La radiologia medica (2021) 126:768–773
https://doi.org/10.1007/s11547-021-01337-9

BREAST RADIOLOGY

Diagnostic accuracy of resection margin in specimen radiography: digital breast tomosynthesis versus full-field digital mammography

Giovanna Romanucci[1] · Sara Mercogliano[2] · Elisabetta Carucci[3] · Alessandro Cina[2] · Elisa Zantedeschi[4] · Andrea Caneva[5] · Chiara Benassuti[6] · Francesca Fornasa[6]

Received: 20 August 2020 / Accepted: 3 February 2021 / Published online: 24 February 2021

Abstract

Objective We investigated the accuracy of digital breast tomosynthesis compared to full-field digital mammography for evaluating tumor-free resection margins in the intraoperative specimen during breast-conserving surgery, reducing re-excision rates.

Materials and Methods In total, 170 patients, with proven breast cancer and eligible for breast-conserving surgery, were enrolled. Intraoperative specimens underwent digital mammography and digital breast tomosynthesis. Two breast radiologists, with ten years of experience in breast imaging, in batch mode, evaluated tumor-free resection margins and the distance between the margins and lesion. Histopathological findings were considered the standard of reference.

Results We used the correlation analysis to evaluate the agreement between measures of tumor-free resection margins obtained with digital mammography and the true value (histopathological findings), and between digital breast tomosynthesis and histopathological findings. The size evaluation determined by digital breast tomosynthesis was more accurately correlated with that found by pathology; the calculated Pearson's correlation coefficient of digital breast tomosynthesis and digital mammography to the pathologically determined tumor-free resection margins were 0.92 and 0.79 in CC view and 0.92 and 0.72 in LL view, respectively. Compared with the pathologically determined tumor-free resection margins, the size determined by both imaging modalities was, on average, overestimated. Bland–Altman analysis showed an excellent inter readers agreement.

Conclusions Digital breast tomosynthesis is more accurate in assessment of margin status than digital mammography; it could be a more accurate technique than full-field digital mammography for the intraoperative delineating of tumor resection margins.

Keywords Digital breast tomosynthesis · Digital mammography · Specimen radiography · Margin assessment · Breast-conserving surgery

✉ Giovanna Romanucci
giovanna.romanucci@aulss9.veneto.it

1 UOSD Breast Unit ULSS9 Scaligera, Fracastoro Hospital, 1 Via Circonvallazione, 37047 San Bonifacio, VR, Italy

2 Department of Diagnostic Imaging, Radiation Oncology and Haematology, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy

3 Department of Diagnostic Imaging, Santa Maria Degli Angeli Hospital, Putignano, BA, Italy

4 Department of Radiology, G. Fracastoro Hospital, San Bonifacio, VR, Italy

5 Department of Anatomy and Pathological Histology, G. Fracastoro Hospital, San Bonifacio, VR, Italy

6 Breast Unit ULSS9, G. Fracastoro Hospital, San Bonifacio, VR, Italy

Introduction

In recent years, breast screening has greatly increased the early detection of cancer and therefore the chances for successful treatment [1]. The standard treatment for early breast cancers is breast-conserving surgery (BCS); indeed, BCS plus radiotherapy is equivalent to mastectomy with respect to long-term survival in these patient [2]. However, being able to predict tumor-free resection margins is crucial for decreasing the risk of local recurrence. Therefore, the radiologist is needed during surgery for communicating with the surgeon in order to ensure a tumor-free resection with or without further excision [2]. Intraoperative specimen radiography is the method of choice to determinate the integrity of resection [3, 4], but it is often difficult on full-field digital mammography (FFDM) due to superimposed structures in a two-dimensional (2D) projection. Digital breast tomosynthesis (DBT), performing a pseudo-3D breast examination [5], overcomes this problem, allowing better view of lesion margins [1, 6]. There are already several studies about the usefulness of DBT in diagnosis of breast cancer [7, 8], but not many on the role of DBT in evaluation of tumor margin status in specimen radiography [4, 6, 9]. The purpose of this study was to compare the accuracy of DBT and FFDM for evaluating tumor-free resection margins in the intraoperative specimen during BCS, with the aim of reducing re-excision rates.

