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The Importance of Intraoperative Surgical Margin Assessment in Breast Conserving Surgery: Our Clinical Experience

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ABSTRACT

Background: Breast cancer is the most common cancer in women. Breast-conserving surgery (BCS) has been increasingly applied to eligible patients. One of the most important points in BCS is to provide clean surgical margins. This study aimed to share the re-excision results of those having positive surgical margins in intra-operative evaluation among BCS patients, and to discuss the intra-operative evaluation in the light of the literature.

Materials and Methods: The data (patient files, surgery notes and pathology reports) of 203 patients who had undergone BCS for breast cancer between January 2016 and January 2022 and whose excision materials had been evaluated with intra-operative frozen sections in terms of surgical margins, were scanned retrospectively. Absence of ink on tumoral cells (“no ink on tumor”) for invasive ductal carcinoma (IDC), and a margin width of ≥ 2 mm for ductal carcinoma in situ (DCIS) were considered as a clean surgical margin.

Results: Median age was 51 years (range, 22-75). There were reportedly 27 patients with positive surgical margins, five of whom had positive margins in re-excision. Re-excision specimens of all these 5 cases (18.5%) had been reported to have no positive surgical margins. No patients had been reported to require a second re-excision or mastectomy.

Conclusion: Intraoperative surgical margin assessment eliminates the need for repetitive surgery. We recommend routine application of intra-operative surgical margin assessment.

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INTRODUCTION

Breast cancer is one of the most common types of cancer in women and it is the second cause of death in women. Breast cancer surgeries continue to be performed in high numbers in surgical clinics. Since breast conserving surgery (BCS) has proven its safety, the frequency of its application has been increasing all over the world. The definition of oncoplastic techniques increases this momentum. Surgical margin

status after BCS is considered the strongest predictive factor for local recurrence.^{1,2} Re-excision is the standard practice to reduce local recurrence in patients with positive surgical margins.³ Mastectomy applications may be required when surgical margin negativity cannot be achieved with re-excision. Re-excision may increase the cost, mortality and morbidity, and may also cause deterioration of cosmetics in the breast.^{4,5} In this study, we aimed to discuss the importance of intra-operative surgical margin assessment in the light of the literature, and to share the re-excision results in patients with positive surgical margins in the intraoperative evaluation of patients who underwent BCS.

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MATERIALS AND METHODS

The files, surgery notes, pathology reports, radiology and oncology records of the patients who had undergone BCS for breast cancer between January 2016 and January 2022 in the institutional database were retrospectively scanned. The patients' age, tumor size, pathologies, axillary involvement, and whether they received neoadjuvant chemotherapy or not were recorded. Permission for our study was obtained from the Tokat Gaziosmanpaşa University Faculty of Medicine Clinical Research Ethics Committee (Date: 17.03.2022 Registration number: 22-KAEK-053). Excised specimens in all patients undergoing BCS in our clinic are routinely evaluated in the pathology department intra-operatively in terms of surgical margins. Surgical margin assessment was performed by a single pathologist with more than 20 years of experience. A manual cryostat device is used in our pathology clinic. While evaluating the surgical margin, all surfaces are painted and radial vertical sections are taken. Extra sections are taken from the fixed tissue. In the evaluation of pathological surgical margins, only frozen section is used but touch smear is not. Sections were taken from all margins and the same method was applied to all patients. The turnover time was between 15 and 20 minutes. Pathology results of the patients undergoing re-excision due to positive surgical margin in intra-operative evaluation were also recorded. Absence of ink on tumoral cells ("no ink on tumor") for invasive ductal carcinoma (IDC), and a margin width of ≥ 2 mm for ductal carcinoma in situ (DCIS) were considered as a clean surgical margin. Intra-operative surgical margin evaluation was performed by frozen section analysis after staining the margins of the specimen. An adequate amount of re-excision was taken from the side reported as positive by pathology and sent to pathology again.

The categorical data were expressed as numbers and percentages, and the continuous data were expressed as the mean \pm standard deviation or median (range).

RESULTS

Two hundred three female patients who had undergone BCS were included in our study. The median age was 51 (range 22-75). The characteristics of the patients are given in Table 1. Of the patients, 168 had invasive ductal carcinoma (IDC) and five had invasive lobular carcinoma (ILC). Concomitant ductal carcinoma in situ (DCIS) was present in 20 patients with invasive cancer. Ten patients had been operated for DCIS. Surgical margins were positive in 27 (13.3%) of 203 patients in intra-operative evaluation reports. Of these 27 patients with positive surgical margins, 18 were diagnosed with IDC, four

with IDC+DCIS, one with LCI, and four with DCIS. Re-excision reports of these 27 patients showed tumor persistence in five (2.46%) patients; however, their new surgical margins were negative in re-excision. Surgical margins according to pathology types are given in Table 2. In addition, we did not have any patients who needed mastectomy because of poor cosmetics when re-excision was required. It was determined that there had been no need for a second re-excision in any of our patients.

