Intraoperative radiological margin assessment in breast-conserving surgery


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Abstract

A prospective study was lead in order to analyze the accuracy of an X-ray device settled in the operating room for margin assessment, when performing breast-conserving surgery.

Patients and methods: One hundred and seventy patients were included. All lesions were visible on the preoperative mammograms. An intraoperative X-ray of the lumpectomy specimen was systematically performed for margins assessment. Final histological data were collected and the accuracy of intraoperative specimen radiography (IOSR) for margin assessment was analyzed.

Results: IOSR allowed an evaluation of margins status in 155 cases (91.2%). After final histological examination, the positive margins rate would have been 6.5% if margin assessment had relied only on IOSR.

Conclusion: Margin assessment with a two-dimensional X-ray device would have allowed the achievement of negative margins in 93.5% of the cases. Moreover, this procedure allows important time-saving and could have a substantial economical impact.

Keywords: Intraoperative specimen radiography; Intraoperative histological examination; Faxitron; Margins status; Breast cancer; Mammograms

In breast-conserving surgery (BCS), the main objective is to obtain negative histological margins which are known to be a major prognostic factor for tumor recurrence. Until now, the intra-operative evaluation of margin status (MS) for palpable cancers has relied on histological examination (HE) by the pathologist. For non-palpable, radio-opaque lesions, the intra-operative MS was assessed using conventional specimen radiography (CSR). However, these two procedures need a specific organization of the breast surgery department (pathologist in the operating room or transport of the lumpectomy specimen to the pathology or radiology unit) and are time consuming. In order to propose an alternative to these intra-operative procedures for lesions visible on mammograms, a prospective study was lead in order to analyze the concordance between margin evaluation with intra-operative HE or CSR and margin assessment using a dedicated X-ray imaging device settled in the operating room (Faxitron MX20, Faxitron Bioptics, Illinois). The potential economical and organizational benefits of this procedure were studied.

Patients and methods

Between 2010 and 2012, one hundred and seventy consecutive, non-selected patients (median age: 61 years-old, range: 32—91) treated with BCS for palpable or non-palpable breast cancers were included.

All lesions were visible on the preoperative mammograms.

Surgical procedures were performed under general anesthesia. For invasive lesions, the operation started with sentinel lymph node biopsy. For non-palpable lesions, tumor resection relied on wire-guided localization. For tumor removal, the surgical procedure was as follows:
Once the skin incision performed, subcutaneous undermining was achieved. The gland was cut, down to the pectoralis muscle fascia one centimeter far from tumor location. The gland was then separated from the pectoralis fascia all around the tumor and the lumpectomy was achieved by cutting the gland all around the tumor. Each lumpectomy specimen was orientated using metallic clips and settled on a radio-opaque grid (Fig. 1, picture 1a). For each patient, intraoperative specimen radiography was performed with a two-dimensional X-ray device settled in the operating room of the lumpectomy [Faxitron (FX)]. The margins surrounding the tumor were then measured (Fig. 1, picture 1b) by the surgeons. The device used was a Faxitron MX-20 equipped with a large camera, which provides 10 line pairs per millimeter (lp/mm) spatial resolution in contact mode and up to 50 lp/mm at full 5 x magnification. When margins were inferior to 10 mm, complementary resections were systematically performed. For non-palpable lesions, the lumpectomy was sent for conventional specimen radiography. For palpable lesions, the specimen was systematically sent for intra-operative HE (Fig. 1, picture 1c): the surgical fresh specimen was inked according to the surgeon’s orientation marks and macroscopical serial sections were performed in order to assess the distance between the tumor and the surgical margins. In rare cases, mainly if preoperative histological diagnosis was doubtful, frozen section of the tumor was performed. Complementary glandular excisions were performed when required by the radiologist or the pathologist.

For each patient the final histological data, provided by the pathology unit 10 days after the operation, were collected. Margins were considered free when tumor cells did not touch ink on final pathology. When margins were inferior or equal to 2 mm, each case was discussed during multidisciplinary team meetings. Re-excision was proposed when the patient had several risk factors of local recurrence.

The primary objective of this study was to analyze the accuracy of FX for the evaluation of margin status. Hence, it was possible to compare the results of the FX procedure with the results of intra-operative HE or CSR.

