Hong Kong J Radiol. 2016;19:269-78 | DOI: 10.12809/hkjr1615317

ORIGINAL ARTICLE

Efficacy of Radioguided Occult Lesion Localisation: How Well are We Doing?

AKY Au, AYH Wan, BST Leung, SSW Lo, WWC Wong, JLS Khoo

Department of Radiology, Pamela Youde Nethersole Eastern Hospital, Chai Wan, Hong Kong

ABSTRACT

Objective: *To assess the radiological, scintigraphic, surgical, and histological success rates of radioguided occult lesion localisation (ROLL).*

Methods: *We retrospectively reviewed 94 consecutive patients who underwent stereotactic-guided ROLL for radiologically indeterminate to highly suspicious microcalcifications from September 2002 to May 2014. Mammograms, scintigraphic records, surgical records, pathology results, and consultation notes of patients were reviewed. Fisher's exact test was used to assess the association between ductal carcinoma in-situ (DCIS), invasive carcinoma, and surgical success.*

Results: *Radiological success was achieved in 88 (93.6%) of 94 patients. There were four cases of inadvertent intraductal injection of iodinated contrast and two cases of contrast staining away from the suspicious microcalcifications. Scintigraphic success was achieved in 93 (98.9%) of 94 patients. There was one failure related to insufficient radio-isotope. Among the 87 cases of successful stereotactic-guided ROLL, 50 (57.5%) tumours were benign and 37 (42.5%) were malignant, including 24 (64.9%) cases of DCIS. There were five (20.8%) low-grade, 15 (62.5%) intermediate-grade, and four (16.7%) high-grade DCIS. Surgical success was achieved in 71 (81.6%) of 87 patients. Margin involvement by DCIS accounted for 14 (16.1%) failures, in which 10 (71.4%) patients had re-excision of margin. Subsequent modified radical mastectomy was performed in six (37.5%) patients and included two patients in whom there was failed re-excision of margin. Histological success was achieved in 82 (94.3%) of 87 patients, in whom 'microcalcifications present' was mentioned in the pathology report. All patients survived with no recurrence on follow-up breast imaging for 12 years except one patient who died from carcinoma of the ovary. There was a significant association between DCIS and lower surgical success ($p = 0.017$).*

Conclusion: *ROLL is effective in localising non-palpable breast lesions with high radiological, scintigraphic, surgical, and histological success. There was a significant association between DCIS and lower surgical success. A wider resection margin may improve surgical success.*

Key Words: *Breast neoplasms; Carcinoma, ductal, breast; Mastectomy, segmental*

Correspondence: *Dr Alice KY Au, Department of Radiology, Pamela Youde Nethersole Eastern Hospital, Chai Wan, Hong Kong. Tel: (852) 2595 6111; Fax: (852) 2975 0432; Email: aky141@ha.org.hk*

Submitted: 18 Mar 2015; Accepted: 10 Jul 2016.

Disclosure of Conflicts of Interest: All authors have disclosed no conflicts of interest.

中文摘要

放射導向隱匿性病灶定位的有效性和目前應用現狀

區嘉殷、尹宇瀚、梁肇庭、盧成瑋、黃慧中、邱麗珊

目的：評估放射導向隱匿性病灶定位（ROLL）的放射學、同位素顯像、手術和組織學成功率。

方法：回顧研究2002年9月至2014年5月期間所有接受立體定向引導ROLL的94例患者，經放射學檢查發現不確定至高度可疑的微鈣化灶的病例。回顧患者的乳房X線照片、顯像掃描紀錄、手術紀錄、病理結果和病歷紀錄。使用Fisher精確檢驗來評估導管原位癌（DCIS）、浸潤性癌和手術成功率之間的關係。