Materials and methods

This prospective study was granted institutional ethics approval and specific written informed consent was required for all patients. From January 1, 2017, to December 31, 2018, women with a suspicious mammographic or clinical abnormality detected at our Institute were considered for inclusion in this study. All these women referred to a second-level assessment that could potentially include additional DBT plus synthetic 2D views, ultrasonography (US) and core needle biopsy or vacuum-assisted breast biopsy (VAB), when indicated. Patients, with histological confirmation of breast cancer, underwent surgical procedures (BCS or mastectomy) with subsequent imaging and/or histopathological confirmation of the radical resection. Patients were recruited in our study according to the following inclusion criteria: no previous breast surgery; histological confirmation of breast cancer (297); BCS procedures (225/297); radical resection confirmed by both FFDM and DBT examinations on the resected specimens (170/225). Exclusion criteria included: histological diagnosis of benign lesions; mastectomy (72/297); surgeon specimens unexamined by DBT imaging (55/225: 54/55 FFDM e 1/55 US). Thus, our study population consisted of 170/297 breast lesions; the lesions were subgrouped according to their features into 4 categories: opacity, architectural distortion, calcifications and opacity plus calcifications. All patients were women, with an average age of 62 years, ranging between 30 and 86 years. All breast lesions were marked with a charcoal suspension under US guidance, one day before surgery. A black trail was left behind from the lesion toward the skin, where a small tattoo mark was visible. Thereafter, surgical local excision was performed. To allow correct specimen orientation, each specimen was clipped in the operating room: 1 clip in the areolar resection margin, 2 clips in the cranial resection margins and 3 clips in lateral resection margins. Intraoperative X-ray of the specimen was obtained to assess the adequacy of the excision margin. In our Institution, if the tumor-free margin width is < 1 mm, supplementary excision is performed; if the margin width is > 1 mm and < 5 mm, a facultative extension is possible. There is no consensus on the width of tumor-free margin after surgery; it varies from 1 to 10 mm [4, 10]. Each specimen was examined using a Selenia Dimensions unit (Hologic, Bedford, MA, USA) with capability for DBT and FFDM acquisitions; examinations included cranio-caudal (CC) and latero-lateral (LL) views (Fig. 1). Two breast radiologists, with at least ten years of experience in breast imaging, in batch mode, analyzed images obtained by DBT and FFDM, rating the distance of the lesion from the closest specimen edge both in CC and LL views in both modalities, using the clip positions for orientation. Following imaging, the surgical specimen was submitted for histological processing, which included estimates of size, grade, type of tumor and the distance (in millimeters) from the lesion to the closest resection margin. Histopathological findings were regarded as reference standard. Given the excellent inter-reader agreement, correlation analysis was performed to compare the measures obtained only by the first reader with each modality and histopathology. All statistical analyses were done using SPSS (SPSS version 22.0, IBM, Chicago, IL, USA) and with a P value < 0.05 considered statistically significant. The size difference in millimeters between the imaging modalities measurements and the pathology measurement was analyzed using the paired t-test, and P-values for comparative performance were calculated. Since measure of distal margins were expressed as continuous data, we employed Bland–Altman analysis to assess quantitative differences among two readers.

Results

The correlation analysis was used to evaluate the agreement between measures of tumor-free resection margins obtained at FFDM and the true value, given by histopathological findings, and between DBT and histopathological findings.

