

Impact of Routine Cavity Shave Margins on Breast Cancer Re-excision Rates

Anne Kobbermann, MD¹, Alison Unzeitig, BS¹, Xian-Jin Xie, PhD², Jingsheng Yan, PhD², David Euhus, MD¹, Yan Peng, PhD³, Venetia Sarode, MD³, Amy Moldrem, MD¹, A. Marilyn Leitch, MD¹, Valerie Andrews, MD¹, Carrie Stallings, MD¹, and Roshni Rao, MD¹

¹Division of Surgical Oncology, Department of Surgery, University of Texas Southwestern Medical Center, Dallas, TX;

²Department of Clinical Sciences, University of Texas Southwestern Medical Center, Dallas, TX; ³Department of Pathology, University of Texas Southwestern Medical Center, Dallas, TX

ABSTRACT

Purpose. Breast-conserving therapy (BCT) is an accepted method of treating early breast cancer. We hypothesized that routine excision of additional cavity shave margins (CSM) at time of initial partial mastectomy reduces the need for additional surgery.

Methods. A single-institution retrospective review was performed of women, 18 years or older, with a new diagnosis of breast cancer who underwent partial mastectomy between 1 January 2004 and 1 October 2009. Five hundred thirty-three charts were reviewed. Of those, 69 patients underwent CSM at time of initial operation. These 69 patients were matched with patients who had undergone partial mastectomy without CSM by tumor size, presence of extensive intraductal component, and primary histology.

Results. The two groups were well matched for age, nuclear grade, associated lymphovascular invasion (LVI), receptor status, and multifocality. We found that 31.9% (44/138) required return to the operating room (OR) for re-excision of margins. Rate of return to the OR was 21.7% (15/69) in the CSM group and 42.0% (29/69) in the matched group ($p = 0.011$). Multivariate analysis found factors significantly associated with need for additional operation included lack of CSM (odds ratio 9.2, 95% CI 2.8–30.5, $p = 0.0003$), larger extent of intraductal component (odds ratio 7.0, 95% CI 1.8–27.0, $p = 0.005$), and lack of directed re-excision (odds ratio 6.4, 95% CI 1.7–25.1, $p = 0.007$).

Conclusions. CSM at time of initial partial mastectomy decreases rate of re-excision by as much as ninefold. CSM should be considered at time of initial operation to reduce the need for subsequent reoperation.

Breast-conserving surgery followed by whole-breast radiation is an accepted therapy for patients diagnosed with early breast cancer.¹ Of the 200,000 women diagnosed in the USA every year, nearly half choose breast-conserving therapy (BCT).¹ Successful BCT requires complete tumor removal with adequate surrounding margins of normal breast parenchyma. This oncologic approach results in low recurrence rates and equivalent survival when compared with total mastectomy.^{2–4} Recent studies have revealed that the majority of surgeons prefer a 2-mm negative margin around the tumor and will perform additional operations in order to achieve this.⁵ Previous reports indicate that 30–50% of breast cancer patients undergo additional operations in order to obtain adequate margins.^{6–8} Additional surgery, which may be oncologically necessary, is clearly difficult for patients and does impose added health care costs on the system.

Techniques to facilitate complete removal of nonpalpable breast cancers at initial surgery following diagnosis of breast cancer are of significant interest to surgeons and patients. Wire localization has been available since the early 1990s, and is a standard approach that requires the placement of a thin wire into the lesion of concern.^{9,10} Although this has allowed increased precision, re-excisions are still commonly required. Other techniques, including ultrasound-guided hematoma localization, ultrasound alone localization, seed localization, radioguided localization, intraoperative specimen mammography, and intraoperative

pathologic margin assessment, have also been utilized to maximize the probability of complete tumor removal at the first surgery.^{8,10-27} While success with these approaches has been reported, they universally require additional equipment, and the vast majority increase operative time.