Table 1. General characteristics of the patients (203 patients, all female)

Tumor Size	N (%)	
T1	119	(58.6%)
T2	72	(35.4%)
T3	12	(6%)
Pathology		
IDC	168	(82.7%)
IDC+DCIS	20	(9.8%)
DCIS	10	(5%)
ILC	5	(2.46%)
Axillary Metastases		
Yes	57	(28%)
No	146	(72%)
Distant Metastasis		
Yes	3	(1.5%)
No	200	(98.5%)
Neoadjuvant chemotherapy status		
Yes	42	(20.7%)
No	161	(79.3%)

As a result, it was observed that surgical treatment had been completed in all patients undergoing BCS without the need for a second operation. Surgical margin was positive in two of the 176 patients who were reported to have negative surgical margins in the intraoperative evaluation. Our false negative rate in intraoperative margin evaluation was 1%. We consider this rate to be acceptable.

DISCUSSION

Since a positive surgical margin in BCS is associated with local recurrence, the width of the surgical margin has been a matter of debate for a long time. While it was previously argued that an intact margin of 10mm is required, Houssami *et al.* reported that there was no significant difference in terms of local recurrence between the surgical margins of 1mm, 2mm, and 5mm.⁶ Currently, a consensus article published by the Radiation Oncology Society reported that the concept of "no ink on tumor" is sufficient for a negative margin.⁷ For DCIS, it is argued that the surgical margins should be slightly



wider. Pilewskie *et al.* have shown that a surgical margin of 2mm is sufficient for DCIS.⁸ Based on these data, we used the presence of tumor in the dyed area for invasive cancers and 2mm for DCIS as surgical margins in our study.

Table 2. Surgical margin positivity distribution according to the pathology results of the patients (Number of patients: 203)

	Number of patients	Percentage
Surgical margin positivity	27	13.3%
IDC	18	66.6%
IDC+DCIS	4	14.8%
DCIS	4	14.8%
ILC	1	3.7%
Surgical margin positivity at reexcision	5	2.46%
IDC	1	20%
IDC+DCIS	1	20%
DCIS	3	60%
ILC	0	0
Second reexcision	none	
Mastectomy	none	

In the literature, re-excision rates in BCS range from 0% to 60%.⁹ Reid *et al.* reported that this rate was more than 20%.¹⁰ In our study, we found that the re-excision rate in our clinic was 13.3%. The fact that the re-excision rates are so different in the literature may be related to how many millimeters the surgical margin is accepted. One of the most important factors in providing a clean surgical margin is the experience of the surgeon.¹¹ It is clear that one of the reasons for this difference in re-excision rates is the experience of the surgeon. When the BCS decision is made, it should be ascertained that surgical margin negativity is achievable without disturbing the cosmetics at the surgical planning stage. The presence of metastatic axillary lymph node, the presence of extra-invasive component, lymphovascular invasion, and the presence of spiculation or microcalcification have been reported to be independent and unfavorable factors affecting the positive surgical margin.¹² After neoadjuvant chemotherapy, it may be more difficult to provide a clean surgical margin, as the tumor may disperse as multifocal or occult foci.¹³ Lobular breast cancer and excisional biopsy are also troubles for providing clean surgical margins. Factors that

negatively affect surgical margin positivity should be carefully investigated and a special planning should be made for each case.

Providing a clean surgical margin in BCS is very important to prevent recurrences. Intra-operative evaluations can reduce mortality, morbidity and costs by eliminating the need for reoperation, and contribute to the preservation of breast cosmetics.¹³ There are studies suggesting that new techniques such as margin probe and protease-activated fluorescent imaging system can be used for this purpose.^{14,15} However, their use has not yet become widespread and they are not easily accessible methods. Racz *et al.* reported that re-operation rates decreased with intra-operative evaluation, and there was no difference in safety between re-operation and intra-operative evaluation.¹⁶ Chapgar *et al.* reported that intra-operative evaluation in DCIS reduces the risk of reoperation while also reducing the amount of the tissue removed.¹⁷ Esbona *et al.* reported that intra-operative use of imprint cytology and frozen section analysis margin evaluation techniques against permanent histopathological section significantly reduced the need for re-operation.⁹ Metcalfe *et al.* Reported that the risk of complications in second surgeries performed after BCS was twice as high as under normal conditions.⁴ Reducing the need for a second surgery is very valuable for reducing morbidity rates and costs in patients. Our results also support the literature.

CONCLUSION

In our series, no patient required reoperation due to positive surgical margins, and no patient required mastectomy. We recommend routine intra-operative margin assessment in all BCS patients. Our study is limited due to its retrospective nature and the relatively small number of patients.

ETHICAL CONSIDERATIONS

Permission for our study was obtained from the Tokat Gaziosmanpaşa University Faculty of Medicine Clinical Research Ethics Committee (Date: 17.03.2022 Registration number: 22-KAEK-053).

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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