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ORIGINAL ARTICLE

Can Intraoperative Specimen Radiograph Predict Resection Margin Status for Radioguided Occult Lesion Localisation Lumpectomy for Ductal Carcinoma In Situ Presenting with Microcalcifications?

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ABSTRACT

Objective: *To determine the accuracy of specimen radiograph in predicting ductal carcinoma in situ resection margin status during radioguided occult lesion localisation.*

Methods: *Retrospective review of cases of stereotactic radioguided occult lesion localisation for radiologically indeterminate-to-highly suspicious microcalcifications from September 2002 to May 2014 in a regional hospital was conducted. All patients diagnosed with ductal carcinoma in situ histopathologically with a specimen radiograph for review were included. An anteroposterior specimen radiograph was taken for each lumpectomy specimen. Retrospective assessments of the radiological margin, defined as the shortest distance from the outermost microcalcification to the specimen edge, in the superior, medial, inferior, and lateral borders were made. Results were correlated with histopathology findings in each border, where resection margin status was defined as positive (≤2 mm), close (2.1-5.0 mm), or clear (>5 mm). Results were analysed by Mann-Whitney* U *test and receiver operating characteristic curve.*

Results: *A total of 24 radioguided occult lesion localisation procedures revealing ductal carcinoma in situ in 23 patients were included. Among the 96 borders assessed, 12 and five had positive and close margins, respectively. Significantly smaller radiological margins were seen in borders with positive pathological margins (range, 0-17.5 mm; mean, 8.7 mm) than in those with close/clear pathological margins (range, 4.8-45.8 mm; mean, 20.1 mm; $p < 0.001$); and in borders with positive/close pathological margins (range, 0-17.5 mm; mean, 9.1 mm) than in those with clear pathological margins (range, 5.1-45.8 mm; mean, 20.7 mm; $p < 0.001$). Receiver operating characteristic curves were plotted from these results. The areas under the curve were 0.87 (95% confidence interval, 0.78-0.96) for positive margins and 0.89 (95% confidence interval, 0.82-0.96) for positive/close margins, indicating that radiological margin possessed good discriminating power for predicting resection margin status. From the receiver operating characteristic curves, a 15-mm radiological margin had the highest combination of sensitivity and specificity for predicting a positive margin (91.7% and 75.0%, respectively) and positive/close margin (94.1% and 73.4%, respectively). A 5-mm or 10-mm radiological margin resulted in higher specificity, while a 20-mm radiological margin had higher sensitivity.*

Conclusion: *Radiological margin assessment on specimen radiograph during radioguided occult lesion localisation showed high accuracy in predicting resection margin status in ductal carcinoma in situ presenting with microcalcifications.*

Key Words: *Carcinoma, ductal, breast; Mammography; Mastectomy, segmental; Radiography*

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中文摘要

術中標本X光片是否可預測因微鈣化而進行放射導向的隱匿性病灶定位乳房腫瘤切除術乳管原位癌病例的切緣狀態？

梁肇庭、尹宇瀚、區嘉殷、盧成瑋、黃慧中、邱麗珊

目的：在放射導向的隱匿性病灶定位過程中，研究標本X線片預測乳管原位癌環周切緣狀況的準確度。

方法：回顧2002年9月至2014年5月期間，因乳腺X線片上性質待定或高度可疑的微鈣化灶而接受立體定向放射導向隱匿性病灶定位術的病例。所有組織學上被診斷為乳管原位癌且有標本X線片的病例均被列入研究範圍。每個乳房腫瘤切除術標本都配有一張前後位X線片。放射學邊緣被定義為從最外層微鈣化至標本邊緣的最短距離，回顧性評估上方、內側、下方和外側幾個方向的邊緣。每個方向邊緣狀況與病理學結果作相關比較，病理上少於2毫米的切緣被介定為切緣陽性，2.1至5.0毫米的被介定為切緣近，多於5毫米的則為切緣清晰。最後利用Mann-Whitney *U*檢驗和ROC曲線分析結果。

結果：共有24項放射導向的隱匿性病灶定位術納入分析，其中確診出23名乳腺原位癌患者。評估的96個邊緣中，12個為切緣陽性，另5個為切緣近。與切緣近／清晰的病例（平均20.1毫米，介乎4.8至45.8毫米）比較，切緣陽性的病例（平均8.7毫米，介乎0至17.5毫米）有較小放射邊緣（$p < 0.001$）；與切緣清晰的病例（平均20.7毫米，介乎5.1至45.8毫米）比較，邊緣陽性／近的病例（平均9.1毫米，介乎0至17.5毫米）有較小放射邊緣（$p < 0.001$）。根據上述結果繪製出ROC曲線。切緣陽性病例的ROC曲線下面積為0.87（95%置信區間，0.78-0.96），而切緣陽性／近病例的曲線下面積為0.89（95%置信區間，0.82-0.96），表明放射學邊緣能有效預測切緣狀態。ROC曲線分析結果顯示15毫米的放射性切緣對於邊緣陽性和邊緣陽性／近病例有最高的敏感性和特異性組合，前者為91.7%和75.0%，後者為94.1%和73.4%。5毫米或10毫米的放射切緣有較高特異性，而20毫米的放射切緣則有更高敏感性。

