

Oncology Clinical Service Line
 System-wide Consensus Guidelines: **Invasive Carcinoma: Management of Surgical Margins and Recommendations for Margin Re-excisions in Patients Having Breast Conserving Therapy**

These guidelines apply to clinical interventions that have well-documented outcomes, but whose outcomes may not be desirable for all patients

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System-wide Ownership Group: Allina Health Breast Program Committee
System-wide Information Resource: Director of Clinical Programs

Hospital Division Quality Council Review: May 2017
Allina Health Group Quality Council Review: May 2017

SCOPE:

Sites, Facilities, Business Units	Departments, Divisions, Operational Areas	People applicable to
All Facilities that perform breast conserving therapy for invasive carcinoma; Abbott Northwestern Hospital, Buffalo Hospital, Cambridge Medical Center, District One Hospital, Mercy Hospital, New Ulm Medical Center, River Falls Area Hospital, Regina Hospital, St. Francis Medical Center, United Hospital	Breast Surgeons Pathology Radiation Oncology Medical Oncology	Physicians, Advanced Practice Providers

PICO(TS) FRAMEWORK

Population Invasive breast cancer patients undergoing breast conserving therapy

Intervention Management of surgical margins

Comparison n/a

Outcomes Ensure adequacy of tumor removal to reduce risk of recurrence

Timing During surgical procedure and subsequent pathologic review

Setting Hospitals where procedure is performed

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CLINICAL PRACTICE GUIDELINES:

1. **Wire or seed localization procedures will be utilized intraoperatively in non-palpable lesions, with confirmatory specimen radiographs obtained** to assess adequacy of removal of designated lesion.
2. **The surgeon will orient the lumpectomy margins** using the standard inking scheme (see below). **The surgeon will orient the mastectomy specimen** with a stitch at 12 o'clock.
3. **Specimens will be sent immediately to pathology for evaluation** of margins (for known cancers) and for handling of specimens according to ASCO/CAP guidelines.
 - a. If a pathologist is not available on site at the time of surgery, the surgeon is responsible for handling the specimen according to ASCO/CAP guidelines (see attached flow charts for mastectomies and lumpectomies).
4. **Invasive tumor at ink is considered a positive margin. All margins with invasive tumor at ink should be considered for re-excision.**
 - a. Exceptions may occur, and some margins may not be amendable to re-excision.
 - b. Clinical aspects including the age of the patient, location of involved margin, history of breast reconstruction, etc. may also influence the decision for re-excision.
 - c. If re-excision is not performed for positive margin, the reason should be documented in the medical record.
5. **Invasive tumor not at ink is considered a negative margin. However, re-excision of close margins <1 mm can be considered in some situations.** Some justifiable reasons include:
 - a. Residual malignant appearing calcifications on post-lumpectomy mammogram.
 - b. Ink-negative margin but close large volume of cancer involvement within 1 mm of the margin.
 - c. Ink-negative margin, but insidiously infiltrating tumor (such as invasive lobular carcinoma).
 - d. Fragmented lumpectomy specimens, or those that have not been appropriately inked, causing uncertainty of margin status.
 - e. If re-excision is performed for a negative margin the reason should be documented in medical record
6. **Close (<1 mm) margins should be discussed in a multi-disciplinary setting if concerns remain regarding margin status**

This recommendation is for invasive cancer and considers the evidence that there are many factors that affect local recurrence that are not altered by the margin status. These factors are related to characteristics such as family history, age, tumor size, grade, tumor

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type, receptor status and HER2 status. Tumor subtypes such as basal cancers are particularly known to have increased local recurrence rates. Additional factors such as lymphovascular invasion (LVI), extensive intraductal carcinoma (EIC), and nodal status may also affect local recurrence rates. Adjuvant therapy and hormonal therapy as well as radiation therapy all help reduce local recurrence rates.

SUPPORTING EVIDENCE:

Margin status is an important issue in the management of patients with breast cancer. The incidence of ipsilateral breast tumor recurrence (IBTR) in patients with breast cancer who undergo breast-conserving therapy (BCT) has been shown to be directly affected by margin status.

