Total-Circumference Intraoperative Frozen Section Analysis Reduces Margin-Positive Rate in Breast-Conservation Surgery

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Objective: One problem existing in breast-conservation surgery is ipsilateral breast tumour recurrence, and one of its major risk factors is surgical margin positivity. We therefore investigated whether total-circumference surgical margin examination can reduce surgical margin-positive rates.

Methods: A total of 122 cases were examined after BCS was performed between March 2004 and March 2006. After partial mastectomy, specimens were taken from the remnant breast side along the total-circumference of the mammary gland (width, approximately 5 mm). Intraoperative frozen section analysis was performed for those specimens. Margin-positive cases were defined as those showing malignancy within ≤5 mm of the final margin as revealed by final diagnosis.

Results: If intraoperative frozen section analysis had not been performed, 33 cases (27%) would have been diagnosed as margin-positive. However, it reduced the number of margin-positive cases to 12 (9.8%), and final margin-positivity rates were thus significantly reduced (P < 0.001). As for the accuracy of intraoperative frozen section analysis, sensitivity was 78.6%, specificity was 100%, correct diagnosis rate was 95.1%, positive predictive value was 100% and negative predictive value was 94.0%. False-negatives were caused by the detection of malignancy as revealed in permanent specimens. Margin-positive sites were not limited to the nipple and distal (peripheral) sites, with equivalent margin-positive cases found laterally.

Conclusions: Total-circumference surgical margin examination by IFSA for BCS significantly reduced margin-positive rates from 27% to 9.8%.

Key words: breast cancer – breast-conservation surgery – frozen section – surgical margin

INTRODUCTION

In recent years, breast-conservation surgery (BCS) has become a standard operative procedure for breast cancers. One problem that arises with BCS is ipsilateral breast tumour recurrence (IBTR), and one of the major risk factors for such recurrence is surgical margin positivity (1–5). Margin examination by intraoperative frozen section analysis (IFSA) is anticipated to significantly facilitate the correct identification of margin status. As a result, margin examination is currently performed in individual facilities. However, many issues require further investigation. For instance, methods of specimen submission and evaluation of accurate diagnosis rates are yet to be standardized. Moreover, few detailed reports have examined margin diagnosis within BCS, and no reports have yet clarified the use of IFSA examining the total-circumference (i.e. ‘circumferential’ examination) of the surgical margin.

Ever since we established an environment for performing intraoperative pathological examinations, we have been submitting total-circumference margins shaved from the
mammary gland of the remnant breast for IFSA, and performing margin diagnoses based on these specimens. The present study examined the extent to which circumferential margin examination can reduce surgical margin-positive rates.

METHODS

The present research was performed in the Department of Breast and Endocrine Surgery at Tohoku University Hospital, in the 2-year period from March 2004 to March 2006, and involved a retrospective study of 122 cases in which BCS had been performed (including three cases of simultaneous dual-breast cancer). During the same periods, 57 patients had received total mastectomy and they were excluded from this study. And cases in which preoperative adjuvant chemotherapy or endocrine therapy had been performed were excluded from analysis, as were cases in which surgical excision biopsy of the main tumour had been performed. Background factors of subjects are shown in Table 1.

Table 1. Characteristics of the 122 patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Count (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (median)</td>
<td>32–87 (56)</td>
</tr>
<tr>
<td>Tumour size, n (%)</td>
<td></td>
</tr>
<tr>
<td>Tis</td>
<td>31 (25.4)</td>
</tr>
<tr>
<td>T1 (≤2 cm)</td>
<td>74 (60.7)</td>
</tr>
<tr>
<td>T2 (&gt;2 cm, ≤5 cm)</td>
<td>17 (13.9)</td>
</tr>
<tr>
<td>Histology, n (%)</td>
<td></td>
</tr>
<tr>
<td>DCIS</td>
<td>31 (25.4)</td>
</tr>
<tr>
<td>IDC</td>
<td>81 (66.5)</td>
</tr>
<tr>
<td>ILC</td>
<td>2 (1.6)</td>
</tr>
<tr>
<td>Mucinous carcinoma</td>
<td>6 (4.9)</td>
</tr>
<tr>
<td>Apocrine carcinoma</td>
<td>2 (1.6)</td>
</tr>
<tr>
<td>Oestrogen receptor status, n (%)</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>103 (84.4)</td>
</tr>
<tr>
<td>Negative</td>
<td>19 (15.6)</td>
</tr>
<tr>
<td>Progestosterone receptor status, n (%)</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>90 (73.8)</td>
</tr>
<tr>
<td>Negative</td>
<td>32 (26.2)</td>
</tr>
<tr>
<td>HER2 status, n (%)</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>24 (19.7)</td>
</tr>
<tr>
<td>Negative</td>
<td>98 (80.3)</td>
</tr>
<tr>
<td>Menopausal status, n (%)</td>
<td></td>
</tr>
<tr>
<td>Premenopausal</td>
<td>45 (36.9)</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>77 (63.1)</td>
</tr>
</tbody>
</table>

