Editorial Commentary

Indications and methods of intraoperative specimen radiography in breast-conserving surgery

Ji Young Kim, Yong Sik Jung, Se Hwan Han, Ji Hyun Sung, Min Hee Hur

Department of Surgery, Ajou University Hospital, Suwon, Republic of Korea

Correspondence to: Min Hee Hur. Department of Surgery, Ajou University Hospital, Suwon, Republic of Korea. Email: hmh1916@gmail.com.

Comment on: Funk A, Heil J, Harcos A, *et al.* Efficacy of intraoperative specimen radiography as margin assessment tool in breast conserving surgery. Breast Cancer Res Treat 2020;179:425-33.

Submitted Sep 08, 2020. Accepted for publication Oct 10, 2020.

doi: 10.21037/tcr-20-2859

View this article at: http://dx.doi.org/10.21037/tcr-20-2859

Breast-conserving surgery (BCS) has been increasingly performed owing to advances in surgical techniques. BCS can provide survival and cosmetic benefits to patients with breast cancer. However, 15–35% patients who undergo BCS subsequently undergo re-excision when histological analysis reveals a positive margin. Accordingly, various methods have been studied to obtain a negative margin in the first BCS, which is one of the most important determinants of the local recurrence rate (1,2). The margin assessment methods approved by the Food and Drug Administration include specimen X-ray, radiofrequency, frozen sectioning, hematoxylin and eosin staining, and touch cytology. In addition, several studies have reported that margin assessment methods have >95% sensitivity using multidimensional data and volumetric three-dimensional (3D) analysis. Furthermore, cellular or molecular level margin assessment methods that do not involve artifacts, large-scale technical issues, or high-cost intraoperative histological assessment tools are being sought (3). Specimen radiography is an easy and cost-effective method widely used alongside mammography/tomosynthesis in the preoperative evaluation of patients and lesions targeting X-ray-guided wire/seed localization. Nevertheless, radiological systems have limited penetration depth and may not provide adequate information regarding internal aspects of the specimen. Therefore, it is more reliable to use a combination of methods to identify the status of the margins instead of a single method. Maloney *et al.* reported that micro-computed tomography is the best system to assess the internal aspects and tissue volume of specimens, whereas spatial frequency domain imaging, spectral imaging, and radiofrequency imaging are ideal for the evaluation of the tissue surface (3). The applicability of current assessment modalities is limited owing to prolonged surgical time, and interpretation of the test results is complex. Therefore, based on the results of previous studies, we aimed to provide information on patient selection for intraoperative specimen radiography and execution of the procedure to improve procedure accuracy.

Type of X-ray imaging

In general, 3D images are considered more useful than two-dimensional (2D) images. In a prospective study, the sensitivity and specificity of 2D and 3D images were 41% and 47% and 78% and 75%, respectively. The treatment plan was changed in only 6.3% patients who underwent 3D imaging (4). In another study comparing digital breast tomosynthesis and full-field digital mammography, digital breast tomosynthesis had a significantly higher sensitivity and demonstrated a reduced rate of re-excisions (5). Therefore, identification of the vertical plane of a specimen using tomosynthesis may be more appropriate than using digital mammography; however, it is possible to reduce the re-excision rate using the latter modality.

Mammographic breast density

The chief limitation of specimen mammography is the lack of specificity for tumor and dense fibroglandular tissue. Radiography is useful for further resection if the tumor has microcalcifications. For non-palpable lesions, preoperative mammographic breast density can be an important variable to target the lesion and perform specimen radiography to assess the status of the margin. Fatty breasts can affect evaluation of the margin by flattening the specimen if compression is applied when performing mammography. However, fatty breasts are excellent for confirming lesions using radiography owing to the small amount of fibroglandular tissue. Evaluation of margins becomes more difficult in cases of higher mammographic density, regardless of the presence of microcalcifications. In a previous study, margin assessment was possible in approximately 69% cases with a preoperative mammographic density of ≥75% (6). Therefore, it may be inappropriate to use specimen radiography as a margin assessment method in patients with extremely dense breasts.

Types of mammographic lesions

The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of margin assessments using specimen radiography differ depending on the inclusion or exclusion of microcalcifications. Several studies including patients with microcalcifications have reported that margin assessment using specimen radiography has a sensitivity of 50–72%, specificity of 52–74%, PPV of 76%, and NPV of 46% (7,8). However, there are no reports on the accuracy of specimen radiography in patients without microcalcifications. In a study by Kim *et al.*, the presence of microcalcifications on mammography was an independent predictor of final positive margin (odds ratio, 4.1; 95% confidence interval, 1.2–13.7) (9). Therefore, it is necessary to radiographically confirm the safety margin of lesions that contain microcalcifications owing to the increased likelihood of positive margins.

