 (0.07-2.00)	
Annual surgeon volume		
0.0-9.9	0.79 (0.31-2.02)	.92
10.0-24.9	0.81 (0.32-2.06)	
25.0-49.9	1.31 (0.31-5.58)	
≥50.0	1 [Reference]	
Tumor size, mm		
0.0-9.9	1 [Reference]	.03
10.0-19.9	0.59 (0.41-0.83)	
20.0-29.9	0.95 (0.61-1.48)	
30.0-39.9	0.81 (0.40-1.65)	
40.0-49.9	1.88 (0.52-6.75)	
≥50	1.32 (0.24-7.27)	
Malignant diagnosis established preoperatively		
No	5.91 (3.74-9.32)	<.001
Yes	1 [Reference]	

^aPatients did not report race/ethnicity.

an increase in local recurrence risk in the presence of close margins (>0-2 mm), while other studies have demonstrated no difference compared with widely negative margins.²³⁻²⁵ Achieving greater margin distance (1 mm vs 2 mm vs 5 mm) was recently demonstrated in a meta-analysis to not be associated with differences in local recurrence rates, especially after adjusting for adjuvant therapy use.¹⁸

Additionally, based on survey reports, there appears to be variation in practice patterns among surgeons regarding the use of reexcision based on both margin distance and tumor histology present at the closest margin (DCIS vs invasive cancer).^{19,26} In light of the large number of new cases of breast cancer diagnosed each year in the United States (182 460 in 2008), this variation in surgical practice patterns could have an enormous outcome on health care costs nationwide (American Cancer Society, <http://www.cancer.org/index>). Given the current degree of practice variation we have demonstrated in the management of close margins, as well as the potential effect on both local recurrence and the number of additional surgical procedures, it is critical that we continue to understand actual clinical practice patterns beyond physician survey reports.

We identified that individual institutions vary significantly in reexcision rates, which to a large degree reflects the summation of individual surgeons' practice patterns at these institutions. Other factors behind institutional differences may represent utilization of multidisciplinary breast cancer teams, the reporting format and sectioning techniques of pathology teams, and perhaps even operative techniques of surgeons at various institutions. We did not examine institutional-specific factors that might contribute to differences in reexcision in our study, because our primary goal was to determine whether any significant differences existed.

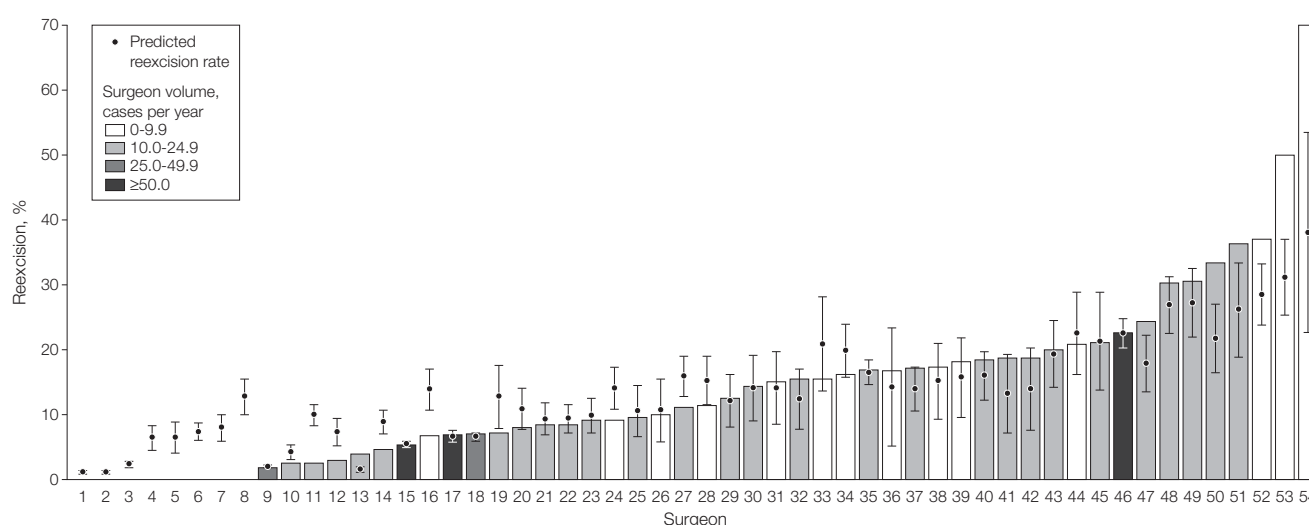
Our finding that the median OR between 2 randomly selected surgeons was 1.6 suggests that patients under similar clinical conditions are likely to undergo reexcision based on the treating surgeon and not just the clinical characteristics. Possible explanations might include differences in surgical training, surgeon confidence in their operative technique in localizing tumors, utilization of intraoperative assessment of margins, and surgeon's and pathologist's coordination of specimen orientation and margin interpretation. Surgical experience may play a role, but we did not observe differences in reexcision rates between high- and low-volume surgeons. Variability of what surgeons accept to be an adequate margin, as demonstrated by the

aforementioned survey data, may therefore be a larger factor in the actual clinical variation in reexcision rates we observed.

