

Does Gross Margin Examination Reduce Re-excision Rate in Breast Conservation for Invasive Carcinoma? CALLER Review

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ABSTRACT

Objective: Determine if Gross Margin Examination reduces margin re-excision rate. Our institutional practice is to perform Gross Margin Examination (GME) with Real-time re-excision (RRE) for all breast conservation specimens with Invasive Carcinoma.

Materials and Methods: Chart review was done to determine if this practice is helpful. 51 CALLER charts were reviewed from December 2016 to December 2017.

Results: Thirty-three underwent margin RRE based on the GME. 11 had cancer in the re-resected margin, 6 of which were cleared with the RRE. The other 5 were reoperated on to clear the margin because on final pathology a margin other than the re-resected margin was positive for malignancy. GME was helpful in preventing reoperation in 55%. None of the remaining 22 patients receiving were found to have a positive margin on final pathology, with 1.6 margins on average re-resected. 13/18 patients did not have RRE and had a final clear margin, but of the other 5, final margin was positive for DCIS in 2 and Invasive Cancer in 3. GME missed invasive disease at the margin in 3 of these 18 patients.

Conclusion: GME was helpful in preventing reoperation in 6 of 11 patients who would have had a positive margin. However, this resulted in the unnecessary removal of additional normal breast tissue in 22 patients. 3 patients' positive margins were missed with GME and required reoperation. 13 patients were able to avoid re-excision and 11 were able to clear their margin in real-time, improving outcomes 24/51 patients. GME therefore does appear useful.

Keywords: CALLER, gross margin examination, re-excision

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Introduction

Breast-conserving surgery (BCS) is the established standard approach for women with early-stage invasive breast cancers. During BCS, the breast tumor is excised with negative margins, yielding a better cosmetic result. Various factors are associated with tumor recurrence after BCS, including margin status, which has been shown to be a very important prognostic factor for local recurrence (1). A positive margin is correlated with a twofold increase in ipsilateral breast tumor recurrence (2). This risk is not completely eliminated with the addition of local or systemic adjuvant therapy. In addition, patients who develop local recurrence have an increased risk of distant disease, which can impact survival (3).

Delays in adjuvant therapy can also occur when additional surgical procedures are needed to obtain clear margins after breast conservation. Cosmesis is also impacted, and up to 50% of patients requiring multiple re-excisions will opt for completion mastectomy (4, 5).

The assessment of lumpectomy margins is an ongoing issue for breast surgeons. Various techniques and technology have been utilized in an attempt to reduce margin re-excision rates. These include imaging techniques such as margin scans, and specimen radiograph and pathological assessment such as frozen section or cytology. To date, none of these intraoperative approaches have been successful in reliably identifying clear margins, resulting in a global re-excision rate of approximately 25% (6). Intraoperative pathologic techniques have the highest sensitivity and specificity on meta-analysis (7).

The simplest intraoperative pathological technique for evaluating lumpectomy margins is examination of the specimen for gross evidence of the tumor. This method is quick, inexpensive, simple, and any additional suspicious margins can be immediately resected.

We sought to determine if our institution's protocol for intraoperative gross margin assessment was successful in reducing the number of patients requiring re-operation.

Materials and Methods

In 2015, the American Society of Breast Surgeons held a multidisciplinary consensus conference entitled a "Collaborative Attempt to Lower Lumpectomy Reoperation rates" (CALLER) and composed a "toolbox" of options to reduce lumpectomy reoperations (8). They then offered surgeons the opportunity to participate in the CALLER Registry, a one-year period during which patients undergoing breast conservation were entered into a special section of the Mastery of Breast Surgery where certain data points regarding re-excision were captured. We performed a retrospective analysis of our institution's patients entered in the CALLER registry during this time.

The most recent consensus for a clear margin for invasive cancer is "no tumor on ink," and this was utilized as our definition of a clear margin for patients with invasive disease (9). We reviewed the operative notes and surgical pathology for all CALLER registry patients. Notation was made regarding the results of intraoperative margin assessment as well as whether reoperation was needed, and why.

Table 1. Patient cohort

Number of patients	51
Median age group	60-69
Median tumor size group (mm)	10-19 mm
ER positivity	43 (84%)
Triple negative	5 (10%)