結果：放射學成功率為93.6%（94例中有88例）。其中4例發生不慎管內注射碘化造影劑，2例為可疑微鈣化灶的造影劑偏離。顯像成功率為98.9%（94例中有93例）。1個失敗病例與放射性同位素不足有關。87例成功進行立體定向引導ROLL中有50例（57.5%）腫瘤為良性，37例（42.5%）為惡性（包括24例DCIS，64.9%）。5例（20.8%）屬低度、15例（62.5%）屬中度，以及4例（16.7%）屬高度分化DCIS。手術成功率為81.6%（87例中有71例）。14（16.1%）例的DCIS切除邊緣呈陽性，其中10例（71.4%）重新進行了邊緣切除。隨後6例（37.5%）進行了根治性乳房切除術，包括2例邊緣切除失敗的患者。組織學成功率為94.3%（87例中有82例），其病理學報告中提及「微鈣化」。除1例死於卵巢癌外，所有患者術後12年的乳腺成像中均未發現復發。DCIS與手術成功率低之間存在顯著相關性（p=0.017）。

結論：ROLL對不可觸及的乳房病變的定位具有很高的放射學、同位素顯像、手術和組織學成功率。DCIS與手術成功率低顯著相關。增加切緣寬度可以提高手術成功率。

INTRODUCTION

Breast cancer is the most common malignant tumour affecting women in Hong Kong. The number of diagnosed cases tripled from 1152 in 1993 to 3508 in 2012. An average of nine women are diagnosed with breast cancer every day.[1] Breast cancer accounts for 25.1% of all newly diagnosed malignancies in female patients locally and 25.2% internationally.[2,3]

Due to the greater availability of breast screening services and increasing public awareness of breast cancer, the incidence of ductal carcinoma in-situ (DCIS) has significantly increased in recent years.[4,5] According to a local large-scale opportunistic breast cancer screening programme,[6] DCIS accounted for 28% of all newly diagnosed breast cancers in Hong Kong. Most cases of DCIS are clinically non-palpable and sonographically occult, therefore requiring the use of radionuclide localisation or stereotactic-guided hookwire insertion to obtain a pathological diagnosis.

Radioguided occult lesion localisation (ROLL) was first introduced in 1996 at the European Institute of Oncology in Milan as a possible superior alternative to hookwire-guided localisation.[7] Inspired by the rationale for sentinel node biopsy, this technique utilises intralesional injection of radiotracer to localise the primary lesion with the guidance of a gamma probe intra-operatively. With the help of a gamma probe, this method provides an opportunity for the surgeon to choose the best route of access and perform a lumpectomy that aims to achieve tumour-free margins, while removing a minimal volume of tissue. This technique also allows the surgeon to check for any residual radioactivity in the breast tissue, thus ensuring complete excision.

Various studies have reviewed the utilisation of ROLL with or without comparison with hookwire-guided localisation. Locally, it has been found that ROLL excels in yielding a much shorter localisation time and is as good as hookwire localisation in terms of specimen margin clearance and the need for re-excision.[8] ROLL also offers the advantage of enabling simultaneous sentinel lymph node biopsy for invasive cancers. Monti et al[9] retrospectively analysed a database of 959 patients who underwent ROLL. These patients

had histologically or cytologically proven malignancy. In 883 (92.1%) of 959 patients, the malignancy was completely removed with tumour-free surgical margins. In a prospective study published by Sarlos et al in 2008,[10] 100 patients with 120 proven malignancy or DCIS underwent ROLL. A sentinel node procedure was performed in 72 patients by placing a second injection of technetium-99m subdermally or in the periareolar area with a success rate of 98.6%. Complete tumour removal with negative margins was noted in 55 (80%) out of 69 patients in the invasive carcinoma group, and 65% in the DCIS group.[10]

A group of patients with non-palpable suspicious lesions of BI-RADS (Breast Imaging–Reporting and Data System) grades 4-5 were prospectively studied by Lavoué et al.[11] During the ROLL procedure, technetium-99m was injected peritumourally at the superficial and deeper poles of the lesion. In all cases, the lesion was localised and removed. Pathological examination showed involvement of margin in only seven (10%) of 72 patients. In four patients, multi-focal tumour was identified. These 11 (15%) patients required re-excision. The sentinel node procedure was also successful in 90% of these patients when the radioactive tracer was combined with a peri-tumoural injection of blue dye during surgery.

Van Esser et al[12] recruited patients with core biopsy–proven invasive carcinoma who required breast-conserving surgery and a sentinel node procedure. One intra-tumoural injection was used for both localisation of the tumour and the sentinel node procedure. In 78% of the 40 enrolled patients, complete excision of the tumour was achieved and the sentinel node was also identified in 88% of patients.