A simpler technique that utilizes existing equipment available in any operative suite that may reduce the need for re-excision in BCT is the performance of cavity shave margins (CSM). This technique has previously been described and does appear to decrease the need for additional surgery.²⁷⁻³² Surgeons either perform directed excisions of specific margins, or excision of all margins adjacent to the lumpectomy cavity. Interpretation of prior studies is difficult because not all patients had a preoperative diagnosis of breast cancer, and some studies do not utilize the detailed pathologic analysis performed in the USA. This study evaluates the impact of CSM on re-excision rates in patients diagnosed with breast cancer by core-needle biopsy in the current era of careful pathologic examination.

METHODS

An Institutional Review Board-approved retrospective analysis was performed to identify all patients undergoing BCT at an academic cancer center. All women, 18 years or older, who underwent partial mastectomy between 1 January 2004 and 1 October 2009 were included. All patients had undergone core-needle biopsy prior to surgical intervention and had a known diagnosis of in situ or invasive breast cancer; patients undergoing excisional biopsy for diagnosis alone were excluded. Patients who had undergone neoadjuvant chemotherapy were excluded to remove this as a confounding factor leading to increased re-excision rates.

Technique of CSM

Patients underwent standard partial mastectomy (PM) with immediate CSM or PM with or without additional margins removed at the discretion of the surgeon. Three surgeons (R.R., A.M., D.E.) began performing CSM routinely on all patients with a known diagnosis of cancer. Directed margins removed at surgeon discretion were primarily removed due to interpretation of the specimen mammogram by the surgeon. Partial mastectomy with CSM involved macroscopic tumor removal with oriented PM followed by removal of six additional shaved margins (superior, inferior, medial, lateral, anterior, and posterior) taken from the entire wall of the residual cavity during the same operation. The additional margin specimens were at least 1 cm in thickness. When a skin ellipse was taken, the anterior margin was taken from beneath the raised flap.

Similarly, when dissection was taken down to the pectoralis muscle, posterior margin came from the tissue surrounding the exposed muscle. Each additional margin was further oriented with clips marking the new margin. These six margins, in addition to the PM specimen, were then sent to pathology for evaluation. Specimen mammography is routinely performed for patients undergoing radiologic localization prior to surgery. This mammogram was interpreted by the operating surgeon, and directed immediate re-excisions were performed at surgeon discretion. As a routine protocol, compression is not used when specimen mammography is performed.

Tumor greater than or equal to 2 mm from the margin of the specimen was considered a negative margin. Tumor less than 2 mm from the margin but not involving the cut edge was considered a close margin. All patients with close or positive margins were taken back to the operating room (OR) for re-excision.

Statistical Analysis

Data collected included patient demographics, pathology, adjuvant therapies, number of surgical interventions, and final treatment outcome. Initial review identified 533 patients who had undergone BCT for a new diagnosis of in situ or invasive breast cancer. Fifty-seven patients were excluded secondary to having received neoadjuvant chemotherapy. Of the remaining 476 patients, 69 (14.50%) patients had undergone immediate CSM at time of PM. Because of the retrospective nature of this study, a case-matched analysis was performed to minimize confounding variables and allow for focused evaluation of the impact of the CSM technique. The 69 patients who underwent immediate CSM at time of PM were matched with an equal number of patients who underwent traditional PM with or without additional margin removal at the discretion of the surgeon. The groups were matched for age at diagnosis, tumor size, extent of intraductal component, and primary histology. These 138 patients formed the study population.

A univariate analysis using Chi-square was performed to ensure that the CSM and control groups were well matched. The groups were compared in terms of race, age at diagnosis, nuclear grade, associated lymphovascular invasion (LVI), multifocality, and estrogen receptor (ER) status. Subsequently, a multivariate logistic regression analysis was performed to identify independent risk factors for return to the OR. Stepwise procedure was conducted with a *p* value of 0.2 or less from the univariate analysis to enter. SAS version 9.1.3 was used for all statistical analysis. Multivariate analysis included age at diagnosis, race, tumor size, primary histology, extent of intraductal component, nuclear grade, associated LVI,

multifocality, ER status, CSM taken, and use of directed re-excision.

