



Surgeon interpretation of margin status utilizing intraoperative 3D tomosynthesis during breast-conserving surgery

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Received: 5 March 2026 / Accepted: 6 June 2026 / Published online: 22 June 2026
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Abstract

Introduction Obtaining negative margins at the time of segmental mastectomy (SM) is important to reduce risk of local recurrence and avoid the need for a second surgery due to positive margins. Our current institutional standard practice (ISP) includes intraoperative assessment of the gross specimen and specimen radiographs by a multidisciplinary team including radiologists and pathologists.

Methods In this study, we utilized digital breast tomosynthesis (DBT) images of SM specimens in the operating room and recorded when additional (selective) shave margins were proposed by the surgeon. A breast radiologist later reviewed the archived DBT images. The timing and accuracy of surgeon and breast radiologists' margin assessment using DBT was then compared to our ISP.

Results There were 193 patients enrolled and included in the analysis. Of 196 SM specimens, 9.7% ($n=19$) had positive margins prior to excision of selective shave margins. Of these, 16 were identified by ISP with a sensitivity of 84%, specificity of 29%, false-negative rate (FNR) of 16%, positive predictive value (PPV) of 11%, and negative predictive value (NPV) of 95%. Surgeon assessment of DBT images identified 16/19 specimens with positive margins, with a sensitivity of 84% ($p>0.05$), specificity of 49% ($p<0.001$), FNR of 16% (>0.05), PPV of 15% ($p>0.05$), and NPV of 97% ($p>0.05$). The median time for surgeon interpretation was 6 (range 2–35) minutes vs. 33 (range 15–88) for ISP.

Conclusions Surgeon interpretation of DBT images offers an alternative to a more time- and labor-intensive ISP for detecting positive margins during breast-conserving surgery, with comparable accuracy and higher sensitivity.

Keywords Breast · Specimen · Intraoperative tomosynthesis images · Surgeon interpretation · Margins

Introduction

Breast-conserving surgery (BCS) is an effective and safe local therapy option for patients with early-stage breast cancer associated with less morbidity, improved patient reported outcomes and comparable survival when compared to mastectomy [1–3]. Achieving negative margins is an essential component of BCS to optimize disease-free survival since positive margins are associated with an increased risk of ipsilateral breast tumor recurrence (IBTR) [3–6]. Many studies have demonstrated that positive margins often require return to the operating room for margin re-excision or completion mastectomy which increases costs, delays delivery of adjuvant therapy and can result in emotional distress to the patient [7–14]. Common strategies utilized for successful BCS include accurate pre-operative

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localization to guide lesion excision, intraoperative specimen radiograph with surgeon review to confirm excision of the target lesion, and cavity shave margins [15–30]. Some centers utilize intraoperative assessment by pathologists with variable use of frozen section or touch imprint analysis of margins. Despite this, published reoperation rates are highly variable with an average rate of ~ 20% and some reports as high as 60% [8, 31–37].

Various techniques have been developed to reduce the rate of positive margins and the need for reoperation, including use of comprehensive cavity shave margins, fluorescence imaging or radio-frequency electrical fields to identify areas for selective shave margins, frozen section, and use of digital breast tomosynthesis (DBT) to allow for three-dimensional (3D) assessment of the excised specimen and margins [8].

Our current institutional standard practice (ISP) includes intraoperative assessment of the gross specimen and specimen radiographs by a multidisciplinary team including breast pathologists and radiologists. This strategy has proved to be highly accurate for predicting positive margins at the time of the index operation allowing for immediate re-excision of close/positive margins and has led to a sustainably low positive margin rate on final pathology [44, 47]. This process involves two-dimensional (2D) whole specimen imaging (WSI) of the intact segmental mastectomy (SM) specimen followed by serial sectioning of the specimen with 2D radiographs of the sectioned specimen. The breast pathologist, radiologist and surgeon discuss the findings to determine the need for excision of selective shave margins. While this multidisciplinary approach to intraoperative margin assessment has previously been shown to be superior to surgeon interpretation of 2D WSI, it is both time and labor intensive [47].