Re-excision of margins for both invasive breast cancer and ductal carcinoma in situ (DCIS) in clinical practice is determined by the closeness of the surgical resection margin. Controversy surrounds the recommendations for re-excision for both invasive carcinoma and DCIS since multiple factors including pathologic handling of specimens; tumor characteristics and biology can have an effect on local recurrence.

Intra-operative and pathologic examination of breast specimens has been standardized for Allina Health that are served by Hospital Pathology Associates (HPA). These include orientation of lumpectomy specimens intra-operatively by using a standardized multi-colored inking scheme (blue=superior, red=inferior, green=medial, yellow=lateral, orange=anterior, black=deep). All mastectomy specimens should be oriented with a stitch at 12 o'clock.

A standardized protocol developed by HPA for sectioning the lumpectomy and mastectomy specimens for gross assessment of margins is utilized on all specimens. Specimens are cut at approximately 0.5 cm sections along the long axis of the specimen. Shaved tangential margins are not used since this overestimates the “positive margin rate” and increases the likelihood of unnecessary re-excisions. Intra-operative touch preps are also not advocated for margin assessment because of inconsistent results. The pathologist evaluates the closeness of the margins on gross examination (and when necessary by frozen section). The decision for immediate re-excision is made by joint decision of the pathologist and surgeon. Final margin status for both invasive and non-invasive breast cancer is reported in pathology report for all 6 margins less than 1 cm from tumor.

Following gross evaluation, the specimens are placed in 10% neutral buffered formalin within 60 minutes from removal from the patient, and are fixed in formalin for a minimum of 6 hours, not to exceed 72 hours, according to American Society of Clinical Oncology (ASCO) and College of American Pathology (CAP) guidelines.

Scientific information regarding margin status and recurrence for invasive cancer include:

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1. In a review of over 5,000 patients, positive margins, defined as tumor on ink, were associated with a 16% IBTR compared to a 6% IBTR for negative margins defined as tumor not touching ink. (2)
2. NSABP trials (B-6, B-17, B-24) used a margin of tumor not touching ink as a definition of a negative margin. (1)
3. Margins of “tumor not touching ink” to margins of <1 mm for invasive cancer have not been shown to increase local recurrence compared to margins of 1 mm or greater (35).
4. Margins between 1 mm and 5 mm have similar LR rates. (2, 11)
5. Younger age (18), ER, PR and Her-2 status (7), size of tumor (14), “basal phenotypes” have all been associated with increased risk of local recurrence. And, tumors with "basal phenotypes" have also been found to recur earlier than “luminal” cancers. (9)
6. Presence of extensive intraductal component (EIC) associated with invasive cancer increases positive margin rate, risk of IBTR and requirement for re-excision. (7)
7. Breast conserving therapy without radiation therapy increases risk of local recurrence. (3,4,5,18,22,33)
8. HER-2 positive tumors have been found to be associated with increased local recurrence, which can be reduced by trastuzumab. (19, 20)
9. Adjuvant therapy and hormonal therapy reduce local recurrence rates of breast cancers. Additionally, the basal type of breast cancers has an increased local recurrence rate, which is reduced by adjuvant therapy. (9)
10. Many experts including surgeons and radiation therapists recommend margin of 1 mm and would recommend re-excision of margin <1 mm for invasive breast cancers. However, the latest SSO/ASTRO consensus did not support such practice (10)
11. Recommendation from national consensus panels suggests a 10-year LR goal of 5-10% (<1%/year).