Despite these advantages, ROLL has drawbacks. Radioactive substance may flow into mammary tissue adjacent to the tumour, or there may be inadvertent intraductal injection of contrast leading to failed or inaccurate localisation. This may hinder localisation of the lesion itself and result in excessively large excision volumes.[13,14]

The aim of this study was to evaluate more comprehensively the utilisation of ROLL in terms of radiological, scintigraphic, surgical, and histological success.

METHODS

We retrospectively reviewed 94 consecutive stereotactic-guided ROLL procedures performed for indeterminate to highly suspicious microcalcifications in a regional hospital of Hong Kong from September 2002 to May 2014. Mammograms, scintigraphic records, intra-operative findings, pathology results, and consultation notes of patients were reviewed. The radiological, scintigraphic, surgical, and histological success rates were determined. Radiological success was defined as accurate localisation of the targeted microcalcifications with radiographic iodinated contrast. Scintigraphic success was defined as accurate localisation of the targeted microcalcifications with radio-isotopes. Surgical success was defined as a ≥1 mm clear margin or no lesion involvement in the surgical specimen. Associations between DCIS, invasive ductal carcinoma (IDC), and surgical success were analysed using Fisher's exact test. Histological success was defined as the inclusion of microcalcifications mentioned in the pathology report. The study was approved by the hospital ethics committee, with the requirement of patient informed consent waived because of its retrospective nature.

Pre-procedural Mammogram

Radiological findings in the pre-procedural mammograms were categorised according to the Royal College of Radiologists Breast Group breast imaging classification[15] into five categories depending on the level of suspicion for malignancy and the need for further investigation (Table 1[15]).

Table 1. Royal College of Radiologists Breast Group breast imaging classification.[15]

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.

The Radioguided Occult Lesion Localisation Procedure

The targeted cluster of indeterminate to highly suspicious microcalcifications was located with the use of paired stereo images obtained at 15 degrees by the mammographic machine. A 21-G spinal needle was inserted to localise the designated microcalcifications. After radiographic confirmation of the position of the spinal needle, 5-10 MBq technetium-99m Tc macroaggregated albumin was injected into the lesion followed by 0.1-0.2 ml of radio-opaque non-ionic iodinated contrast to ensure correct location of the injected radio-isotope without inadvertent injection into the intramammary ducts. Post injection views were obtained to confirm contrast staining at the area of the targeted microcalcifications (Figure 1). The patient was then transported to the Department of Nuclear Medicine for scintigraphic examination to ensure focal concentration of radio-isotope tracer (Figure 2).

After a successful ROLL procedure, the patient underwent radioguided surgery in which a gamma-detecting probe was used to measure the radioactivity intra-operatively and to identify the area with maximal activity corresponding to the site of the suspicious microcalcifications. The lesion was excised and complete excision confirmed by the absence of residual radioactivity in the surgical bed. The surgical specimen was then sent to the Department of Radiology for a specimen radiograph to verify inclusion of the targeted lesion in the excised surgical specimen (Figure 3). The intra-operative specimen radiograph was read by a dedicated radiologist who immediately communicated the findings to the surgeon.

