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What is an Adequate Margin for Breast-Conserving Surgery? Surgeon Attitudes and Correlates

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ABSTRACT

Background. Re-excision is common in breast-conserving surgery (BCS), partly due to lack of consensus on margin definitions. A population-based surgeon sample was used to determine current attitudes toward margin width and identify characteristics associated with margin choice.

Methods. Breast cancer patients treated from 2005 to 2007 were identified from Los Angeles and Detroit Surveillance, Epidemiology, and End Results (SEER) registries. Pathology reports were used to identify their surgeons, who were surveyed ($n = 418$). Response rate was 74.6% ($n = 312$). Mean surgeon age was 51.9 years, 17.8% were female, and mean number of years in practice was 18.5.

Results. Wide variation in margin selection was noted among surgeons, and did not differ for invasive cancer and ductal carcinoma in situ (DCIS). In a scenario of T1 invasive cancer, 11% of surgeons endorsed margins of tumor not touching ink (TNTI), 42% of 1–2 mm, 28% of ≥5 mm, and 19% >1 cm as precluding need for re-excision before radiotherapy. On multivariate analysis, having 50% or more of practice devoted to breast cancer independently predicted smaller margin choice ($p = 0.03$). For a patient with a 1.4-cm grade 2 estrogen receptor (ER)-positive DCIS without radiotherapy (RT) planned, 3% of surgeons chose TNTI, 12% 1–2 mm, 25% ≥5 mm, and 61% >1 cm as sufficient without re-excision. In the scenario of DCIS without RT, breast specialization independently predicted larger margin choice ($p = 0.03$). Gender and years in practice were not predictive of margin choice.

Conclusions. Wide variation in BCS margin definition exists. Variation is similar for invasive cancer and DCIS with RT, with more specialized surgeons choosing smaller margins. In DCIS without RT, more specialized surgeons favored larger margins. A standardized margin definition may significantly affect re-excision rates.

There is no widely adopted definition of an adequate margin in patients with invasive or in situ breast carcinoma undergoing breast-conserving surgery (BCS) with subsequent radiation therapy. In the prospective randomized trials of breast-conservation therapy (BCT) that showed survival to be equivalent to that seen with mastectomy, only the National Surgical Adjuvant Breast and Bowel Project (NSABP) B06 study used a microscopic definition of a negative margin, which was tumor not touching ink.[1] While it is clear that positive margin status, defined as tumor touching ink, is an important predictor of ipsilateral breast tumor recurrence (IBTR), consistent evidence that more widely clear margins decrease the risk of IBTR is lacking.[2–5] Re-excision is a common procedure in women undergoing BCS, and reported rates of re-excision vary widely.[6–8] In a population-based survey of 704 women with DCIS and stage 1 and 2 cancer undergoing successful BCS in 2005–2006, 26% reported that they had a re-excision.[9] We hypothesized that the lack of a standard definition of an adequate negative margin among surgeons contributes to high rates of re-excision, sought to determine the current definition of a negative margin among surgeons, and sought to define what surgeon characteristics are associated with margin preference for patients with ductal carcinoma in situ (DCIS) and invasive breast cancer.

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METHODS

We performed a survey of a population-based sample of 2,680 women in the metropolitan areas of Los Angeles, CA, and Detroit, MI, aged 20–79 years and diagnosed with primary DCIS and invasive carcinoma (American Joint Committee on Cancer stage 1–3) between August 2005 and February 2007 using Surveillance, Epidemiology, and End Results (SEER) program registries.[10] The details of the patient study are reported elsewhere.[9,11,12] Pathology reports were used to identify one surgeon or more for 98.9% of the patient sample. Surgeons were contacted by mail and asked to participate in a brief, self-administered survey which used clinical scenarios to evaluate preferences regarding margins for BCS. Surgeons were mailed a packet containing a letter of introduction, the survey, and a US $40 subject fee approximately 14 months after the start of the patient survey. We used a modified version of the Dillman method to optimize responses.[13] A second survey was mailed to nonrespondents 4 weeks after the first survey; a phone call was made to nonrespondents 4 weeks after the second survey; a third survey was mailed on a case-by-case basis. We identified 418 surgeons of whom 318 returned completed questionnaires (response rate, 76.1%). Surgeon survey measures were developed based on an extensive review of the literature, our prior research, and a conceptual model. The content included questions pertaining to demographics (age, gender, years in practice), practice volume (percentage of total practice time devoted to breast cancer treatment, number of definitive breast carcinoma surgery procedures per year), and hospital practice setting. Breast surgery practice volume was created by recording the percentage of total practice time devoted to breast-carcinoma-related surgery into three categories: <15%, 16–49%, and >50%. We chose this measure rather than surgeon recall of the number of procedures performed per year because there were fewer missing observations. However, the same results were obtained when data was analyzed with the number of procedures as the independent variable.