結論：放射導向的隱匿性病灶定位乳腺腫瘤切除術中標本X線片上放射學邊緣評估可準確預測含微鈣化灶的乳管原位癌病例切緣狀態。

INTRODUCTION

Breast cancer is the most common malignancy in women, accounting for 26.4% and 25.2%, respectively, of all newly diagnosed malignancies in women locally and internationally.[1,2] With improving public awareness and increasing availability of breast screening, there has been a substantial increase in the incidence of ductal carcinoma in situ (DCIS) in recent decades.[3,4] Locally, DCIS accounts for 28% of all newly diagnosed breast cancers according to a large-scale opportunistic breast cancer screening programme.[5] Most of these DCISs are clinically and sonographically occult (80%) and require stereotactic-guided hookwire insertion or radionuclide localisation for pathological diagnosis and operative treatment planning.

Breast-conserving therapy with lumpectomy and radiotherapy as treatment for DCIS is well established.[6-9] Resection margin status is shown to be one of the most important prognostic factors in predicting future tumour recurrence.[10-12] If histopathology shows a positive resection margin during the primary surgery, patients will undergo a second operation for margin re-excision, which can lead to negative cosmetic, psychological, and economic outcomes.[10] Therefore, achieving a clear resection during the primary surgery, while maintaining an optimal amount of tissue for better cosmetic outcome, is of utmost importance.

The tendency of DCIS for multifocal and multicentric disease, however, renders achieving clear resection margins a challenge during the primary surgery.[13] A large portion of clinically occult disease further increases the difficulty of complete surgical resection.

Previous studies have shown that 48% to 72% of patients did not have clear resection margins after the primary surgery.[14,15] To improve success in achieving complete resection, various methods have been proposed for intraoperative assessment of the resection margin. These include intraoperative frozen section, imprint cytology, ultrasound, radiofrequency spectroscopy, and specimen radiography.[11,13] However, there is currently no standardised intraoperative evaluation for DCIS.[14]

Specimen radiography is often being utilised during hookwire or radionuclide-guided localisation for clinically occult breast lesions undergoing operation.[16] The primary aim is to ensure that complete removal of the targeted lesion is established.[17] However, its accuracy in predicting resection margin status remains controversial and there are no representative local data available.

Therefore, the aim of this study was to determine the accuracy of intraoperative specimen radiography in predicting the resection margin status in DCIS presenting with microcalcifications in patients with clinically occult DCIS who underwent radioguided occult lesion localisation (ROLL) lumpectomies.

METHODS

A retrospective review of 94 consecutive stereotactic-guided ROLLs performed on 88 patients in a regional hospital in Hong Kong from September 2002 to May 2014 was conducted. DCIS was found in the specimens of 31 (33.0%) stereotactic-guided ROLL procedures and were included for further analysis. The remaining procedures revealed the presence of benign diseases (n = 50) or invasive ductal carcinoma (n = 6). There were also seven procedural failures due to unsuccessful localisation of target microcalcification by radioisotope.

Among the 31 procedures showing DCIS, 7 were later excluded due to unavailability of specimen radiographs for assessment. Patients' background demographics, preprocedure mammographic findings, procedural details, intraoperative specimen radiograph findings, and pathology reports were analysed.

Preprocedure Mammogram

Preprocedure mammographic findings and locations of the lesions were recorded. Mammographic findings were graded according to the Royal College of Radiologists Breast Group breast imaging classification.[18] Findings were graded into five categories according to the level of suspicion for malignancy and the need of further investigations (Table 1[18]).

Radioguided Occult Lesion Localisation Procedure

ROLL was performed under stereotactic guidance for clinically and sonographically occult indeterminate-to-highly suspicious microcalcifications (Figure 1). All procedures were performed for diagnostic intent without preprocedural pathological diagnosis. Stereotactic-guided ROLL was offered to patients when the target microcalcifications were clinically and sonographically occult and technically difficult for stereotactic-guided biopsy.

The mammographically detected target lesion or cluster of microcalcifications was located using a stereo pair of images obtained at 15° by a mammographic machine. A 21-gauge spinal needle was inserted at the designated region and technetium-99m macroaggregate albumin was injected into the lesion site. This was followed by injection of 0.1 to 0.2 ml of radio-opaque non-ionic iodinated contrast to confirm the correct location of the radioisotope placement without inadvertent erroneous intraductal injection. After a successful ROLL procedure, the site of the lesion was identified by a hand-held gamma probe during operation. The lesion was excised and complete excision was confirmed by the absence of residual radioactivity in the surgical bed.

