THE COMPARISON OF RADIOCOLLOID, BLUE DYE AND A COMBINED METHOD FOR SENTINEL LYMPH NODE BIOPSY IN EARLY-STAGE BREAST CANCER

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Abstract
This study aims to compare the performance of radiocolloid, blue dye and a combined method for sentinel lymph node biopsy in early breast carcinoma. One hundred seventy-two clinically node-negative, early-stage breast cancer patients who underwent combined method sentinel lymph node biopsy (SLNB) with ^{99m}Tc-nanocolloid and blue dye were recruited. The peri-areolar injection is the method used in both techniques. The hot node contained only radiocolloid, the blue node contained only blue dye, and the hot-blue node contained both tracers. The detection, metastatic, and failure rate of the combined, radiocolloid, and blue dye methods were determined by analysing the number of hot and blue nodes in all patients, all excised nodes, and metastatic nodes. The association between clinicopathological factors and the detection of sentinel lymph nodes (SLN) was analysed. The overall SLN detection rate was 98.2% (169/172) for radiocolloid, 95.9% (165/172) for blue dye, and 99.4% (171/172) for the combined method. The metastatic rate was 19.2% (33/172). Among the 33 metastatic-node cases, the combined, radiocolloid and blue dye method failed to identify 1, 1 and 4 cases, respectively. Therefore, the failure rate of the combined, radiocolloid, and blue dye method was 3.0% (1/33), 3.0% (1/33) and 12.1% (4/33), respectively. No significant association between clinicopathological factors and SLN detection was observed. The combined method of SLNB yielded the highest detection rate when compared to the radiocolloid-alone and blue-dye-alone methods. The radiocolloid method detected more SLN than the blue dye method. Therefore, incorporating the radiocolloid method in the blue dye method will improve the SLN identification rate and reduce the failure rate of metastatic detection.

Keywords: Early-stage Breast Cancer; Sentinel Lymph Node Biopsy; Blue Dye; ^{99m}Tc-nanocolloid

Introduction

The status of the axillary lymph node is crucial in early-stage breast cancer as it determines the staging and treatment strategies. Traditionally, axillary lymph node dissection (ALND) was the standard procedure to evaluate the axillary lymph node status. However, due to many significant complications associated with this procedure, it has been replaced by the less-invasive alternative, sentinel lymph node biopsy (SLNB). The concept of a sentinel lymph node (SLN) is based on a biological assumption that the primary tumour drains into the afferent lymphatic pathway to a principal "sentinel" node in the regional lymphatic basin that is most likely to harbour metastasis if they are present (1). This concept facilitates the surgeons to stage the axilla from the sentinel node information and avoid axillary dissection if the sentinel is negative for metastasis.

Despite the widespread practice of the SLNB for the axillary staging of breast cancer, the gold-standard method of performing lymphatic mapping is not yet achieved and still evolving. Currently, the most preferred method is a dual tracer using blue dye and radiocolloid (combined method) (2). According to the American Society of Oncology (ASCO) guideline, the combined method or dual localisation of sentinel lymph nodes (SLNs) with these two reagents is considered the most optimal technique as it has the highest identification rate compared to the single reagent

technique (3). The first study of lymphatic mapping using dual reagents was in 1996 when they found a high SLN identification rate of 92% (4). Multiple studies have been conducted and reported over the years, confirming the claim and increasing the popularity of this combined method.

In contrast with the recommendation, a study by Marrow et al. in the earlier history of SLNB suggested no advantage for using a combined technique compared to using blue dye alone (5). On the other hand, a study by Schmidt et al. of 391 SLN biopsy procedures in 2011 suggested that additional blue dye is unnecessary when the radiocolloid can identify the node (6). These debates regarding which method is superior to the other are still ongoing even these days (7).