RESULTS

On univariate chi-square analysis the two groups were found to be well matched in terms of patient demographics, tumor characteristics, and surgical localization technique. Patient demographics included age, race, and method of tumor detection. Tumor characteristics included primary histology, nuclear grade, associated LVI, receptor status, and multifocality. No statistically significant differences were noted between the groups (Table 1).

Overall reoperation rate was 31.9% (44 of 138). Patients who underwent CSM at time of PM had significantly lower rates of re-excision ($p = 0.015$) when compared with patients who underwent traditional PM (Table 1). Of the patients requiring reoperation, there was no statistically significant difference in terms of patient demographics, tumor characteristics, or surgical localization technique.

Of the patients who underwent CSM at time of primary PM, 15 of 69 (21.7%) required second operation for close or positive margins (Table 1). Detailed chart review indicated that 9 of 15 (60.0%) required reoperation for close margins whereas 6 of 15 (40.0%) required reoperation for positive margins. Of the patients who did not undergo CSM at time of PM, 29 of 69 (42.0%) required reoperation for close or positive margins (Table 1). Of these 29 patients, 15 of 29 (51.7%) were due to close margins whereas 14 of 29 (48.3%) were due to positive margins.

Upon reoperation, patients who had undergone previous CSM were less likely to have residual tumor found in re-excision specimens. Twelve of 15 (80.0%) of CSM patients had no residual tumor as compared with 20 of 29 (69.0%) of the patients who had undergone traditional PM (Fig. 1).

Our study then focused on the 44 patients who required reoperation. Upon multivariate analysis, CSM was the strongest factor associated with complete removal of the primary tumor at initial operation (Table 2). Additional factors contributing to lower re-excision rates included extent of intraductal component, and directed excision of additional margins performed at the discretion of the operative surgeon, typically based on interpretation of the specimen mammogram (Table 2).

DISCUSSION

An integral part of BCT involves complete tumor removal. Positive or microscopically close margins have been associated with increased rates of local recurrence.³³ There is evidence that local recurrence is associated with both decreased disease-free and overall survival.³⁴ One

particular challenge with breast-conserving surgery is ensuring complete tumor removal at time of initial partial mastectomy. The operating surgeon must remove enough tissue to guarantee high rates of local control while preserving healthy breast tissue in order to achieve the best possible cosmetic result.

There is significant variability in the literature as to what constitutes a negative margin. Initial National Surgical Adjuvant Breast and Bowel Project (NSABP) studies comparing more aggressive surgery with BCT defined a negative margin as no tumor at the inked edge of the specimen.³⁵ However, more recent studies have focused on microscopic histologic evaluation of the specimen edge. Studies evaluating BCT have utilized a range of definitions for what constitutes a negative margin. This creates some difficulty in comparing outcomes. At our institution, we utilize the College of American Pathologists protocol for micro-evaluation of margins.³⁶ We return patients to the OR for both positive margins and close margins as defined by tumor less than 2 mm from the inked edge of the specimen. Without adherence to this stringent oncologic benchmark, overall re-excision rates would likely have been lower. It is important when evaluating the literature regarding BCT to ensure that an accurate comparison is being made based on this definition.

Return to the OR for re-excision of margin exposes the patient to both additional physical and psychological risks. Physically, the patient incurs risks associated with additional anesthetic. Additionally, cosmetic outcome may be compromised by additional surgical manipulation of breast tissue with further development of scar tissue. Psychologically, the patient may experience the anxiety of a second surgery, which may be associated with a loss of confidence in the treatment strategy.