DBT produces 3D images and reduces tissue superimposition thus providing a clearer view of the specimen and target lesion. It has also been shown to be superior to traditional 2D specimen radiograph images for margin assessment [21, 25, 38–46]. This technology also provides mobile digital specimen radiography allowing for immediate imaging of the excised specimen in the operating room, eliminating the need for transportation of the specimen to radiology. This can reduce time under anesthesia and operating room costs [45]. A recent retrospective study from our institution demonstrated that interpretation of DBT images by breast radiologists is an acceptable alternative method for detecting positive margins in patients undergoing SM [44]. In this study, we aimed to compare both intraoperative surgeon interpretation of DBT images and interpretation of DBT images by a breast radiologist to our ISP for intraoperative specimen and margin evaluation.

Methods

After approval from the University of Texas MD Anderson Cancer Center Institutional Review Board (IRB), we prospectively enrolled patients planned for SM from March 2024 to June 2025. Patients > 18 years old with a breast cancer diagnosis at any stage undergoing a SM were eligible, with or without receipt of neoadjuvant systemic therapy. Patients were excluded if they had a multi-site SM of the ipsilateral breast. Patients signed informed consent prior to study enrollment. Participating surgeons received training on DBT imaging. The study included review of archived images by breast radiologists, surgeon evaluation of margins utilizing intraoperative DBT, and the institutional ISP multidisciplinary intraoperative assessment of specimens, images and margins (Fig. 1). Clinical, imaging, surgical, and pathology data were analyzed.

Institutional intraoperative assessment of margins

Our institutional standard practice (ISP) of SM specimen evaluation includes four steps, as detailed in Fig. 2. Intact specimen radiographs are acquired using 2D imaging (Faxitron MX20; Faxitron Bioptics, LLC, Tuscon, AZ, USA). The SM specimens are sectioned in 3–5 mm slices and 2D images of the sectioned specimen are acquired. Gross examination of the whole specimen and sectioned specimen is performed by the breast pathologist. The analysis from the breast pathologist and breast radiologist is then communicated to the surgeon to guide excision of selective shave margins targeted to the specific anatomic margin(s) interpreted by ISP as being concerning for a positive margin.

Final margin status was determined by the breast pathologists by examining formalin-fixed, paraffin-embedded sections from the primary SM specimen and any additional selective shave margins. The margin width was reported in millimeters. For patients with ductal carcinoma in situ (DCIS), invasive carcinoma, and mixed DCIS and invasive cancer, margin status was defined according to the American Society of Breast Surgeons Breast Conservation Margin guidelines [47]. For the cases where the primary specimen had ink on tumor at the junction of multiple edges (i.e. anterior/lateral), these margins were considered as separate margins for statistical analysis.

Surgeon assessment of margins

Twelve surgeons participated in this study with years of experience in practice ranging from 1 to >20 years and all were in a dedicated breast surgical oncology practice. Departmental training sessions for surgeons participating on

