

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 are not clearly desirable for all patients

Origination Date: June 2011
Next Review Date: August 2017
Effective Date: August 2011

Approved Date: 6/2011, 8/2014 Approval By: Allina Health Breast Program Committee

System-wide Information Resource: Director of Clinical Programs

SCOPE:

Sites, Facilities, Business Units	Departments, Divisions, Operational Areas	People applicable to (Physicians, NP, Administration, Contractors etc.)
Allina – all facilities	Breast Surgeons, Pathology, Radiation Oncology, Medical Oncology	MD, NP, PA

CLINICAL PRACTICE GUIDELINES:

- 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.
- The surgeon will orientate the lumpectomy margins** using the standard inking scheme (see below). **The surgeon will orientate the mastectomy specimen** with a stitch at 12 o'clock.
- Specimens will be sent immediately to pathology for evaluation** of margins (for known cancers) and for handling of specimens according to ASCO/CAP guidelines.
- Invasive tumor at ink is considered a positive margin. All margins with invasive tumor at ink should be considered for re-excision.**

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- 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 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 Hospitals & Clinics that are served by Hospital Pathology Associates (HPA). These include orientation of lumpectomy specimens intra-operatively by using a standardized multi-colored

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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:

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 pheontypes" 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)

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9. Adjuvant therapy and hormonal therapy reduce local recurrence rates of breast cancers. Additionally, the basal type of breast cancers has an increase 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. (10)
11. Piper Breast Center and Abbott Northwestern Pathology group have used <1 mm margin for recommendation for re-excision for invasive cancer for 13 years. PBC five-year LR rate for 325 patients following lumpectomy and radiation therapy for T1 and T2 tumors was 5%.
12. Recommendation from national consensus panels suggests a 10-year LR goal of 5-10% (<1%/year).

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