Systematic CSM sampling has been proposed to reduce rates of reoperation for positive or microscopically close margins. While this technique has been reported in the literature, a consistent definition of what defines CSM is lacking. Consequently, there is not much definitive data indicating the effectiveness of this technique. Given the low risk involved with adopting this technique, and the fact that it does not require additional equipment or expertise, we accepted that 5% would be an appropriate decrease in return to the OR. Sample size calculation (95% confidence interval) indicates we would have needed 65 patients who had undergone CSM. This study has 69 matched patients, and although retrospective, our data indicate that performing CSM at time of initial PM results in a statistically significant reduction in reoperation rates.

A recent prospective analysis of specimen orientation out of the University of Miami revealed an overall mis-orientation rate of 31.1% of partial mastectomy specimens,

TABLE 1 Chi-square analysis of patient demographics, tumor characteristics, and surgical localization as well as surgical and pathologic characteristics of patients requiring reoperation

	All patients N (%)	Shave margins N (%)	Standard PM N (%)	p Value
<i>Patient demographics</i>				
Race				<i>p</i> = 1.0000
White	67 (48.6)	34 (49.3)	33 (47.8)	
Non-White	71 (51.4)	35 (50.7)	36 (52.2)	
Median age at diagnosis (years)	58.78	58.83	58.72	<i>p</i> = 0.9602
<i>Method tumor detected</i>				
Radiographic ^a	104 (75.4)	49 (71.0)	55 (79.7)	<i>p</i> = 0.3239
Other ^b	28 (20.3)	20 (29.0)	14 (20.3)	
<i>Tumor characteristics</i>				
<i>Histology</i>				
In situ	40 (29.0)	20 (29.0)	20 (29.0)	<i>p</i> = 1.0000
IDC	76 (55.1)	38 (55.1)	38 (55.1)	
ILC	12 (8.7)	6 (8.7)	6 (8.7)	
Other	2 (1.4)	1 (1.4)	1 (1.4)	
Combination	8 (5.8)	4 (5.8)	4 (5.8)	
<i>Nuclear grade</i>				
Grade I	44 (31.9)	22 (31.9)	22 (31.9)	<i>p</i> = 0.7166
Grade II	57 (41.3)	31 (44.9)	26 (37.7)	
Grade III	35 (25.4)	16 (23.2)	19 (27.5)	
Unknown	2 (1.4)	0 (0.0)	2 (2.9)	
<i>Associated LVI</i>				
Yes	9 (6.5)	6 (8.7)	3 (4.3)	<i>p</i> = 0.4882
No	93 (67.4)	46 (66.7)	47 (68.1)	
Unknown	36 (26.1)	17 (24.6)	19 (27.5)	
<i>ER status</i>				
Positive	114 (82.6)	60 (87.0)	54 (78.3)	<i>p</i> = 0.3576
Negative	22 (15.9)	9 (13.0)	13 (18.8)	
Unknown	2 (1.4)	0 (0.0)	2 (2.9)	
<i>Multifocality</i>				
Yes	10 (7.2)	4 (5.8)	6 (8.7)	<i>p</i> = 0.5114
No	128 (92.9)	65 (94.2)	63 (91.3)	
<i>Percentage of DCIS in final specimen</i>				
None	42 (30.4)	21 (30.4)	21 (30.4)	<i>p</i> = 1.0000
1–25%	44 (31.9)	22 (31.9)	22 (31.9)	
>25%	52 (37.7)	26 (37.7)	26 (37.7)	
<i>Surgical localization</i>				
<i>Breast surgery localization</i>				
Wire	96 (69.9)	43 (62.3)	53 (76.8)	<i>p</i> = 0.1552
Seed	4 (2.9)	3 (4.3)	1 (1.4)	
None	38 (27.5)	23 (33.3)	15 (21.7)	
<i>Patients requiring 2nd operation</i>				
<i>Need for 2nd operation to achieve adequate margins</i>				
Yes	44 (31.9)	15 (21.7)	29 (42.0)	<i>p</i> = 0.0105
No	94 (68.1)	54 (78.3)	40 (58.0)	
<i>Reason for 2nd operation</i>				
Positive margin	20 (45.5)	6 (40.0)	14 (48.3)	<i>p</i> = 0.6013
Close margin (< 2 mm)	24 (54.5)	9 (60.0)	15 (51.7)	
<i>Residual tumor present at 2nd operation</i>				
Yes	12 (27.3)	3 (20.0)	9 (31.0)	<i>p</i> = 0.4360
No	32 (72.7)	12 (80.0)	20 (69.0)	