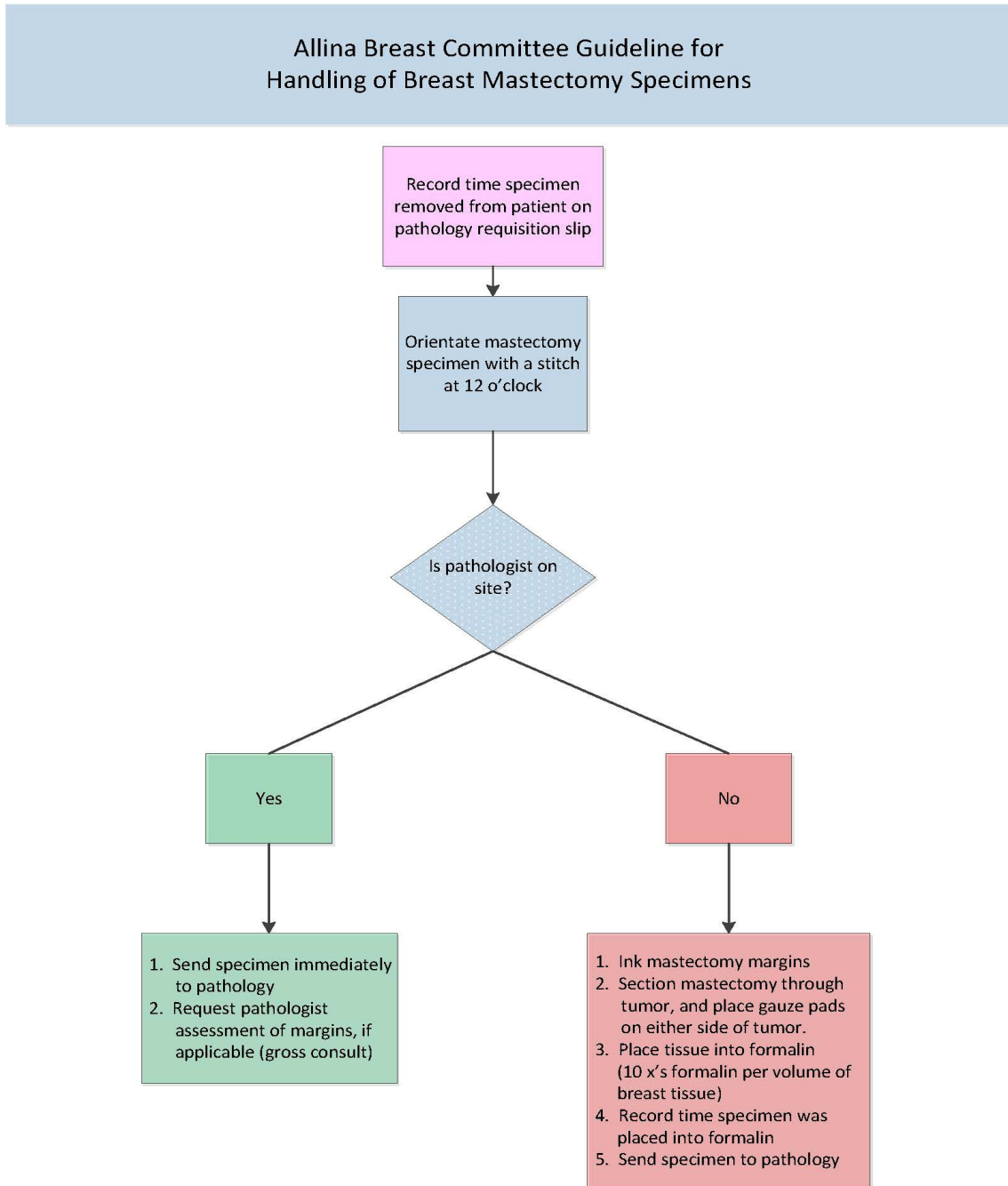
DEFINITIONS: N/A

SPECIAL ENTITIES: N/A

FORMS: N/A

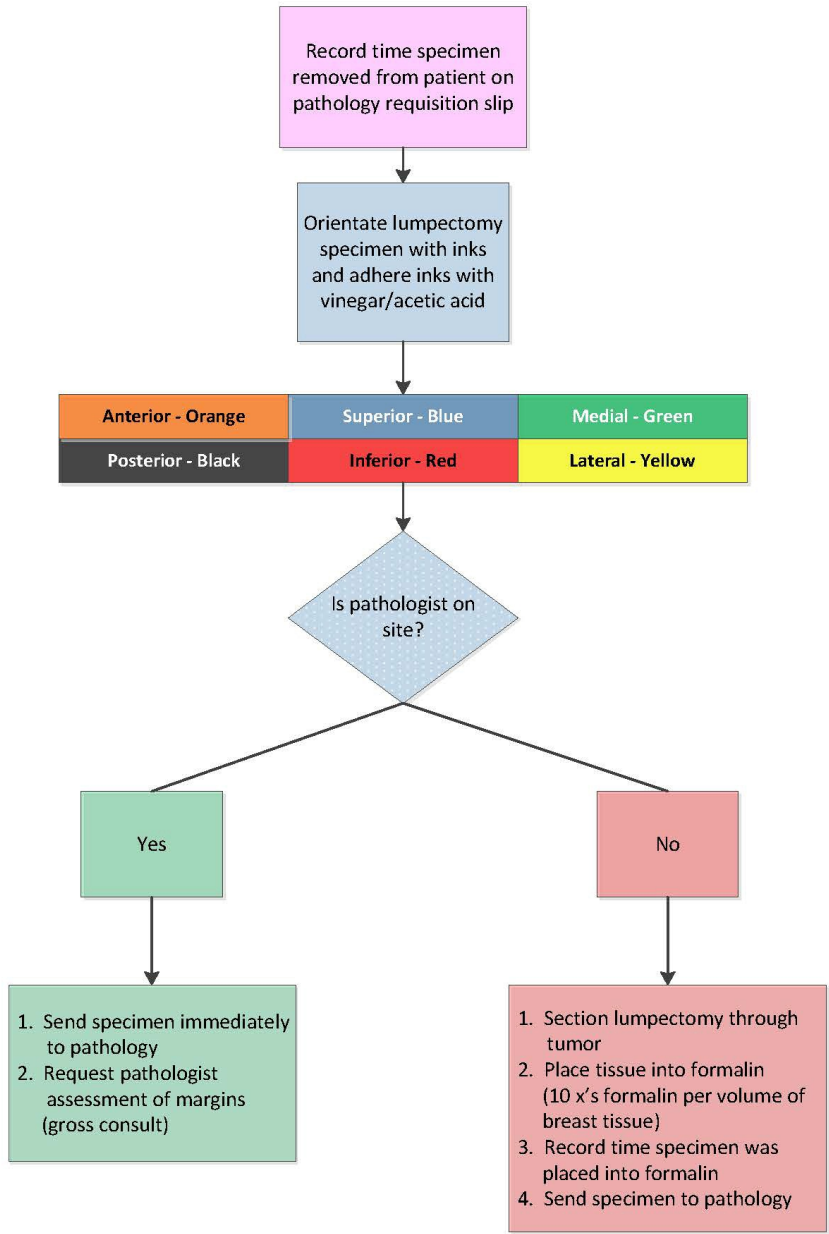
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ALGORITHM:



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**Allina Breast Committee Guideline for
 Handling of breast Lumpectomy Specimens**



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ADDENDUM:

Plan for Monitoring and Adherence

Who will be measured for guideline adherence?

- Breast Surgeons

What will be measured? Just in time monitoring will be performed to make certain appropriate handling of specimens is followed. Outliers will be addressed. And, re-excision rates will ultimately be gathered for surgeons.

Where is the data located? The data will be obtained from pathology reports, and additional information may be obtained from the surgeon's operative note.

How will the guideline adherence be monitored?

- It will be monitored through the Breast Program Committee

When will adherence data be collected? TBD – need the dashboard to be built

REFERENCES:

1. Morrow M. Breast conservation and negative margins: how much is enough? *Breast* 2009;18(S3):S84-6.
2. Singletary SE. Surgical margins in patients with early-stage breast cancer treated with breast conservation therapy. *Am J Surg* 2002;184:383-93.
3. Kumar S, Sacchini V. The surgical management of ductal carcinoma in situ. *Breast J* 2010;16(suppl 1):S49-S52.
4. Virnig BA, Tuttle TM, Shamlivan T, Kane RL. Ductal carcinoma in situ of the breast: a systematic review of incidence, treatment, and outcomes. *J Natl Cancer Inst* 2010;102:170-8.
5. Rudloff U, Brogi E, Reinger AS, Goldberg JI, Brockway JP, Wynveen CA, et al. The influence of margin width and volume of disease near margin on benefit of radiation therapy for women with DCIS treated with breast-conserving therapy. *Ann Surg* 2010;251(4):583-91.
6. Sanchez C, Brem RF, McSwain AP, Rapelyea JA, Torrente J, Teal CB. Factors associated with re-excision in patients with early-stage breast cancer treated with breast conservation therapy. *Am Surgeon* 2010;76:331-4.
7. Morrow M. Trends in the surgical treatment of breast cancer. *Breast J* 2010;16(suppl 1):S17-9.
8. Rudloff U, Jacks LM, Goldberg JI, Wynveen CA, Brogi E, Patil S, et al. Nomogram for predicting the risk of local recurrence after breast-conserving surgery for ductal carcinoma in situ. *J Clin Oncol* 2010;28(3):3762-9.
9. Millar EKA, Graham PH, O'Toole SA, McNeil CM, Browne L, Morey AL, et al. Prediction of local recurrence, distant metastases, and death after breast-conserving therapy in early-stage invasive breast cancer using a five-biomarker panel. *J Clin Oncol* 2009;27(28):4701-8.
10. Schwartz GF, Veronesi U, Clough KB, Dixon JM, Fentiman IS, Heywang-Kobrunner SH, et al. Consensus conference on breast conservation. *J Am Coll Surg* 2006;203(2):198-207.
11. Dunne C, Burke JP, Morrow M, Kell MR. Effect of margin status on local recurrence after breast conservation and radiation therapy for ductal carcinoma in situ. *J Clin Oncol* 2009;27(10):1615-20.

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12. McCahill LE, Privette A, James T, Sheehey-Jones J, Ratliff J, Majercik D, et al. Quality measures for breast cancer surgery, initial validation of feasibility and assessment of variation among surgeons. *Arch Surg* 2009;144(5):455-62.
13. Kaufman CS, Shockney L, Rabinowitz B, Coleman C, Beard C, Landercasper J, et al. National Quality Measures for Breast Centers (NQMBC): A robust quality tool. *Ann Surg Oncol* 2010;17:377-85.
14. Rausei S, Rovera F, Gianlorenzo D, Tornese D, Fachinetti A, Boni L, et al. Predictors of loco-regional recurrence and cancer-related death after breast cancer surgery. *Breast J* 2010;16(suppl 1):S29-33.
15. Kouzminova NB, Aggarwal S, Aggarwal A, Allo MD, Lin AY. Impact of initial surgical margins and residual cancer upon re-excision on outcome of patients with localized breast cancer. *Am J Surg* 2009;198:771-80.
16. Allegra CJ, Aberle DJ, Ganschow P, Hahn SM, Lee CN, Millon-Underwood, S, et al. National Institutes of Health State-of-the-Science Conference Statement: Diagnosis and management of ductal carcinoma in situ September 22-24, 2009. *J Natl Cancer Inst* 2010;102(3):161-9.
17. Dick AW, Sobrero MS, Ahrendt GM, Hayman JA, Gold HT, Schiffhauer L, 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.
18. Anderson SJ, Wapnir I, Dignam JJ, Fisher B, Mamounas EP, Jeong JH, et al. Prognosis after ipsilateral breast tumor recurrence and locoregional recurrences in patients treated by breast-conserving therapy in five national surgical adjuvant breast and bowel project protocols of node-negative breast cancer. *J Clin Oncol* 2009; 27(15):2466-73.
19. Romond EH, Perez EA, Bryant J, Suman VJ, Geyer CE Jr, Davidson NE. Trastuzumab plus adjuvant chemotherapy for operable HER2-positive breast cancer. *N Engl J Med* 2005;353(16):1673-84.
20. Wiechmann L, Sampson M, Stempel M, Jacks LM, Patil SM, King T, Morrow M. Presenting features of breast cancer differ by molecular subtype. *Ann Surg Oncol* 2009;16:2705-10.
21. Wright MJ, Park J, Fey JV, Park A, O'Neill A, Tan LK, et al. Perpendicular inked versus tangential shaved margins in breast-conserving surgery: does the method matter? *J Am Coll Surg* 2007;204:541-9.
22. Clarke M, Collins R, Darby S, Davies C, Elphinstone P, Evans E, et al.; 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 randomized trials. *Lancet* 2005;366:2087-106.
23. Fisher B, Dignam J, Wolmark N, et al. Tamoxifen in treatment of intraductal breast cancer: National Surgical Adjuvant Breast and Bowel Project B-24 randomised controlled trial. *Lancet* 1999;353:1993-2000.
24. Silverstein MJ, Lagios MD, Groshen S, Waisman JR, Lewinsky BS, Martino S, et al. The influence of margin width on local control of ductal carcinoma in situ of the breast. *N Engl J Med* 1999;340:1455-61.
25. Wong JS, Kaelin CM, Troyan SL, Gadd MA, Gelman R, Lester SC, et al. Prospective study of wide excision alone for ductal carcinoma in situ of the breast. *J Clin Oncol* 2006;24:1031-6.
26. Horiguchi J, Lino U, Takei J, et al. Surgical margin and breast recurrence after breast- onserving therapy. *Oncol Reports* 1999;6:135-8.