The implications of variation in clinical practice of reexcision for positive and close margins warrants additional study, specifically as it relates to local recurrence health care costs and patients' perceived quality of health. We are aware of 1 recent comparative effectiveness study²⁷ that reported individual surgeon variation may contribute to long-term differences in breast cancer ipsilateral recurrence rates in patients with DCIS. Whether these findings would be similar for patients with invasive breast cancer warrants additional study.

A major limitation of our study is the absence of data regarding decision making factors influencing treatment options. For example, we do not know how patient preferences affect observed reexcision rates. Additionally, we were not able to control for factors such as specific pathology methods or reporting structure of breast cancer specimens. Our study, however, is likely more generalizable to community-

Figure. Observed Reexcision Rates for Each of 54 Surgeons With at Least 10 Patients in the Study



Predicted reexcision rates, based on the random effects logistic regression model controlling for clinical covariates, are plotted as a circle above the encrypted surgeon identifiers along the horizontal axis. Error bars indicate 95% CIs. Surgeon-level predicted values were computed by averaging the patient-level predicted probabilities for all patients treated by that surgeon. Bars are shaded to indicate categories of annual surgeon volume (average cases per year, see "Methods" section). Surgeons 1 through 8 had zero observed reexcisions, thus there is no bar associated with these surgeons. These surgeons had average annual volumes of 0 to 9.9 cases per year, with the exception of surgeons 2 and 5 who had average volumes of 10.0 to 24.9 cases per year.

based breast cancer management in which reporting of breast pathology also has considerable variability.²⁸ Not including local recurrence data limited our ability to evaluate any beneficial outcome of reexcisions. However, our primary focus was to explore variations in practice patterns for reexcision.

In conclusion, we found individual surgeons and institutions were associated with variation in reexcision rates following initial partial mastectomy for invasive breast cancer. This variability cannot be explained entirely by patients' clinical factors. Our study highlights the value of multicenter observational studies in demonstrating variability in health care across geographic regions and different health systems, with uniform data collection instruments. The long-term effect of this variability is beyond the scope of our study, but it is feasible that outcomes such as local recurrence and even over-

all survival could be affected by variability in initial surgical care. Even in the absence of effects on local control, the wide level of unexplained clinical variation itself represents a potential barrier to high-quality and cost-effective care of patients with breast cancer. Continued comparative effectiveness research of breast cancer surgery requires further attention to better determine the association of initial surgical care with long-term patient outcomes.

Author Contributions: Dr McCahill had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: McCahill, Aiello Bowles, Single, Feigelson, James, Engel, Onitilo.

Acquisition of data: Aiello Bowles, Single, Feigelson, Barney, James, Engel, Onitilo.

Analysis and interpretation of data: McCahill, Aiello Bowles, Single, Feigelson, James, Onitilo.

Drafting of the manuscript: McCahill, Aiello Bowles, Single, Onitilo.

Critical revision of the manuscript for important intellectual content: McCahill, Aiello Bowles, Single, Feigelson, Barney, James, Engel, Onitilo.

Statistical analysis: Single.

Obtained funding: McCahill, Aiello Bowles, Single, Feigelson, James, Onitilo.

Administrative, technical, or material support: Barney, Engel, Onitilo.

Study supervision: McCahill, Aiello Bowles, Feigelson, James.

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

Funding/Support: This work was funded by grant 1RC1CA145402-01 from the American Recovery and Reinvestment Act of 2009 by the National Institutes of Health.

Role of the Sponsor: The funding source had no role in the design and conduct of the study, in the collection, analysis, and interpretation of the data, or in the preparation, review, or approval of the manuscript.

Online-Only Material: The Author Video Interview is available at <http://www.jama.com>.

Additional Contributions: Turner Osler, MD, PhD (University of Vermont), provided helpful discussions regarding the modeling of surgeon level variation; Johanna Sheehy-Jones, RN (Fletcher Allen Health Care), provided training of institutional medical abstractors for the project; and Marie Fleisner (Marshfield Clinic Research Foundation's Office of Scientific Writing and Publication) provided editorial assistance with the manuscript. Dr Osler and Ms Fleisner received no compensation for their contributions. Ms Sheehy-Jones received partial salary support in her efforts of training abstractors by the National Institutes of Health grant.