The surgical specimen was then transferred to the

Table 1. Royal College of Radiologists Breast Group breast imaging classification.[18]

Category		Level of suspicion for malignancy
1	Normal	There is no significant imaging abnormality
2	Benign findings	The imaging findings are benign and further investigation purely on the basis of the imaging findings is not indicated
3	Indeterminate / probably benign findings	There is a small risk of malignancy, and further investigation is indicated
4	Suspicious of malignancy	There is a moderate risk of malignancy and further investigation is indicated
5	Highly suspicious of malignancy	There is a high risk of malignancy and further investigation is indicated

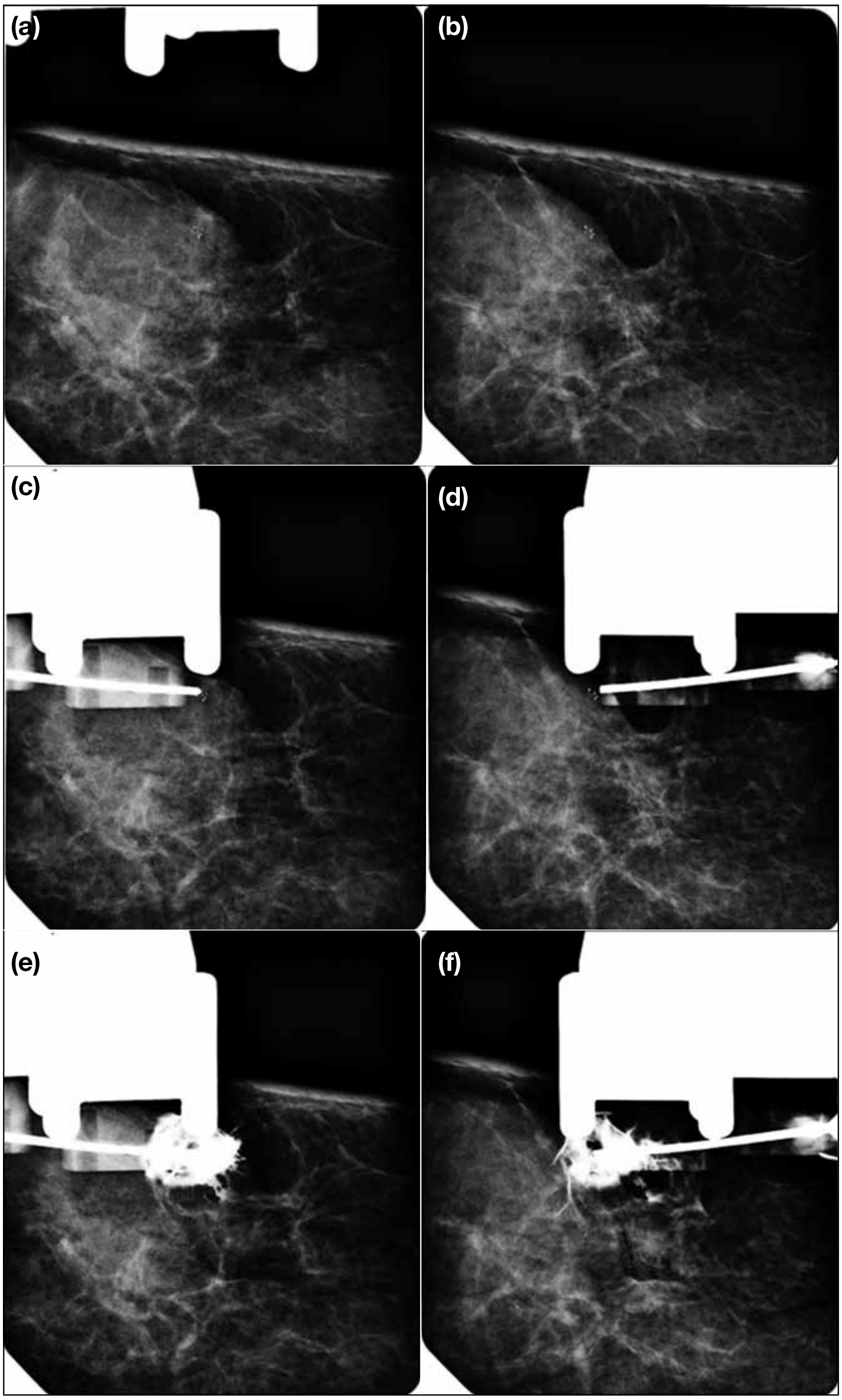

Figure 1. Radiography images of the stereotactic-guided radioguided occult lesion localisation procedure. (a and b) The mammographically detected target lesion is located using a pair of stereo images; (c and d) a 21-gauge spinal needle is inserted into the target lesion with the location confirmed by the pair of stereo images; and (e and f) iodinated contrast is injected to confirm the correct location of the radioisotope placement without inadvertent erroneous intraductal injection.