Surgical success in this study was defined as a ≥1 mm

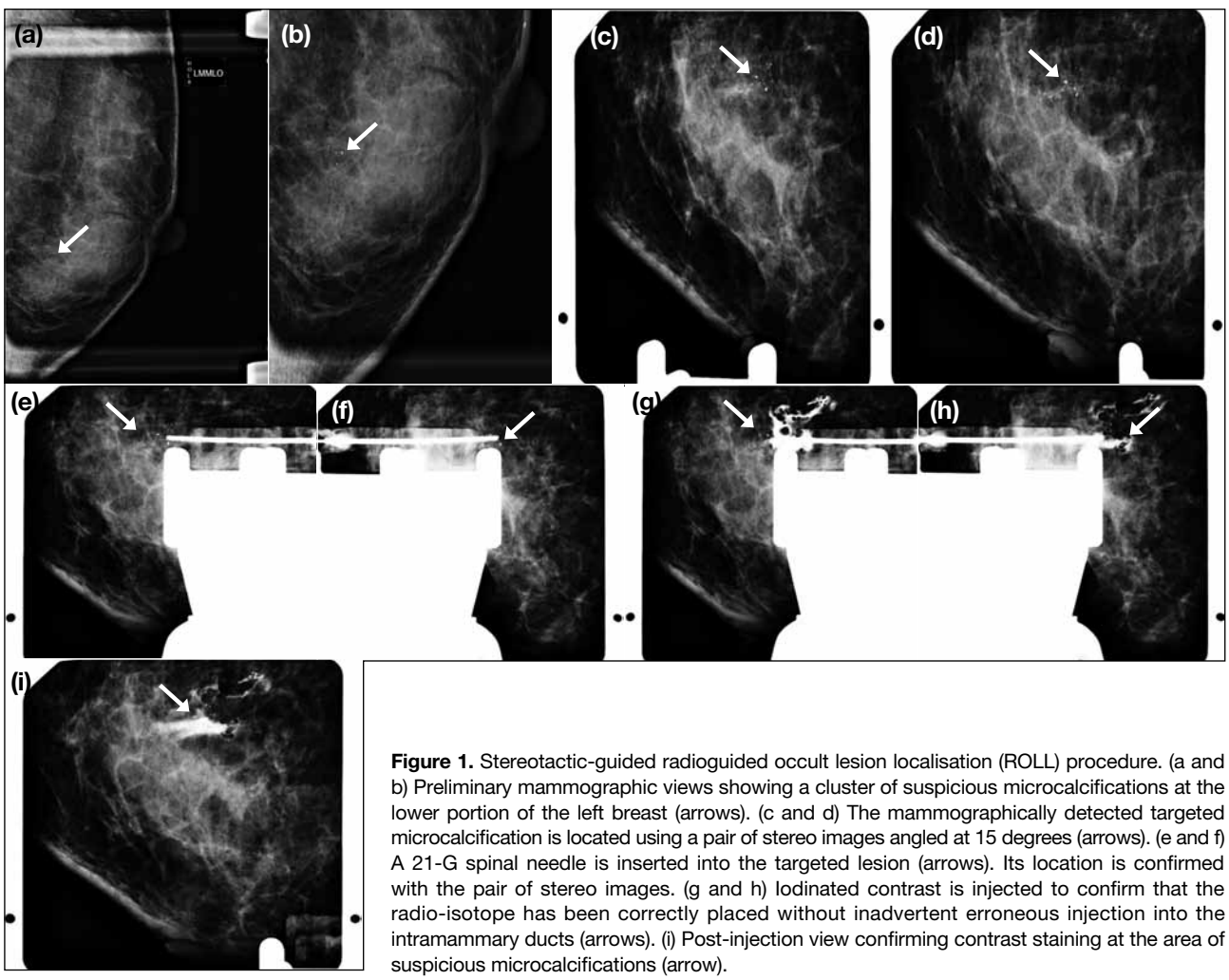

Figure 1. Stereotactic-guided radioguided occult lesion localisation (ROLL) procedure. (a and b) Preliminary mammographic views showing a cluster of suspicious microcalcifications at the lower portion of the left breast (arrows). (c and d) The mammographically detected targeted microcalcification is located using a pair of stereo images angled at 15 degrees (arrows). (e and f) A 21-G spinal needle is inserted into the targeted lesion (arrows). Its location is confirmed with the pair of stereo images. (g and h) Iodinated contrast is injected to confirm that the radio-isotope has been correctly placed without inadvertent erroneous injection into the intramammary ducts (arrows). (i) Post-injection view confirming contrast staining at the area of suspicious microcalcifications (arrow).