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27. Vicini FA, Kestin LL, Goldstein NS, et al. Relationship between excision volume, margin status, and tumor size with the development of local recurrence in patients with ductal carcinoma in situ treated with breast-conserving therapy. *J Surg Oncol* 2001;76:245–54.

28. Fisher ER, Costantino J, Fisher B, et al. Pathologic findings from the National Surgical Adjuvant Breast Project (NSABP) Protocol B-17. *Cancer* 1995;75:1310–9.

29. Holland PA, Gandhi A, Knox WF, et al. The importance of complete excision in the prevention of local recurrence of ductal carcinoma in situ. *Br J Cancer* 1998;77:110–4.

30. Cheng L, Al-Kaisi NK, Gordon NG, et al. Relationship between the size and margin status of ductal carcinoma in situ of the breast and residual disease. *J Natl Canc Inst* 1997;89:1356–60.

31. Fowble B, Hanlon MS, Fein DA, et al. Results of conservative surgery and radiation for mammographically detected ductal carcinoma in situ. *Int J Radiat Oncol Biol Phys* 1997;38:949–57.

32. Weng EY, Juillard GJF, Parker RG, et al. Outcomes and factors impacting local recurrence of ductal carcinoma in situ. *Cancer* 2000;88:1643–9.

33. Solin LJ, Fourquet A, Vicini FA, et al. Mammographically detected ductal carcinoma in situ of the breast treated with breast-conserving surgery and definitive breast irradiation: long-term outcome and prognostic significance of patient age and margin status. *Int J Radiat Oncol Biol Phys* 2001;50:991–1002.

34. Tartter PI, Kaplan J, Bleiweiss I, et al. Lumpectomy margins, reexcision, and local recurrence of breast cancer. *Am J Surg* 2000;179:81–5.

35. Moran MS, Schnitt SJ, Giuliano AE, Harris JR, Khan SA, Horton J, Klimberg S, Chavez-MacGregor M, Freedman G, Houssami N, Johnson PL, Morrow M. Society of Surgical Oncology–American Society for Radiation Oncology Consensus Guideline on Margins for Breast-Conserving Surgery With Whole-Breast Irradiation in Stages I and II Invasive Breast Cancer. *J Clin Oncol* 2014 jco.ascopubs.org/cgi/doi/10.1200/JCO.2013.53.3935

Alternate Search Terms: N/A

Related Guidelines/Documents

Name	Content ID	Business Unit where Originated
Ductal Carcinoma In Situ (DCIS): Management of Surgical Margins and Recommendations for Margin Re-excisions in Patients Having Breast Conserving Therapy	SYS-PC-OCSL-CG-005	System-wide

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