



# Digital Breast Tomosynthesis as a Tool in Confirming Negative Surgical Margins in Non-palpable Breast Lesions

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## Abstract

Breast cancer is one of the leading killers among women the world over. Widespread mammographic screening programs have led to almost 20% of breast cancers being detected when they are radiologically visible but clinically impalpable. For the localization of these cancers before surgical excision, the Kopan hook wire is the standard technique, but the extent of margins excised still needs to be determined. In this study, we have evaluated the accuracy of specimen mammogram (SM) with digital breast tomosynthesis (DBT) for margin assessment by comparing it to the excised margins as measured in final histopathology. This is a prospective observational study of patients with radiologically suspicious impalpable breast lesions. The patients underwent ultrasound-guided hook wire placement followed by excision of the lesion, subjected to digital tomosynthesis mammogram, and margins were revised on table when indicated. These findings were correlated with final histopathological margin. Our study included 30 patients and out of the 6 lesions, which showed positive margins on specimen mammography, 4 were histologically confirmed to have tumour at the surgical margin and 2 were confirmed to be tumour free. All DBT-positive margins were re-excised at the time of primary surgery. Individual comparison of the margins revealed a good agreement and high level of correlation between DBT and histopathology margins. None of the cases required a second surgery for margin revision. It can be concluded that specimen mammogram with DBT can be used as a reliable tool for intraoperative surgical margin assessment in non-palpable breast lesions to reduce rate of margin revision as well as reduce the volume of breast excised without compromising the oncological safety of the procedure.

**Keywords** Digital breast tomosynthesis · Breast conservation surgery · Non-palpable breast lesion · Breast cancer

## Introduction

Breast cancer is a major cause of mortality and morbidity in India. It has been ranked as the number one cancer in India, with an incidence of 25.8 per 100,000 women and mortality of 12.7 per 100,000 women [1]. According to Globocan 2012 [2], India along with the USA and China collectively shares

one-third of the global cancer burden. In India, the trend has been late and advanced breast cancer at presentation leading to increased mortality and morbidity. However, with the advent of mammographic breast cancer screening, there has been a shift in clinical scenario towards early cancer so much so that almost 20% of newly detected cancers are now non-palpable leading to new challenges in how to excise these tiny lesions which cannot be felt but are radiologically suspicious and sometimes histologically proven to be malignant [3]. Various techniques of localization of impalpable breast lesions have been described such as ultrasound- or stereotactic-guided wire insertion (WGL) [4–6], radioguided occult lesion localization (ROLL) [7], radioactive iodine (<sup>125</sup>I) seed localization (RSL) [8], cryo-assisted techniques (CAL) [9], and intraoperative ultrasound (IOUS)-guided excision [10]. All the above procedures allow for the excision of tiny cancers most of which cannot be felt even intraoperatively by the surgeons thus facilitating breast conservative surgery followed by adjuvant radiotherapy which is the standard of care for early breast

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cancers. Cochrane meta-analysis of 2015 compared ROLL and RSL with WGL, which is the most commonly employed technique and concluded that ROLL and RSL have comparable outcomes with WGL whereas other techniques need more validation [11]. Though WGL has its drawbacks like wire migration, wire transection, wire injuries, and longer operating time, it still continues to be the gold standard of localization due to its availability, flexibility, and ease whereas other techniques do require more advanced equipment and infrastructure. Whatever the technique of localization, they are all followed by wide local excision of the tumour or removal of the tumour with a rim of tumour-free breast tissue and complete removal with no residual tumour left behind. Herein lies the challenge to a breast surgeon. How much more to remove and how little? Thus, the breast surgeon treads the fine line between excising too much breast tissue thereby compromising cosmetic outcome or excising too little and leaving behind positive margins which may warrant another procedure. Walking the tight rope between breast cosmesis and oncological safety and with no guidance from the feel of the fingers, the lesion being too small to be felt, specimen mammogram (SM) along with digital breast tomosynthesis (DBT) takes an important place in guiding the surgeon regarding confirmation of excision of the suspicious lesion as well as the adequacy of the margins removed. Frozen section for margin assessment comes with its limitations in terms of availability and accuracy in certain pathologies like lobular carcinoma and DCIS [12, 13]. Since the lesion to start with was a radiological abnormality, radiology of the specimen for confirmation of the lesion in the excised specimen as well as margin status around the lesion when communicated to the surgeon enables on table revision of the involved margin sparing the patient another admission and surgery, which in countries like India holds a lot of importance as there is no state-sponsored health insurance and most patients have to bear the expense of the entire treatment themselves. A study conducted by Amer et al. comparing digital specimen mammography and mammography with digital breast tomosynthesis showed significant superiority of the latter in margin evaluation [14]. Subjecting the specimen to mammography along with DBT in assessing surgical margins of the excised lesion significantly reduced the re-operation rate for positive margins.