In Malaysia, the radiocolloid method is expensive to widely practise on top of the risks of handling radiation and strict legislation regarding radioactive materials. The blue dye method is much cheaper and readily available, but it has been associated with serious complications like life-threatening severe anaphylactic reactions (8) and skin necrosis when the dye is injected in a subdermal fashion (9). However, as there have been few reports of these severe side effects, blue dye continues to be widely used due to its greater accessibility than radiocolloids (10). However, the high identification rate of combination radiocolloid and blue dye needs to be validated in the Malaysian population to justify the high cost of technical complexity in terms of radiation handling and facility maintenance. In this study, we evaluated the performance of radiocolloid, blue dye and combined method of SLNB procedure in early-stage breast cancer patients.

Materials and Methods

Patient selection

Clinical and histological data from a prospectively maintained database were analysed on 173 consecutive breast cancer patients who underwent SLNB between June 2018 and November 2020 at the National Cancer Institute/Hospital Putrajaya, Putrajaya, Malaysia. Eligible patients were above 18 years old at registration and diagnosed with T1 to T2 (less-than-50-mm) primary breast cancer, clinically non-palpable nodes, and no distant metastasis. In every case, pre-operative histological confirmation of breast cancer was performed. This research protocol was approved by the MREC (Medical Research and Ethics Committee; NMRR-19-594-47141), JEPeM (The Human Research Ethics Committee of USM; USM/JEPeM/19030194), and the hospital research committee. Due to the retrospective nature of the study, informed consent of the patients was not required because the study analysed anonymous clinical data of the patients. Exclusion criteria include patients who had already undergone treatment such as axillary drainage procedure or neo-chemotherapy/radiotherapy to the axillary area and pregnant patients.

SLN detection

At nuclear medicine department

The lymphatic system was mapped using a radiocolloid one day prior to the scheduled operation. A trained nuclear medicine doctor administered one injection of 37 – 74 MBq (2 – 3 mCi) ^{99m}Tc-nanocolloid (Nanocoll, GE Healthcare Ltd. UK) in 0.2 ml aliquot at the peri-areolar area, upper quadrant, away from the palpable breast mass. The main benefit of ^{99m}Tc-nanocolloid is its size (6-80 nm), which enables faster migration through the lymphatic system and optimal retention within the SLN. Following the injection, the breast was massaged for five minutes to assist the passage of the ^{99m}Tc-nanocolloid from the subcutaneous space into the lymphatic system. Initial static image acquisition was made at 5 minutes. SLN localisation was done using a dedicated SPECT-CT at 30 minutes (Philips BrightView XCT, Philips Healthcare, Netherlands).

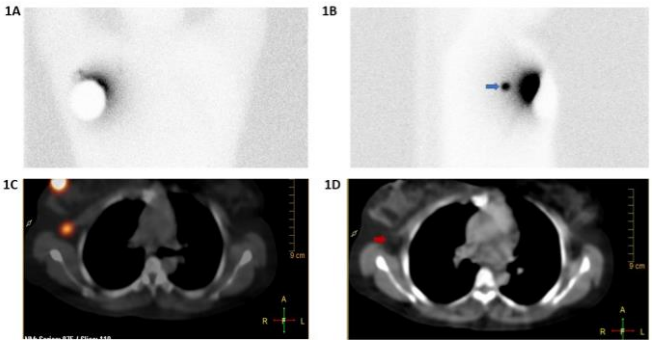

Figure 1: Lymphoscintigraphy images of successful radiocolloid mapping. (1A) Planar anterior image. The blue arrow shows a focus of uptake at the right axillary area. (1B) Planar lateral view with a clearer view of tracer uptake. (1C) SPECT-CT image shows a focus of radiotracer uptake at level I of the right axilla. (1D) CT component shows a sub-centimetre node (red arrow)