In order to evaluate the time-saving induced by FX, the time needed to obtain the results of CSR and/or HE was calculated for each patient. Thus, the secondary objective of this study was to evaluate the impact of the FX procedure in a surgical department from an organizational point of view.

Statistical analysis was performed using Student’s and Fisher’s tests.

Results

The treated lesions were ductal carcinoma in situ DCIS in 16 cases (9.4%), invasive ductal carcinomas IDC in 127 cases (74.7%), invasive lobular carcinomas ILC in 20 cases (11.8%) and a combination of histological subtypes (ductal and lobular carcinomas in the same sample) in 7 cases (4.1%). Breast lesions were palpable in 48.2% of the cases. Median tumor size was 12 mm [2–80].

FX provided an X-ray image of the lumpectomy specimen in 90 s. The surgeons by themselves evaluated the specimen obtained by FX in less than 2 min thanks to the radio-opaque grid. The FX allowed an evaluation of the margins status (MS) in 155 cases (91.2%). In the 15 remaining cases, the image provided by FX did not allow an accurate evaluation of the margins. These patients were excluded from the analysis of FX’s accuracy for the evaluation of margin status. Nevertheless, these 15 patients had high breast density (type 3 or 4) and a smaller median tumor size (8 mm vs. 12 mm) (p = 0.035).

After intraoperative HE and/or CSR, complementary excisions were required in 16 cases (10.3%) (14 after HE and
2 after CSR). Hence, MS evaluation with FX was corroborated by the intraoperative HE or CSR in 89.7% (139/155) of the cases.

On final histological examination, from the 14 complementary excisions required by the pathologist, 6 allowed to obtain negative margins and 5 were not necessary as margins were already negative after the FX procedure. In the three remaining cases, the final margins were positive in spite of intraoperative HE. Moreover, on final pathology, none of the two complementary resections required after CSR were necessary as margins were already clear after the FX procedure.

On final pathology, only four patients (2.6%) required secondary operation for positive margins for DCIS. All these results are summarized in Table 1 and Fig. 2.

Hence, if MS evaluation had relied only on the FX procedure, 10 patients would have had positive margins (four patients with positive margins on final pathology + six patients for whom intra-operative histological examination allowed to obtain negative margins) and the positive margin rate would have been 6.5% (10/155).

Interestingly, when the margins, measured using FX were superior or equal to 10 mm, the final margin status, evaluated by HE, were negative in 98.5% of the IDC cases (125/127), in 90% of the ILC cases (16/18) and in 68.75% of DCIS cases (5/16) \( (p = 0.0001) \).

The median time required to obtain CSR results was 20 min [12–40]. The median time required to obtain intraoperative HE results was 20 min in our series [14–45]. The median time required to obtain the results of both CSR and HE was 40 [25–65] minutes.

**Discussion**

The main objective, when performing BCS, is to obtain clear tumor margins as positive margins on final pathology hold a major risk of local relapse. The intra-operative assessment of margin status (MS) is essential in breast-conserving surgery as it helps reducing the positive margins and re-excision rates. Several teams perform BCS without intra-operative histological margin assessment. This approach is questionable because complementary excisions performed during a secondary operation may not be as precise as excisions performed during initial surgery. Moreover, from a psychological point of view, the perspective of a re-operation may cause anguish to patients treated for breast cancer. Last, this approach is also debatable from an economical point of view. Indeed, adding a supplemental operation might increase the costs of breast cancer handling.

Faxitron has been initially used for non-palpable lesions. Its use has then been extended to all types of lesions provided they are visible on mammograms. The use of intra-operative specimen radiography (IOSR) with FX for margin evaluation has been described by several teams which have brought to light the benefits of this procedure. Indeed, Layfield et al. have shown that IOSR reduced specimen weights without increasing the re-excision rate. Reducing specimen weights might limit the risk of having cosmetic sequelae after breast-conserving surgery. Moreover, Bathla et al. have shown that the use of FX allowed a decrease of the rates of margins positivity for patients requiring a second operation for re-excision. Thanks to this procedure, these patients thus avoided having a mastectomy. Muttalib et al. have compared IOSR with CSR and with FX. Although not statistically significant, the re-excision rate was 19.8% with the Faxitron and 31.5% with CSR. This could be explained by the fact that FX is a high-resolution device. It enables the surgeon to adjust the specimen image contrast and allows a better visualization of the tumor and a better evaluation of tumor margins.