## Material and Methods

This was a prospective observational study conducted from May 2016 to October 2018. The study was approved by the

institutional review board and the institute's Ethics Committee.

## Inclusion Criteria

1. Asymptomatic patients who were detected to have radiologically suspicious lesions (BI-RADS 4 or 5) on screening mammogram but clinically did not have any palpable mass
2. Patients who presented with breast symptoms other than that of a palpable lump and on radiological evaluation were found to have suspicious abnormality mandating histology and excision
3. Patients willing for breast conservation therapy.

All patients with BI-RADS 5 had a preoperative histological diagnosis confirmed by a US-guided core needle biopsy.

## Exclusion Criteria

1. Patients with radiological suspicious lesions, which were clinically palpable
2. Patients with history of surgery done to the breast before
3. Patients with BI-RADS 1, 2, or 3 lesions
4. Patients unwilling for breast conservation
5. Patients with features of locally advanced or metastatic breast cancer.
6. Patients with contraindications for radiotherapy
7. Pregnant patients

## Objective

The objective of this study was to compare the margins of the surgically resected radiologically suspicious non-palpable breast lesion by post-excision specimen mammography with DBT and correlate these margins to the margins as determined in the final histopathological analysis and evaluate the accuracy of DBT for margin assessment.

## Study Design

All patients who reported to this institution with suspicious radiological lesions and who fitted the inclusion criteria were taken into this study. After complete evaluation and triple assessment, the patients were discussed in multidisciplinary tumour board (MDTB) and after the MDTB decision, the patients underwent preoperative counselling. The procedure was explained to them and an informed consent was taken. The procedure was done under general anaesthesia after preanaesthesia evaluation.

**Table 1** Comparison of surgical margins between specimen mammography and histopathology report

		HPR margins			<i>p</i> value > 0.05
		Positive	Negative	Total	
SM margins	Positive	4 (13.3%)	2 (6.7%)	6 (20%)	
	Negative	2 (6.7%)	22 (73.3%)	24 (80%)	
Total		6 (20%)	24 (80%)	30	

On the day of the surgery, the patients were moved to radiology where under US guidance and local anaesthesia, the radiologist placed a Kopan hook wire into the lesion. The placement was confirmed by post-insertion imaging. Thereafter, the patient was moved to the operating theatre, and on the table with the help of guide wire and the preoperative mammogram, the surgeon approached and excised the entire lesion with a margin of the normal breast tissue. It was important on table to not expose the wire tip as it indicated the transgression into the tumour. After excision, the specimen was marked for the margins by silk sutures as per standard guidelines and was sent to radiology where it was subjected to SM and DBT, the margins measured, and conveyed to the surgeon. If the tumour was reaching up to a margin or was within 1 mm of the margin, the margin concerned was revised by the surgeon on table. If the margin was more than 1 mm away, it was considered negative and the surgeon proceeded to close the breast cavity. Subsequently, the specimen was sent for histopathological examination and all the margins were assessed on gross as well as paraffin sections.

### Statistical Analysis

Statistical analysis was done using the IBM SPSS Statistics 20 Windows (SPSS Inc., Chicago, USA). Pearson's correlation was used for finding the degree of correlation between the imaging of the lesion in specimen mammography and histopathological examination. Bland-Altman analysis and intraclass correlation (ICC) were used to determine to what extent the imaging of the lesion in specimen mammography correlated with the histopathological examinations. A *p* value of < 0.05 was considered with statistically significant difference. All tests of statistical significance were two-tailed.

### Results

A total of 30 patients were included in our study. The mean age of the patients was  $55.67 \pm 9.31$  years. The mean size of the lesions on ultrasound was  $1.09 \pm 1.29$  cm and that on mammogram was  $1.74 \pm 1.30$  cm. The mean size of the lesions on histopathological examination was  $1.53 \pm 1.70$  cm. 63.3% of the lesions were incidentally detected on screening

mammogram whereas 26.67% of patients presented with nipple discharge and 10% of patients presented with mastalgia.

Out of the 6 lesions, which showed positive margins in specimen mammography, 4 were histologically confirmed to have tumour at the surgical margin and 2 were confirmed to be tumour free. These margins in question while performing SM and DBT were re-excised at the time of the primary surgery. Out of the 24 lesions, which showed negative margins in specimen mammography, 2 were histologically confirmed to have tumour at the surgical margin and 22 were confirmed to be tumour free. However, this was statistically insignificant which in turn showed a good association among the two. This comparison yielded a sensitivity of 66.67% and a specificity of 91.67%. The accuracy of assessing margins between HPR and SM was 86.67% (Table 1).

