



POSITION STATEMENT ON BREAST CANCER LUMPECTOMY MARGINS

Breast-conserving surgery (BCS) with partial mastectomy is an option for the treatment of patients with invasive or in situ breast carcinoma. The presence or absence of malignant cells on the edge or close to the edge of a partial mastectomy specimen is called the surgical margin status. This margin status serves as a surrogate marker of residual disease in the breast and has an impact on patient risk of in-breast tumor recurrence (IBTR). There is evidence of significant variation in margin definitions, positive margin rates, and re-excision lumpectomy rates (RELR) in patients undergoing BCS.¹⁻¹⁵ Surgeon opinion of a negative surgical margin ranges from “ink negative” to greater than 1 cm, providing one potential explanation for variation in surgical re-excision rates.^{1-4,8-10,12,15-18} This position statement summarizes the current evidence in this controversial field and recommends an algorithmic approach toward assessing surgical margins.

Surgical Approach and Specimen Handling

Indeterminate, high-risk, or confirmed breast cancer tissue specimens should have margins oriented intraoperatively by the surgeon, accompanied by clear communication with pathology and radiology.¹⁹⁻²² After the surgeon orients the specimen, the surgeon or pathologist should ink the margins to identify the surfaces of the excised specimen. The operative report should document whether the specimen and fascia was removed from the muscle. The removal of any skin should also be noted. Nonpalpable, image-detected lesions require radiographic confirmation of excision by mammogram or ultrasound (US) to confirm removal of the targeted lesion.²⁰⁻²³ Resultant specimen imaging findings should be communicated intraoperatively to the surgeon and should also be available for the pathologist. The pathologist should document grossly and microscopically the orientation, and distance and extent of involvement between the invasive and in situ cancer for each specific margin, compliant with the College of American Pathologists (CAP) breast cancer reporting protocol.²⁴

Multiple techniques have been described to reduce the chance of microscopically positive lumpectomy margins, including, but not limited to (1) radioactive seed localization instead of wire guidance, (2) routine or selective cavity shave excisions, (3) hematoma ultrasound (US)-guided excisions, (4) intraoperative US by surgeon, (5) large-volume oncoplastic lumpectomy or reduction mammoplasty procedures, and (6) immediate intraoperative margin assessment with frozen section (FS) or touch prep analysis (TP).^{13,25-31} There are limitations of FS of fatty tissue and there is a need for cytopathology expertise if TP is performed. Not all of these techniques are universally available and they have not been compared to each other for effectiveness.

Positive Margin

Patients with invasive or in situ breast carcinoma with histologic positive margins (ink positive) after lumpectomy have increased IBTR compared to patients with negative margins.^{1,6,7,9,10,32} IBTR and local regional recurrence (LRR) after BCS for invasive cancer can influence patient survival. The Early Breast Cancer Trialists Collaborative Group (EBCTCG) concludes that 1 life is saved at 15-year follow-up for every 4 local recurrences prevented by 10 years after lumpectomy.³³ Re-excision to achieve negative margins is therefore desirable and should be performed in most patients with ink-positive margins. Many factors, including patient age, co-morbidities, life expectancy, extent of excision, extent of margin involvement, tumor characteristics, and whether the patient will receive adjuvant therapies, should be taken into account before proceeding with re-excision. The “margin index,” based on margin status and tumor extent at the margin, may assist prediction of residual malignancy in the breast.^{34,35} National Comprehensive Cancer Network (NCCN) guidelines state, “It may be reasonable to treat selected cases with breast conserving therapy with a microscopically focally positive margin in the absence of an extensive intraductal component. For these patients, the use of a higher radiation boost dose to the tumor bed should be considered.”¹⁶ Re-excision may not be necessary for involved anterior and posterior margins if underlying muscle fascia or overlying skin has been removed. If re-excision is not performed for a positive margin, then the reason should be documented in the medical record.

Negative Margin

When margins are ink-negative, there is variation of opinion of adequacy of margin width that does not require re-excision, resulting in differences of definition and practice among surgeons, pathologists, and radiation oncologists.^{2,3,8,9,12,15} In the 1970s, the National Surgical Adjuvant Breast and Bowel Project (NASBP) B-06 study defined a negative margin as no tumor cells found on the inked edge of a surgical specimen.³⁶ In a recent meta-analysis, the effect of margin status and margin distance on IBTR in patients with early-stage invasive breast cancer was evaluated in 21 studies that identified 1026 local recurrences in 14,571 patients.⁶ The odds ratio for recurrence was 2.42 ($P < 0.001$) for positive vs negative margins. Greater radial width of a negative margin had borderline significance for improvement in LRR for 1 mm compared to wider margins, but no significance when adjusted for patients receiving a radiation boost or endocrine therapy.⁶ Another meta-analysis from trials evaluating BCS and radiation therapy for DCIS in 4,660 patients concluded that a 2-mm margin was not associated with decreased IBTR, compared to more than 2 mm.⁷ Current NCCN guidelines for DCIS state, “margins less than 1 mm are considered inadequate. However, close surgical margins (<1 mm) at the fibroglandular boundary of the breast (chest or skin) do not mandate surgical re-excision but can be an indication for higher boost dose radiation to the involved lumpectomy site.”¹⁸ The value of re-excision is unclear after BCS for patients with invasive breast cancer when margins are negative, but close (<1-2 mm) if these patients receive appropriate adjuvant radiation and systemic therapies.⁹ Re-excision can be considered for this group, but current evidence does not support mandatory re-excision. If re-excision is performed for a negative margin, then the reason for re-excision should be documented in the medical record. Justifiable reasons could include, but are not limited to (1) residual adjacent malignant appearing calcifications identified on post-lumpectomy mammography, (2) an ink-negative margin but proximate “large” volume cancer involvement within 1-2 mm of the margin, and (3) fragmented lumpectomy specimens, causing uncertainty of margin status. Avoiding re-excisions to obtain wider margins in patients with documented negative margin status can potentially lower RELR nationally.⁹