To assess surgeon attitudes about appropriate margin width, we used the following case scenarios. Scenario A: A 60-year-old woman presents with a 0.8-cm mass in the upper outer quadrant of a large breast. A core biopsy shows grade 3 infiltrating ductal carcinoma, ER/progesterone receptor (PR) negative, human epidermal growth factor receptor-2 (HER-2) negative. The patient received lumpectomy and sentinel node biopsy with radiotherapy planned. Scenario B: A 60-year-old woman presents with a cluster of calcifications in the upper outer quadrant of the right breast on screening mammogram. A core biopsy shows DCIS. Needle localization and excision demonstrate a 1.4-cm grade 2 DCIS, ER positive. The patient opts for radiation therapy. Scenario C: A 60-year-old woman presents with a cluster of calcifications in the upper outer quadrant of the right breast on screening mammogram. A core biopsy shows DCIS. Needle localization and excision demonstrate a 1.4-cm grade 2 DCIS, ER positive. The patient opts not to receive radiotherapy. For each scenario, surgeons were asked "Which negative margin width precludes the need for re-excision?" Choices offered were tumor cells not touching ink, greater than 1–2 mm, greater than 5 mm, and greater than 1 cm.

Analysis

We first described characteristics of the respondent surgeon population. We then described the distribution of responses to the three scenarios and examined the effect of surgeon age, gender, practice setting, and proportion of practice devoted to breast cancer on response using the chi-squared test. Logistic regression was then used to examine the interaction between surgeon volume and selected demographic variables.

RESULTS

The mean age of the 318 respondent surgeons was 51.9 years (range 40–63 years), the mean number of years in practice was 18.5, and 17.8% of surgeons were female. Breast cancer surgery accounted for 15% or less of the practice of 46% of respondents, and 16–49% of the practice of 37% of respondents, while 17% of the surgeons studied devoted greater than 50% of their practice to breast surgery. Practice characteristics related to cancer program status, participation in a multidisciplinary tumor board, and use of preoperative radiation oncology consultation and degree of specialization are summarized in Table 1.

Responses to the margin width question for each of the three scenarios are shown in Table 2. No significant differences in preferred margins for the invasive cancer with radiotherapy (RT) scenario (A) versus the DCIS with RT scenario (B) were seen, and 82% of those surveyed chose the same response to both questions. A margin of tumor not touching ink was the least frequently endorsed margin for either of these scenarios, and was selected by only 11 and 10% of respondents, respectively. For each of these scenarios, approximately half of the surgeons favored margins of 5 mm or less, and half favored larger margins. For scenario C (DCIS with no RT) only 14% of surgeons favored margins less than 5 mm, and 61% endorsed margins greater than 1 cm.

Consistent patterns across both the invasive cancer scenario (A) and the DCIS with RT scenario (B) were not observed for most demographic characteristics. For

example, a significant difference in margin preference on the basis of gender was seen for invasive cancer, where 67% ($n = 37$) of female surgeons endorsed a margin of 2 mm or less compared with only 50% of male surgeons ($n = 124$; $p = 0.007$), In contrast, no gender-based differences in margin preference were seen for the DCIS with RT scenario, with 52% of male surgeons and 54% of female surgeons selecting a margin of 2 mm or less. Gender was also not predictive of margin selection in the DCIS with no RT scenario. Age was also not a significant determinant of margin preference. In the invasive scenario, the mean surgeon ages for those who selected margin widths of tumor not touching ink, >1–2 mm, and >5 mm were 53.7 ± 10 years, 50.7 ± 10 years, and 52.4 ± 10 years, respectively. A similar lack of significant differences on the basis of age was seen in the other scenarios.