Department of Radiology and an anteroposterior intraoperative specimen radiograph was taken. The orientation of the specimen was indicated by placement of stitches or surgical clips at different borders during the operation. The preoperative stereotactic-guided ROLL and intraoperative specimen radiograph were assessed by the same radiologist to verify the inclusion of the target lesion in the excised surgical specimen. The findings from the intraoperative specimen radiographs were immediately communicated to the operating surgeon.

Intraoperative Specimen Radiograph

Retrospective analysis of all intraoperative radiographs

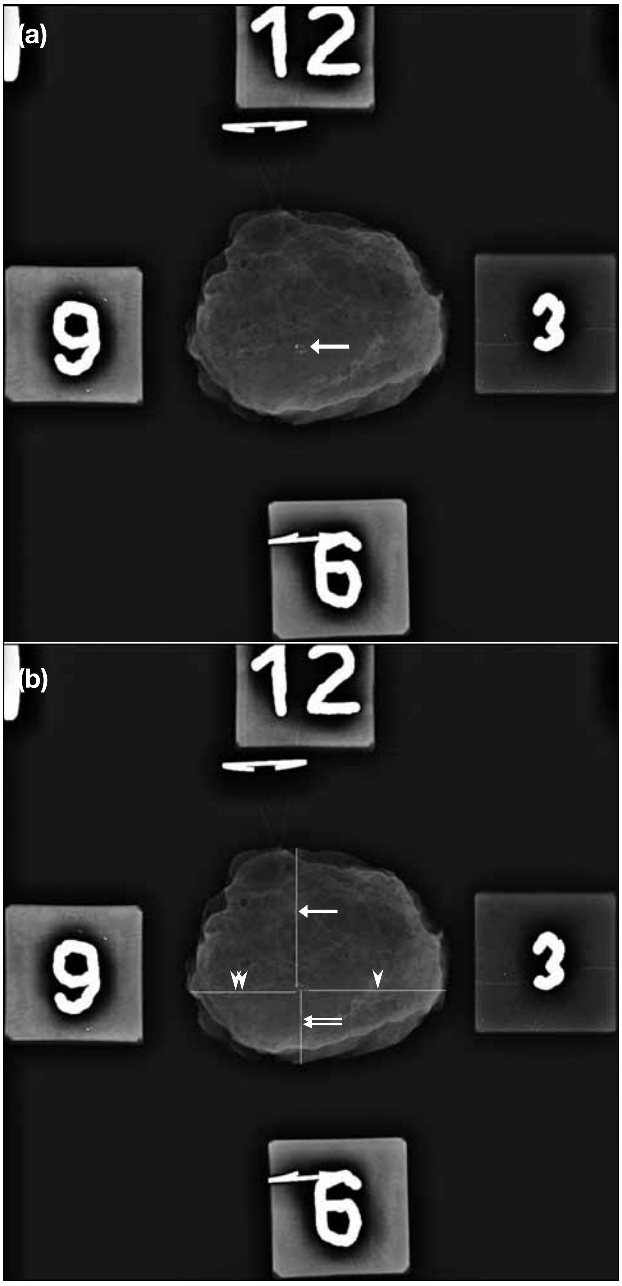

Figure 2. Radiological margin measurement on intraoperative specimen radiograph. (a) The specimen radiograph confirms inclusion of the target cluster of microcalcifications (arrow) in the surgical specimen from the left breast; and (b) the radiological margins are measured from the outermost microcalcification to the edge of the specimen in each of the superior (arrow), lateral (arrowhead), inferior (double arrows), and medial borders (double arrowheads).

of the ROLL-lumpectomy specimens was done. The radiological margin was measured in each of the superior, medial, inferior, and lateral borders of the specimen, which was defined as the shortest distance from the outermost microcalcification to the edge of the specimen (Figure 2).

Histopathology

The histopathology results were reviewed and analysed for each specimen. The size and grading of DCIS were documented, and coexistence of any invasive carcinoma component was recorded. Grading of DCIS was made according to the Van Nuys classification.

The pathological margin status was documented in each of the superior, medial, inferior, and lateral borders in every specimen. The margins were categorised as a clear, close, or positive margin — a clear margin was defined as more than 5 mm of margin clear of DCIS involvement; a close margin was defined as presence of DCIS involvement within 2.1 mm to 5.0 mm of the resection margin; and a positive margin was defined as presence of DCIS involvement within 2 mm of the resection margin.