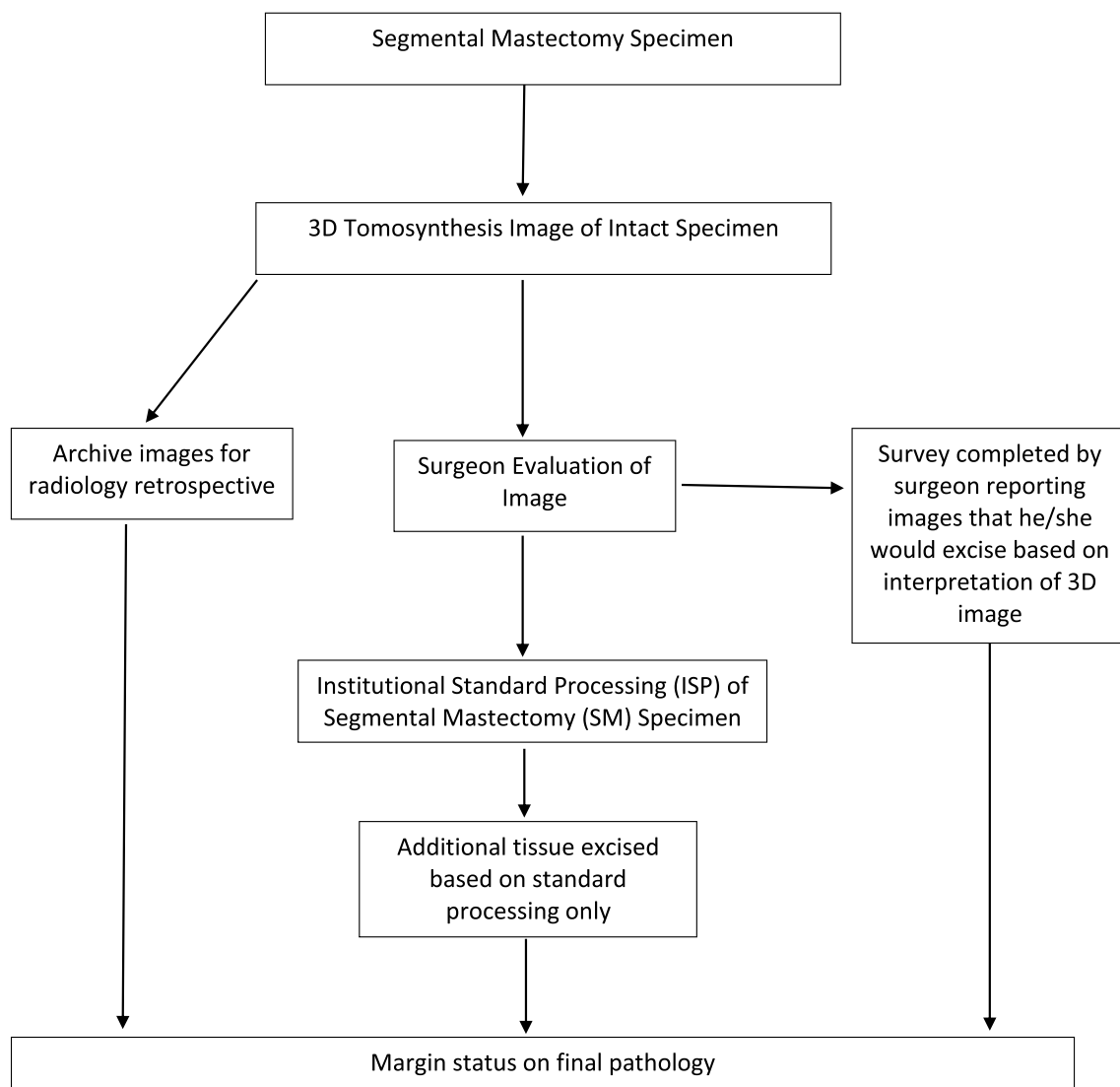


Fig. 1 Study Schema

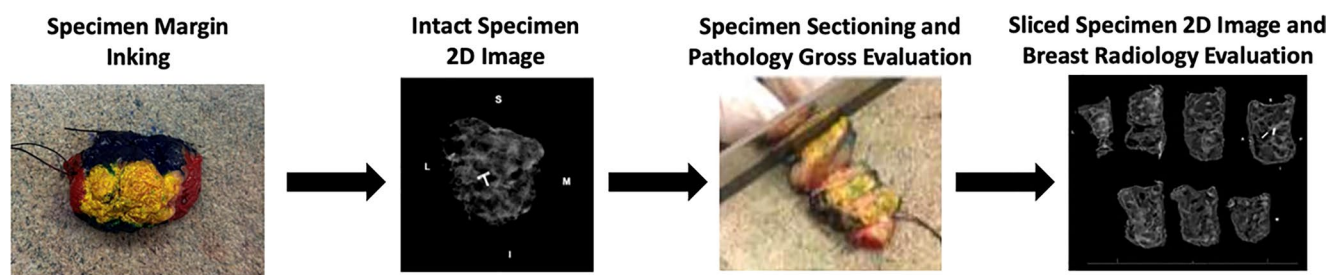


Fig. 2 Schematic of the multidisciplinary Institutional Standard Process (ISP) for Segmental Mastectomy (SM) Margin Evaluation

study were conducted with representatives from the company. Specimens preloaded into the system were reviewed by surgeons for margin assessment of mass lesions, distortion, and calcifications. Surgeons were trained on how to utilize features of the device for precise interpretation, such as tumor distance from the margins.

