Vacuum intraoperative specimen mammography: A novel technique

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ABSTRACT

Objective: Intraoperative specimen mammography (ISM) is a diffuse technique that allows surgeons to check specimens immediately after lumpectomy. Although the specimen is slightly compressed, the radiological image can be distorted by tissue overlap, and this may affect the evaluation of tumour borders, resulting in extension of the lumpectomy. As ISM may be less precise due to inadequate compression, a vacuum effect was applied to the specimen to increase the precision of margin detection. Study design: This study was conducted at St. Anna Hospital Breast Unit, Turin, Italy. Women who underwent lumpectomy for cancer were eligible for inclusion. Both standard ISM (sISM) and vacuum ISM (vISM) were performed. Eighteen specimens obtained after lumpectomy from 1 April 2018 to 31 April 2018 were scanned. sISM (two orthogonal projections) was performed. Next, the specimen was placed in a vacuum, and vISM was performed. The examination was completed with a second orthogonal projection after removal of the vacuum, replacement of the specimen and repositioning of the vacuum. Additional tissue was removed if the surgeon considered that excision was inadequate. Finally, the specimen was sent for definitive histopathological analysis, which is the gold standard for the assessment of surgical margins. Intraoperative histological margin assessment was not performed. The sISM and vISM images and final histopathology reports were compared.

Results: For sISM, specificity was 47% (95% confidence interval [CI] 25–70), sensitivity was 67% (95% CI 21–94), positive predictive value (PPV) was 20% (95% CI 6–51) and negative predictive value (NPV) was 88% (95% CI 53–98). For vISM, specificity was 100% (95% CI 80–100), sensitivity was 67% (95% CI 21–94), PPV was 100% (95% CI 34–100) and NPV was 94% (95% CI 72–99).

Conclusion: These data suggest that the vacuum technique is feasible, cost-saving and yields results that are similar to those from frozen sections but without the limitations, such as prolonged operating time, high variability in sensitivity due to pathologists’ abilities, risk of compromising the histological report, and unreliability for small lumps and ductal carcinoma in situ.

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Objective

A free margin is regarded as an essential outcome for a correct surgical procedure. According to currently available evidence, the presence of a free margin correlates with a better postoperative prognosis. The concept of a free margin surgical intervention goes beyond the idea of an excessive margin procedure. In this context, the St. Gallen consensus conference stated that ‘no ink on tumour’ is the standard goal for conservative surgery for invasive cancer [1].

Standard specimen mammography (SSM) is used routinely to confirm the presence of the target breast lesion within the excised specimen and to evaluate the adequacy of the margin. SSM requires transport of the specimen to the radiology department, evaluation by an expert radiologist and communication of the results to the operating room. In the case of an inadequate margin or partial excision of the tumour, the surgeon can excise additional tissue in the same surgical session. All of the procedures listed above are time consuming, and they are executed while the patient is under local or systemic anaesthesia. Intraoperative specimen mammography (ISM) is a diffuse technique that enables surgeons to check specimens immediately after lumpectomy, directly in the operating room. Specimen images can also be transmitted to the radiology picture archiving and communication system. ISM

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consists of a radiography-oriented specimen in two projections. Radiological images are available, at the same time, for both the surgeon and the radiologist, who analyse the images and decide whether the margin is free.

Although the specimen is slightly compressed in ISM, radiological images are sometimes distorted by tissue overlap. The tissue overlap during the intraoperative radiological procedure may alter the evaluation of tumour borders, resulting in wider extension of the lumpectomy. Although the limits of the current practice are well known, no other options are clinically available at present. In this context, this study was designed to evaluate a novel technique consisting of ISM of the surgical specimen after vacuum sealing, with the purpose of reducing tissue overlap, increasing the accuracy of imaging and minimizing unnecessary resections.

**Study design**

This pilot study was conducted at St. Anna Hospital Breast Unit, Turin, Italy, which was founded in 2015. Each year, approximately 500 patients are treated for breast cancer at this unit. The surgical team at the breast unit includes six certified surgeons, and each surgeon performs approximately 70–90 procedures per year.

All of the patients underwent mammography and breast ultrasound preoperatively. Patients with small and localized lesions were selected for breast-conserving surgery (BCS) in order to preserve the cosmetic appearance of the breast, together with complete resection of the neoplastic lesion. Non-palpable and ultrasound-detectable tumour resections were guided by skin markers. Non-palpable and ultrasound-undetectable tumour resections were guided by metallic hook wire.

BCS resection was performed with a free margin, and the surgical specimen was imaged immediately by SSM and evaluated by an expert radiologist and surgeon. A lymph node biopsy was performed in the same surgical procedure.