Statistical Analysis

Results of radiological margin measurement on intraoperative specimen radiographs were correlated with the pathological margin status in each of the borders for every specimen. Statistical analyses were performed using the Statistical Package for the Social Sciences (Windows version 19.0; SPSS Inc, Chicago [IL], US). A p value was calculated by Mann-Whitney *U* test for any statistically significant difference in radiological margins between borders with different pathological margin status. A significance level of 0.05 was used.

In addition, receiver operating characteristic (ROC) curves were plotted according to the radiological margins and corresponding pathological margin status for each of the borders. Two ROC curves were plotted for the presence of (1) positive resection margin (DCIS involvement within 2 mm of resection margin) and (2) positive or close resection margin (DCIS involvement within 5 mm of resection margin) on histopathology. The discriminating power of radiological margin assessment in predicting resection margin status was determined by the area under the curve (AUC). The sensitivity and specificity of using different radiological margin cutoff values in predicting the resection margin status were also determined from the ROC curves.

RESULTS

A total of 24 stereotactic-guided ROLLs in 23 female patients were included. Patients' ages ranged from 33 to 73 years, with a mean of 52 years.

Preprocedure Mammogram

All patients underwent stereotactic-guided ROLL for microcalcifications detected on a preprocedure mammogram. The characteristics of the microcalcifications are summarised in Table 2.

Table 2. Grading and location of microcalcifications on preprocedure mammogram (n = 24).

Microcalcification characteristic	No. (%) of lesions
Mammographic grading	
Benign (category 2)	0 (0)
Indeterminate (category 3)	15 (62.5)
Suspicious of malignancy (category 4)	7 (29.2)
Highly suspicious of malignancy (category 5)	2 (8.3)
Location of lesions	
Side	
Left breast	13 (54.2)
Right breast	11 (45.8)
Quadrant	
Upper outer	15 (62.5)
Lower inner	6 (25.0)
Upper inner	1 (4.2)
Subareolar	2 (8.3)

All microcalcifications were graded as indeterminate (category 3) to highly suspicious of malignancy (category 5) according to the Royal College of Radiologists Breast Group breast imaging classification.[18] Indeterminate (category 3) lesions were most commonly seen.

Most lesions were located in the upper outer quadrant. Similar left and right breast involvement was observed.

Table 3. Histopathology findings of DCIS in stereotactic-guided radioguided occult lesion localisation (n = 24).

Pathology result	No. (%) of lesions*
Grade	
Low	5 (20.8)
Intermediate	15 (62.5)
High	4 (16.7)
Maximum dimension (mm)	
Mean	10.2
Range	1.5-40.0
Co-existing carcinoma	
Invasive ductal	3 (12.5)
Invasive lobular	1 (4.2)
Pathological margin status (n = 96)	
Positive (DCIS involvement ≤2 mm of resection margin)	12 (12.5)
Close (DCIS involvement 2.1-5.0 mm of resection margin)	5 (5.2)
Clear (DCIS involvement >5 mm of resection margin)	79 (82.3)

Abbreviation: DCIS = ductal carcinoma in situ.
* Unless otherwise stated.

Histopathology

The histopathology results are summarised in Table 3. Intermediate-grade DCIS was most commonly seen. The maximum dimensions ranged from 1.5 mm to 40.0 mm. A few patients (n = 4) had smaller components of co-existing invasive ductal carcinoma or invasive tubular carcinoma on histopathology. The maximum dimension of co-existing invasive ductal carcinoma ranged from 1.5 mm to 5 mm, and co-existing invasive tubular carcinoma measured 1 mm in maximum dimension.

A pathological clear margin was achieved in 79 (82.3%) of the 96 borders assessed. Twelve (12.5%) positive margins and 5 (5.2%) close margins were found on histopathological assessment.

Intraoperative Specimen Radiograph

As shown in Table 4, borders with a positive margin on histopathology (DCIS involvement within 2 mm of the resection margin) had a significantly smaller radiological margin on intraoperative specimen radiographs than borders with a close or clear margin ($p < 0.001$). The radiological margin for borders with a positive margin on histopathology ranged from 0 mm to 17.5 mm (mean, 8.7 mm) and borders with a close or clear margin on histopathology showed a radiological margin of 4.8 mm to 45.8 mm (mean, 20.1 mm).

Table 4. Results of radiological margin measurement for borders with different resection margin status on histopathology.

Resection margin status on histopathology	Mean (range) [mm]	p Value
Using 2 mm as a cutoff		
Positive margin (DCIS involvement ≤2 mm of margin)	8.7 (0-17.5)	<0.001
Close/clear margin (DCIS involvement >2 mm of margin)	20.1 (4.8-45.8)	
Using 5 mm as a cutoff		
Positive/close margin (DCIS involvement ≤5 mm of margin)	9.1 (0-17.5)	<0.001
Clear margin (DICS involvement >5 mm of margin)	20.7 (5.1-45.8)	

Abbreviation: DCIS = ductal carcinoma in situ.