After excision of the SM specimen, the surgeon placed the intact specimen within the MOZART iQ[®] 3D Specimen Radiography System (Kubtec Medical Imaging, Stratford, CT, USA) in the operating room. After DBT image acquisition, the surgeon interpreted the specimen images and completed a survey indicating which margins appeared to be

positive (Appendix 1). Survey answers were immediately recorded. The specimen was then submitted to pathology for standard processing after which the pathologist reported directly to the surgeon and recommended additional selective shave margins for a guided excision based on the ISP. These recommendations were also documented in the surgeon survey. All tissue was submitted for permanent evaluation as per standard protocol. The survey also recorded various time points: (1) time of specimen excision (2) time of completion of surgeon assessment of margins using DBT (3) time of pathologist's verbal report to the surgeon of ISP margin evaluation results.

Radiologist assessment of margins using DBT imaging

DBT images of the intact SM specimen were acquired using the MOZART system prior to serial sectioning of the specimen. Images were obtained using the standard tomosynthesis technique, which generated multiple low-dose projection images over a 30-degree arc and were reconstructed into a series of 1-mm sections to create a set of parallel slices. DBT images were stored and all images were retrospectively reviewed by two breast radiologists, independently. These radiographs were de-identified and final pathology

results were not available to the radiologists. Inter-reader agreement for radiologist assessment of archived images was evaluated. This retrospective review was not available for intraoperative specimen analysis and did not guide additional tissue excision.

Statistical analysis

We evaluated and compared the accuracy of the ISP to both surgeon and radiology evaluation of DBT images for identifying SM primary specimens having positive margins and correctly detecting the specific specimen edge (margin) that was positive. Sensitivity, specificity, false-negative rate (FNR), positive predictive value (PPV), and negative predictive value (NPV) were calculated with 95% confidence intervals. Summary statistics were provided, including mean, standard deviation, median, and range for continuous variables. The frequency counts and percentages for categorical variables were summarized. A chi-square test was used to evaluate associations between categorical variables. The Wilcoxon rank sum test or t-test was used to evaluate differences in continuous variables between different patient groups. Inter-reader agreement for radiologist assessment of archived images was calculated using Cohen's Kappa. The *p* values were calculated using McNemar's test, and a *p* value ≤ 0.05 was considered statistically significant. Statistical analyses were performed using R (version 4.3.1, R Development Core Team).

Results

The final analysis included 196 specimens from 193 patients (3 bilateral SM cases), the median age was 61.3 years (range 29.8–89.7 years). The majority (76.0%) of cases had a pre-operative diagnosis of invasive ductal carcinoma ($n=149$) of which 13 were associated with DCIS. There were 34 (17.3%) cases of pure DCIS, and 9 (4.6%) cases of invasive lobular carcinoma. For invasive tumors, the median tumor size was 1.3 cm (range 0.3–7.9 cm). Imaging findings were a mass in 85 (43.4%) cases, architectural distortion in 14 (7.1%) cases and calcifications (either with or without a mass) were noted in 43 (22%) cases. There were 24 (12.2%) patients who received neoadjuvant therapy (either chemotherapy or endocrine therapy). The clinicopathologic features of the study population are presented in Table 1.

On permanent pathology, 19 of the 196 SM specimens (9.7%) had a positive margin at one or more of the specimen edges prior to excision of any additional selective shave margins. In 16 of these 19 (84.2%) SM specimens, positive margins were identified by the ISP for a sensitivity of 84%, specificity of 29%, FNR of 16%, PPV of 11%, and

Table 1 Clinicopathologic features of patients undergoing segmental mastectomy (SM)