PM partial mastectomy, IDC invasive ductal carcinoma, ILC invasive lobular carcinoma, LVI lymphovascular invasion, ER estrogen receptor, PR progesterone receptor, DCIS ductal carcinoma in situ, NA not applicable

^a Mammogram, US, or combination

^b Physician examination, breast self-examination (BSE), or other (nonradiographic)

FIG. 1 Flow diagram for study population demonstrating patients requiring reoperation and findings of re-excision specimen. *PM* partial mastectomy, *CSM* cavity shave margins

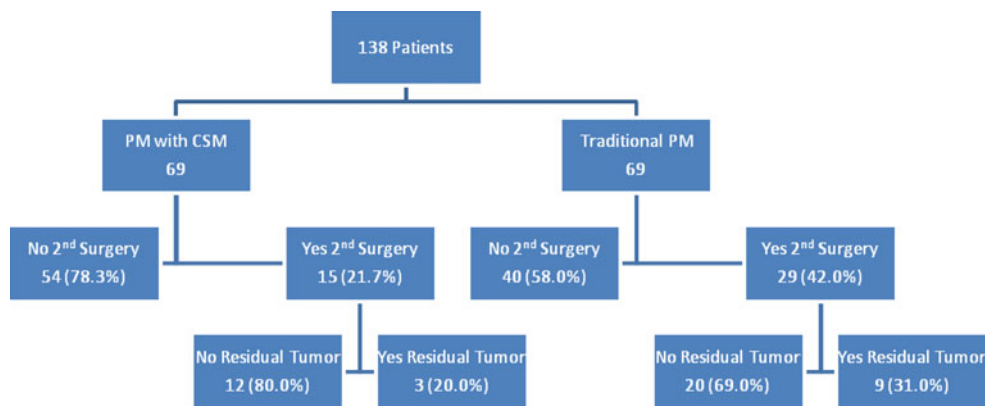


TABLE 2 Multivariate analysis of predictors of second operation for re-excision of margins

All patients	Odds ratio estimate	Odds ratio 95% confidence interval	Odds ratio <i>p</i> value	Overall <i>p</i> value
Shave margins taken				
Yes				0.0003
No	9.237	(2.798, 30.488)	0.0003	
Extent of intraductal component				
NA				
1–25%	1.673	(0.424, 6.599)	0.4623	0.0062
>25%	6.953	(1.793, 26.968)	0.0050	
Additional margins taken				
Yes				0.0071
No	6.457	(1.659, 25.131)	0.0071	

NA not applicable

despite suture markings placed by the operative surgeon.³⁷ One challenge of reoperation for close or microscopically positive margins remains accurate identification of involved margin when returning to the OR. Due to the friability of the PM specimen and its ability to be distorted during handling or specimen mammography, there is a risk of false positivity during margin assessment. A benefit derived from CSM sampling is more accurate removal of oriented margins during primary surgery. CSM sampling allows the multidisciplinary team certainty that any close or positive margin on the initial partial mastectomy specimen was correctly and accurately re-excised.

Literature Review

Review of the literature reveals consistently lower rates of re-excision with CSM (Table 3). There remain few published series in the literature that address a surgical approach similar to that described herein. There remains some limitation in comparing these published accounts as the definition of “shave margin” varies in both number and thickness. Many of the published studies involving this technique do not provide specific information regarding the definition used. Also, the threshold for reoperation was

based on varying standards of what constituted a negative margin. However, despite these limitations, there is consistency in lowered reoperation rates.