The proportion of the practice devoted to breast cancer surgery was a significant predictor of margin preference in univariate analysis. Surgeons devoting 50% or more of their practice to breast cancer patients favored smaller margins ($p = 0.002$) for the invasive cancer scenario. A similar trend was seen for the DCIS with RT scenario, but did not reach statistical significance. In contrast, surgeons treating more breast cancer were likely to favor larger margins for DCIS treated without RT. These results are summarized in Table 3. Most other structural attributes of practice were not associated with margin preference in any consistent fashion. Discussion of the treatment plan with a radiation oncologist, medical oncologist or plastic surgeon prior to surgical therapy or participation in a multidisciplinary tumor board was not associated with margin preference. Practice setting [National Cancer Institute (NCI)-designated cancer center, university affiliation, or practice in a hospital with an American College of Surgeons-approved cancer program] was also not associated with margin preference. However, surgeons favoring smaller margins for the invasive cancer scenario and the DCIS with RT scenario were more likely to have residents associated with their practice (invasive cancer 59 vs. 49%, $p = 0.01$; DCIS plus RT 59 vs. 47%; $p = 0.007$) than those favoring larger margins. Finally, surgeon propensity for BCS in the invasive scenario, measured using a six-point Likert scale of strongly, moderately, weakly favor lumpectomy plus RT, or strongly, moderately, weakly favor mastectomy, did not correlate with choice of margin width, although almost all respondents strongly or moderately favored lumpectomy.

The logistic regression analysis examining correlates of a larger margin width is shown in Table 4. Surgeons devoting more than 50% of their practice to breast cancer surgery were *much less likely* to favor large margins than their counterparts with 15% or less of the practice devoted to breast surgery for the invasive cancer scenario. In contrast, for DCIS treated without RT, surgeons treating a high proportion of breast cancer cases were *much more likely* to favor a larger margin than surgeons for whom breast cancer

TABLE 1 Characteristics of surgeon practices

Characteristic	No. of surgeons ($n = 318$)	%
Cancer program status		
None	96	30.2
American College of Surgeons	129	40.5
National Cancer Institute	93	29.3
Tumor board		
Weekly	187	58.8
Biweekly	52	16.4
Monthly	49	15.4
None	30	9.4
Frequency of patients having preoperative radiation oncology consultation		
Few or none	137	43.5
About 1/3	62	19.7
About 1/2	37	11.7
About 2/3	20	6.4
Almost all	59	18.7
No response	3	0.3
Proportion of practice devoted to breast surgery		
≤15%	146	46.0
16–49%	118	37.0
≥50%	54	17.0

TABLE 2 Margin preferences

Margin width				
Scenarios	Not touching ink (%)[a]	>1–2 mm (%)	>5 mm (%)	>1 cm (%)
A: 60-year-old, 0.8 cm invasive ER/PR/HER2−, RT planned	11.2	42.0	27.9	18.9
B: 60-year-old, 1.4 cm DCIS ER+, RT planned	10.2	42.2	32.6	15.0
C: 60-year-old, 1.4 cm DCIS ER+, no RT planned	2.6	11.6	24.8	61.0

[a] Percentage of surgeon respondents who selected a given margin width for each clinical scenario, $n = 318$

TABLE 3 Relationship between margin preference and surgeon specialization

	Scenario A[a]			Scenario B			Scenario C[b]		
	Invasive cancer + RT[c]			DCIS + RT[d]			DCIS, no RT[e]		
	Percentage of practice devoted to breast cancer								
Preferred margin	≤15	16–49	≥50	≤15	16–49	≥50	≤15	16–49	≥50
Not touching ink	19 (13.4)	9 (7.8)	6 (11.5)	16 (11.3)	10 (8.5)	5 (9.6)	6 (4.3)	1 (0.9)	1 (1.9)
>1–2 mm	51 (35.9)	45 (39.1)	34 (65.4)	53 (37.6)	51 (43.6)	27 (51.9)	23 (16.3)	10 (8.7)	3 (5.8)
>5 mm	37 (26.1)	40 (34.8)	9 (17.3)	45 (31.9)	37 (31.6)	19 (36.5)	39 (27.7)	28 (24.3)	10 (19.2)
>1 cm	35 (24.7)	21 (18.3)	3 (5.8)	27 (19.1)	19 (16.2)	1 (1.9)	72 (51.1)	76 (66.1)	38 (73.1)