Median age years (range)	61.3 (29.8–89.7)
Median BMI (range)	28.9 (17.9–49.3)
Mammographic tumor characteristic	
N (%)	
Mass	85 (43.4%)
Focal Asymmetry	47 (24.0%)
Calcifications	35 (17.9%)
Architectural distortion	14 (7.1%)
Mammographically occult	7 (3.6%)
Mass and calcifications	8 (4.1%)
Histology	
N (%)	
Ductal carcinoma in situ (DCIS)	34 (17.3%)
Invasive ductal carcinoma (IDC)	136 (69.4%)
Invasive ductal carcinoma and DCIS	13 (6.6%)
Invasive lobular carcinoma (ILC)	9 (4.6%)
Other	4 (2%)
Median size of tumor (cm)	1.3 (0.3–7.9)
Prior Surgery	
Yes	2 (1.0%)
No	194 (99.0%)
Prior Radiation	
Yes	1 (1.0%)
No	195 (99.0%)
Neoadjuvant Therapy	
Yes	24 (12.2%)
No	172 (87.8%)

Table 2 Comparing the accuracy of the institutional standard practice (ISP) process to surgeon interpretation of digital breast tomosynthesis (DBT) images to predict segmental mastectomy (SM) specimens with positive margins. Values represent frequencies

SM permanent pathology (<i>n</i> = 196)	ISP interpreted as negative margin	ISP interpreted as positive margin	Surgeon interpreted DBT images as negative margin	Surgeon inter- preted DBT images as posi- tive margin
SM specimen with negative margins (<i>n</i> = 177)	52	125	87	90
SM specimen with one or more positive margins (prior to selective shave margin excision) (<i>n</i> = 19)	3	16	3	16
		ISP (%)	DBT (%)	p value
Sensitivity		84	84	>0.99
Specificity		29	49	<0.001
False negative rate (FNR)		16	16	>0.99
Positive predictive value (PPV)		11	15	0.08
Negative predictive value (NPV)		95	97	0.55

SM=segmental mastectomy; ISP=Institutional Standard Practice, DBT= digital breast tomosynthesis

Table 3 Comparing the accuracy of the institutional standard practice (ISP) process versus surgeon interpretation of digital breast tomosynthesis (DBT) images versus radiologist interpretation of DBT images to predict the location of the segmental mastectomy (SM) edge with a positive margin. Values represent frequencies

Permanent pathology of individual SM edges (<i>n</i> = 1,176)	ISP inter- preted as a negative margin	ISP inter- preted as a positive margin	Surgeon interpreted DBT images as a nega- tive margin	Surgeon inter- preted DBT images as a positive margin	Radiologist interpreted DBT images as a negative margin	Radiologist interpreted DBT images as a positive margin
Edges with a negative margin (<i>n</i> = 1,138)	860	278	990	148	942	196
Edges with a positive margin (prior to additional excision of tissue) (<i>n</i> = 38)	9	29	12	26	10	28
			ISP (%)	DBT (%)	Radiologist (%)	p value
Sensitivity			76	68	74	0.61
Specificity			76	87	83	<0.001
False negative rate (FNR)			24	32	26	0.61
Positive predictive value (PPV)			10	15	12	0.005
Negative predictive value (NPV)			99	98	99	0.69

SM=segmental mastectomy; ISP=Institutional Standard Practice, DBT= digital breast tomosynthesis

NPV of 95%. Similarly, 16 of 19 (84.2%) of the primary specimens with positive margins were identified by intra-operative surgeon evaluation of the DBT images, with no difference in sensitivity or between surgeon interpretation of margins and the ISP. Surgeon evaluation of the margins resulted in higher specificity compared with the ISP (49% vs. 29%, $p < 0.001$) Table 2.

On permanent pathology, there were 16 SM specimens with a positive margin at one edge and 3 SM specimens with two or more positive margins. Of the 1,176 total margins from the 196 SM specimens, 38 (3.2%) were positive prior to excision of additional selective shave margins. The ISP did not predict 9 positive margins, resulting in a sensitivity of 76%, specificity of 76%, FNR of 24%, PPV of 10%,

and NPV of 99%. Surgeon evaluation did not identify 12 positive margins, and radiologist evaluation did not identify 10 positive margins. In comparing the ISP, surgeon evaluation, and radiologist evaluation, there were no differences in sensitivity (76% vs. 68% vs. 74%, $p > 0.05$) but there was higher specificity for surgeon and radiologist evaluations of the DBT images (76% (ISP) vs. 87% vs. 83%, $P < 0.001$) (Table 3). There was fair inter-reader agreement between the two radiologists who independently assessed tumor margins on DBT images (Cohen's $\kappa = 0.33$, Table 4).