Cao et al. retrospectively identified 126 patients who had undergone CSM of anywhere from four to six additional margins.³⁸ Margins were considered negative if no tumor was identified within 2 mm of the inked surface. Of the 103 patients who had at least one histologically positive margin on primary PM specimen, 61 (59.2%) did not require reoperation due to CSM sampling.

Jacobson et al. reported on 125 women who had undergone CSM, where the majority had all six margins sampled.²⁷ However, specific numbers of patients who had fewer than six margins excised or how many margins those patients had sampled were not reported. Margins were considered positive if tumor existed less than 2 mm from the inked margin. Of the 83 patients who had at least one histologically positive margin on primary PM specimen, 61 (73.5%) did not require reoperation for re-excision due to CSM.

Marudanayagam et al. compared 394 patients who had undergone PM with four CSM with 392 who had undergone traditional PM alone.³¹ All patients had a preoperative diagnosis of cancer. CSM were defined as at least 1 cm in

TABLE 3 Comparison of recent literature evaluating CSM

References	Preoperative diagnosis of carcinoma	N for CSM	N for standard PM	Routine CSM of margin	Definition of CSM (number of additional margins)	Definition of negative margin	Reduction in re-excision	p Value
Cao et al. ³⁸	Unknown	126	NA	Yes	4–6	2 mm	61/103	
Jacobson et al. ²⁸	Unknown	125	NA	Yes	“Most had all 6 margins”	2 mm	61/83	
Marudanayagam et al. ³²	Yes	394	392	Yes	4	No tumor at inked margin	6.92% ^a	<0.01
Rizzo et al. ³⁹	Yes	121	199	Yes	4–5	1 mm	27.9% ^b	<0.05
Tengher-Barna et al. ³⁰	Yes	107	NA	Yes	4	3 mm	27/47	

CSM cavity shave margins, PM partial mastectomy, NA not applicable

^a 49/392 (12.5%) versus 22/394 (5.58%) requiring reoperation

^b 183/320 (57.2%) versus 272/320 (85.1%) with negative margins

thickness. Negative margins were defined as absence of tumor at the resected margin. Forty-nine of 392 (12.5%) of the traditional PM group required re-excision for positive margins as compared with 22 of 394 (5.6%) of the CSM group ($p < 0.01$).

Rizzo et al. compared 320 patients who had undergone PM with four to five CSM with 320 who had undergone traditional PM alone.³⁹ All patients had a preoperative diagnosis of cancer. Margins were defined as positive if tumor was within 1 mm of the inked specimen surface. Of the traditional PM patients, 57.2% were found to have negative margins after primary surgery as compared with 85.1% of those who underwent CSM.

Tengher-Barna et al. reported on 107 consecutive patients who had undergone four CSM.²⁹ Margin positivity was defined as tumor within 3 mm of the inked specimen edge. Of the 107 patients, 47 (43.9%) were found to have positive primary PM margins, however only 27 of those (25.2%) required reoperation for re-excision because of CSM sampling.

Future Directions

One potential downside of performing CSM is the risk of increased tissue removal at time of initial operation with diminished cosmetic result. It is possible that the decrease in return to operation rates is simply due to more tissue being removed at time of primary operation. The single study, however, that evaluates this particular issue, does not support this conclusion.³⁹ This study reports that the converse is true: less tissue is actually removed when taking CSM.³⁹ We would speculate that the reason for this, in part, is that the operative surgeon is more comfortable excising closer to the tumor on initial PM specimen when six additional margins will be resected. However, this was not something that was evaluated in this analysis but will be the focus of a planned prospective protocol.

CONCLUSIONS

Our study demonstrates that routine use of CSM sampling at time of partial mastectomy significantly reduces reoperation rates. This is a simple technique that does not require additional training or specialized surgical equipment, and can reduce the number of necessary surgical interventions for breast cancer treatment. We would recommend adopting systematic CSM sampling at time of primary partial mastectomy.