Numbers in cells are the number of surgeons in each group. Figures in parenthesis are percentages

[a] $p = 0.002$ for differences between groups

[b] $p = 0.075$

[c] Missing nine observations

[d] Missing eight observations

[e] Missing ten observations

TABLE 4 Correlates of larger margin width

Odds ratio (95% confidence interval)[a]		
	Scenario A Invasive	Scenario C DCIS, no RT
Percentage of practice devoted to breast cancer		
≤15%	Reference	Reference
16–49%	1.05 (0.66–1.70)	1.61 (0.96–2.71)
≥50%	0.44 (0.23–0.87)	2.72 (1.24–5.95)
Wald test, *p*-value	7.27, $p = 0.026$	7.23, $p = 0.027$
Female surgeons	0.71 (0.39–1.32)	1.12 (0.54–2.32)
Years in practice	0.99 (0.97–1.02)	0.99 (0.97–1.01)

[a] Adjusted for all other covariates in the model

comprised 15% or less of their practice. The proportion of practice devoted to breast cancer was not predictive of margin status for DCIS treated with RT, and neither gender nor years in practice were predictive of margin width for any scenarios.

DISCUSSION

Our study demonstrates wide variation among surgeons in the Los Angeles County and Metropolitan Detroit areas regarding the definition of an adequate negative margin. None of the margin definitions provided (tumor not on ink, >1–2 mm, >5 mm, >1 cm) were endorsed by more than half the respondents when treatment with BCS included radiotherapy, regardless of whether the diagnosis was invasive cancer or DCIS. More specialized surgeons (i.e., those with >50% of their practice devoted to breast disease) were significantly more likely to endorse smaller margins in the invasive cancer scenario than their non-specialized counterparts, but years in practice and gender did not influence margin preference. Somewhat surprisingly, other measures of surgeon practice were not correlated with attitudes about margin status, including affiliation with a specialized cancer treatment setting or the extent of multidisciplinary treatment decision-making (presence of a tumor board, extent to which the surgeon discussed treatment plans with other specialists prior to surgery).

Similar variation in the definition of a negative margin has been observed among North American and European radiation oncologists. Taghian et al. surveyed 702 North American radiation oncologists and 431 European radiation oncologists.[14] Tumor not touching ink was accepted as a negative margin by 46% of North Americans and only 28% of Europeans. No regional variations in the definition of a negative margin were observed within different parts of the USA, suggesting that our findings from Los Angeles and Detroit are generalizable to surgeons throughout the country. Similar to the findings of our study, Taghian et al. did not observe variation in the definition of a negative margin based on practice in an academic or a nonacademic setting.[14] We extend this finding as we did not find significant correlations between surgeon attitudes about margin width and factors such as gender, surgeon specialization, institutional specialization, or degree to which the practice has multidisciplinary decision support models.

The lack of consensus in margin definition reflects the lack of a standardized definition of a negative margin in the original randomized trials of BCT. While the NSABP-06 study used the definition of tumor cells not touching ink, other randomized trials appeared to employ more widely clear margins.[1] Entrance criteria for the Institute Gustave Roussy study included a gross margin of 2 cm, while the Milan I trial specified removal of a "quadrant" of the

breast.[15,16] The use of these gross definitions means that the actual microscopic margin widths in these studies ranged from margins involved with tumor to margins negative by several centimeters depending upon the microscopic extent of disease and the location of the tumor within the quadrant. This unmeasured variation precludes the use of data from the randomized trials to analyze the impact of negative margin width on ipsilateral breast tumor recurrence (IBTR) after controlling for other variables. It is not particularly surprising that retrospective studies have not resulted in consistent findings regarding margin width and IBTR.[5] Margin assessment is a sampling of the surface of the lumpectomy specimen, and both the technique of sampling and the number of specimens examined are variable. Wright et al. reported that the positive margin rate at Memorial Sloan-Kettering Cancer Center increased from 15 to 49% when the technique of pathologic assessment of margins changed from perpendicular margins to shaved margins, although surgical practice did not change in that interval.[17] Graham et al. noted that the mean height of the lumpectomy specimen (anterior to posterior distance) as measured by the surgeon in the operating room was decreased by 54% when measured in the pathology laboratory when compression devices were used for specimen X-rays, and by 41% when these devices were not used, introducing a major source of variation in the measurement of anterior and posterior margin width.[10] In addition, Wiley et al. observed that the likelihood of identifying residual invasive cancer after an initial lumpectomy decreases in a statistically significant way as the time from the initial surgical procedure increases, introducing another source of variation in margin assessment.[18] Given all these potential sources of variation, it is not surprising that differences of millimeters in margin width have not been shown to correlate with rates of IBTR. In addition, it has become clear that factors other than tumor burden, as measured by margin width, have a major impact on the risk of IBTR. The use of adjuvant systemic therapy significantly reduces IBTR, and newer information suggests that the intrinsic biologic subtype of the breast cancer may also be related to the risk of IBTR.[19,20] This is a rapidly evolving field, and it is possible that surgeons who devote a greater proportion of their practice to breast cancer management may be more aware of the impact of factors other than margin width on IBTR than their counterparts who treat breast cancer less frequently, and therefore place less emphasis on obtaining more widely clear margins.