Borders with positive or close margins on histopathology (DCIS involvement within 5 mm of resection margin) also showed significantly smaller radiological margins on specimen radiograph than borders with clear margins ($p < 0.001$). For borders with a positive or close margin on histopathology, the radiological margin ranged from 0 mm to 17.5 mm (mean, 9.1 mm). These were compared with borders with a clear margin on histopathology, which had radiological margins ranging from 5.1 mm to 45.8 mm (mean, 20.7 mm).

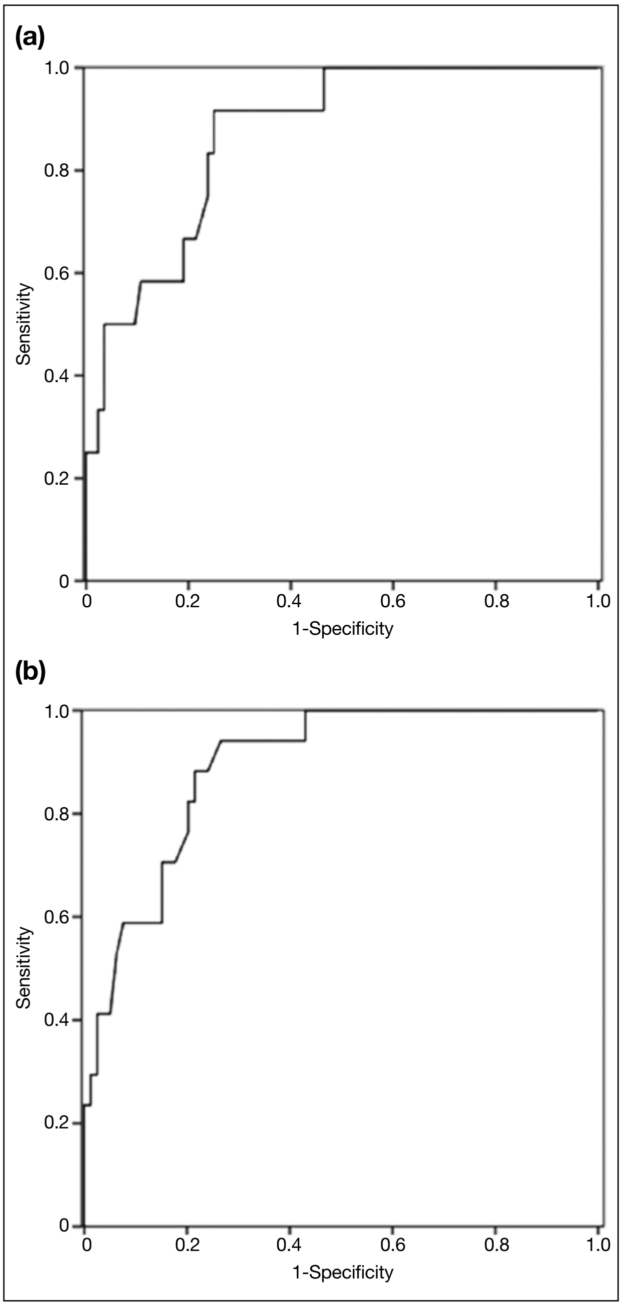

Figure 3. Receiver operating characteristic curves for discriminating the power of radiological margin assessment in predicting (a) a positive margin and (b) positive or close margins on histopathology.

Two ROC curves were plotted according to the radiological margins measured and corresponding histopathological margin status for each border (Figure 3). The AUC was 0.87 (95% confidence interval [CI], 0.78-0.96) for prediction of a positive margin and 0.89 (95% CI, 0.82-0.96) for prediction of a positive or close margin.

From the ROC curve, using a 15-mm radiological margin would yield the highest combination of sensitivity and specificity in predicting resection margin status. Using a 5-mm or 10-mm radiological margin would yield a higher specificity, but lower sensitivity. Similarly, using a 20-mm radiological margin would yield a high sensitivity, but lower specificity. The sensitivity and specificity of using 5 mm, 10 mm, 15 mm, and 20 mm as the radiological margin cutoff values are shown in Table 5.

DISCUSSION

The accuracy of specimen radiograph in predicting resection margin status in early breast carcinoma has been evaluated by various authors in the literature (Table 6[17,19-26]), yet no consensus has been reached. Different authors have demonstrated varying degrees of success in predicting resection margin status by specimen radiograph. Mazouni et al[19] showed a correlation between specimen radiograph and histopathology in terms of lesion size and margin status, Goldfeder et al[20] concluded that specimen radiograph could aid in margin assessment for patients undergoing breast-conserving therapy, and Ciccarelli et al[21] demonstrated that specimen radiograph was reliable in identifying clear margins and reducing the intervention rate. However, there are several publications showing a lack

Table 5. Sensitivity and specificity of using different radiological margin cutoff values in predicting positive margin or positive/close margin on histopathology.