On comparing the individual margins of the lesions in specimen mammography and DBT with histopathological examination using Pearson's correlation and ICC, they showed a high level of significant positive correlation and a good agreement respectively. The comparison of surgical margins between specimen mammography and histopathological examination using Pearson's correlation and ICC is summarized in Table 2.

### Discussion

The management of non-palpable breast lesions that have suspicious characteristics on radiography requires an effective

**Table 2** Pearson's correlation and ICC of surgical margins between specimen mammography and histopathology

SM vs HPR margins	Pearson's correlation		Intraclass coefficient correlation		<i>p</i> value < 0.05 is statistically significant
	<i>r</i> value	<i>p</i> value	ICC	<i>p</i> value	
Superior	0.854	< 0.001	0.720	< 0.001	
Inferior	0.731	< 0.001	0.729	< 0.001	
Medial	0.881	< 0.001	0.881	< 0.001	
Lateral	0.651	< 0.001	0.647	< 0.001	
Anterior	0.634	< 0.001	0.620	< 0.001	
Posterior	0.728	< 0.001	0.720	< 0.001	

method of lesion localization. This is of prime importance because the surgeon is unable to feel the lesion at the time of surgery, thereby decreasing the chances of acquiring adequate margins. Proper localization of the non-palpable lesion under imaging guidance, ultrasound or mammogram, can help the surgeon to tackle this issue. This coupled with specimen mammography supplemented by digital breast tomosynthesis can assist the surgeon in margin assessment and to decide whether there is a need to excise more tissue or not. This not only helps in achieving negative surgical margins but also reduces the amount of normal tissue excised thereby maintaining the cosmetic appeal.

Although specimen mammography and now even digital breast tomosynthesis are being used in the West as a part of their routine treatment, we were unable to find any Indian literature with regard to using specimen mammography along with digital breast tomosynthesis in assessing surgical margins in cases of non-palpable breast lesions.

The mean age of our patients was  $55.67 \pm 9.31$  years and majority of the lesions were in the upper outer quadrant, which is in line with the current literature [1, 4]. Majority of our patients (63.33%) had incidental findings on screening mammogram, which appeared suspicious, needing further surgical intervention. US-guided wire localization is a well-established alternative for diagnosing early subclinical breast cancers, which requires a close cooperation of the surgeon, radiologist, and pathologist for successful results [4, 5].

Graham et al. [15] in his study showed a sensitivity and specificity of 62% and 95%, respectively, in using specimen radiography to assess surgical margins. Amer et al. [14] in his study showed that SR along with DBT was far superior to FFDM in assessing surgical margins with a sensitivity of 77% versus 62%. Overall accuracy was stated to be 69% for SR with DBT in assessing surgical margins. However, Bimston et al. [16] suggested that specimen mammography was not beneficial in the management of non-palpable breast lesion. McCormick et al. [17] in their study were able to show that with specimen mammography, they were able to reduce their re-operation rates from 12 to 5%. In our study, out of the 30 cases, 9 of them required re-excision of margins at the time of surgery. Out of the 9 cases, 6 of them had positive specimen mammography findings prompting the need for a revision of margins, which was performed on table. But none of our patients required a second surgery for revision of their margins. In our study, we were able to show that specimen mammography along with digital breast tomosynthesis yielded a sensitivity of 66.67% and a specificity of 91.67% in assessing surgical margins. We were able to get an accuracy of 86.67%. Specimen mammography along with digital breast tomosynthesis can be used as a useful tool in assessing surgical margins during surgery, thereby reducing the chances of a re-operation for revision of margins, if they turn out to be inadequate.

## Conclusion

Our study yielded a sensitivity of 66.67% and a specificity of 91.67% with an accuracy of 86.67%. On comparing the specimen mammography + digital breast tomosynthesis margins with the histopathological margins, we were able to find a high level of significant positive correlation with the ICC showing a good agreement between the two. Our study shows that specimen mammography along with digital breast tomosynthesis can be used as a reliable tool, intraoperatively to assess the surgical margins in cases of non-palpable breast lesions.

**Data Availability** The data used to support the findings of this study are available from the corresponding author upon request.

**Compliance with Ethical Standards** The study was approved by the institutional review board and the institute's Ethics Committee. The procedure was explained to them and an informed consent was taken.

**Conflict of Interest** The authors declare that they have no conflicts of interest.

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