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Review of Third and Fourth Re-Excision for Narrow or Positive Margins of Invasive and Intraductal Carcinoma

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The trend in breast surgery has shifted toward breast conservation. We reviewed our third and fourth breast re-excision cases, with an analysis of various factors used in making this decision. A retrospective analysis identified 585 patients who underwent re-excision surgery for positive or close margins of invasive carcinoma or ductal carcinoma *in situ* (DCIS). Of these patients 75 (13%) and 17 (3%) underwent third and fourth re-excisions, respectively. The indication for a third re-excision was the presence of positive and/or close (≤1 mm) margins for invasive carcinoma or DCIS in 72/75 patients. A third re-excision was done 31 days (range 8–123 days) after the second re-excision. Re-excision of margins was done in 45 (60%) patients, whereas 30 (40%) patients underwent mastectomy. Residual tumor mandated a fourth re-excision in 17 patients, which was done 45 days (range 14–87 days) after the third surgery. Re-excision of margins was done in 6 patients, whereas 11 patients underwent mastectomy. Involved or close margins with DCIS were the most common indication for re-excision, accounting for 61/75 (82%) of third and 16/17 (94%) of fourth re-excisions. Histopathology revealed that 28/75 (37%) of third and 7/17 (41%) of fourth re-excision patients had no residual tumor. In conclusion, the majority of re-excisions was done for margins <1 mm. Lower rates of re-excision were noted in well-differentiated invasive carcinomas. A close or involved DCIS margin was more likely to lead to a third and even a fourth re-excision. The absence of residual tumors in 40% of patients undergoing third and fourth re-excisions calls for a review of margin guidelines for breast re-excision.

Key words: Re-excision – Breast – *In situ* carcinoma

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Breast conservation therapy has been established as an appropriate alternative to mastectomy in early-stage invasive cancers as well as ductal carcinoma *in situ* (DCIS). Breast conservation surgery combined with radiation therapy has shown to result in survival rates that compare favorably with modified radical mastectomy.[1]

The margin status in breast-conserving treatment of early-stage breast cancer is important. In general most would agree that negative margins are preferable to close or positive margins. In most series, the risk of ipsilateral breast tumor recurrence after breast-conserving surgery and radiotherapy has been shown to be 2 to 3 times greater in the presence of a positive or close (<2 mm) margin compared with negative margins. However, many other series have not found an increased risk of ipsilateral breast tumor recurrence with a close compared with a negative margin.[2]

Studies have reported different re-excision rates and factors leading to them. A fine balance needs to be maintained between cosmesis and excision of the tumor. Too much excision will ensure removal of tumor and lesser chance of necessity of re-excision, but will affect the cosmesis. Patients have needed multiple re-excision surgeries because of positive or near margins. We reviewed our third and fourth breast re-excision cases, with an analysis of various factors used in making this decision.

Materials and Methods

A retrospective analysis of 3246 patients was done who underwent either a lumpectomy for a palpable mass or a needle localization biopsy. These surgeries were performed by 8 general surgeons during a 5-year period between January 2003 and December 2007. We identified 585 patients who needed a re-excision surgery because of their margin status. On further analysis of these patients we found 75/585 (13%) and 17/585 (3%) patients who underwent third and fourth re-excisions, respectively. These patients formed our study group.

Involved (positive) margins were defined as tumor cells (either focal or extensive) directly at the cut edge of the specimen. Close margins were defined as tumor cells <2 mm from the cut edge of the specimen. Residual disease was defined as the persistence of invasive or intraductal carcinoma in the re-excision or mastectomy specimen.

Results

In the 585 patients who needed re-excision the mean patient age was 59 years (range 25–93 years). Needle localization was used to guide initial excision in the majority of patients [372/585 patients (64%)]. Four hundred twenty-four patients underwent re-excision of margins, whereas 168 underwent mastectomy as the second surgery.

Invasive carcinoma was seen in 69% (n = 402), which included 308 patients who had both invasive carcinoma. Thirty-one percent (n = 183) of the patients had DCIS only. Moderately or poorly differentiated carcinomas accounted for most of the re-excisions (76%; n = 258) when compared to well-differentiated carcinomas (24%; n = 78). Comedo necrosis was seen in 64 (35%) patients with DCIS only and in 140 (45%) patients with invasive and *in situ* carcinoma with DCIS. Tumor size ranged from 0.1 to 6 cm, with the majority being <2 cm (51%).