After ISP-guided excision of selective shave margins, 9 patients had a positive margin on final pathology resulting in a margin positivity rate of 4.6%. Of the 9 cases with positive final margins, 8 patients underwent re-excision (Table 5).

Table 4 Comparison of radiologist interpretation of digital breast tomosynthesis (DBT) images for inter-reader agreement

	Radiologist 2			Cohen's Kappa (<i>p</i> -value)
	Margins Interpreted as Negative	Margins Interpreted as Positive	Total	
Radiologist 1				0.33 (<i>p</i> < 0.0001)
Margins interpreted as Negative	894 (76%)	58 (4.9%)	952 (81%)	
Margins Interpreted as Positive	147 (13%)	77 (6.5%)	224 (19%)	
Total	1,041 (89%)	135 (11%)	1,176 (100%)	

Table 5 Comparison of permanent pathology, the institutional standard practice (ISP), and the surgeon interpretation of the digital breast tomosynthesis (DBT) images for the 8 patients with final positive margins undergoing a second surgery

Mammogram Finding	SM pathology and margin status	Selective shave margin pathology	ISP interpreted (+) margins for SM	Surgeon interpreted (+) margins for SM	Second Surgery Performed
Calcifications	IDC with DCIS (+)margin: Inferior	Inferior (+) DCIS Medial/superior (-)	Inferior Medial Superior	Inferior Medial Superior	Re-excision SM: Inferior margin (-)
Mass	Mixed IDC and ILC (+)margin: medial	Anterior/medial (+) ILC Posterior (-)	Anterior Medial Posterior	Medial Posterior	Re-excision SM: Anterior/medial (-) Posterior/medial (-)
Calcifications	Microinvasive carcinoma and DCIS (+)margin: superior	Anterior/medial (-) Superior/Lateral (+) DCIS Posterior (-)	Anterior Medial Superior Lateral Posterior	Superior Anterior Lateral	Re-excision SM: Superior/Lateral margin (-)
Density	IDC (+)margin: inferior	Inferior (+) IDC Posterior (-)	Inferior Posterior	Lateral Anterior	Re-excision SM: Inferior (-)
Calcifications	IDC with DCIS (+) margin: medial	N/A (no shave margins excised)	Inferior	Inferior	Re-excision SM: Medial (-)
No abnormality (MRI detected)					
Mass	IDC with DCIS (+) margin: lateral and anterior	Lateral (-)	Lateral	Lateral	Re-excision SM: Anterior/lateral (-) Anterior/medial (-)
Mass	IDC+DCIS (+) margin: superior and posterior	Superior (+) DCIS Posterior(+) DCIS	Superior Posterior	Superior Posterior	Completion mastectomy (No additional carcinoma identified)
Mass	IDC (+)margin: superior	N/A (no shave margins excised)	None	None	Re-excision SM: Superior (-)

SM=segmental mastectomy; ISP=Institutional Standard Practice, DBT= digital breast tomosynthesis

There was no additional disease identified on pathology from re-excision in these 8 patients. Of these 8 patients who underwent re-excision surgery at a second operation, 5 had ISP-guided margins recommended for excision intraoperatively at the index operation that yielded additional disease; surgeons correctly identified 4 of these cases by DBT image interpretation. ISP-directed selective shave margins were persistently positive in all 5 cases and ultimately cleared by re-operation. The ISP evaluation did not identify 2 SM specimens having a positive margin and neither of these were identified by surgeon DBT image interpretation. Of note, in one of these cases, the lesion was a mammographically-occult lesion and only detected on MRI. In addition, one patient had a SM with two positive margins, only one of which was identified at the index operation by the ISP as well as the surgeon.