DCIS, ductal carcinoma in situ; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma.

Preoperative Evaluation

For the preoperative diagnosis of lesion spread, mammography, ultrasonography, computed tomography (CT) and magnetic resonance imaging were used concomitantly. An overall determination was made for each finding, and the excision range was determined. Particularly with CT, imaging was performed using body surface markers, three-dimensional images were created, and detailed width diagnoses were made (6).

Surgical Method

For surgery, wide excision or quadrantectomy was performed after making a skin flap, in principle securing a 2-cm margin from the conjectured lesion. As for lymph node dissection, depending on the case, sampling of Level I to Level III dissection was performed (7).

Adjuvant Therapy

Indication for adjuvant chemotherapy was decided in consideration with histological evidence and according to the report of St Gallen Oncology Conference or Guideline of National Comprehensive Cancer Network. As for adjuvant radiotherapy, most patients underwent except those who refused or contraindicated patients. In this study, 35 patients did not undergo adjuvant radiotherapy.

Margin Diagnosis

After partial mastectomy, specimens were taken from the remnant breast side of the mammary gland with a width of approximately 5 mm, and these specimens were submitted for IFSA (Fig. 1). The outermost surface of the specimen was set as the evaluation surface [Fig. 1 (asterisks)].

Figure 1. Schematic diagram of a total-circumference surgical margin examination. After partial mastectomy, specimens were taken from the remnant breast side of the mammary gland with a width of approximately 5 mm, and these specimens were submitted for IFSA. The outermost surface of the specimen (asterisks) was set as the evaluation surface.
According to the adipose content of the submitted specimen, penetration was made with the proper surfactant, and the sample was frozen in liquid nitrogen. For each specimen, a minimum of two slides were prepared and stained using haematoxylin and eosin. As for margin diagnosis, the basic policy set was that additional excisions would be made of margin-positive portions until the specimen was found to be margin-negative. These frozen specimens were defrosted after evaluation and embedded in paraffin to create permanent specimens. An optical microtome was then used to create sections, and slides were prepared. The diagnosis obtained using these final specimens was considered final.

**PATHOLOGICAL EXAMINATION OF SURGICAL SAMPLES**

For the pathological examination of surgical samples, whole serial slices (width, 5 mm) were created and examined under microscopy. Margin-positive status was defined as the existence of cancer cells (either invasive or non-invasive carcinoma) within 5 mm of the final margin. Written consent was obtained from all patients for the use of specimens in the present investigation. The $\chi^2$ test was used for statistical analyses, and values of $P < 0.05$ were determined significant.

**RESULTS**

The median number of slices submitted for IFSA was seven slices per case (range, 4–12 slices per case). An average of eight slides per case (range, 8–24 slides per case) were prepared and stained using haematoxylin and eosin. It took an average of 53 min per case to perform total-circumference IFSA.

As for margin status according to the need for IFSA, cases were divided into three groups:

- **Group 1**: Could have been determined as margin-negative without IFSA (79 cases).
- **Group 2**: Determined as margin-negative from IFSA (31 cases).
- **Group 3**: Margin-positive despite performance of IFSA (12 cases).

A more detailed investigation of Groups 1–3 was therefore undertaken.

**GROUP IN WHICH MARGIN-NEGATIVE STATUS COULD HAVE BEEN DETERMINED WITHOUT IFSA**

For this group [79 cases (65%), Table 2], preoperative imaging diagnoses were valid, and excisions could thus be made while securing a sufficiently safe margin. Margin diagnoses from excised sample margin, IFSA or final margin diagnosis were divided into types A–H.

