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Intraoperative Use of Methylene Blue for Sentinel Lymph Node Detection in Breast Cancer Surgery: A Prospective Study

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ABSTRACT

Background: SLNB is suggested for breast cancer patients with histologically negative axillary nodes. It inhibits axillary lymph node dissection. Excellent intrinsic accuracy and low axillary nodal metastatic load (subject to patient selection) explain SLNB's low false negative rate, especially with blue dye. Location, injection site, mapping agent, volume, axillary nodal metastatic burden, and dissection competency impact SLN identification.

Objective: The purpose of this research is to evaluate the efficacy of incisional and excisional biopsy methods for determining the rate of methylene blue injection into sentinel lymph nodes in patients with early-stage breast cancer.

Methods: Participants in this study were women who had undergone a breast cancer biopsy and were in the early stages of the disease, meaning there was no lymph node metastases (N0). In this investigation, 110 people were considered. Methylene blue was injected into the peritumoral region before the sentinel lymph node biopsy. A positive lymph node biopsy result was indicated by blue nodes in the axilla, which were then sent for histopathology analysis.

Results: In our study mean age of the included females was 47.13±10.76 years and had mean BMI 26.13±27.59 kg/m^2. Majority of the cases 73 (66.4%) had tumor on right side of breast and 37 (33.6%) cases had tumor on left side.The sensitivity rate for patients who had excisional biopsy surgery was 84% and the specificity rate was 92%, whereas the accuracy rate for patients who had incisional biopsy surgery was 78% and the specificity rate was 81%.

Conclusion: In this study, we found no difference in the accuracy of SLNB using methylene blue in patients with early-stage breast cancer with N0 and a history of either incisional or excisional biopsy.

Keywords: *breast cancer, biopsy, sentinel lymph nodes, methylene blue*

1. INTRODUCTION

It is currently well-established that sentinel lymph node biopsy (SLNB) is beneficial for breast cancer patients who have histologically negative axillary nodes. This allows them to avoid axillary lymph node dissection (ALND) [1]. With an enhanced quality of life, the chances of ipsilateral upper limb lymphoedema, painful paraesthesiae, and pain syndromes linked to ALND are decreased. With a false negative rate of less than 5% in appropriately selected patients (those with primary breast tumours less than 5 cm [3] and clinically negative axillae), SLNB accurately determines whether axillary nodes have metastasised [2]. Consequently, it is not surprising that SLNB has also been proven to be a safe and adequate procedure for oncology, with disease-free and overall survival rates comparable to those of stage-matched patients with ALND [3,4].

With the exception of skin necrosis, which can be prevented by using careful injection technique during breast conserving surgery, methylene blue dye is equally effective as, if not better than, isosulfan blue at SLN mapping [6,7], and it is

significantly less expensive than isosulfan blue [5]. Temporary and harmless side effects include a blue tint to the urine, faeces, and skin (not tattoo-causing) around the injection site [7]. The use of radio-tracer mapping in conjunction with blue dye has the potential to increase the SLN identification rate in North America and Europe compared to using blue dye alone [7,8], but, not all studies have shown this to be the case [8].

Every foreign entity, including cancer cells and materials brought in from the outside, will be phagocytosed by lymph nodes if they enter them by an afferent vasa.[9, 10] This suggests that regional lymphatic flow might be helpful in identifying if the enlargement of the initial lymph nodes along the coloured lymphatic flow is a result of cancer cells being phagocytosed. The fact that the contrast travels to the lymph nodes of the subsequent station before leaving the first station is another finding. The chemical formula of methylene blue, C16H18CIN3S, makes it a dark blue contrast agent that is commonly employed for staining bacteria and other biological samples. Especially in situations of breast conserving surgery, methylene blue contrast is a cost-effective option because it does not induce hypersensitivity responses or other serious problems, with the exception of a small amount of skin necrosis that may be

prevented with proper stenting technique. Minor and transient side effects, including as injection site skin discolouration, stools, and urine, are possible.[10]
Checking for blue lymph nodes in the axillary lymphatic ducts ensures precise methylene blue injections.the eleventh First, about 5 cc of 1% methylene blue was infiltrated into the skin around the tumour to begin the sentinel lymph node biopsy. After that, the breast was massaged for five minutes. It is possible to locate the axillary lymph nodes following tumourremoval.[11] A biopsy would be conducted if the number of blue axillary lymph nodes, also known as sentinel nodes, was less than three. It would be necessary to do an axillary dissection if the number of tumours exceeded three. Checking whether blue axillary lymph nodes that came back positive on histology were indeed metastasising was the way the accuracy was measured. False negative rates were between 5.5% and 16.7%, whereas SLNB's sensitivity was between 77% and 94.5 percent.[12]
Methylene blue has historically been utilised in conjunction with other approaches, rather than in isolation, and the findings of most investigations using it have been favourable.[4,5] In situations with limited resources, methylene blue dye is the most convenient choice since it is inexpensive, readily accessible, water-soluble, and has no significant negative effects. Prior research on the reliability of sentinel lymph node biopsy (SLNB) found no statistically significant difference between incisional and core biopsy results for breast cancer patients.Two sources: [11,12] This study seeks to compare the accuracy rate of incisional and excisional biopsies in early-stage breast cancer patients by injecting methylene blue into sentinel lymph nodes.