Inclusion criteria were: breast cancer detected by a screening test, and treatment with surgical lumpectomy. Eighteen specimens obtained after lumpectomy from 1 April 2018 to 30 April 2018 were scanned. Lumps were oriented with metallic stiches. Both standard ISM (sISM) and vacuum ISM (viSM) were performed. A dedicated breast surgeon at the study institution performed both surgery and radiological scans, and their interpretation. A dedicated radiologist reviewed all of the images. ISM was performed by a digital specimen mammography system (Faxitron, Bioptics Inc., Tucson, AZ, USA) in the operating room. Specimen registration and ISM analysis took 3 min. sISM (two orthogonal projections) was performed. Specimens were sealed in plastic bags in the vacuum apparatus (TissueSAFE Milestone Medical, Sorisole, Italy); this process took a few seconds. Next, viSM was performed, and the examination was completed with a second orthogonal projection after removing the vacuum, replacing the specimen and repositioning the vacuum. Additional tissue was removed if the surgeon considered that excision was inadequate. Finally, the specimen was sent for definitive histopathological analysis, which is the gold standard for the surgical assessment of margins. Intraoperative histological margin assessment was not performed. Patient characteristics and pathology and treatment-related data were collected via medical record review. The siSM and viSM images and final histopathology reports were compared.

**Results**

In total, 72 % (13/18) of lesions were seen on mammography as masses, 5 % (1/18) as microcalcifications and 23 % (4/18) as parenchymal distortions. The average tumour diameter on mammography/ultrasound was 12 mm. Fifty percent (9/18) of tumours were palpable. Sixty-one percent (11/18) of specimens were invasive ductal cancer, 11 % (2/18) were invasive lobular cancer, 11 % (2/18) were in-situ lesions, 11 % (2/18) were invasive papillary cancer and 5 % (1/18) were tubular carcinoma. The average tumour diameter on histopathological analysis was 11.8 mm (range 1–23 mm). The tumoural target was identified in the specimen by the surgeon in all 18 cases.

Concordance between margin interpretation by the surgeon using sISM and viSM, and then between ISM (siSM and viSM) and histological margin assessment was evaluated. Concordance was 44 % (8/18) for margin interpretation between siSM and viSM. Eight patients were considered to have positive margins on siSM but negative margins on viSM; only one of eight patients had a positive margin on pathology (viSM false-negative case). One patient was considered to have a free margin on siSM but a positive margin on viSM; the margin was positive on pathology (siSM false-negative case). Surgical margins were radiologically involved in 55 % (10/18) of specimens analysed with siSM and 11 % (2/18) of specimens analysed with viSM, while 16 % (3/18) of specimens were histopathologically involved (Table 1).

Table 2 shows the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for identification of positive margins for siSM and viSM using the pathologic margin status of the specimen. For siSM, specificity was 47 % [95 % confidence interval (CI) 25–70], sensitivity was 67 % (95 % CI 21–94), PPV was 20 % (95 % CI 6–51) and NPV was 88 % (95 % CI 53–98).

For viSM, specificity was 100 % (95 % CI 80–100), sensitivity was 67 % (95 % CI 21–94), PPV was 100 % (95 % CI 34–100) and NPV was 94 % (95 % CI 72–99).

**Discussion**

Positive microscopic margins for lumpectomies are associated with a significantly higher rate of local recurrence than negative margins. The St. Gallen Panel reiterated the ‘no ink on tumour’ rule for the surgical margin of invasive breast cancer [1]. According to recent guidelines from the Surgical Society of Oncology, American Society of Clinical Oncology and American Society for Radiation Oncology, a 2-mm margin is sufficient for in-situ lesions [2] and a 1-mm margin is sufficient for invasive lesions.

Re-operation after conservative surgery of the breast leads to additional costs, non-aesthetic results and patient discomfort. Intraoperative histopathological assessment of surgical margins guarantees a complete lump excision, but requires time and has additional costs. ISM provides two digital x-ray specimen images to provide rapid confirmation of complete excision of the breast mass. Performing ISM in the same operating room or nearby saves time and reduces anaesthesia and useless re-interventions.

Previous studies have shown that specimen radiography can limit the number of patient recalls [3,4]. Compared with SSM, ISM has comparable accuracy and a shorter operative time [1,2,4]. ISM is a valid, safe and quicker alternative to intraoperative histopathological study, but has been reported to be limited due to less compression than standard SSM. Consequently, ISM may result in a high percentage of false-positive results, meaning unnecessary wider resections that lead to increased operative times and worse aesthetic results.