The mean distance from the lesion to the closest resection margin determined pathologically was 7.7 mm in CC view and in 11 mm in LL view (standard deviation [SD], 5.40 and 5.59, respectively). The mean distance determined on DBT was 8.8 mm (range, 1–27 mm) in CC view and 11.2 mm in LL view (range, 2–27 mm), and the mean distance determined by FFDM was 10.3 in CC view (range, 2–33 mm) and 12.5 in LL view (range, 2–32 mm) (Table 1). When compared with the pathology results, the measure of tumor-free resection margins was, on average, overestimated for both imaging modalities.

Size measurement determined by DBT was in stronger agreement with that of pathology than that measured by FFDM. The calculated Pearson's correlation coefficient of DBT and FFDM in whole specimens compared to the size

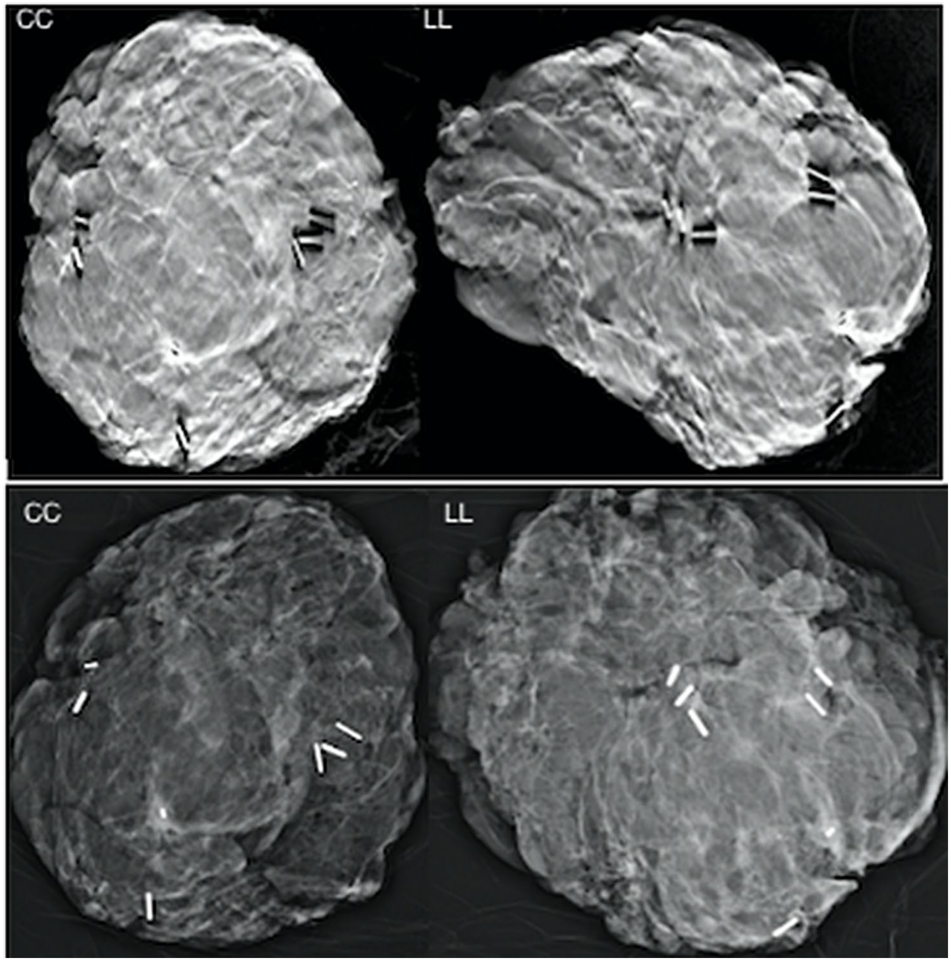

Fig. 1 Surgical specimen submitted to DBT (**a** CC view, **b** LL view) and FFDM (**c** CC view, **d** LL view)

Table 1 Descriptive statistic: average measurements determined by imaging modalities and pathology; mean errors between the imaging modalities measurements and the pathology. Measurement