Radiological margin	Positive margin		Positive or close margin	
	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
5 mm	25.0	98.8	23.5	100
10 mm	58.3	89.3	58.8	91.1
15 mm	91.7	75.0	94.1	73.4
20 mm	100	40.5	100	43.0

Table 6. Studies reviewing accuracy of specimen radiography in predicting resection margin status in early breast cancers.[17,19-26]

Study	No. of cases	Lesion nature	No. of views of specimen radiograph	Radio-logical margin (mm)	Patho-logical margin (mm)	Localisation method	Sen-sitivity (%)	Spec-ificity (%)	PPV (%)	NPV (%)
Graham et al,[23] 1994	119	All malignancy	1	0	0	Wire	62	95	98	32
Coombs et al,[22] 2006	61	All malignancy	NA	5	1	Wire	52	86	75	69
							67*	82*	74*	77*
McCormick et al,[24] 2004	93	Invasive carcinoma	2	0	NA	Wire	55	88	38	94
Mazouni et al,[19] 2006	164	DCIS	1	1	1	Wire	33	84	77	43
				5			50	74	76	46
				10			75	41	68	49
Goldfeder et al,[20] 2006	112	All malignancy	1 (with 1-view specimen radiographs)	0	1	Wire	50	78	65	65
			2 (with 2-view specimen radiographs)				44	65	47	63
Ciccarelli et al,[21] 2007	123	All malignancy	2	NA	2	Charcoal	68	86	74	81
Britton et al,[17] 2011	106	All malignancy	1	11	5	Wire	68	68	NA	NA
				9.5	2		68	70	NA	NA
Rua et al,[25] 2012	118	DCIS	NA	10	1	Wire/skin marker	33	80	52	61
		IDC					50	77	36	85
Buggi et al,[26] 2013	272	DCIS	1	15	2	ROLL	81% (accuracy)			

Abbreviations: DCIS = ductal carcinoma in situ; IDC = invasive ductal carcinoma; NA = not available; NPV = negative predictive value; PPV = positive predictive value; ROLL = radioguided occult lesion localisation.
* Assessment by surgeon.

of satisfactory accuracy in the evaluation of resection margin status by specimen radiograph.[17,22]

The reported sensitivity and specificity of specimen radiography in predicting resection margin status for early breast cancer ranges from 33% to 75% and 65% to 95%, respectively.[17,19-26] Such heterogeneous data may be partially explained by the lack of international consensus regarding the optimal pathological and radiological margin to be used. Pathological margins of no ink on tumour, 1 mm, 2 mm, and 5 mm have all been used in previous studies, while the radiological margins used varied from 0 mm (lesion reaching specimen border) to 15 mm.

The calibre of an acceptable negative surgical margin in breast-conserving therapy for DCIS remains controversial, and values between 1 mm and 10 mm have been proposed.[15] A large group of breast surgeons in the United States were surveyed for the minimal acceptable resection margin for DCIS. Around 12% would accept any negative margin, 22% would accept a 1-mm margin, 52% would accept a 2-mm margin, 10% would accept a 5-mm margin, and 4% would accept a 10-mm margin.[27] The fact that a 2-mm margin is a more commonly accepted value was supported by the study by Neuschatz et al.[28] These researchers have shown that the incidence of residual DCIS at re-excision was correlated with the margin width free of DCIS involvement on the initial surgical specimen: 41% with a <1-mm margin, 31% with a 1- to 2-mm margin, and 0% with a greater than 2-mm margin.[28] A review of 4,660 DCIS patients treated with postoperative radiotherapy found that patients with no ink on tumour or a 1-mm margin had a significantly greater ipsilateral breast tumour recurrence rate than patients with a greater-than-5-mm clear margin. However, no statistically significant difference in the ipsilateral breast recurrence rate was seen between patients with a 2-mm margin and a greater-than-5-mm margin.[29] Therefore, our study adopted a cut-off of 2 mm for a positive margin and 5 mm for a close margin.

Only a few studies specifically investigated the accuracy of specimen radiography in predicting resection margin status in DCIS.[19,25,26] The radiological margins used in these studies ranged from 1 mm to 15 mm. In this study, one of the objectives was to determine the optimal cutoff value of radiological margin to be used for predicting resection margin adequacy for DCIS, and ROC curves showed that a 15-mm radiological margin had the highest combination of sensitivity and specificity. Using a radiological margin of 15 mm was supported by Buggi et al,[26] who reported 81% accuracy in predicting a clear resection margin. However, it was understood that choosing cutoff values for radiological margin assessment is a trade-off between sensitivity and specificity, which has been shown by Mazouni et al.[19] Therefore, an optimal cutoff value should be chosen with consideration of whether a patient would benefit from a more sensitive or more specific assessment. Hence the sensitivity and specificity for different radiological margins were calculated for reference.