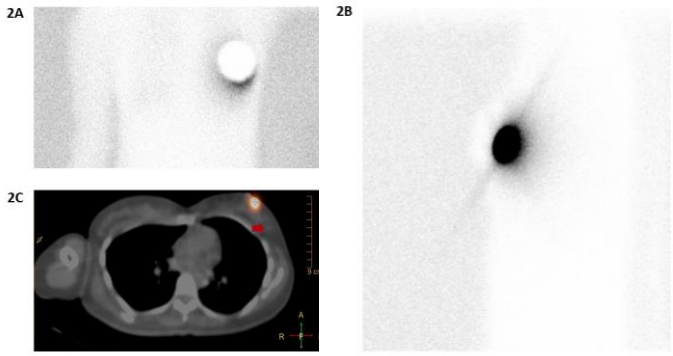

Figure 2: Lymphoscintigraphy images of a failed mapping with radiocolloid. (2A) Planar anterior image. (2B) Planar lateral image. (2C) SPECT-CT image shows

no tracer in the left axillary area. The red arrow shows a sub-centimetre node

A nuclear medicine specialist reported the scan findings. A portable gamma-ray detecting probe was used to indicate the hot nodes on the skin (C-Trak® Surgical Guidance System, Care Wise, USA). The same portable gamma-ray detecting probe was used intraoperatively to locate the hot nodes.

At operation theatre

A subareolar injection was used to administer 2 ml of methylene blue dye (Laboratories Sterop, Belgium) at four quadrants. The breast was massaged for 5 minutes prior to the skin incision.

Surgical procedure

During axillary exploration, the SLNs were identified by the surgeon's visual evaluation of the blue colouration of a node (blue node) and the nuclear medicine physicist's detection of radioactivity using a portable gamma-ray detecting probe (hot node). Apart from that, any suspicious, palpable, neither hot nor blue nodes were surgically removed as international guidelines recommended (11, 12). Excision of all hot and blue nodes was continued until the axilla's background count was less than 10% of the hottest excised lymph node. The excised lymph nodes were labelled in the sequence of excision (A - first node, B - second node) and further categorised as containing both radiocolloid and blue dye (hot-blue node), radiocolloid alone (hot only node), blue dye alone (blue only node), and neither radiocolloid nor blue dye (no-hot-blue node). SLNB was successful if a true sentinel lymph node was found to be either blue or hot, or contain both hot and blue. Any immediate adverse events and reactions after the injection of blue dye during surgery were recorded.

Histopathological examination (HPE) of sentinel lymph nodes

All SLNs were sent to the frozen section for pathological evaluation intraoperatively, which involved haematoxylin and eosin (H&E) staining at serial sectioning 200 – 300 mm of cutting interval, per national protocols.

Patients with metastatic SLNs (positive node) underwent axillary clearance. The final pathological reports were written following the American Joint Committee on Cancer (AJCC) tumour/node/metastasis (TNM) classification. A tumour-positive or metastatic node was defined as micrometastases (> 0.2 and < 2.0 mm) or macrometastases (> 2.0 mm).

Data analysis

The number of cases with hot-only and blue-only nodes, hot-blue nodes, and no-hot-blue nodes which were clinically suspicious was determined and correlated with HPE findings. The detection and failure rate of radiocolloid, blue dye and combined method were also calculated. The detection rate was determined by dividing the number of patients whose SLNs were detected by the total number of patients. The failure rate of each tracer agent and the combined method were figured out by the number of patients with metastatic nodes whose tracers failed to localise a sentinel node. The presence or absence of the hot-blue node, hot-only node, and blue-only node in the metastatic node was analysed to determine its association with metastatic node frequency.

Kruskal Wallis or Pearson Chi-square test was used to analyse the association between clinicopathological factors and the presence of a hot-blue, hot-only and blue-only node. The clinicopathological factors analysed in this study were age, tumour histology, tumour size, tumour grade, and the presence of oestrogen, progesterone and HER2 receptor. Finally, a simple linear regression analysis was used to determine any correlation between the detection of nodes and clinicopathological factors (pathology, tumour size, tumour grade, the presence of oestrogenic receptor, progesterone receptor and HER2 receptors).

Statistical analyses were performed using the IBM SPSS software (Version 26). The average values are presented as mean ± SD. A p-value of less than 0.05 is considered statistically significant.

Results

Per patients' analysis

One hundred seventy-three patients were recruited. One patient received a radiocolloid injection only due to chronic kidney disease and was excluded from the study. The final analysis was based on 172 early-stage breast cancer women with an average age of 53 years old (range 29 – 78 years). Among these patients, 130 (75.6%) are Malay, 25 (14.5%) are Chinese, 16 (9.3%) are Indian and 1 (0.6%) is from other ethnic group.