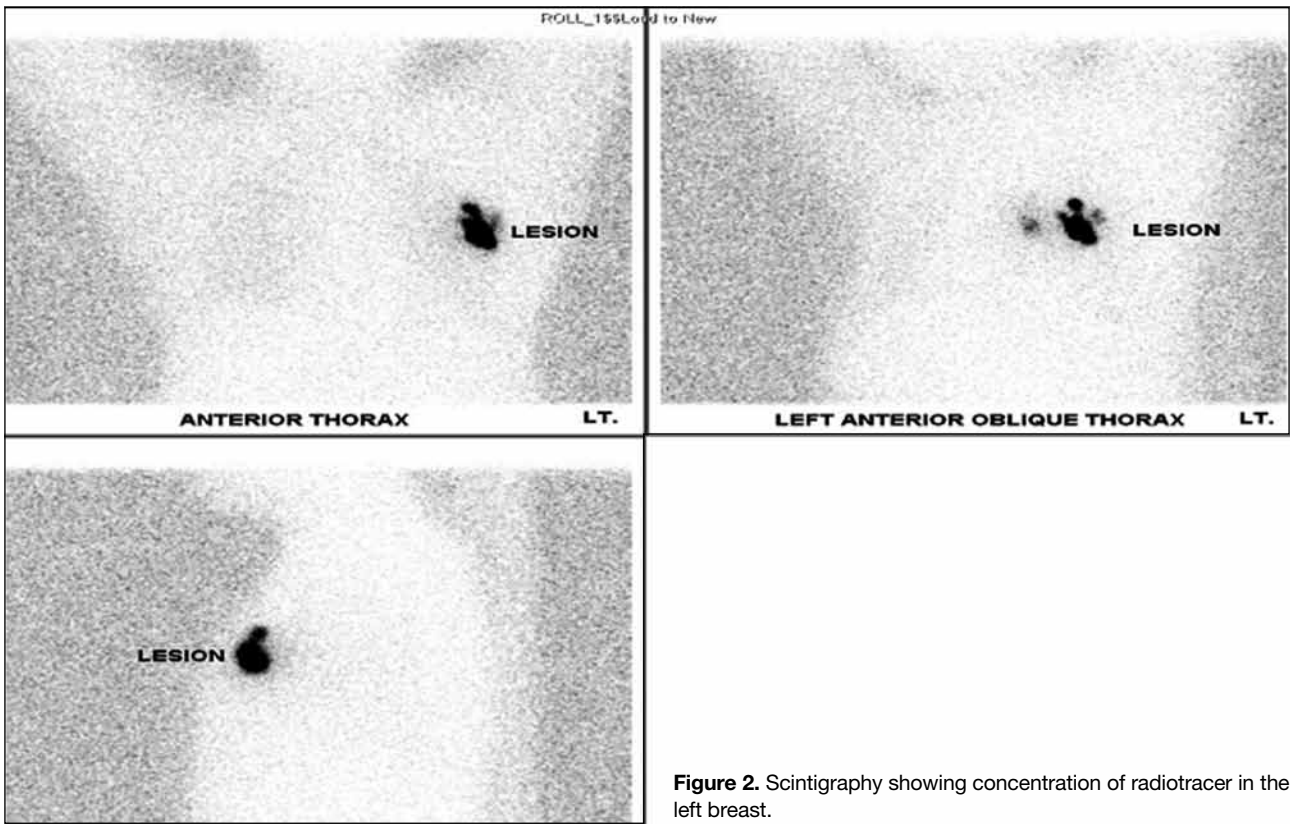

Figure 2. Scintigraphy showing concentration of radiotracer in the left breast.

Figure 3. Specimen radiograph is taken to show that the suspicious microcalcifications marked by radioguided occult lesion localisation are all excised.

clear margin or no lesion involvement in the specimen radiograph. The calibre of acceptable negative surgical resection margin in breast-conserving treatment for DCIS remains controversial: figures between 1 mm and 10 mm have been used.[16] In a local study,[8] a clear margin was defined as a >1 mm margin clear of any lesion involvement. In a study conducted by Neuschatz et al,[17] the incidence of residual DCIS at re-excision correlated with the margin-width free of DCIS involvement on the initial surgical specimen: 41% with a <1 mm margin, and in 31% when using a margin of 1-2 mm. In a large survey of breast surgeons carried out in the USA,[18] 22% stated that the minimal acceptable resection margin for DCIS was 1 mm. The diversity in the data can be partly related to the paucity of international consensus regarding the optimal

pathological and radiological margin to be adopted, and is a topic for future studies.