**GROUP IN WHICH MARGIN-NEGATIVE STATUS WAS DETERMINED FROM IFSA**

For this group [79 cases (65%), Table 2], preoperative imaging diagnoses were valid, and excisions could thus be made while securing a sufficiently safe margin. Margin diagnoses from excised sample margin, IFSA and final diagnosis were all negative.

**GROUP IN WHICH MARGIN-NEGATIVE STATUS WAS DETERMINED FROM IFSA**

Upon investigation of cases that were finally determined as margin-negative based on IFSA, patterns A, B and C were identified:

(i) Although margins in the excised sample were negative, skip lesions were identified on slices submitted for IFSA. Since these were considered IFSA-positive, additional excision was performed, and a final diagnosis of margin-negative was obtained. Six cases showed this pattern (Table 2 and Fig. 2A). All these skip lesions were confirmed as cancer occupying in only one or several ducts. There were not multifocal lesions.

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**Table 2. Results of intraoperative frozen section analysis (IFSA) for the 122 cases and classification of diagnosis pattern**

<table>
<thead>
<tr>
<th>Excised sample margin</th>
<th>IFSA</th>
<th>Final margin diagnosis</th>
<th>No. of cases</th>
<th>Classification of diagnosis$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>–</td>
<td>–</td>
<td>–</td>
<td>79</td>
<td></td>
</tr>
<tr>
<td>–</td>
<td>+</td>
<td>–</td>
<td>6</td>
<td>A</td>
</tr>
<tr>
<td>+</td>
<td>–</td>
<td>–</td>
<td>15</td>
<td>B</td>
</tr>
<tr>
<td>+</td>
<td>+</td>
<td>–</td>
<td>10</td>
<td>C</td>
</tr>
<tr>
<td>+</td>
<td>+</td>
<td>+</td>
<td>4</td>
<td>D, E</td>
</tr>
<tr>
<td>–</td>
<td>–</td>
<td>+</td>
<td>3</td>
<td>G</td>
</tr>
<tr>
<td>–</td>
<td>–</td>
<td>+</td>
<td>1</td>
<td>H</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>122</td>
<td></td>
</tr>
</tbody>
</table>

$^a$Cases with lesions detected in the excised sample margin, IFSA or final margin diagnosis were divided into types A–H.

$^b$Cases in which margin positivity could have been diagnosed without IFSA.

$^c$Cases in which margin positivity was diagnosed in the final specimen.
Although a lesion existed within 5 mm of the excised sample margin, additional cutting of the remnant breast used for IFSA submission secured a sufficient distance between the lesion and the final margin, which was margin-negative. Fifteen cases showed this pattern (Table 2 and Fig. 2B).

Since IFSA showed margin-positive status, additional excision was performed and final diagnosis was margin-negative. Ten cases showed this pattern (Table 2 and Fig. 2C).

In 12 cases (10%), final margin status was margin-positive despite the performance of IFSA. Investigation of cases that finally became margin-positive revealed patterns D–H.

Since these cases were IFSA-positive, additional excision was performed until negative margins were obtained. However, in the additionally excised slice, permanent specimens revealed lesions. Two cases showed this pattern (Table 2 and Fig. 3A).

In two cases, a lesion was confirmed in all of the following: margin of excised sample, IFSA and final margin diagnosis. Of these, a widespread lesion was confirmed in one case even in the additionally excised slice. In that case, total mastectomy was subsequently performed. In the other case, malignancy was also confirmed in the slice submitted for final IFSA, but was limited to just one glandular duct, and the decision was made to achieve control via postoperative radiotherapy. Surgery was therefore considered complete (Table 2 and Fig. 3B).

Although these cases showed negative margins in IFSA, cancer was revealed in permanent samples from IFSA slices, resulting in a final diagnosis of margin-positive status. Four cases showed this pattern (Table 2 and Fig. 3C).

Figure 2. Surgical margin-negative cases shown schematically.

Figure 3. Surgical margin-positive cases shown schematically.
Although these cases were negative on IFSA, a skip lesion was revealed in the IFSA-slice permanent specimens, and the final diagnosis was thus margin-positive status. Three cases showed this pattern (Table 2 and Fig. 3D).

Although this case was negative in the excised sample margin, a skip lesion was found in the IFSA slice, and despite additional excision, cancer was revealed in permanent samples from IFSA slices. One case showed this pattern (Table 2 and Fig. 3E).

Among the cases finally determined as margin-positive, with the exception of the two type E cases, all were cases in which the lesion was revealed when sections were made from permanent specimens.