Range of microcalcifications

Most ductal carcinomas in situ (DCISs) often demonstrate microcalcifications and are a known risk factor for positive resection margins. In previous studies, approximately 78–96% of the involved margins were owing to DCIS (10-13). Several studies have been conducted to assess the possible effects of the range of microcalcifications on the accuracy of specimen radiography. In particular, the size of the DCIS tends to be underestimated on radiological imaging based on the range of microcalcifications on mammography, leading to a positive margin (14-17). Radiopathological discrepancies may exist; however, Layfield *et al.* have reported a statistically significant increase in re-operation rates when the range of microcalcifications exceeded 30 mm (18). Therefore, in cases with a wide range of microcalcifications, it is advisable to use alternative margin assessment methods.

Specimen volume and height

In most cases, the volume and height of the specimen measured tended be lower than those measured by the surgeon during BCS. The height decreases by at least 5 mm; therefore, the results of pathological analysis might be closer to the margin. In a study by Graham *et al.*, the decrease in specimen volume and height was associated with five factors—patient age, breast tissue density, mammographic lesion type, specimen size, and use of compression during specimen radiography. The only variable that independently contributed to the flattening was the use of compression during specimen radiography. Flattening was more severe when specimen radiography with compression was performed than when specimen radiography without compression was performed; the height decreased by 54% and 41%, respectively (19). In another study, margin distortion owing to compression was inevitable while performing specimen radiography (20). One study found that a 25- or 28-kV Mo/Mo target/filter setting was optimal for smaller breasts (21–32 mm in thickness), whereas a 34-kV beam with Rh/Rh target/filter was ideal for larger breasts (>45 mm in thickness) (21). Therefore, the necessity of compression when performing specimen radiography may be questioned in such situations. In a previous study, adequate radiographic confirmation of lesions was possible without compression in cases that underwent mammography-guided localization (22). However, compression of the specimen could be misinterpreted as a wider excision than the actual margin. Hence, it is necessary to compare the status of the margin in each situation. Furthermore, safety margins should be determined in either situation (compressed or uncompressed situations.

Width of safety margin

There is no consensus regarding the distance (mm) from the tumor to the resection margin during specimen radiography to recommend excision of additional tissue. A greater threshold may be associated with fewer with positive margins, but it leads to unnecessary resection of healthy tissue. Some studies have noted an increased sensitivity when a greater radiological margin was considered; however, the specificity inversely decreased (23-25). Studies have attempted to define the optimal threshold and proposed radiologic margin widths of 4–11 mm (7,11). One study has specifically suggested a 15-mm marginal width for optimal sensitivity and specificity using receiver operating characteristic curves (24). However, the optimal radiological threshold for DCIS-associated specimens is unknown.

Histological characteristics

The final histological characteristics are determined after surgery; therefore, their prediction before surgery is difficult. However, it is possible to predict invasive carcinoma, DCIS component in invasive carcinoma, and pure DCIS based on the results of various preoperative imaging studies and core biopsy. Most studies have retrospectively investigated the effectiveness of specimen radiography based on each histological characteristic. As expected, histological DCIS >20 mm was found to be an independent predictor of surgically involved margins, while a specimen radiography margin <4 mm trended toward significance (7).

In summary, assessment of lesions containing microcalcifications <30 mm should be performed using intraoperative specimen radiography in patients with a mammographic breast density of ≤75%. Considering the tendency of a decrease in the volume and height of specimens during histological analysis, radiography should be performed in two views (with and without compression), and the safety margin should be confirmed at 15 mm. In this manner, intraoperative radiography can be efficiently performed in most patients.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Translational Cancer Research*. The article did not undergo external peer review.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/tcr-20-2859). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Schnitt SJ, Abner A, Gelman R, et al. The relationship between microscopic margins of resection and the risk of local recurrence in patients with breast cancer treated with breast-conserving surgery and radiation therapy. Cancer 1994;74:1746-51.
2. Silverstein MJ, Lagios MD, Groshen S, et al. The influence of margin width on local control of ductal carcinoma in situ of the breast. N Engl J Med 1999;340:1455-61.
3. Maloney BW, McClatchy DM, Pogue BW, et al. Review of methods for intraoperative margin detection for breast conserving surgery. J Biomed Opt 2018;23:1-19.
4. Chagpar AB, Butler M, Killelea BK, et al. Does three-dimensional intraoperative specimen imaging reduce the need for re-excision in breast cancer patients? A prospective cohort study. Am J Surg 2015;210:886-90.
5. Amer HA, Schmitzberger F, Ingold-Heppner B, et al. Digital breast tomosynthesis versus full-field digital mammography- Which modality provides more accurate prediction of margin status in specimen radiography? Eur J Radiol 2017;93:258-64.
6. Jin M, Kim JY, Kim TH, et al. Intraoperative specimen mammography for margin assessment in breast-conserving surgery. J Breast Cancer 2019;22:635-40.
7. Lange M, Reimer T, Hartmann S, et al. The role of specimen radiography in breast-conserving therapy of ductal carcinoma in situ. Breast 2016;26:73-9.
8. Mazouni C, Rouzier R, Balleyguier C, et al. Specimen radiography as predictor of resection margin status in non-palpable breast lesions. Clin Radiol 2006;61:789-96.