Statistical Analysis

Association between DCIS, IDC, and surgical success was evaluated using the Fisher's exact test. The analysis was performed using the Statistical Package for the Social Sciences (Windows version 19.0; SPSS Inc, Chicago [IL], USA). A p Value was calculated for any statistically significant difference in surgical success between DCIS and IDC; significance level was set at 0.05.

RESULTS

The total number of stereotactic-guided ROLL performed was 94. Patient age ranged from 33 to 73 years with a mean of 51.5 years. The location of the targeted microcalcifications is summarised in Table 2.

Radiological success was achieved in 88 (93.6%) of 94 cases. There were four cases of inadvertent intraductal injection of iodinated contrast and two cases of contrast staining away from the suspicious microcalcifications. Scintigraphic success was achieved in 93 (98.9%) cases. There was one failure related to injection of an insufficient amount of radio-isotope. There were a total of 87 successful cases of stereotactic-guided ROLL. Histological success where the presence of microcalcifications was mentioned in the pathology report was achieved in 82 (94.3%) of 87 patients.

Histopathology

Histopathology of the benign and malignant breast lesions is summarised in Tables 3 and 4, respectively. In the benign lesions, fibrocystic changes were most commonly observed (62%). Malignant cases accounted for 42.5%, of which 64.9% were DCIS. Intermediate grade accounted for most of the DCIS (62.5%). Surgical success was achieved in 71 (81.6%) of 87 patients. Margin involvement of DCIS accounted for 14 failures, while that of IDC accounted for two failures. The 2x2 contingency table for Fisher's exact test is shown in Table 5. There was a significant association of DCIS with lower surgical success (p = 0.017).

Of the cases with margin involvement of DCIS, 10 (62.5%) patients had re-excision of margin and six (37.5%) underwent subsequent modified radical mastectomy of whom two had failed re-excision of margin. All patients survived with no recurrence on follow-up breast imaging for 12 years except one patient who died from carcinoma of the ovary.

Table 2. Location of the targeted microcalcifications on pre-procedural mammograms.

Location	No. (%) of lesions*
Side	
Left	46 (48.9)
Right	48 (51.1)
Quadrant	
Upper outer	54 (57.4)
Upper inner	10 (10.6)
Lower outer	6 (6.4)
Lower inner	22 (23.4)
Subareolar	2 (2.1)

* Because of rounding, not all percentages total 100.

Table 3. Histopathology findings of benign lesions in stereotactic-guided radioguided occult lesion localisation (n = 50).

Histopathology findings	No. (%) of lesions
Fibrocystic changes	31 (62)
Atypical ductal hyperplasia	6 (12)
Sclerosing adenosis	4 (8)
Intraductal papilloma	3 (6)
Focal ductal hyperplasia	2 (4)
Stromal fibrosclerosis	1 (2)
Papillomatosis	1 (2)
Peripheral papilloma	1 (2)
Apocrine cysts	1 (2)

Table 4. Histopathology findings of malignant lesions in stereotactic-guided radioguided occult lesion localisation (n = 37).

Histopathology findings	No. (%) of lesions
DCIS	24 (64.9)
Low grade	5 (20.8)
Intermediate grade	15 (62.5)
High grade	4 (16.7)
Invasive ductal carcinoma*	16 (43.2)
Invasive lobular carcinoma*	1 (2.7)
Co-existing carcinoma	
Invasive ductal carcinoma	3 (12.5)
Invasive lobular carcinoma	1 (4.2)

Abbreviation: DCIS = ductal carcinoma in-situ
* Including co-existing DCIS

Table 5. A 2x2 contingency table for Fisher's exact test.

	Surgical success	Surgical failure	**Marginal row totals**
Ductal carcinoma in-situ	10	14	**24**
Invasive ductal carcinoma	11	2	**13**
Marginal column totals	**21**	**16**	**37 (grand total)**