Summarizing the above findings, even if IFSA had not been performed, margin evaluation of the excised sample margin itself would have become the final diagnostic evaluation. That is, in the present investigation of 122 cases, 33 cases (27%; Groups shown in Figs 2B and C, and 3A–C) were diagnosed as margin-positive (Table 2). However, use of IFSA reduced the number of margin-positive cases to 12 (9.8%; Table 2). Final margin-positive rate was thus significantly reduced ($P < 0.001$).

**INVESTIGATION OF MARGIN-POSITIVE SITES**

With regard to 33 cases that became margin-positive within the first excised sample margin (Table 2), investigation was made of the direction in which margin-positive results were identified. In these cases, tumour cells were identified at the nipple-side margin in 10 cases, the distal-side margin in 11 cases, and lateral-side margins in 23 cases (with some overlap; Fig. 4). Among lateral-side margin-positive cases, 14 cases were diagnosed as positive except for the side nearest to the tumour.

**INVESTIGATION OF THE ACCURACY OF INTRAOPERATIVE FSA**

For the estimation of correct diagnosis rate, sensitivity, specificity, false-positive rate and false-negative rate, positive cases were defined as IFSA-positive cases showing positive results on permanent samples from IFSA slices. Likewise, negative cases were defined as IFSA-negative cases showing negative results on permanent samples from IFSA slices. IFSA made in this study showed a sensitivity of 78.6%, a specificity of 100%, and a correct diagnosis rate of 95.1%, and a positive predict value of 100%, and a negative predict value of 94.0%. Cases determined as negative on IFSA, but in which a cancer was afterwards revealed by slicing in the permanent sample, were determined as final margin-positive, and included as ‘false-negative’ cases.

**HISTOLOGICAL CHARACTERISTICS**

Histological characteristics in the cases with final margin-positive and IFSA-negative are shown in Table 3. The group of IFSA-negative cases included only those which met the requirements of final margin-negative and IFSA-negative. The frequencies of pathological factors compared the group of final margin-positive cases with the other cases. In a similar way, the group of IFSA-negative cases were compared. Patients who had extensive intraductal component (EIC) were more likely to have final margin-positive compared with patients without this characteristic, although there was no significant difference.

**DISCUSSION**

Many reports have examined relationships between status of surgical margins and IBTR in BCS, and a high rate of IBTR has been seen in cases with positive surgical margins (1–5).
Surgical margins must be taken into consideration when BCS is to be performed, and IFSA is now being performed to ensure negative margins.

In several previous studies, risk factors have been investigated to identify those patients with a high likelihood of having positive margin during BCS (5,8–11). Histological characteristics including ductal carcinoma in situ (DCIS), presence of EIC, presence of lymphovascular invasion, multifocality, lobular carcinoma, have all been associated with positive margins. In this study, our result was similar to the previous studies of cases with EIC. It has been shown that the case with EIC has increased the risk of IBTR, particularly severe positive-margin cases. Therefore, these cases must be followed carefully. However, there was not so much of difference about other histological characteristics. The case with multifocal lesions was only two. One was final margin-positive and the other was margin-negative case. There were a few cases of final positive margin in our study. If there were more final margin-positive cases in our study, we might also have been obtaining the data similar to previous studies.

No clear standard currently exists that defines ‘margin-positive’ within surgical specimens, with a variety of standards existing for different institutions. In the ‘Breast Conservation Therapy Guidelines’ used in Japan, a determination of margin-positive status is considered reasonable in cases when a cancer is confirmed within 5 mm. Other countries show a broad range of definitions, with some institutions defining ‘margin-positive’ only when a cancer is exposed at the excision margin, and others diagnosing ‘margin-positive’, when a cancer has been confirmed within 2 mm or 5 mm (12–18). The accuracy (i.e. correct diagnosis rates) of IFSA thus cannot be determined simply by comparing values from existing reports, and no meaningful discussion can be made regarding the superiority or inferiority of accuracy rates.