The median time for the multidisciplinary ISP margin assessment was 33 min (range 15–88 min) which was

longer than the median time for the surgeon interpretation of margins using the intraoperative DBT images (6 min, range 2–35 min). The review of prospectively obtained DBT images by the breast radiologists was performed retrospectively and was not timed.

Discussion

Overall, the current institutional ISP of SM specimen and margin evaluation yielded an extremely low rate of positive margins on final pathology (4.6%). This is similar to previously reported rates of positive margins from our institution which demonstrate the reliability of this multidisciplinary method of intraoperative margin assessment over time [43, 46]. Previous work by Tevis et al. demonstrated that this multidisciplinary ISP margin assessment was more accurate than surgeon interpretation of 2D images of both whole SM

specimens and sectioned specimens [46]. However, given the time- and labor-intensive nature of the current ISP, new technologies, including the use of 3D DBT images, for margin assessment continue to be explored as possible alternatives. In a recent pilot study, Park et al. demonstrated that breast radiology assessment of DBT images of intact specimens was an accurate method for detecting positive margins in breast cancer patients undergoing SM and yielded similar results to the ISP [43]. The results of our current study reinforce that breast radiology review of DBT images is comparable to our institutional multidisciplinary ISP for specimen and margin evaluation.

Importantly, our study demonstrates that surgeon interpretation of DBT images is similar to radiologist interpretation of images and yields similar results to our ISP process. Previously, Miller et al. demonstrated that surgeons are able to accurately identify the target lesion on standard (2D) intraoperative specimen radiography and have similar accuracy to breast radiologists in identifying positive margins by radiographs [23]. However, this is in contrast to the prior study by Tevis et al. which demonstrated that the surgeon interpretation of 2D whole and sectioned specimens was inferior to a multidisciplinary margin assessment involving review of whole and sectioned specimen radiographs by a dedicated breast radiologist (ISP) [46]. The improved accuracy of margin assessment by surgeons in our study may be due to the superiority of the DBT imaging over 2D mammography. This concept is supported by prior studies which have also shown that tomosynthesis is superior to 2D mammography for lesion identification and margin assessment of whole specimens, particularly for women with dense breasts [24, 25, 38–41].

While the cost of our current ISP process has not been explored, Osborne et al. demonstrated that the routine use frozen-section analysis of lumpectomy margins, a similarly labor-intensive process, was cost-effective compared to no intraoperative margin assessment due to the number of re-operations avoided by the use of frozen-section analysis during the index operation [29]. Given the extremely low rate of positive margins with our current standard practice, a similar argument has been made for maintaining the current multidisciplinary ISP for margin assessment [46]. However, comparing a current practice to omission of intraoperative margin assessment is not meaningful given that any new techniques or technologies for margin assessment should not only compete with the sensitivity and specificity of the ISP but also offer an advantage of efficiency, cost, labor reduction and/or scalability [21]. Our results demonstrate comparable accuracy to standard practice, with the added benefit of lower resource utilization. Surgeon interpretation of DBT images reduces labor by eliminating the need for a dedicated breast pathologist and radiologist for

intraoperative specimen assessment. Additionally, it results in a significant reduction in time to final recommendation for margin re-excision which translates to less time in the operating room.

We also found that surgeon and radiologist interpretation of DBT images demonstrated improved specificity compared to the ISP process which would have resulted in removal of fewer selective shaves with no impact on oncologic outcomes. This may result in improved patient satisfaction, particularly for cases in which even a small volume of additional tissue excised can lead to poor cosmesis [48]. For more complicated cases, such as those with multiple localizing devices to target a large volume of tissue, or those in which more extensive reconstructive techniques are employed to improve cosmetic outcome, the multidisciplinary ISP process of specimen and margin analysis may be replicated through collaboration between surgeon and radiologist review of DBT images.