2. MATERIALS AND METHODS

Following the guidelines established by STrengthening the Reporting of OBservational studies in Epidemiology (STROBE),[21,22] this prospective observational research was conducted at District Headquarter Hospital Mardan during January 2024 to march 2025.This study only included women who had previously undergone a biopsy and had a confirmed diagnosis of breast cancer. If breast or lymphatic node cancers in stages I, IIA, IIB, or IIIA have not spread, they are called early-stage [17,23]. Additionally, these patients did not have any lymph node metastases (N0). Immunohistochemistry using ER, PR, Ki67, and Her2Neu was used to establish the kind of cancer following the initial biopsy. Participants could not have received chemotherapy or a mastectomy for their early-stage N0 breast cancer; instead, they needed to have undergone a core, incisional, or excisional biopsy, as confirmed clinically by physical examination and ultrasound. Since the malignancy may still be detected with minimum disturbance to the surrounding tumour tissue, researchers felt that combining the incisional biopsy with core biopsy was the best course of action. If a participant has a history of lymph disorders or cancer or any other condition that could impair renal function, they are not eligible to participate in this study. Neither are they able to have had surgery in the axillary area, breast area under investigation, for non-malignant breast disease, nor are they able to have been allergic to injections of foreign agents.
Levels I and II underwent axillary lymph node dissection (ALND). Following this, the tissues were transferred for histopathologic analysis. The histological data was obtained by assessing the positivity or negativity of the metastatic nodes after the samples were stained with haematoxylin and eosin (H&E). The histopathology results were categorised using a pathological type categorisation that was based on the College of American Pathologists version 1.2.0.0. Using chi-square analysis, we looked for inconsistencies. The sensitivity and specificity of SLNB were assessed by comparing patients who had incisional and excisional biopsies with histopathologic confirmation. We used SPSS (Statistical Package for the Social Sciences), version 25, for our statistical analysis. There is a statistically significant association if the p-value is less than 0.05.

3. RESULTS

In our study mean age of the included females was 47.13±10.76 years and had mean BMI 26.13±27.59 kg/m^2. Majority of the cases 73 (66.4%) had tumor on right side of breast and 37 (33.6%) cases had tumor on left side. Incisional biopsy was found in 60 (54.5%) cases and excisional biopsy in 50 (45.5%) cases. Mean size of tumor was 24.16±8.39 mm.(table 1)

Table-1: Demographics of the presented females

Variables	**Frequency/Percentage**
Mean age (years)	47.13
Mean BMI (kg/m^2)	26.13
Tumor size (mm)	24.16
Side of Tumor	
Left	37 (33.6%)
Right	73 (66.4%)
Biopsy	
Incisional	60 (54.5%)
Excisional	50 (45.5%)

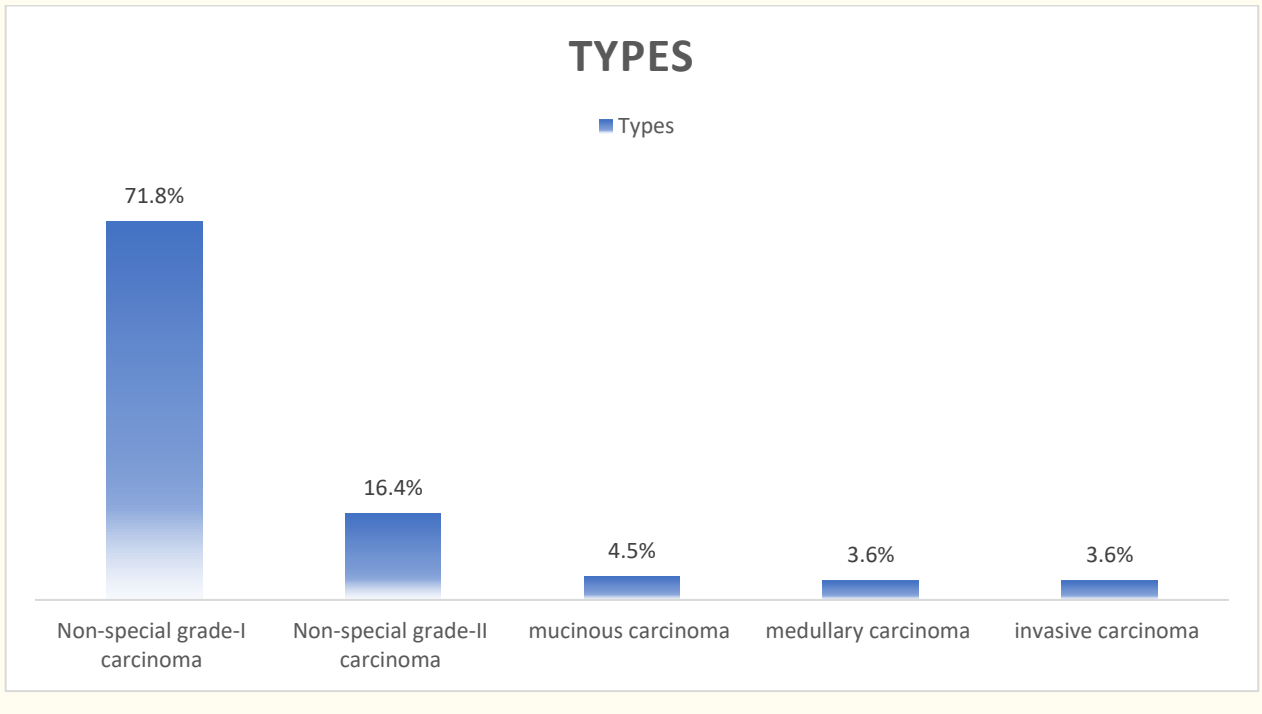
According to SLNB results, 69 (62.7%) cases were positive and 51 (37.3%) were negative and as per histopathological findings, 77 (70%) were positive and 33 (30%) were negative.(Table 2)