The most prevalent tumour type is ductal carcinoma, which accounts for 140 (81.4%) of 172 patients, followed by lobular carcinoma (4.1%) and others (4.6%). Forty-eight cases (27.9%) had tumours smaller than 20 mm, while 124 patients (72.1%) had tumours between 20 and 50 mm. Patient and clinic-pathological characteristics are summarised in Table 1.

Table 1: Patients and tumour characteristics

Characteristics	Study group, n (%)
No. of patients	172
Age, years, mean (range)	53 (29 - 78)
Race	
Malay	130 (75.6)
Chinese	25 (14.5)
Indian	16 (9.3)
Others	1 (0.6)
Tumour types	
Ductal	140 (81.4)
Lobular	7 (4.1)
Others*	25 (14.5)
Grade	
1	46 (26.7)
2	89 (51.7)
3	37 (21.6)
Hormone receptor status	
Oestrogen receptor	125 (72.7)
Positive	47 (27.3)
Negative	113 (65.7)
Progesterone receptor	59 (34.3)
Positive	37 (21.5)
Negative	135 (78.5)
HER2	
Positive	
Negative	

Note. HER2 = human epidermal growth factor receptor 2
*mucinous, papillary and tubular

A total of 406 nodes were removed in 172 patients. The total number of patients that were successfully mapped (hot and/or blue) was 171 (99.4%). Analysis of SLN biopsy is shown in Table 2.

Table 2: Analysis of SLN biopsy

Analysis of SLNB cases	
Total number of patients	172
Number of patients successfully mapped	171/172 (99.4%)
Number of SLN removed	406
Number of SLN successfully mapped	382/406 (94.1%)
Number of SLN removed (per patient)	50
1	68
2	25
3	19
4	10
>5	
The mean number of SLN successfully mapped/patient	2.2 ± 1.5

Note. SLN = sentinel lymph nodes

One patient (0.6%) had neither radiocolloid nor blue dye accumulation in the SLN. However, an enlarged axillary node which was neither hot nor blue, was found and excised.

Among 172 patients, 169 (98.2%) had at least one hot SLN, and 165 patients (95.9%) had at least one blue SLN. Hot-blue nodes were detected in 163 patients (94.8%), hot-only nodes were present in 6 patients (3.5%), and blue-only nodes were present in 1 patient (1.2%). Therefore, radiocolloid was distributed in 169 (98.2%) patients whereas blue dye was distributed in 165 (95.9%) patients. The frequency of hot or cold nodes is shown in Table 3.

Table 3: Frequency of the presence of hot or blue nodes

		Blue					
		Number of patients (n = 172)			Number of SLN (n = 406)		
		Presence	Absence	Total	Presence	Absence	Total
Hot node							
	Presence	163 (94.8)	6 (3.5)	169 (98.2)	289 (71.2)	66 (16.4)	355 (87.4)
	Absence	2 (1.2)	1 (0.6)	3 (1.8)	27 (6.7)	24 (5.9)	51 (12.6)
Total		165 (95.9)	7 (4.1)	172 (100)	316 (77.8)	90 (22.2)	406 (100)

Note. Values in parentheses are percentages.

SLN = sentinel lymph nodes

Among 172 patients, 33 (19.2 %) were confirmed to have SLN metastasis by HPE of frozen section and/or immunohistochemistry. A total of 29 (87.9 %) patients had hot-blue nodes; 3 (9.1%) patients had hot-only nodes; and 0 (0.0 %) patients had blue-only node. One patient (3.0%) had neither of these reagents distributed, making the failure rate of 3.0% from the combined method. Only one patient had the metastatic SLN not identified by radiocolloid, whereas 4 of these metastatic node patients failed to be identified by the blue dye. Therefore, the failure rates of the radiocolloid and blue dye methods were 3.0% (1/33) and 12.1% (4/33), respectively. The frequency of the hot or blue nodes in metastatic-node patients is shown in table 4.