DISCUSSION

ROLL has been shown in various studies to be effective in localising breast lesions. A prior local study[8] demonstrated that ROLL yields a much shorter localisation time and is as good as hookwire in terms of specimen margin clearance and the need for re-excision. It also offers the benefit of enabling simultaneous sentinel lymph node biopsy for invasive cancers. ROLL has a further advantage of delivering less radiation to patients and staff. As low-dose gamma radiation is employed and technetium-99m has a short half-life of 6 hours, radiation safety is ensured. In a study carried out by Cremonesi et al,[19] the effective dose for a patient in ROLL was 9.25 μSv, less than half the dose of a chest radiograph (0.02 mSv). ROLL also offers an advantage to breast surgeons and radiologists in that the finger doses are minimal. Rampaul et al[20] performed a randomised trial to determine the need for extra-radiation protection procedures using dosimetry data from patients and hospital personnel involved in the procedure of ROLL. The finger dose was 9.3 ± 3.3 mSv to breast surgeons and 0.5 ± 0.1 mSv to radiologists. Therefore, a surgeon who performs 100 ROLL procedures per annum would receive a finger dose of around 1 mSv, which is well within the annual dose limit of 150 mSv. The study also showed that no additional protective equipment was required because no contamination was evident in the garbage and the porters received no radiation.

Our study showed that ROLL was associated with high success rates radiologically (93.6%), scintigraphically (98.9%), and surgically (81.6%). In addition to high success rates and assured radiation safety, ROLL has also been shown to offer advantages such as reduced excision volume of breast tissue, more accurate centricity of a lesion within the surgical specimen, better cosmetic outcome, and a higher percentage of tumour-free margins.[7,21-23] Many publications have reported satisfactory success rates of ROLL ranging from 99.6%[9] to 100%,[11,24,25] and good margin clearance ranging from 75%[26] to 100%.[27] A local study by Chu et al[8] reported a 84% margin clearance rate. The use of an intra-operative specimen radiograph in ROLL to predict resection margin status in cases of DCIS can be further investigated in future studies.

ROLL can also be performed to localise markers previously placed to help surgeons achieve a wide local excision in pathologically high-risk cases yielded by stereotactic-guided biopsy. Stereotactic-guided vacuum-assisted biopsy with a large needle (9-Gauge) can retrieve a large amount of breast tissue, and achieve whole-lesion excision and complete removal of grouped microcalcifications. Vacuum-assisted biopsy outperforms biopsy with a core biopsy needle in terms of larger specimen size and higher calcification retrieval rate; and lower targeting error, false negative rate, underestimation rate, and the need for re-biopsy or further multi-treatment surgery.[28,29]

Pathologically high-risk cases encountered in our practice include atypical ductal hyperplasia (ADH), atypical lobular hyperplasia (ALH), lobular carcinoma in-situ (LCIS), and DCIS.

Large-scale studies have shown that there was an underestimation of cancer in cases of ADH diagnosed by vacuum-assisted core needle biopsy in 9% of patients.[30] Another study by Jackman et al[31] demonstrated that surgical excision revealed carcinoma in 22 (21%) of 104 ADH lesions.

It has also been shown that in cases of ALH diagnosed with stereotactic-guided vacuum-assisted biopsy, subsequent surgical excision demonstrated cancer in one (14.3%) of seven lesions.[32] Thus Irfan and Brem[32] recommended that surgical excision be performed for lesions that demonstrate ALH on stereotactic-guided vacuum-assisted biopsy to exclude malignancy. In a study performed by Polom et al[33] of 16 cases of LCIS, invasive ductal cancer was observed in two (12.6%) patients, invasive lobular cancer in two (12.5%) patients, and DCIS in one (6.3%). The underestimation of DCIS by stereotactic-guided vacuum-assisted biopsy was also documented in a local study performed by Wan et al,[34] where one (14.3%) of seven cases showed DCIS in a histological specimen retrieved by vacuum-assisted biopsy, with excisional biopsy showing IDC. It is clear that some DCIS will progress over the lifetime of a patient. Erbas et al[35] showed that 14% to 53% of DCIS misdiagnosed as benign will progress to invasive carcinoma over 10 to 15 years. In another study by Sanders et al,[36] low-grade DCIS progressed in 11 out of 28 patients, with most occurring after 10 years; while three were diagnosed between 23 and 42 years after the initial biopsy, and five out of 11 died of breast cancer. It is important to obtain a wide surgical clearance in cases of DCIS.

In the aforementioned pathologically high-risk cases, ROLL is performed to localise previously placed

vacuum-assisted biopsy markers to assist surgeons to achieve a wide local excision.