Description	N	Mean	SD	SE
2D CC	170	10.3	5.06	0.39
3D CC	170	8.8	4.99	0.38
Histopat. findings in CC	170	7.7	5.40	0.41
2D LL	170	12.5	5.36	0.41
3D LL	170	11.2	5.06	0.39
Histopat. findings in LL	170	11.0	5.59	0.43
Error 2D CC	170	2.58	3.41	0.26
Error 3D CC	170	1.11	2.12	0.16
ABS Error 2D CC	170	3.46	2.51	0.19
ABS Error 3D CC	170	1.78	1.59	0.12
Error 2D LL	170	1.56	4.13	0.32
Error 3D LL	170	0.25	2.21	0.17
ABS Error 2D LL	170	3.59	2.55	0.20
ABS Error 3D LL	170	1.63	1.51	0.12

determined by pathology were 0.92 and 0.79 in CC view (Fig. 2) and 0.92 and 0.72 in LL view (Fig. 3), respectively (Table 2).

Measurement of 2D and 3D errors (difference between the imaging modalities measurements and the pathology measurement) was reported as mean ± standard errors (95% confidence interval was calculated). Student's *t* test was adopted to assess significant differences among data (Table 3). Although Student's t test assessed a significant differences ($p < 0.001$) for both methods, the mean error with DBT was lower than with FFDM: The mean error between the tumor-free resection margins and surgical findings was 1.11 ± 0.32 by DBT and 2.58 ± 0.51 by FFDM in CC view, and 0.25 ± 0.33 by DBT and 1.56 ± 0.62 by FFDM in LL view, respectively.

Bland–Altman analysis showed a good inter readers agreement. Mean differences and standard deviation of DM measure among readers are reported in Table 4. A more evident inter-reader agreement was founded in the 3D evaluation, particularly for LL.

