

# Intraoperative Margin Assessment in Breast Cancer Management



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## KEYWORDS

- Breast cancer • Breast-conserving surgery • Breast-conserving therapy
- Lumpectomy • Re-excision • Margin • Intraoperative assessment

## KEY POINTS

- Rates of margin re-excision vary widely in the literature.
- Efforts to reduce re-excision rates must begin at the time of diagnosis with high-quality imaging, minimally invasive breast biopsy, and multidisciplinary planning.
- A variety of techniques to reduce rates of re-excision have been described; however, careful tracking of re-excision rates and cosmetic outcomes must be undertaken when using these techniques.

## INTRODUCTION: NATURE OF THE PROBLEM

Numerous trials have demonstrated equivalent survival outcomes for mastectomy and breast-conserving therapy (BCT) in early-stage breast cancer.<sup>1–6</sup> For patients with unifocal, early-stage breast cancer, BCT is often the preferred treatment. The goal of breast-conserving surgery (BCS) is to excise the tumor with negative margins while providing satisfactory cosmesis. Positive margins after BCS represent a significant risk factor for recurrence and patients with positive margins have rates of ipsilateral breast tumor recurrence twice those of patients with negative margins.<sup>7</sup> Patients who choose to undergo BCT are counseled about the possibility of having to return to surgery for re-excision of positive or close margins. The rates of re-excision reported in the literature range from less than 10% to greater than 50%.<sup>8–15</sup> Importantly, this variability is not explained by characteristics of either the patients or their disease.

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Achieving a negative margin at initial surgical intervention spares patients from undergoing additional operative intervention, thus sparing patients additional cost and risk. A return to the operating room for margin re-excision results in additional exposure to the risks of anesthesia, increased surgical complications including increased surgical site infections, increased health care costs, and even increased conversion to bilateral mastectomies.<sup>16–19</sup>

The definition of a negative margin has varied widely over time and across practices. The National Surgical Adjuvant Breast and Bowel Project B-06 trial defined a negative margin as “no ink on tumor,” whereas the Milan trials required quadrantectomy with a 2-cm to 3-cm gross margin.<sup>1,2</sup> For patients undergoing BCS, the margin width required for a negative margin has varied widely in clinical practice.<sup>20,21</sup> These different definitions of margin negativity influence re-excision rates. The Society of Surgical Oncology–American Society for Radiation Oncology (SSO-ASTRO) consensus guideline on margins for BCS with whole-breast irradiation in patients with stages I and II invasive breast cancer suggest that “no ink on tumor” be considered the standard for a negative margin.<sup>22</sup> This guideline is based on 33 studies that included more than 28,000 patients with analysis failing to indicate an association between increased margin width and decreased risk of local recurrence. Some investigators have suggested, however, that physicians should consider each case individually, taking into account clinical, pathologic, and treatment variables to determine the need for re-excision rather than using solely margin width.<sup>23</sup> Soon after publication of the guideline, a survey of members of the American Society of Breast Surgeons revealed that a majority of surgeons did not perform re-excision of margins when tumor was not touching the inked margins, but for more complex margin scenarios individual surgeon judgment was used to determine if re-excision was needed.<sup>24</sup> The recently published SSO-ASTRO–American Society of Clinical Oncology consensus guideline on margins for BCS with whole-breast irradiation in patients with ductal carcinoma in situ (DCIS) suggested that a 2-mm margin be considered the standard for a negative margin in these patients.<sup>25</sup> This guideline is based on 20 studies that included 7883 patients with analysis indicating that a 2-mm margin decreased the risk of local recurrence in comparison to smaller margins.

Although eliminating re-excisions for patients undergoing BCS is not feasible, several intraoperative margin assessment strategies are available to reduce the need for re-excision. It is important to recognize, however, that this effort must start at the time of diagnosis. High-quality diagnostic mammography must be performed with supplemental imaging when necessary, the diagnostic biopsy should be obtained in a minimally invasive manner, and multidisciplinary discussions should be undertaken especially for those patients receiving neoadjuvant therapy.<sup>26</sup>

## PREOPERATIVE LOCALIZATION

Since the introduction of the SSO-ASTRO guideline of “no ink on tumor,” attention to margin status has increased, particularly in regards to intraoperative techniques.<sup>22</sup> Breast cancers removed by segmental mastectomy most commonly require preoperative localization to identify the lesion to be removed. After resection, regardless of which preoperative localization modality is used, meticulous attention to proper specimen orientation is critical. It is recommended that 3 or more margins are labeled to ensure accuracy and improve results.<sup>26</sup> Positive margins increase the risk of local recurrence and proper preoperative localization is critical to ensuring complete excision.<sup>22,27</sup> A variety of techniques to localize breast lesions have been implemented, ranging from needle localization to radioguidance to electromagnetics.

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