Residual invasive carcinoma and DCIS was seen in 31% and 50%, respectively. Residual invasive carcinoma was seen more when lumpectomy (68%) was the initial surgery compared with residual intraductal carcinoma, in which the majority was seen when needle localization surgery (57%) was the initial surgery. Residual carcinoma was seen in 75 of 198 (38%) patients with involved margins, compared with 26 of 109 patients (24%) with <1 mm margins and only 8 of 67 patients (12%) with >1 mm margins. The figures for residual DCIS were 65% of patients with involved margins, 50% with <2 mm margins, and 35% with 2 to 5 mm margins.

In the 75 patients who underwent third and fourth re-excision, the mean patient age was 57 years (range 33–87 years). The indication for a third re-excision was the presence of positive and/or close (≤1 mm) margins for invasive carcinoma or DCIS in 72/75 patients. A third re-excision was done 31 days (range 8–123 days) after the second re-excision. Re-excision of margins was done in 45 (60%) patients, whereas 30 (40%) patients underwent mastectomy. Residual tumor mandated a fourth re-excision in 17 patients, which was done 45 days (range 14–87 days) after the third surgery. Re-excision of margins was done in 6 patients, whereas 11 patients underwent mastectomy. Involved or close margins with DCIS were the most common indication for re-excision, accounting for 61/75 (82%) of third and 16/17 (94%) of fourth re-excisions. Histopathology revealed that 28/75 (37%) of third and 7/17 (41%) of fourth re-excision patients had no residual tumor.

Discussion

Breast conservation has become the trend for early breast cancer treatment because of better cosmesis

and good cure rates. Randomized trials have shown that overall survival of women undergoing breast conservation surgery with adjuvant radiation therapy is equivalent to mastectomy.[3,4] Rate for re-excision has been reported to be more than 50%.[4] Negative final margins result in a 5-year risk of local failure in 2% to 8% of cases, whereas the risk is 0 to 22% for positive margins, 2% to 11% for close margins, and 7% to 16% for unknown margins.[5]

Patients in whom the cancer is fully excised with clear margins in the first excision will have less of a chance of local recurrence compared with patients who need further re-excision to achieve clear margins.[6] But a fine balance exists between removing more margins while achieving a desirable cosmesis after breast conservation surgery. The decision to take extra margins should be based on the surgeon's judgment.[7]

The factors significantly associated with positive re-excision findings were initial positive margins and extensive DCIS.[2] We found similar results in our study with a increased rate of residual tumors in patients with involved margins for both invasive and intraductal carcinoma. Mai *et al*[8] studied serially sectioned lumpectomy specimens and found a relation between extensive DCIS in the specimen and the incidence of margin involvement. In our study DCIS in the margins were the common reason for re-excision surgery. Also residual DCIS was found in 50% compared with 31% for invasive tumors. It is the volume of residual disease, and not the likelihood of its presence alone, that is important in determining the effectiveness of radiotherapy on local control.[2]

Studies have shown grade of the tumor as a predictive factor for re-excision surgery and residual tumors.[1] Well-differentiated invasive carcinomas and low grade DCIS had low re-excision rates and lower incidence of residual tumors in our study.

Persistently involved re-excision margins create a diagnostic dilemma for clinicians regarding recommendations for further surgical therapy. Currently other than patient preference and habitus, no clear guidelines exist as to whether the next procedure should be the resection of additional margins or a mastectomy. Also the time taken for multiple re-excision attempts may not be worth the delay in administration of adjuvant therapy.[9] In our study 75 and 17 patients needed third and fourth re-excision surgeries, respectively.

Our study has some limitations. It is a retrospective study. We did not correlate with nodal involvement, and we did not look at the local recurrence rates.

Conclusions

The majority of re-excisions was done for margins <1 mm. Lower rates of re-excision were noted in well-differentiated invasive carcinomas. A close or involved DCIS margin was more likely to lead to a third and even a fourth re-excision. The absence of residual tumors in 40% of patients undergoing third and fourth re-excisions calls for a review of margin guidelines for breast re-excision.

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