Our study shows that the intra-operative evaluation of margin, for lesions that are visible on mammograms, can be rapidly and successfully achieved using a two-dimensional X-ray device settled in the operating room. FX allows a two-dimensional margin assessment but the analysis of the anterior and posterior margins is possible by pinning the lumpectomy specimen on a vertical polystyrene support. However, in our practice, it is seldom necessary as we perform tumor resection from the subcutaneous

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**Table 1**

Complementary excisions following the Faxitron Procedure (when the Faxitron was contributory).

<table>
<thead>
<tr>
<th>Lesions</th>
<th>Number of patients</th>
<th>Complementary excision after CSR</th>
<th>Complementary excision after HE</th>
<th>Negative margins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palpable</td>
<td>78</td>
<td>2</td>
<td>9</td>
<td>77</td>
</tr>
<tr>
<td>Non-palpable</td>
<td>77</td>
<td>0</td>
<td>5</td>
<td>74</td>
</tr>
</tbody>
</table>
plane to the pectoralis major fascia. Hence, the margins, which have to be evaluated, are the lateral ones.

In this study, the margin status (MS), evaluated with FX, was corroborated by intra-operative CSR and/or HE in more 89.3% of the cases. Moreover, the positive margins rate in our series, for patients with contributory FX procedure, would have been 6.5% if the MS evaluation had relied only on FX. This rate is low when compared to the positive margins rates found in the literature which range from 10 to 40%. Our rate compares well with the findings of McCormick et al. who observed a decrease of their positive margins rate from 12% to 5% thanks to the use of systematic specimen radiography. Furthermore, in our study, positive margins were only found in patients with DCIS for which MS intra-operative evaluation is known to be difficult. The re-operation rate for DCIS in this series was 18.2% and compares well with the data found in the literature for this histological sub-type.

Moreover, this study tends to show that having margins on FX superior or equal to 10 mm leads to negative final margins in 98.5% of the IDC, 90% of ILC and 78.5% of DCIS (p = 0.0001) which often are ill-defined lesions. To our knowledge, this is the first study that analyzes the accuracy of FX depending on the histological subtype of the tumor.

This approach has however some limitations. First, in our series, FX did not allow margin assessment in 8.8% of the cases (15 patients) that were excluded from the analysis of FX’s accuracy. Although not statistically significant, these 15 patients had type 3 or 4 breast density and a smaller median tumor size. These elements might explain the fact that FX was not contributory. Another limitation of this approach is that it can only be used for lesions that are visible on mammograms. However, for non-visible lesions, tumor resection can be guided by intra-operative ultrasonography. Indeed, several studies analyzing the use of this technique showed low positive margin rates ranging from 3 to 11%.

From an organizational point of view, the FX procedure has many advantages. Indeed, intraoperative HE takes 20−30 min. When compared to HE, The FX procedure is almost 20-times faster (90 s versus 30 min). Thus, FX might be able to decrease the operating time and increase the number of operations per theater list. For instance, in our surgery department, the achievement of a lumpectomy and sentinel lymph node biopsy requires 2 h including operating room preparation, anesthesiology, surgery and intraoperative margin assessment. A 30-min time-saving would reduce the operating time by 25% and might allow a supplementary intervention every operating day as stated by Mutallib et al.

Conclusion

The evaluation of MS with FX, when contributory, would have allowed the achievement of negative margins in 93.5% of the cases. The accuracy of the FX in the evaluation of MS seems to depend on the histological subtype of the cancer. A better selection of the patients might enhance the accuracy of the FX procedure. Indeed, this approach may be limited for high-density breasts and/or small lesions.

This procedure allows important time-saving which could have a major economical impact. If our data are confirmed the FX procedure might be an alternative notably to intra-operative HE in some specific indications with substantial economical and organizational benefits.

Conflict of interest statement

The authors have no conflict of interest to disclose.

References