In the present investigation, results were obtained under an extremely strict standard compared with those of previously existing reports. As stated earlier, our results regarding the accuracy of margin diagnoses were as follows: sensitivity, 78.6%; specificity, 100%; correct diagnosis rate (diagnostic accuracy rate), 95.1%; positive predictive value, 100%; and negative predictive value, 94.0%. The following rates have been reported previously: sensitivity, 65.0–96.0%; specificity, 84.0–100%; correct diagnosis rate, 83.8–98.0%; positive predictive value, 81.4–97.1%; and negative predictive value, 81.0–100% (12–23). Our values for IFSA were calculated under extremely strict standards of a definition stating ‘existence of cancerous cells within 5 mm’ and ‘cancer identified by slicing with optical microtome from a permanent sample previously determined as negative on IFSA shall be included as a ‘false-negative’ case’. In previous investigations, no mention has been made of reinvestigation of permanent samples; that is, of slices that had been used for IFSA evaluation after unfreezing. Despite this, accuracy of our IFSA was comparable to results described elsewhere (Table 4). In this study, if margin-positive status was defined as the existence of cancer cells within 2 mm of the final margin, only six margin-positive cases were identified (4.9%). Accuracy rates were as follows: sensitivity, 95.7%; specificity, 100%; correct diagnosis rate, 99.2%; positive predictive value, 100%; and negative predictive value, 99.0%. These values were superior to results described elsewhere.

Furthermore, the majority of cases finally identified as margin-positive were cases in which the lesion first appeared when a reinvestigation was made in the FSA-slice permanent sample. Mammary gland tissue is surrounded by adipose tissue, and thin slices of such adipose tissue are difficult to obtain from frozen samples. As a result, not all gland tissue may show up in the evaluated surface. This is an unavoidable phenomenon characteristic of IFSA, and has been considered as one of the key limitations of IFSA.

Conversely, even in cases where a cancer appears on evaluated surface, frozen specimens are inferior in quality to formalin-fixed permanent samples, and this is thought to have a major impact on the diagnosis. Singletary et al. have stated that since evaluation of structural atypia and nuclear atypia is difficult owing to artefacts from the freezing operation, low-grade DCIS and atypical ductal hyperplasia is

Table 4. Comparison of IFSA accuracy of previous reports and our study

<table>
<thead>
<tr>
<th>Author</th>
<th>No.</th>
<th>Positive</th>
<th>Positive rate (%)</th>
<th>Accuracy (%)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive predictive value (%)</th>
<th>Negative predictive value (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olson et al. (13)</td>
<td>290</td>
<td>c</td>
<td>4.1</td>
<td>98.0</td>
<td>73.0</td>
<td>99.5</td>
<td>91.9</td>
<td>98.3</td>
</tr>
<tr>
<td>Cabioglu et al. (12)</td>
<td>154</td>
<td>&lt;2 mm</td>
<td>20.0</td>
<td>87.4</td>
<td>77.8</td>
<td>91.7</td>
<td>88.9</td>
<td>86.1</td>
</tr>
<tr>
<td>Cendan et al. (14)</td>
<td>97</td>
<td>exposure</td>
<td>22.7</td>
<td>96.0</td>
<td>65.0</td>
<td>100</td>
<td>94.0</td>
<td>100</td>
</tr>
<tr>
<td>Weber et al. (15,20)</td>
<td>80</td>
<td>&lt;1 mm</td>
<td>12.5</td>
<td>83.8</td>
<td>80</td>
<td>87.5</td>
<td>81.4</td>
<td>86.5</td>
</tr>
<tr>
<td>Ikeda et al. (21)</td>
<td>56</td>
<td>exposure</td>
<td>32.1</td>
<td>91.1</td>
<td>94.4</td>
<td>89.5</td>
<td>97.1</td>
<td>81.0</td>
</tr>
<tr>
<td>This study</td>
<td>122</td>
<td>&lt;5 mm</td>
<td>9.8</td>
<td>95.1</td>
<td>78.6</td>
<td>100</td>
<td>100</td>
<td>94.0</td>
</tr>
</tbody>
</table>