REFERENCES

- Morrow M, White J, Moughan J, et al. Factors predicting the use of breast-conserving therapy in stage I and II breast carcinoma. *J Clin Oncol.* 2001;19:2254–62.
- Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med.* 2002;347:1233–41.
- Veronesi U, Cascinelli N, Mariani L, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *N Engl J Med.* 2002;347:1227–32.
- Camp ER, McAuliffe PF, Gilroy JS, et al. Minimizing local recurrence after breast conserving therapy using intraoperative shaved margins to determine pathologic tumor clearance. *J Am Coll Surg.* 2005;201:855–61.
- 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;209:608–13.
- Sabel MS, Rogers K, Griffith K, et al. Residual disease after re-excision lumpectomy for close margins. *J Surg Oncol.* 2009;99:99–103.
- Wiley EL, Diaz LK, Badve S, Morrow M. Effect of time interval on residual disease in breast cancer. *Am J Surg Pathol.* 2003;27:194–8.
- Gray RJ, Salud C, Nguyen K, et al. Randomized prospective evaluation of a novel technique for biopsy or lumpectomy of nonpalpable breast lesions: radioactive seed versus wire localization. *Ann Surg Oncol.* 2001;8:711–5.

9. Rissanen TJ, Makarainen HP, Kiviniemi HO, Suramo, II. Ultrasonographically guided wire localization of nonpalpable breast lesions. *J Ultrasound Med.* 1994;13:183–8.
10. Rissanen TJ, Makarainen HP, Mattila SI, et al. Wire localized biopsy of breast lesions: a review of 425 cases found in screening or clinical mammography. *Clin Radiol.* 1993;47:14–22.
11. Gray RJ, Pockaj BA, Karstaedt PJ, Roarke MC. Radioactive seed localization of nonpalpable breast lesions is better than wire localization. *Am J Surg.* 2004;188:377–80.
12. Thompson M, Henry-Tillman R, Margulies A, et al. Hematoma-directed ultrasound-guided (HUG) breast lumpectomy. *Ann Surg Oncol.* 2007;14:148–56.
13. Smith LF, Henry-Tillman R, Harms S, et al. Hematoma-directed ultrasound-guided breast biopsy. *Ann Surg.* 2001;233:669–75.
14. Kaufman CS, Jacobson L, Bachman B, Kaufman LB. Intraoperative ultrasonography guidance is accurate and efficient according to results in 100 breast cancer patients. *Am J Surg.* 2003;186: 378–82.
15. Smith LF, Rubio IT, Henry-Tillman R, Korourian S, Klimberg VS. Intraoperative ultrasound-guided breast biopsy. *Am J Surg.* 2000;180:419–23.
16. Rahusen FD, Bremers AJ, Fabry HF, van Amerongen AH, Boom RP, Meijer S. Ultrasound-guided lumpectomy of nonpalpable breast cancer versus wire-guided resection: a randomized clinical trial. *Ann Surg Oncol.* 2002;9:994–8.
17. Ngo C, Pollet AG, Laperlee J, Ackerman G, Gomme S, Thibault F, Fourchette V, Salmon RJ. Intraoperative ultrasound localization of nonpalpable breast cancers. *Ann Surg Oncol.* 2007;14:2485–9.
18. Jakub JW, Gray RJ, Degnim AC, Boughey JC, Gardner M, Cox CE. Current status of radioactive seed for localization of non palpable breast lesions. *Am J Surg.* 2010 April;199(4):522–8.
19. Rao R, Moldrem A, Sarode V, et al. Experience with seed localization for nonpalpable breast lesions in a public health care system. *Ann Surg Oncol.* 2010. doi:10.1245/s10434-010-1139-4.
20. Lavoue V, Nos C, Clough KB, et al. Simplified technique of radioguided occult lesion localization (ROLL) plus sentinel lymph node biopsy (SNOLL) in breast carcinoma. *Ann Surg Oncol.* 2008;15:2556–61.
21. Monti S, Galimberti V, Trifiro G, et al. Occult breast lesion localization plus sentinel node biopsy (SNOLL): experience with 959 patients at the European Institute of Oncology. *Ann Surg Oncol.* 2007;14:2928–31.