ROC curves were used in three previous studies to determine the accuracy of specimen radiographs in predicting resection margin status in breast carcinoma.[17,19,23] The ROC curve is a graphical representation of the trade-off between sensitivity and specificity of each possible cutoff value. The AUC of the ROC curves in these studies ranged from 0.63 to 0.79, showing a variable discriminating power of specimen radiography in predicting resection margin status. Only one of these three studies focused on DCIS, and the AUC of its ROC curve was 0.63.[19]

Whether a one-view or two-view specimen radiograph should be obtained is another area of debate. Graham et al[23] have suggested that assessment on a single-view specimen radiograph could localise the lesion in only two planes, that is, a lesion that appears to have a clear radiological margin may actually have a positive margin if an appropriate tangential view was obtained. We had a similar experience, and found that some patients had superficial or deep margin involvement despite apparent clear craniocaudal and mediolateral radiological margins on the anteroposterior specimen radiograph. In the current study, assessments of superficial and deep margins were not included in the statistical analysis because the corresponding radiological margin assessments were not available for histopathological correlation.

The correlation between radiological and histological margins was analysed by border instead of by patient in this study as this better reflects a real-life clinical situation, in which presence or absence of a clear radiological margin should be commented on for each specimen border separately. Only this can provide useful information for surgeons to decide which border requires further excision. For instance, a surgical specimen can have multiple positive margins on histopathology, and the radiological assessment should address the number and location of borders suspected of margin involvement to guide further surgical resection. Britton et al[17] have compared the orientation of the nearest radiological margin with the nearest histological margin, and found that they correlated in less than half of the cases. In 35% of patients, the nearest radiological margin and nearest histological margin showed a difference of 90° rotation, and in 8% of patients there was a difference of 180° rotation.[17] We suggested that margin assessment should be done on a per-border basis instead of a per-patient basis to reflect such discrepancy. A single patient can have a combination of false-positive and false-negative borders, so we tried to reflect the actual radio-pathological correlation in each border separately.

Since its introduction by Luini et al in 1996,[30] ROLL has been widely used for localisation of clinically occult lesions prior to surgery. Compared with traditional wire localisation, ROLL has the advantages of more accurate and faster localisation, easier subsequent surgery, and better cosmetic outcome.[31] It has been reported that ROLL can achieve a comparable or superior negative margin rate to wire localisation.[32] Local data have shown that preoperative localisation by ROLL can give a shorter localisation time with a similar negative margin rate when compared with wire localisation.[32] In addition, ROLL has the advantage of allowing simultaneous lymph node biopsy to be performed (sentinel node and occult lesion localisation). The radiation dose to patients and staff has been shown to be minimal. The mean absorbed dose to the patient was 0.45 mGy and was low compared with that of other diagnostic examinations. The finger dose to surgeons, radiologists, and other allied staff was well below the annual acceptable limit.[33,34] As shown in Table 6, we only identified one study in the literature evaluating the accuracy of specimen radiograph in predicting resection margin status utilising ROLL as the localising procedure.[26] However, due to the study design, this study did not provide data on the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV), and only provided an overall accuracy rate according to the final outcome of the management protocol. To the best of our knowledge, there has been no previous study reporting the sensitivity, specificity, PPV, and NPV of specimen radiograph in prediction of resection margin status using ROLL as the localisation method.

The specificity of specimen radiography in prediction of resection margin status from our study was similar to previous studies, but the sensitivity appeared higher.

This may be accounted for by the intrinsic differences in study design in terms of the values of radiological and pathological margins used, unit of assessment (per-border assessment vs. per-patient assessment), and the use of different specimen radiograph protocols (one view vs. two views). Furthermore, there may be differences in patients' disease spectra, as this study focused on DCIS patients and most of our patients had intermediate-grade DCIS, with only a small number having co-existing invasive carcinoma. The difference in the AUC of the ROC curves compared with prior studies may also be accounted for by these factors.

There are a few limitations to this study. As a retrospective study, it has inherent limitations. The small sample size from a single centre may limit the generalisability of the results. The lack of radiological assessment of superficial and deep resection margins due to the use of one-view specimen radiographs limits a full assessment of all resection margins. Nevertheless, the results of this study have shown that radiological margin assessment in specimen radiography is a potentially useful tool for predicting resection margin status. By obtaining specimen radiographs to confirm target lesion inclusion within the surgical specimen during hookwire or radionuclide localisation for clinically and sonographically occult lesions, radiological margin evaluation requires no additional tests in contrast to other intraoperative assessment modalities. A larger-scale, prospective, multicentre trial will be useful for further assessment based on the results of this study.

CONCLUSION

Radiological margin assessment on specimen radiography during ROLL showed high accuracy and could be a potentially useful tool for predicting resection margin status in patients with DCIS presenting with microcalcifications.

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