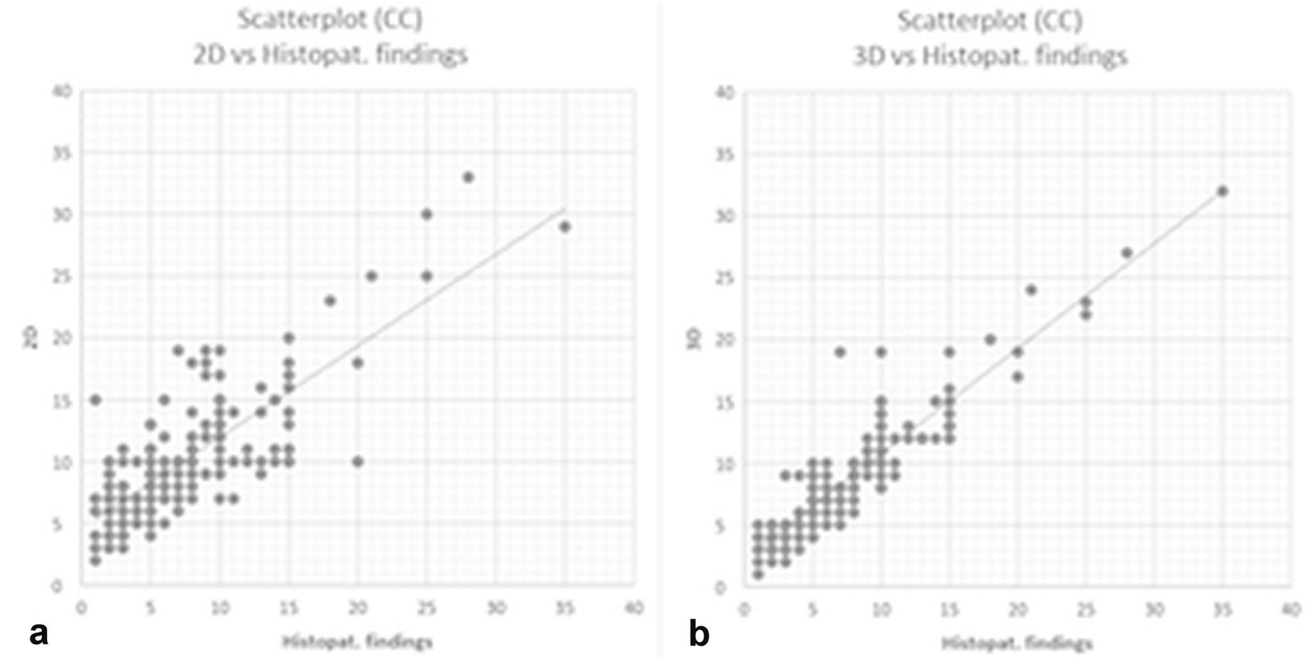

Fig. 2 Scatterplot for measurements of tumor-free resection margins obtained at FFDM (**a**) and DBT (**b**) in CC view and the histopathological findings with the solid line representing linear regression

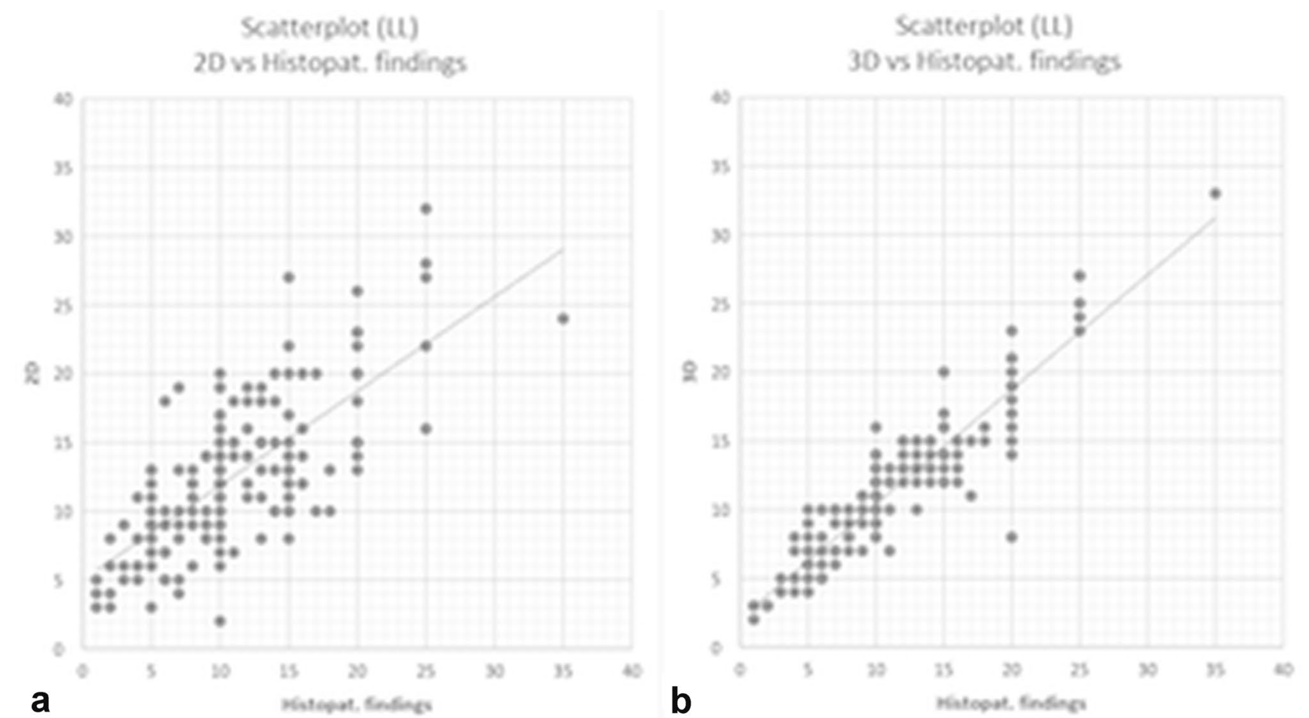

Fig. 3 Scatterplot for measurements of tumor-free resection margins obtained at FFDM (**a**) and DBT (**b**) in LL view and the histopathological findings with the solid line representing linear regression