Table 4: Frequency of hot or blue node in metastatic-node patients

		Blue		Total
		Presence	Absence	
Hot	Presence	29 (87.9)	3 (9.1)	32 (97.0)
	Absence	0 (0.0)	1 (3.0) *	1 (3.0) †
Total		29 (87.9)	4 (12.1) ‡	33 (100.0)

Note. Values in parentheses are percentages.
*False-negative rate of the combined method
† Failure rate of radiocolloid
‡ Failure rate of blue dye

Per SLN analysis

A total number of 382 nodes were successfully mapped either by radiocolloid or blue dye. The mean number of sentinel nodes identified by mapping was 2.2 ±1.5 per patient, as shown in Table 2. The remaining 24 'para-sentinel' nodes were removed due to being clinically conspicuous. Altogether, the total number of nodes removed was 406.

Out of the 406 SLNs that had been removed, 289 (77.2%) were observed as hot-blue, 66 (16.4%) were distinguished as hot-only, and 27 (6.7%) showed blue-only nodes. Therefore, the radiocolloid was distributed into 355 (87.4%) nodes, and blue dye was distributed into 316 (77.8%) nodes. This is shown in table 3.

Among the 406 SLNs removed from the 172 patients, metastatic nodes were found in 36 (12.5%) of 289 hot-blue, 6 (9.1%) of 66 hot-only, and 0 (0.0%) for blue-only nodes. The incidence of nodal metastasis was highest for the hot-blue node, followed by the hot-only node and finally the blue-only node with $p < 0.05$. The presence of metastatic tumours in sentinel lymph nodes associated with hot-blue, blue-only, and hot-only nodes is shown in table 5.

Table 5: Type of sentinel lymph node associated with the presence of metastatic

Type of SLN	No. of Nodes	Metastasis		p-value
		Yes n (%)	No n (%)	
Hot-blue	289	36 (12.5)	253 (87.5)	<0.05*
Hot-only	66	6 (9.1)	60 (90.9)	
Blue-only	27	0 (0.0)	27 (100)	

Note. SLN = Sentinel Lymph Node.
*Pearson Chi-square

Clinicopathological association with SLN detection

There is no association between clinicopathological features (age, histology, tumour size, tumour grade, ER, PR and HER2 receptor) with the distribution of the tracers, shown in table 6.

Table 7 represents the univariable (Simple Linear Regression) analysis of the detection of nodes with clinicopathological factors. As presented in the table, none of the factors has a significant association with the detection of nodes. Therefore, no additional analysis is required (multiple linear regression) since the minimum requirement is not fulfilled

Table 6: Association of hot-blue, hot-only, and blue-only nodes with clinicopathological factors

	Presence of Hot-Blue (%)	Presence of Hot-only (%)	Presence of Blue-only (%)	p-value
Age (mean±SD)	52.39 (11.1)	63.33 (12.0)	49.50 (6.4)	0.125 †
Tumour types				
Ductal	136 (84.0)	5 (83.3)	2 (100.0)	0.987 ‡
Lobular	7 (4.3)	0 (0)	0 (0.0	
Others*	19 (11.7)	1 (16.7)	0 (0.0)	
Tumour size				
< 20 mm	46 (28.2)	1 (16.7)	1 (50.0)	0.739 ‡
20-50 mm	117 (71.8)	5 (83.3)	1 (50.0)	
Grade				
Grade 1	43 (26.4)	3 (50.0)	0 (0.0)	0.503 ‡
Grade 2	86 (52.8)	1 (16.7)	1 (50.0)	
Grade 3	34 (20.9)	2 (33.3)	1 (50.0)	
Oestrogen receptor				
Negative	45 (27.6)	1 (16.7)	0 (0.0)	0.639 ‡
Positive	118 (72.4)	5 (83.3)	2 (100.0)	
Progesterone receptor				
Negative	56 (34.4)	1 (16.7)	1 (50.0)	0.754 ‡
Positive	107 (65.6)	5 (83.3)	1 (50.0)	
HER2 receptor				
Negative	122 (74.8)	6 (100.0)	1 (50.0)	0.771 ‡
Positive	41 (25.2)	0 (0.0)	1 (50.0)	