In DCIS the situation is slightly different since the identification of subtypes of DCIS with a different propensity to develop invasive cancer has proven elusive. In the randomized studies that examined the use of RT in DCIS, the only microscopic margin definition employed was tumor not touching the ink.[21,22] So it is reassuring that our study indicates that surgeons who favor this definition for invasive cancer have a similar approach in DCIS treated with RT. The selection of patients with DCIS for treatment without RT remains a matter of controversy. However, a well-publicized single-institution study has suggested that excision to a margin of 1 cm or greater obviates the need for RT in DCIS.[23] Although the results of this study have not been reproduced prospectively, it is likely that these data account for the overall preference for more widely clear margins in the scenario of DCIS treated with excision alone.[24,25] The difference between high- and low-volume surgeons observed in this scenario, which is in the opposite direction of that observed for patients treated with RT, is not readily explainable but may reflect a greater tailoring of margin status to the individual patient scenario by more specialized surgeons.

Our study has important implications for clinical care. Re-excision rates in the literature are highly variable and range from 20 to 60%.[6,8] In a population-based study of 800 women attempting BCS in 2006, the procedure was successful in 88%, but 26% required re-excision.[9] Re-excision necessitates a second trip to the operating room with its attendant costs, delays the initiation of adjuvant systemic therapy, and leads to patient anxiety. Our results suggest that a significant proportion of re-excisions are done in patients with negative margins (tumor not touching ink) because of the use of alternate margin definitions not supported by consistent high-quality clinical data. The variability in margin definition is increasingly being recognized as a problem and led participants at both the 2008 Bidenkopf International Consensus Conference on the Local Therapy of Breast Cancer and the 2009 St. Gallen Consensus Conference on Early Stage Breast Cancer to endorse tumor not touching ink as the standard definition of an adequate negative margin in women with invasive carcinoma, and to suggest that margins be considered in the context of multiple factors known to influence the risk of IBTR.[26] Our results suggest that better standards need to be broadly adopted by the surgical community at large, because variation in surgeon attitudes was observed across surgeon and practice subgroups.

Our study does have limitations. The margin widths reported are based on surgeon responses to case scenarios and may not reflect actual clinical practice, particularly the use of re-excision when the ideal margin is not achieved. Additionally, the survey population is geographically limited to two large metropolitan areas which may not be reflective of United States practice patterns as a whole, although a study examining this issue in the radiation oncology community did not demonstrate differences in margin preference based on geographic location within the United States.[14] In spite of these concerns, our study documents clear variation among surgeons in the definition of

what negative margin width precludes the need for re-excision. Achieving a more widespread consensus on this issue has the potential to reduce costs, to decrease the use of unnecessary mastectomies, and perhaps to increase patient acceptance of BCS at a time when mastectomy rates are rising.

CONCLUSION

Definition of an adequate margin varies, and clinical trials data supporting tumor not touching ink are not widely accepted. Definition of acceptable margin width is similar for invasive cancer and DCIS with RT, with more specialized surgeons favoring smaller margins. In DCIS treated without RT, more specialized surgeons are significantly more likely to favor larger margins. Factors not significantly associated in either invasive cancer or DCIS include age, gender, years in practice, and multidisciplinary specialist perioperative consultations. Adoption of a standard margin definition has the potential to significantly affect re-excision rates.

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