Although ROLL has gained popularity in recent years, it is not without pitfalls. Radiological success in this study was high (93.6%) with four cases of inadvertent intraductal injection of contrast and two cases of contrast staining away from the suspicious microcalcifications. In the case of inadvertent injection of contrast, it signified that there was failed localisation of the lesion due to migration of radio-isotope away from the injection site. In a study performed by Rampaul et al,[14] two of 38 ROLL procedures were associated with intraductal injection of isotope, and were diagnosed on check mammograms since non-ionic iodinated contrast was mixed with the isotope. In one of these cases, conversion to wire localisation was required. A post-injection radiograph is important as it allows early recognition and timely intervention including alternative methods of lesion localisation. Although it is difficult to predict the probability of inadvertent intraductal injection of contrast, the chance may be higher when the lesion is closer to the subareolar area where a greater abundance of intramammary ducts is expected.

This study showed a statistical association between DCIS and lower surgical success ($p = 0.017$). At present, conservative management of DCIS largely conforms to the principles of breast-conserving treatment for invasive breast carcinoma. Nonetheless, there may be challenges for successful breast-conserving treatment in DCIS. Approximately 80% to 90% of DCIS are calcified[37,38]; and the extent of calcified DCIS detected by screening mammography is a determinant of breast-conserving treatment. Mammogram, however, may miss DCIS that does not present with suspicious patterns of microcalcifications. In a study performed by Hayward et al,[39] almost a quarter of patients with DCIS treated initially by breast-conserving surgery either required a second operation (39%) or were noted to have unexpected invasive disease following surgery (24%). These findings are also compatible with another study performed by Holland et al,[40] in which the authors concluded that mammographic estimates, based on the extent of microcalcifications, frequently underestimated the histological size of tumour, the extent of the discrepancy being related to the histological type (8 / 50 predominantly micropapillary / cribriform). The authors therefore concluded that adequate excision of DCIS will require a wide excision, even involving up to a whole quadrant. In another large-scale retrospective review on 'Sloane Project',[41] it was found that out of 2564 patients, 2013 (79%) had attempted breast-conserving surgery and 1430 (71%) had a successful single operation. In 30% of patients who undergo breast-conserving treatment for DCIS, preoperative imaging underestimates the extent of disease resulting in further surgeries.

To ascertain the extent of disease involvement in these cases, magnetic resonance imaging (MRI) may have a complementary role in aiding the diagnosis of DCIS that is uncalcified or does not display a suspicious morphological pattern of microcalcifications. Most MRI studies of DCIS have analysed a mixed patient cohort of pure DCIS and DCIS with invasive components.[42] Several studies have reported that the MR kinetic and morphologic appearance of pure DCIS correlates with histopathology findings.[43-50] In a study performed by Kuhl et al,[48] only 56% of pure DCIS was detected by mammography, whereas MRI could detect more than 90%. In another study of 33 cases of pure DCIS performed by Vag et al,[49] the sensitivity of mammography and MRI was 64% and 88%, respectively. In the study performed by Chan et al,[42] the typical morphological appearance of pure DCIS on MRI was a mass– or a non-mass–like lesion with heterogeneous or clumped enhancement.

Ironically, poor visualisation of DCIS combined with its frequency to be multifocal leads most surgeons to remove wider surgical margins. In a study by Macdonald et al,[51] local recurrence in DCIS patients treated with excision alone with margins of ≥10 mm compared favourably with local recurrence in DCIS patients with non-transected margins and treated with postoperative radiation. They concluded that the risk of invasive recurrence following widely excised DCIS was extremely low. This is in accordance with our finding of a statistically significant association of DCIS with lower surgical success, thus a wider resection margin for DCIS is necessary. The primary aim of specimen radiography in ROLL is to ensure complete removal of the targeted lesion or microcalcifications and its role has been well-established.[52] Based on the findings discussed above, further investigations on the use of specimen radiographs in ROLL to predict resection margin status in cases of DCIS can be carried out in a large-scale and prospective manner to facilitate better surgical success.

CONCLUSION

ROLL is effective in localising non-palpable breast lesions with high radiological, scintigraphic, surgical, and histological success. There is a significant association between DCIS and lower surgical success. A wider resection margin may improve surgical success.

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