Note. Using the Kruskal Wallis test of analysis for Age and Pearson Chi-Square test for Ethnicity, Pathology, Tumour Size, Grade, Oestrogen, Progesterone and Her2 Receptor, we analysed the association between clinicopathological features with the detection of the node. HER2 = human epidermal growth factor receptor 2
*mucinous, papillary and tubular
† Kruskal Wallis test of analysis; ‡ Pearson Chi-Square

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Table 7: The univariable analysis of the detection of nodes with clinicopathological factors

Factors	Simple Linear Regression	
	Crude β (95% CI)	p-value
Tumour types	-0.01 (-0.07,0.06)	0.851
Tumour size	-0.01 (-0.11,0.08)	0.777
Grade	0.02 (-0.05,0.08)	0.580
Oestrogen receptor	0.06 (-0.03,0.14)	0.171
Progesterone receptor	0.03 (-0.05,0.11)	0.515
HER2 receptor	0.01 (-0.09,0.11)	0.853

Note. HER2 = human epidermal growth factor receptor 2

Adverse reactions

Two people experienced adverse reactions from the blue dye out of the 172 subjects. One patient experienced an anaphylactic reaction with the development of hypotension and urticaria at the blue dye injection site. The other patient's oxygen saturation level dropped to 93% after the injection of the blue dye. There is no documented adverse reaction after the injection of the radiocolloid.

Discussion

SLN identification

The locoregional spread of breast cancer occurs mainly through the lymphatic system in which cells migrate from the primary tumour and are carried away by the

interstitial fluid in the lymphatics (13). As described by Morton et al. in a melanoma study, the tumour cells migrate in an orderly fashion, affecting the first or few sentinel lymph nodes before affecting others. Therefore, the sentinel lymph node (SLN) is described as the first to receive lymphatic flow directly from the primary tumour before spreading to subsequent nodes (14). As of now, the "standard of care" of SLNB is the combined technique with radiocolloid and blue dye. It has the highest SLN identification rates and is recommended for all patients (15, 16).

This study demonstrated that the combined method produced an excellent SLN detection rate of 99.4% (171/172), with the detection of at least one hot node in 98.2% (169/172) and a blue node in 95.9% (165/172) of patients. This finding is consistent with a previous pooled analysis that showed the combination of radioisotope and blue dye was superior to a single tracer alone for the successful SLN detection (17). Nonetheless, the study also acknowledged that the superiority of dual tracers is limited and does not significantly reduce the false-negative rate compared to radioisotope alone. In this study, there was high concordance of radiocolloid and blue dye pattern distribution as similarly reported by previous studies, especially if the intradermal and subareolar injection were employed (7, 18). However, He PS et al. (17) concluded that the high concordance of blue dye and radiocolloid may reduce the additional value of blue dye if the superficial injection was used.

Several studies also suggested that the added value of blue dye over radioisotope alone is minimal with the increased surgical experience in the radioisotope technique (19, 20). The marginal benefit of blue dye was shown to be significant during the initial learning period but declined with increased experience in using radioisotope alone (19). Conversely, the learning curve with radioisotope might be shortened particularly in the progress of a handheld portable gamma probe that is more manoeuvrable, with better shielding for directional detection of gamma rays (21). Furthermore, the radiocolloids are efficiently trapped in the SLN while blue dyes are more likely to pass into second echelon nodes (22) which enables the hot nodes to be detected more effectively.

Metastatic nodes and false-negative rate

The failure rate of metastatic detection in the blue dye method was higher compared to the radiocolloid (12.1% versus 3.0%) in this study (Table 3). There was no difference in the failure rates between the combined method versus the radiocolloid only (both 3.0%). The findings are in concordance with the previous meta-analysis by Kang et al. (23). Thus, there was no relevant contribution of the blue dye method for the metastatic node detection shown in this study. Furthermore, this study also presented that hot-only nodes were more likely to have metastatic tumours than blue-only nodes (Table 4). These results demonstrate that the distribution of radiocolloids to metastatic nodes was superior to that of blue dye. The radiocolloid or blue dye appears to be confined in the metastatic SLNs by a particular mechanism that has to be clarified.