Tumor biology, adjuvant treatment, and surgical margins all contribute to recurrence risk

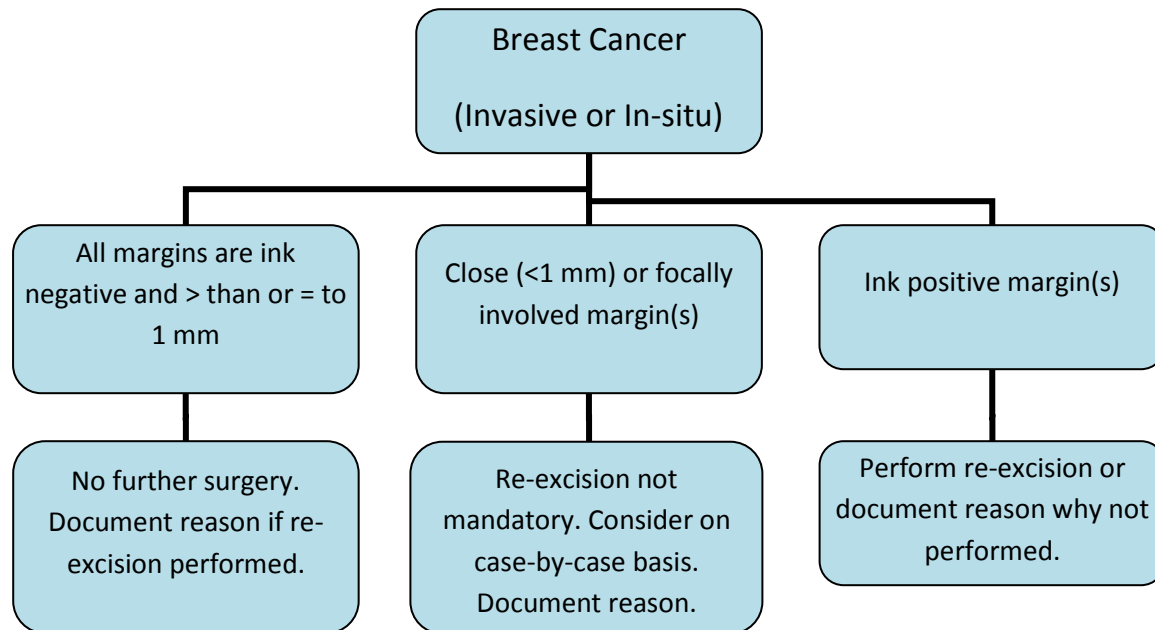
Future comparative effectiveness research regarding lumpectomy tissue processing, margin status, margin width, and subsequent effects on IBTR are encouraged, but margin status is not the only determinant of LRR. Historically the risk of IBTR has been decreasing, probably due more to improved adjuvant treatments than to changes in patient management regarding margin status, because re-excision of ink-positive margins has been usual practice for decades. With better understanding of the influence of molecular and genomic profiling on tumor behavior and the introduction of targeted therapies, width of negative margin status becomes only one of many factors that govern local recurrence. Moreover, it is widely recognized that not all breast cancer is removed in many patients undergoing BCS, even with negative margins. Histopathology research demonstrates that only about one third of breast cancers are unifocal; the rest are multifocal or diffuse.^{37,38} Breast MRI finds some of these cancers. Comprehensive histology finds even more. These extra sites of cancer are usually controlled with adjuvant therapies, as evidenced by the low IBTR in trial patients receiving adjuvant endocrine therapy, chemotherapy, and radiation therapy after lumpectomy.^{33,39-42}

Is re-excision lumpectomy rate a measure of quality?

The use of margin status and RELR as a measure of quality is controversial.^{4,9,14,15} RELR ranges from 0% to 70% (by individual surgeon) in the United States.⁴ Recent publications also document wide variability in Canada (17-56% by province) and England (12%-30% by National Health Service trust)^{14,15} The European Society of Breast Cancer Specialists (EUSOMA), the National Consortium of Breast Centers (NCBC), and multiple institutions use RELR as a quality measure (QM).^{4,14,15,43-47} Arguments against the use of RELR as a QM include (1) the lack of evidence defining the minimum or optimal quality threshold for RELR, and (2) the concern that unintended adverse consequences may occur if the importance of RELR is elevated too high by using it as a QM. For example, surgeons may demonstrate “risk aversion,” changing their criteria for eligibility for breast-conserving therapy, in patients with inherently high risk for positive margins, increasing mastectomy rates, in their effort to lower RELR. Surgeons may also potentially increase their lumpectomy excisional volume, worsening cosmesis. Despite these concerns, RELR as a QM is already in use as referenced above. The American Society of Breast Surgeons advises caution in the use of RELR as a QM. If RELR is used as a quality measurement tool, then it should be incorporated into a program that simultaneously measures other aspects of BCS quality, such as cosmetic outcome, patient satisfaction, IBTR, and breast-conserving therapy rate.^{15,47,48} International variability of the performance of RELR deserves investigation, but RELR should not be used as the singular determinant of the quality of BCS.

The following algorithm is proposed, based on best available data and recognition of the controversy surrounding surgical margin status:

Re-excision not mandatory. Consider on case-by-case basis. Document reason.



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This statement was developed by the Society's Research Committee and on January 16, 2013, was approved by the Board of Directors.