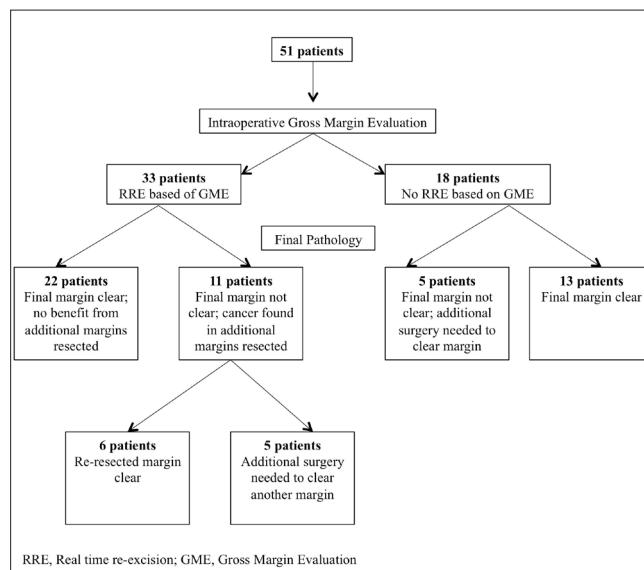


Figure 1. Summary of patient outcomes following gross margin evaluation

Our institutional standard of care is to perform gross margin evaluation (GME) of all lumpectomy specimens done for invasive breast cancer. Each lumpectomy specimen is removed, marked with sutures for orientation, and sent fresh to the pathologist for examination. All lumpectomy specimens were evaluated by a single pathologist. The pathologist inks and sections the specimen. The sections are grossly examined to determine if the tumor appears to be close to or abutting a margin. The pathologist then calls into the operating room and reports the findings, making a recommendation about any margins that might grossly appear to benefit from re-excision. No tissue is frozen or evaluated microscopically. Based on this evaluation, additional margins may be re-resected in real time (RRE) in hopes of avoiding a second operation.

Results

A total of 61 patients were entered into the CALLER Registry from December 2016 to December 2017. 10 of these patients were excluded because they had pure DCIS, resulting in a total of 51 cases of invasive disease analyzed for review. Information on the patient cohort is provided in Table 1.

Of these 51 patients, 33 (65%) underwent margin RRE based on the results of the GME. 11 were found to have cancer in the newly resected margin, and 6 of these had the margin cleared with the RRE. However, the other 5 required a second surgical procedure to completely clear the margins. In all 5 cases this was due to a positive margin other than the one re-excised based on GME based on final pathology. Thus, the GME was helpful in preventing a second operation in only 6 of the 11 patients who had a real-time re-excision.

However, of the other 22 patients who were recommended for and received RRE based on GME, none were found to have a positive margin on the final pathology. The average number of margins resected on these patients was 1.6 as the majority had 1 or 2 margins resected. Thus, the GME did not actually improve the outcome for these patients and increased tissue removed and operative time.

Therefore, of the 33 patients who did receive RRE based on GME, only 6 (18%) of these received a true benefit from the protocol.

Conversely, 18 patients were not recommended to undergo RRE based on GME. Of these patients, the margin was clear on final pathology report in 13 (72%). However, the remaining 5 patients were found to have positive margins at final pathology. Two of these were for DCIS and 3 were for invasive cancer. All but one underwent additional surgery to clear the margins (this patient's margin was anterior and beneath de-epithelialized skin so was felt not to be a candidate for re-excision). Consequently, 3/18 (17%) of patients with invasive disease at the margin were missed during GME.

Overall, of the 51 patients who underwent gross margin evaluation, a total of 19 patients (37%) benefitted from intraoperative gross margin evaluation. This includes the 6 out of 33 patients who underwent RRE based on GME and had a true benefit, and the 13 out of 18 patients who were correctly not recommended for RRE based on GME (Figure 1).

Discussion and Conclusion

Ongoing efforts to decrease the rate of positive margins for patients have been challenging and despite several techniques being explored worldwide, the positive margin continues to be a struggle for patients

who choose breast conservation. Patients must then undergo additional surgical procedures which may reduce cosmesis or delay adjuvant therapy. A number of methods of reducing re-excision rates have been developed. Our institution has a longstanding practice of intraoperative gross margin evaluation with real-time re-excision based on the findings. In our experience, this process does decrease the need for a return to operating room for re-excision for those with invasive disease. A margin positive for DCIS presents an even greater challenge because it is not visualized on GME.

We performed an analysis using data collected from our Mastery of Breast Surgery CALLER registry to determine whether GME reduces re-excision rates for invasive carcinoma. Our analysis revealed an 18% reoperation rate, which compares favorably with other studies, and is below the reported national database average of 25% (6). Balch and colleagues reported a 25% re-excision rate with gross margin assessment, with tumors <2 mm from a margin considered as margin positive (10). Fleming et al. (11) reports a lower re-excision rate of 9.1% with utilization of gross margin assessment, adopting a margin of 10 mm as an acceptable margin. Differences in definitions of margin negativity may influence re-excision rates.

Other intraoperative pathological techniques include frozen section analysis (FSA) of biopsies or cytological examination. A recent systematic review of the literature reported lower re-excision rates with FSA (12). However these methods are more time-consuming, and require further technology or training that may not be necessary if a low margin-positive rate can be achieved with gross evaluation alone.

Ultimately, the use of gross margin examination with real-time re-excision is not as foolproof and helpful as hoped. It may result in excess tissue removal and increased operative time. Additionally, the specimen needs to be directly transferred to the pathology department for real-time consultation, which is not available in every institution. It also depends on reliable orientation of the specimen by the surgeon to ensure that the correct margin is being excised; incorrect orientation has been shown to lead to incomplete resection (13).

Therefore, each surgeon should consider this option and discuss whether it would be helpful in their institution. Because at least 37% of our patients did benefit from this process, we do plan to continue our current practice of intraoperative gross margin evaluation and remain mindful of its limitations.

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