22. Intra M, de Cicco C, Gentilini O, Luini A, Paganelli G. Radio-guided localisation (ROLL) of non-palpable breast lesions and simultaneous sentinel lymph node biopsy (SNOLL): the experience of the European Institute of Oncology. *Eur J Nucl Med Mol Imaging.* 2007;34:957–8.
23. Young ES, Hogg DE, Krontiras H, et al. Specimen radiographs assist in identifying and assessing resection margins of occult breast carcinomas. *Breast J.* 2009;15:521–3.
24. Mazouni C, Rouzier R, Balleyguier C, et al. Specimen radiography as predictor of resection margin status in non-palpable breast lesions. *Clin Radiol.* 2006;61:789–96.
25. Cabioglu N, Hunt KK, Sahin AA, et al. Role for intraoperative margin assessment in patients undergoing breast-conserving surgery. *Ann Surg Oncol.* 2007;14:1458–71.
26. Ramanujam N, Brown J, Bydlon TM, et al. Quantitative spectral reflectance imaging device for intraoperative breast tumor margin assessment. *Conf Proc IEEE Eng Med Biol Soc.* 2009;1:6554–6.
27. Gibson GR, Lesnikoski BA, Yoo J, Mott LA, Cady B, Barth RJ, Jr. A comparison of ink-directed and traditional whole-cavity re-excision for breast lumpectomy specimens with positive margins. *Ann Surg Oncol.* 2001;8:693–704.
28. Jacobson AF, Asad J, Boolbol SK, Osborne MP, Boachie-Adjei K, Feldman SM. Do additional shaved margins at the time of lumpectomy eliminate the need for re-excision? *Am J Surg.* 2008;196:556–8.
29. Hewes JC, Imkampe A, Haji A, Bates T. importance of routine cavity sampling in breast conservation surgery. *Br J Surg.* 2009;96:47–53.
30. Tengher-Barna I, Hequet D, Reboul-Marty J, et al. Prevalence and predictive factors for the detection of carcinoma in cavity margin performed at the time of breast lumpectomy. *Mod Pathol.* 2009;22:299–305.
31. Janes SE, Stankhe M, Singh S, Isgar B. Systematic cavity shaves reduces close margins and re-excision rates in breast conserving surgery. *Breast.* 2006;15:326–30.
32. Marudanayagam R, Singhal R, Tanchel B, O'Connor B, Balasubramanian B, Paterson I. Effect of cavity shaving on reoperation rate following breast-conserving surgery. *Breast J.* 2008;14:570–3.
33. Singletary SE. Surgical margins in patients with early-stage breast cancer treated with breast conservation therapy. *Am J Surg.* 2002;184(5):383–93.
34. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials. *Lancet.* 2005;366:2087–106.
35. Fisher B, Bauer M, Margolese R et al. Five-year results of a randomized clinical trial comparing total mastectomy and segmental mastectomy with or without radiation in the treatment of breast cancer. *NEJM.* 1985;312:665–73.
36. Lester SC, Bose S, Yunn-Yi C, et al. Protocol for the examination of specimens from patients with invasive carcinoma of the breast. *Arch Pathol Lab Med.* 2009 Oct;133(10):1515–38.
37. Molina MA, Snell S, Franceschi D et al. Breast specimen orientation. *Ann Surg Oncol.* 2009;16:285–8.
38. Cao D, Lin C, Woo S, Vang R, Tsangaris TN, Argani P. Separate cavity margin sampling at the time of initial breast lumpectomy significantly reduces the need for reexcisions. *Am J Surg Pathol.* 2005;29:1625–32.
39. Rizzo M, Iyengar R, Gabram SGA, Park J, Birdsong G, Chandler KL, Mosunjac MB. The effects of additional tumor cavity sampling at the time of breast-conserving surgery on final margin status, volume of resection, and pathologist workload. *Ann Surg Oncol.* 2010;17:228–34.