The primary limitation of this study is its single institutional design, which limits generalizability to other institutions. The ISP process we describe has been well established but remains resource intensive and therefore may not be reproducible at other centers. Additionally, while the use of the Kubtec MOZART iQ[®] 3D Specimen Radiography System for intraoperative margin assessment by the surgeon and breast radiologists at our center was new, both the surgeons and breast radiologists at our institution routinely participate in the assessment of 2D specimen radiographs. This regular, real time participation of surgeons in specimen radiograph margin assessment alongside breast radiologists may have contributed to the accuracy of surgeon interpretation of 3D specimen radiographs. Therefore, our findings may not be generalizable to centers where surgeons are less routinely involved in intraoperative specimen radiograph review. While we included patients undergoing SM for a variety of indications (DCIS, invasive carcinoma, mass, calcifications, etc.), our study was not powered to detect differences in the accuracy of margin assessment between these different histologies and imaging findings. Lastly, we did not evaluate the cost effectiveness or scalability of using the Kubtec MOZART iQ[®] 3D Specimen Radiography System for intraoperative margin assessment relative to the ISP in the current study, however, this will be important to examine prior to broader implementation of this new method.

While our ISP has resulted in extremely low positive margin rates for patients undergoing breast-conserving surgery, it is a resource-intensive process and may contribute to the unnecessary excision of additional selective cavity margins. Surgeon interpretation of DBT images is a less time- and labor-intensive alternative to ISP for detecting positive margins in patients undergoing SM with comparable sensitivity and increased specificity. Further studies

are needed to assess the impact on cosmetic outcomes and patient satisfaction.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s10549-026-08005-4>.

Author contributions L.L. made substantial contributions to the conception or design of the work, the interpretation of data, and drafting of the work. E.C. made substantial contributions to the conception or design of the work, the acquisition of and interpretation of data, and revised the work critically for important intellectual content. R.P. made substantial contributions to the conception or design of the work, the acquisition of and interpretation of data, and revised the work critically for important intellectual content. J.S. made substantial contributions to the conception or design of the work, the analysis and interpretation of data and revised it critically for important intellectual content. R.E. made substantial contributions to the acquisition of data and revised the manuscript critically for important intellectual content. A.R. made substantial contributions to the acquisition of data and revised the manuscript critically for important intellectual content. H.J. made substantial contributions to the acquisition of data and revised the manuscript critically for important intellectual content. C.A. made substantial contributions to the acquisition of data and revised the manuscript critically for important intellectual content. J.S.C made substantial contributions to the acquisition of data and revised the manuscript critically for important intellectual content. S.D. made substantial contributions to the acquisition of data and revised the manuscript critically for important intellectual content. F.F. made substantial contributions to the acquisition of data and revised the manuscript critically for important intellectual content. R.H. made substantial contributions to the acquisition of data and revised the manuscript critically for important intellectual content. K.H. made substantial contributions to the acquisition of data and revised the manuscript critically for important intellectual content. Y.W. made substantial contributions to the design of the work and revised the manuscript critically for important intellectual content. N.T. made substantial contributions to the conception or design of the work, the interpretation of data, drafted the work and revised it critically for important intellectual content. All authors reviewed the manuscript and approved the version to be published and agree to be 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.

Funding This study was not funded by any sources.

Data availability The data and survey results that support the findings of this study are available within an MD Anderson Database, but restrictions apply to the availability of these data, which were used for the current study and so are not publicly available.

Declarations

Disclosures Kelly K. Hunt reports the following outside of the submitted work: Medical advisory board – ArmadaHealth, AstraZeneca, Daiichi Sankyo; Paid travel – Daiichi Sankyo, Merck; Research funding to MD Anderson – Cairn Surgical, Lumicell. Rosa F. Hwang reports the following outside of the submitted work: Travel compensation and grant funding to MD Anderson Cancer Center – Intuitive Surgical. Nina Tamirisa reports the following outside of the submitted work: Travel compensation – Kubtec; Medical advisory board- Med-Cognetics. Funding of processing charges was processed through Nina Tamirisa's Physician Referral Services funds through the MD Ander-

son Cancer Center. This research did not receive specific funding and was performed as part of employment at the MD Anderson Cancer Center. The preliminary findings for this study were reported as a poster presentation at the American Society of Breast Surgeons Annual Meeting in Las Vegas, Nevada May 2, 2025.

Competing interests The authors declare no competing interests.

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