9. Kim SHH, Cornacchi SD, Heller B, et al. An evaluation of intraoperative digital specimen mammography versus conventional specimen radiography for the excision of nonpalpable breast lesions. Am J Surg 2013;205:703-10.
10. Kurniawan ED, Wong MH, Windle I, et al. Predictors of surgical margin status in breast-conserving surgery within a breast screening program. Ann Surg Oncol 2008;15:2542-9
11. Britton PD, Sonoda LI, Yamamoto AK, et al. Breast surgical specimen radiographs: how reliable are they? Eur J Radiol 2011;79:245-9.
12. Miller AR, Brandao G, Prihoda TJ, et al. Positive margins following surgical resection of breast carcinoma: analysis of pathologic correlates. J Surg Oncol 2004;86:134-40.
13. Mai KT, Chaudhuri M, Perkins DG, et al. Resection margin status in lumpectomy specimens for duct carcinoma of the breast: correlation with core biopsy and mammographic findings. J Surg Oncol 2001;78:189-93.
14. Holland R, Hendriks JH, Vebeek AL, et al. Extent, distribution, and mammographic/histological correlations of breast ductal carcinoma in situ. Lancet 1990;335:519-22.
15. Thomas J, Evans A, Macartney J, et al. Radiological and pathological size estimations of pure ductal carcinoma in situ of the breast, specimen handling and the influence on the success of breast conserving surgery: a review of 2654 cases from the Sloane Project. Br J Cancer 2010;102:285-93.
16. Aziz D, Rawlinson E, Narod SA, et al. The role of reexcision for positive margins in optimizing local disease control after breast-conserving surgery for cancer. Breast J 2006;12:331-7.
17. Dillon MF, Mc Dermott EW, O'Doherty A, et al. Factors affecting successful breast conservation for ductal carcinoma in situ. Ann Surg Oncol 2007;14:1618-28.
18. Layfield DM, See H, Stahnke M, et al. Radiopathological features predictive of involved margins in ductal carcinoma in situ. Ann R Coll Surg Engl 2017;99:137-44.
19. Graham RA, Homer MJ, Katz J, et al. The pancake phenomenon contributes to the inaccuracy of margin assessment in patients with breast cancer. Am J Surg 2002;184:89-93.
20. Clingan R, Griffin M, Phillips J, et al. Potential margin distortion in breast tissue by specimen mammography. Arch Surg 2003;138:1371-4.
21. Young KC, Oduko JM, Bosmans H, et al. Optimal beam quality selection in digital mammography. Br J Radiol 2006;79:981-90.
22. Méndez JE, ter Meulen D, Padussis J, et al. Tissue compression is not necessary for needle-localized lesion identification. Am J Surg 2005;190:580-2.
23. Schmachtenberg C, Engelken F, Fischer T, et al. Intraoperative specimen radiography in patients with nonpalpable malignant breast lesions. Rofo 2012;184:635-42.
24. Leung BST, Wan AYH, Au AKY, et al. Can intraoperative specimen radiograph predict resection margin status for radioguided occult lesion localisation lumpectomy for ductal carcinoma in situ presenting with micro-calcifications? Hong Kong J Radiol 2015;18:11-21.
25. Fouché CJ, Tabareau F, Michenet P, et al. Specimen radiography assessment of surgical margins status in subclinical breast carcinoma: a diagnostic study. J Gynecol Obstet Biol Reprod (Paris) 2011;40:314-22.

Cite this article as: Kim JY, Jung YS, Han SH, Sung JH, Hur MH. Indications and methods of intraoperative specimen radiography in breast-conserving surgery. Transl Cancer Res 2020;9(11):6625-6628. doi: 10.21037/tcr-20-2859