aBlanks in table represent data not described in that report.
bDefinition of positive margin.
cMargin-positive rate for final margin diagnosis.
extremely difficult to discern from IFSA (24). And papillary lesions were also difficult. Therefore, it was impossible to discern benign and malignant perfectly. IFSA had a limited diagnostic capability. In our institution, several pathologists have diagnosed a sample to avoid misdiagnoses. Fortunately, no misdiagnoses were made in the present investigation; however, this is the point of greatest concern for a pathologist involved in diagnosis, and is thought to be a factor in making IFSA of mammary glands more difficult. To perform accurate IFSA, it is indispensable that the pathologist work together with the surgeon when performing the diagnosis, as a significant portion of this diagnosis can be swayed by the capabilities of the individual pathologist. Inasmuch as there are limitations to any IFSA, margin-positive cases will be impossible to reduce to 0%. Cases diagnosed as margin-positive in the final margin diagnosis have a high possibility of IBTR. Numerous reports have described further excisions or total mastectomy at a later date for such cases (19–21). In the present investigation with 10 cases that finally became margin-positive, only one patient subsequently underwent total mastectomy. In the remaining nine cases, a diagnosis of residual cancer was made for only a limited number of glandular ducts, or, in accordance with the wishes of the patient, further excision was not performed and radiotherapy was used instead. As of the time of writing, although no IBTR has been observed, the mean observation period of 61.4 months has been short, and further observation is obviously required. Strict observation of the clinical course will be especially necessary in these nine cases.

Another novel point in the present investigation was the fact that data were collected over the total-circumference of mammary gland margins. Although other institutions within Japan are performing total-circumference (i.e. circumferential) diagnostic assessments, these are extremely few in number. One reason that can be given for this is the shortage of pathologists in Japan. In IFSA, the diagnosis must be made within a limited time period, and trying to ensure diagnostic accuracy with few pathologists entails limiting the number of slices. Looking at both domestic Japanese and foreign reports, institutions that are performing IFSA over the total-circumference of the mammary margin are rare, with most institutions performing partial IFSA. Many institutions submit IFSA for a total of four sites: both sides of the margins nearest to the tumour (i.e. lateral), in addition to the nipple-side margin and the distal-side margin (19,21). As breast carcinoma has a tendency to undergo intraductal extension on the nipple- and distal-sides along the breast duct lobular unit (7,25,26), emphasis is placed on the nipple- and distal-side margins. However, in the present investigation, margin-positive cases were not limited to nipple and distal sides, and equivalent rates were apparent laterally. Ikeda et al. have reported similar results, and noted as a contributing factor that even in cases of quadrantectomy with the margin set at 2 cm, many cases were seen where margins in the nipple and distal directions were ≥2 cm, meaning that lateral margins were relatively short (21). Akiyama et al. stated about factor of this result that owing to the breast becoming ptotic, the line of the mammary duct becomes curved, with intertwining breast ducts and lobular unit (27). We simulated the case that we submitted IFSA for a total of four sites, and 19 cases would be diagnosed as final margin-positive. This was more than the actual result. Among lateral-side margin-positive cases, approximately 60% cases were diagnosed as positive except for side nearest to the tumour. This thing was thought to increase margin-positive cases. Therefore, nipple and distal directions and lateral margins all need to be considered, and examination only at the nearest portion of the tumour side is an imperfect procedure.

In the present investigation, even supposing that IFSA had not been performed, evaluation of the specimen margins themselves would have constituted the final margin evaluation. In other words, among the 122 cases, 33 (27%) (Groups shown in Figs 2B and C, and 3A–C) were diagnosed as margin-positive (Table 2). However, because of the performance of IFSA, the number of margin-positive cases could be reduced to 12 (9.8%; Table 2). Final margin-positive rates were thus significantly reduced (P < 0.001). Among cases successfully diagnosed as margin-negative because of the performance of IFSA, with regard to the six cases of Group A, no continuity was seen between lesions in these specimens and those in slices submitted for IFSA. Skip lesions existed coincidentally among the portions submitted as margins, and the possibility of lesions existing even further outside the final margins cannot be denied. Thus, in the strictest sense, evaluating whether margin-positive status was successfully determined by IFSA is difficult.

Whether ideal circumferential margin examinations would always be possible is a difficult issue, and the necessity is controversial. There are problems such as securement of pathologists, labour of making many histological preparation and restriction of operating time. Therefore, it is unreal to perform total-circumference margin examination in all patients. Nevertheless, performance of total-circumference surgical margin examination can save cases. Therefore, even more accurate determination of cases warranting total-circumference surgical margin examination is needed in the future.

**CONCLUSION**

Currently, the number of facilities performing total-circumference surgical margin examination by IFSA is limited, and performing this examination for every case of BCS is unrealistic. In the present study, because of the use of this examination on the basis of an extremely strict standard, we reduced surgical margin-positive status from 27% to 9.8%. Thus, with the performance of this examination that is appropriate for each specific case, it should be possible to save even more cases.
Conflict of interest statement

None declared.

References