REFERENCES

- Weissman JS, Hasnain-Wynia R. Advancing health care equity through improved data collection. *N Engl J Med*. 2011;364(24):2276-2277.
- Birkmeyer JD, Dimick JB, Birkmeyer NJ. Measuring the quality of surgical care: structure, process, or outcomes? *J Am Coll Surg*. 2004;198(4):626-632.
- McCahill LE, Privette A, James T, et al. Quality measures for breast cancer surgery: initial validation of feasibility and assessment of variation among surgeons. *Arch Surg*. 2009;144(5):455-462.
- El-Tamer MB, Ward BM, Schiffner T, Neumayer L, Khuri S, Henderson W. Morbidity and mortality following breast cancer surgery in women: national benchmarks for standards of care. *Ann Surg*. 2007;245(5):665-671.
- Katipamula R, Degnim AC, Hoskin T, et al. Trends in mastectomy rates at the Mayo Clinic Rochester: effect of surgical year and preoperative magnetic resonance imaging. *J Clin Oncol*. 2009;27(25):4082-4088.
- Kotwall C, Ranson M, Stiles A, Hamann MS. Relationship between initial margin status for invasive breast cancer and residual carcinoma after re-excision. *Am Surg*. 2007;73(4):337-343.
- Waljee JF, Hu ES, Newman LA, Alderman AK. Predictors of re-excision among women undergoing breast-conserving surgery for cancer. *Ann Surg Oncol*. 2008;15(5):1297-1303.
- Menes TS, Tarrter PI, Bleiweiss I, Godbold JH, Estabrook A, Smith SR. The consequence of multiple re-excisions to obtain clear lumpectomy margins in breast cancer patients. *Ann Surg Oncol*. 2005;12(11):881-885.
- Morrow M, Jagsi R, Alderman AK, et al. Surgeon recommendations and receipt of mastectomy for treatment of breast cancer. *JAMA*. 2009;302(14):1551-1556.
- Lovrics PJ, Cornacchi SD, Farrokhay F, et al. Technical factors, surgeon case volume and positive margin rates after breast conservation surgery for early-stage breast cancer. *Can J Surg*. 2010;53(5):305-312.
- Cellini C, Hollenbeck ST, Christos P, et al. Factors associated with residual breast cancer after re-excision for close or positive margins. *Ann Surg Oncol*. 2004;11(10):915-920.
- Bowles EA, Feigelson HS, Sterrett A, et al. Improving quality of breast cancer surgery through development of a national breast cancer surgical outcomes database. *Clin Med Res*. 2011;9(3-4):144. doi:10.3121/cmr.2011.1020.ps2-03.
- Hornbrook MC, Hart G, Ellis JL, et al. Building a virtual cancer research organization. *J Natl Cancer Inst Monogr*. 2005;(35):12-25.
- Olsen MK, DeLong ER, Oddone EZ, Bosworth HB. Strategies for analyzing multilevel cluster-randomized studies with binary outcomes collected at varying intervals of time. *Stat Med*. 2008;27(29):6055-6071.
- Larsen K, Petersen JH, Budtz-Jørgensen E, Endahl L. Interpreting parameters in the logistic regression model with random effects. *Biometrics*. 2000;56(3):909-914.
- Spiegelhalter DJ, Abrams KR, Myles JP. *Bayesian Approaches to Clinical Trials and Health Care Evaluation*. Chichester, NY: John Wiley & Sons; 2007.
- Singletary SE. Surgical margins in patients with early-stage breast cancer treated with breast conservation therapy. *Am J Surg*. 2002;184(5):383-393.
- Houssami N, Macaskill P, Marinovich ML, et al. Meta-analysis of the impact of surgical margins on local recurrence in women with early-stage invasive breast cancer treated with breast-conserving therapy. *Eur J Cancer*. 2010;46(18):3219-3232.
- Taghian A, Mohiuddin M, Jagsi R, Goldberg S, Ceilley E, Powell S. Current perceptions regarding surgical margin status after breast-conserving therapy: results of a survey. *Ann Surg*. 2005;241(4):629-639.
- Blair SL, Thompson K, Rococco J, Malcarne V, Beitsch PD, Ollila DW. Attaining negative margins in breast-conservation operations: is there a consensus among breast surgeons? *J Am Coll Surg*. 2009;209(5):608-613.
- Azu M, Abrahamse P, Katz SJ, Jagsi R, Morrow M. What is an adequate margin for breast-conserving surgery? surgeon attitudes and correlates. *Ann Surg Oncol*. 2010;17(2):558-563.
- Papa MZ, Zippel D, Koller M, Klein E, Chetrit A, Ari GB. Positive margins of breast biopsy: is reexcision always necessary? *J Surg Oncol*. 1999;70(3):167-171.
- Dillon MF, McDermott EW, O'Doherty A, Quinn CM, Hill AD, O'Higgins N. Factors affecting successful breast conservation for ductal carcinoma in situ. *Ann Surg Oncol*. 2007;14(5):1618-1628.
- Kunos C, Latson L, Overmoyer B, et al. Breast conservation surgery achieving >or=2 mm tumor-free margins results in decreased local-regional recurrence rates. *Breast J*. 2006;12(1):28-36.
- Chan KC, Knox WF, Sinha G, et al. Extent of excision margin width required in breast conserving surgery for ductal carcinoma in situ. *Cancer*. 2001;91(1):9-16.
- Young OE, Valassiadou K, Dixon M. A review of current practices in breast conservation surgery in the UK. *Ann R Coll Surg Engl*. 2007;89(2):118-123.
- Dick AW, Sorbero MS, Ahrendt GM, et al. Comparative effectiveness of ductal carcinoma in situ management and the roles of margins and surgeons. *J Natl Cancer Inst*. 2011;103(2):92-104.
- Persing S, James TA, Mace J, Goodwin A, Geller B. Variability in the quality of pathology reporting of margin status following breast cancer surgery. *Ann Surg Oncol*. 2011;18(11):3061-3065.