Table 2 Correlation analysis

	2D CC	3D CC	Histopat. Findings CC
2D CC	1	//	//
3D CC	0.85	1	//
Histopat. findings in CC	0.79	0.92	1
	2D LL	3D LL	Histopat. Findings LL
2D LL	1	//	//
3D LL	0.76	1	//
Histopat. findings in LL	0.72	0.92	1

Table 3 Paired *t*-test

			t	df	*p*
Error 2D CC	–	Error 3D CC	6.99	169	< .001
ABS Error 2D CC	–	ABS Error 3D CC	9.89	169	< .001
Error 2D LL	–	Error 3D LL	4.73	169	< .001
ABS Error 2D LL	–	ABS Error 3D LL	9.71	169	< .001

Table 4 Bland–Altman analysis

Measurement	Mean difference ± SD
DM CC 3D	− 0.07 ± 6.13
DM CC 2D	− 0.07 ± 5.99
DM LL 3D	− 0.12 ± 6.54
DM LL 2D	0.20 ± 6.42

Discussion

Intraoperative imaging of specimen during BCS is of fundamental importance because it helps the surgeon complete procedures with improved safety, efficiency and clinical outcome. In fact, positive tumor margins following cancer resection often require additional treatments, involving significant prognostic implications. FFDM is the current modality of choice for intraoperative investigation of margin status in specimen radiography, although several intraoperative image-guided methods have been reported [11]. However, Pleijhuis RG et al. [12] suggested that FFDM is of limited use in assessing small, noncalcified lesions.

The potential use of DBT for the detection of breast cancer in the intraoperative specimen during BCS has been recently investigated in several studies. Urano et al. [1], in a study including 65 patients, emphasized the usefulness of DBT, showing that DBT demonstrated more accuracy, compared to FFDM, in LL view and concluded that the former modality could help to diagnose vertical invasion because of its more clearly depiction of whole lesions. They also suggested the potential use of intraoperative DBT in assessing the margin positivity in BCS. This hypothesis was supported by our results, which showed the superiority of DBT over FFDM in the evaluation of the intraoperative specimen in a larger sample of 170 patients. In our experience, moreover, DBT is more accurate than FFDM in assessing margins in both views (Pearson's correlation coefficient of DBT and FFDM were 0.92 and 0.79 in CC view and 0.92 and 0.72 in LL view, respectively). That is in accordance with the study of Amer et al. [3], who published a large series of 102 breast specimens which underwent FFDM and DBT. They demonstrated a significant superiority of DBT (overall accuracy 40%) compared to FFDM (overall accuracy 69%) regarding identification of closest margin and sensitivity (FFDM: 62%; DBT: 77%) in assessment of margin status.

Furthermore, recent studies have been continuously showing more promising results. Park et al. [9] studied 99 breast specimens with DBT and found that DBT was accurate in detecting positive margins, reducing the need of additional surgery. Garlaschi et al. [13] published an article about the higher accuracy of intraoperative DBT with a dedicated device (Mozart system) than FFDM in the identification of positive surgical margins at first excision in 89 operative specimens. Our experience has been quite similar, demonstrating that DBT allows high accuracy in the identification of margin status.

By evaluating a large sample of specimens, there are some limitations of our study. First, this is a monocentric study. Second, data on additional excision or re-excision rates are lacking. Further studies are needed to assess these aspects.

In conclusion, DBT is more accurate, both in CC and LL views, in the assessment of margin status than FFDM; it could be the gold standard for the radiological intraoperative delineating of tumor resection margins.

Funding No funding was received for this study.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethics approval All procedures performed in the studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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