Only one patient (3.0%) in our study had failed metastatic node detection using the combination technique. In this patient, the size of the node was larger than 1cm which was not accumulating either radiocolloid or blue dye. One possible explanation for this was that the lymphatic pathway to the nodes might be obstructed by the tumour, inhibiting the drainage of the radiocolloid and blue dye to the node (23). Given this, it is recommended that all suspicious nodes need to be removed to reduce the chance of locoregional recurrence.

Among the six hot-only metastatic nodes, two were micro metastatic nodes. Micro metastasis is defined as clusters of tumour cells ranging between 0.2 and 2 mm (24). To this day, the role of micro metastatic node removal remained controversial. Although some studies suggested that the detection of micro metastases does not affect the prognosis (25), some studies proposed that this metastatic lymph node may represent an adverse prognostic factor in terms of increased risk of distant metastases, especially in the triple-negative receptor, due to higher chance of peritumoral lymphovascular invasion which influences the survival of patients independently (26). Because of this, it is essential to identify all nodes in order to lower the chance of subsequent metastases, even though micro metastases nodes. A previous study showed that ALND might be avoided if SLNs were found to harbour only micro metastatic tumours due to the low incidence of non-sentinel lymph node micro metastases (27). This shows that SLNB may be able to accurately predict the presence of nodal metastases in patients with early breast cancer, where the high-morbidity axillary dissection can be avoided when the sentinel node is negative.

Patient and tumour characteristics

The injection site (7) and the size of the colloid particles used (28) may influence the SLN detection. In our study, we performed constant peri areolar SLN injection hoping that the technical variance would not influence the study analysis. Previous studies have reported that factors such as age (29) tumour size (30) and BMI (31) may affect SLN identification. In our study, BMI was not included in the data sampling. Our study showed that age and tumour size did not significantly influence SLN detection. Histopathological characteristics which include tumour grade, ER, PR and

HER2 receptors also have no association with the overall detection of SLN.

Side effects

One major concern regarding the utilisation of the blue dye is the adverse effect, especially significant anaphylaxis reaction (32). Omitting blue dye can avoid morbidities ranging from skin tattooing, allergic reactions, interference with pulse oximetry and severe anaphylaxis with hypotension (33). In this study, anaphylaxis reaction occurred in one patient and intraoperative oxygenation desaturation occurred in one patient. On the contrary, there was side effects when performing the radiocolloid method. However, considering the side effects as well as the minimal improvement in identification rates and false-negativity rates by the blue dye, concerns have arisen as to whether the use of the blue dye procedure should be continued in the presence of the radiocolloid method.

This study might contain bias due to the relatively small sample size compared to the previous studies. Furthermore, heterogenous groups of surgeons performed nodal identification and sampling in the operation theatre using blue dye. This may result in operator-dependent bias in SLNB using blue dye.

Despite the study's results that indicated the superiority of the radiocolloid method over the blue dye method, this study was not formulated to test each method individually. Instead, all patients received radiocolloid and blue dye for the SLNB before their operating procedure. There is a possibility that each method, to some degree, influenced the result of the other, as previously pointed out by Cody et al. (34). Therefore, the results must be interpreted cautiously only in a combined technique using radiocolloid and blue dye.

Conclusion

In conclusion, the combined method of SLNB yielded the highest detection rate compared to the radiocolloid-alone and blue-dye-alone methods. The radiocolloid method detected more SLN than the blue dye method. Therefore, incorporating the radiocolloid method in the blue dye method will improve the SLN identification rate and reduce the failure rate of metastatic detection. Furthermore, concerns over the blue dye associated side effects may give rise to whether the blue dye is still needed, given the minimal improvement in efficacy in the presence of the radiocolloid method.

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Competing interests

The authors declare that they have no competing interests.

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