The sensitivity of ISM reported in the literature ranges from 20 % to 50 %, specificity ranges from 89 % to 94 %, PPV is 50 % and NPV is 82–89 % [5,6].

As ISM may be less precise due to inadequate compression, a vacuum effect was performed on the specimen to increase the precision of margin detection. viSM images seem to be easier to interpret than siSM images (Figs. 1–4) as they are characterized by a vacuum-created radiolucent rim that better defines the tumour margins. Moreover, the vacuum technique stretches the removed
tissue, thus preventing overlaps, and helps to prevent underestimation of the surgical margin, even in the case of micro-calculcations. In this study, the sensitivities for ISM and SSM were the same (67 %), but the specificity of vISM was higher than that of sISM (100 % vs 47 %); these data reflect the ability of vISM to identify the real involved margins that are sometimes identified incorrectly on sISM. Consequently, the PPV and NPV of vISM were higher compared with sISM (100 % vs 20 % and 94 % vs 88 %, respectively).

In total, 50 % (9/18) of patients were considered to have positive margins on sISM but negative margins on vISM. As a result, no further excision was performed. Only one of eight patients had a positive margin on pathology, but no further excision was performed because a 1-mm extension of the tumour on the surgical margin was reported. As such, the patient was treated with adjuvant radiotherapy alone. Furthermore, by reviewing the sISM and vISM images of the patients retrospectively, the part of the margin with tumour involvement could be detected correctly on vISM (Fig. 5).

These data suggest that the vacuum technique is feasible, cost-saving and yields results that are similar to those from frozen sections but without the limitations, such as prolonged operative time, high variability in sensitivity due to pathologists’ abilities, risk of compromising the histological report, and unreliability for small lumps and ductal carcinoma in situ [3,7,8]. Furthermore, vISM allows more accurate evaluation of the surgical margin without requiring additional equipment, such as intra-operative three-dimensional tomography imaging, which is not available at the study centre at present.

Recently, hand-held 18F-fluoro-2-deoxy-D-glucose (18F-FDG) positron emission tomography has been proposed as a novel technique based on overexpression of the facilitative glucose

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**Table 1**

<table>
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<tr>
<th>Patient</th>
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<th>Tumour diameter on mammogram (mm)</th>
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<th>vISM margina</th>
<th>Histology</th>
<th>Histological type</th>
<th>Grading IC (mm)</th>
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</table>

IC, invasive cancer; DCIS, ductal carcinoma in situ; ADH, atypical ductal hyperplasia; ILC, invasive lobular carcinoma; B3, lesions of uncertain malignant potential; IMPC, invasive micropapillary carcinoma; NST, no special type; sISM, standard intraoperative specimen mammography; vISM, vacuum intraoperative specimen mammography.

*a Margin: 0, free; 1, involved.

**Table 2**


<table>
<thead>
<tr>
<th>Histopathology margins</th>
<th>Statistic</th>
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<tr>
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<td>Total</td>
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transporter GLUT1 in cancer cells. Although sensitivity and specificity are relatively high, spatial resolution remains a strong limitation of this technique, especially below 1 cm. Additionally, 18F-FDG has a limited role in well-differentiated and lobular breast tumours, has non-specific uptake in inflammatory areas, is very expensive, and is associated with non-negligible radiation exposure for the operating personnel [7,8].

In the authors’ experience, the positive margin rate at the first surgical attempt at breast conservation is approximately one in six, which is far less than reported previously [9,10]. This could be related to routine use of the Faxitron in the operating room, as reported by Bathla et al., who reported a histologically clean margin rate of 84% [3]. This rate is consistent with the present results. Moreover, this novel technique overcomes some reported
bias in specimen handling between the operating room and the pathology department. The specimen undergoes an alteration called the ‘pancake phenomenon’, resulting in significant variation in tumour shape, mean volume and size. The flattening of specimens by the vacuum is obtained immediately after tumour removal by the surgeon; thereafter, the specimen is transported immediately to the pathology department, avoiding the dehydration process that likely causes the pancake phenomenon [11].

**Conclusion**

This was a pilot study, so the population analysed was very small. The authors’ intention is to continue using the vacuum technique before acquiring ISM images, and to verify if the technique effectiveness doesn’t change according to histological type of the tumor, radiological aspect (mass, microcalcifications or opacity), breast size and density.

**Funding**

None.

**Declaration of Competing Interest**

None declared.

**Appendix A. Supplementary data**

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ejogrb.2020.07.004.

**References**


[6] Miller Cl, Coopey Sr, Rafferty E, Gadd M, Smith Bl, Specht MC. Comparison of intra-operative specimen mammography to standard specimen mammogra-