Table-2: Histopathological findings and SLNB results

Variables	**Frequency/Percentage**
SLNB Results	
Positive	69 (62.7%)
Negative	51 (37.3%)
Side of Tumor	
Positive	77 (70%)
Negative	33 (30%)

Non-special grade-I carcinoma was found in 79 (71.8%) cases, followed by non-special grade-II carcinoma in 18 (16.4%),mucinous carcinoma in 5 (4.5%),medullarycarcinoma in 4 (3.6%) and invasive carcinoma in 4 (3.6%) cases.(figure 1)

Figure-1: Histopathological types of carcinoma



The sensitivity rate for patients who had excisional biopsy surgery was 84% and the specificity rate was 92%, whereas the accuracy rate for patients who had incisional biopsy surgery was 78% and the specificity rate was 81%.(table 3)

Table-3: Biopsy accuracy for Sentinel Lymph Nodes

Variables	Sensitivity	Specificity	P value
Biopsy			
Incisional	78%	81%	0.324
Excisional	84%	92%	

4. DISCUSSION

While the non-special type accounts for 70–75% of tumours, the most frequent kind in our study is the non-special type (88.2%), which is higher than in the literature.in [13] The role of tumour cells in lymph nodes in determining whether the disease has progressed locally or has disseminated throughout the body is still up for discussion. Lymph node involvement, on the other hand, is associated with a very bad prognosis in breast cancer, with a 5-year survival rate of about 28-40%. Axillary lymph node dissection is a common procedure that helps with cancer staging and cancer management, which ultimately improves survival rates. Risks of arm lymphoedema, axillary sensory impairment, and shoulder adduction deficits, as well as pathologically cancer cell-free lymph nodes, are increased in the 70-80% of patients who undergo axillary lymph node dissection in the absence of metastasised lymph nodes (cN0).[14]

No statistically significant correlation between SLNB and biopsy type was found in this investigation. Patients' chances of surviving breast cancer are impacted by their SLNB status, which is a prognostic factor. Previous studies have shown that lymphatic mapping during SLNB does not change significantly in breast cancer patients who have already had excisional biopsy. That lines up with what this study found: that the type of biopsy done had no impact on the SLNB results.[15] There has been research on the correlation between SLNB and prior excisional biopsies. Problems with lymphatic mapping following an excisional biopsy prompted them to carry out the research. The sensitivity and predictive value of SLNB conducted with a pre-operative lymphoscintigram were shown to be similar in a prospective investigation.[16]

Similarly, Azhar Y et al. saw comparable results in their study of lymphatic mapping in patients undergoing breast conserving surgery with axillary staging using SLNB or ALND. They found that lymphatic mapping is still doable after BCT surgery, however the identification rate is low.[17] And in a case study published by Alavifard et al., a 24-year-old female patient had invasive ductal carcinoma surgically excised during a left breast excisional biopsy. She had SLNB to remove a mass in her left axillary three weeks later. Lymphatic mapping disturbance was not observed during the excisional biopsy of breast

cancer patients.[18]
Following an excisional biopsy of the primary tumour, this study's findings contradict the hypothesis that SLNB will be less dependable in breast cancer patients. The excisional biopsy causes inflammatory changes that impair lymphatic flow, which in turn causes lymphatic mapping to fail. Wibisana IG et al. found a sevenfold increase in the identification of lymph nodes following excisional biopsy, which further supports this.Only patients with a history of excisional biopsy were found to have false-negative rates in the trials [19]. According to Feldman et al., adjustments to the biopsy procedure, such adjusting the amount and volume of injections, improved accuracy.[20]

5. CONCLUSION

In this study, we found no difference in the accuracy of SLNB using methylene blue in patients with early-stage breast cancer with N0 and a history of either incisional or excisional biopsy.

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