# **Original Research Article**

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# Role of sentinel lymph node biopsy in assessing the cancer spread to axilla in early breast cancer

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#### **ABSTRACT**

**Background:** Sentinel lymph node (SLN) biopsy is a minimally invasive alternative to axillary lymph node dissection as a way to stage breast cancer in clinically node-negative patients. Objective of the study was to determine the safety and reliability of sentinel lymph node biopsy without axillary lymph node dissection (ALND) in early breast cancer patients.

**Methods:** This prospective study was conducted in patients with operable breast cancer in a single surgical unit of our hospital. Patients with T1-T3 breast cancer with clinically negative axilla and patients with previous lumpectomy were included. All the patients had undergone complete axillary lymph node dissection after sentinel lymph node biopsy. All the specimens were sent separately for paraffin section histopathology.

**Results:** Mean age of 35 female patients included was 54 years. SLN was identified in 94.29% cases and it could not be identified in 2 cases. SLN (96.97%) was most commonly identified at level I. Mean numbers of sentinel node and axillary node were 1.52 and 16.11 respectively. Study of SLN biopsy with methylene blue dye for staging the axilla was done with 81.25% sensitivity and 100% specificity. Positive predictive value was 100% and was able to negatively predict the axilla in 86.36% with an overall accuracy of staging of 96.97% and false negative rate of 18.75%.

**Conclusions:** Sentinel lymph node biopsy without axillary lymph node dissection in sentinel lymph node negative breast cancers appears to be a safe and reliable procedure for determining the nodal status and ensuring the locoregional control.

Keywords: Axillary lymph node, Biopsy, Early breast cancer, Minimally invasive, Sentinel lymph node

#### INTRODUCTION

The disease status of the axillary lymph nodes is the most significant prognostic factor for patients with early-stage breast cancer. Predictors of nodal metastasis include tumor size, tumor grade, lymphovascular invasion and patient age. Receptor status, DNA content (ploidy), tumor location, method of detection and presence of casting-type calcifications on mammography has some predictive value. However, no combination of predictors of axillary node status has replaced surgical resection and

histopathological examination of the lymph nodes. While advances in computed tomography, magnetic resonance imaging, positron emission tomography and ultrasonography can often identify suspicious nodes in the axilla; false-negative findings and failure to detect small metastasis are common.<sup>2</sup> Thus reliance on histological examination of removed lymph nodes at the time of axillary lymph node dissection (ALND) is thought to be the most accurate method for assessing spread of disease to the lymph nodes. The anatomic disruption caused by ALND may also result in

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lymphedema, nerve injury, shoulder dysfunction and other complications that may compromise functionality and quality of life. <sup>3,4</sup>

Morton introduced the sentinel lymph node hypothesis at the Annual Meeting of the Society of Surgical Oncology in Washington DC (USA) in 1990.5 Sentinel lymph node biopsy is based on the hypothesis that the lymph from a primary solid neoplasm drains initially to one or more sentinel lymph nodes, which are therefore the first nodes at risk for harbouring occult metastatic disease. The sentinel lymph node concept has evolved from an underestimated principle to a generally accepted and applied procedure. Various systematic studies in breast cancer have shown that breast cancer spreads to one or a few lymph nodes, the sentinel lymph nodes (SLNs), before it spreads to other axillary lymph nodes and that these SLNs can be identified using vital blue dye, a radiolabelled colloid or both.<sup>6,7</sup> The findings of these early studies suggested that the use of a sentinel lymph node identification and sampling procedure referred to here as sentinel node biopsy (SNB) could be reliably performed in selected patients with early stage breast cancer by a carefully trained multidisciplinary team (surgeon, pathologist, radiologist, nuclear medicine doctor), thus reducing the need for ALND and avoiding the associated morbidity.

There is a general agreement that regional lymph node dissection is recommended for patients who have clinically suspicious nodes or pathologically proven metastasis to the regional lymph nodes. However, major controversy exists regarding the utility of regional lymph node dissection for patients with clinically unaffected (i.e. no palpable) lymph nodes, because most of these patients are without nodal metastasis and therefore, can derive no benefit from regional lymph node dissection. Currently the two most widely accepted clinical applications of sentinel lymph node biopsy are for melanoma and breast cancer. So, this present study was conducted to determine the safety and reliability of sentinel lymph node biopsy without axillary lymph node dissection in early breast cancer patients.

## **METHODS**

This prospective study was conducted in tertiary care teaching institute after getting approval from institutional ethics committee. All patients with operable breast cancer in a single surgical unit of hospital were included during study period. Patients with T1-T3 breast cancer clinically negative axilla and patients with previous lumpectomy were included in study after taking written informed consent from all the patients. Patients with palpable clinical nodes in the axilla, neoadjuvant chemotherapy patients, multicentric tumours on mammography, recurrent lesions, noninvasive breast carcinoma, breast sarcoma patients, T4 lesions, pregnancy, prior axillary surgery, and prior non-oncological breast surgery were excluded.

All the patients had undergone complete axillary lymph node dissection (level 1/2) after sentinel lymph node biopsy. All the sentinel lymph nodes and axillary dissection specimens were sent separately for paraffin section histopathology.

After anaesthetic induction, patient was painted and draped. 2 ml methylene blue dye was taken in dilution with 2 ml saline (total 4 ml) and 1 ml each injected peritumorally towards the axilla in 4 quadrants (3, 6, 9 and 12 o'clock positions). Gentle massage was done for 2-3 minutes. Mastectomy started and proceeded till the flaps were raised (10-15 minutes). After that the blue lymphatics and the lymph nodes were identified. All blue lymph nodes were removed separately and then complete axillary clearance was performed in all the cases. The resected lymph nodes and the axillary dissection specimen were sent separately for final histology. Multiple serial sectioning of the lymph nodes was performed by the pathologist.

#### RESULTS

Total 35 female patients who underwent lymphatic mapping, SLN biopsy with methylene blue and routine standard ALND were included in our study.

**Table 1: Patients' characteristics.** 

	Number of				
Patients' characteristics	patients (%)				
	n = 35				
Mensturation					
Premenopausal	08 (22.86)				
Postmenopausal	27 (77.14)				
Tumor size					
T1	02 (5.71)				
T2	31 (88.58)				
T3	02 (5.71)				
Tumor location					
UOQ (upper outer quadrant)	13 (37.14)				
UIQ (upper inner quadrant)	09 (25.71)				
LOQ (lower outer quadrant)	09 (25.71)				
LIQ (lower inner quadrant)	01 (2.86)				
Central	03 (8.57)				
Pathology					
Invasive ductal carcinoma	31 ((88.58)				
Invasive lobular carcinoma	01 (2.86)				
Medullary carcinoma	03 (8.57)				
Type of surgery					
Modified radical mastectomy	33 (94.29)				
Breast conservative surgery	02 (5.71)				
Prior lumpectomy	08 (22.86)				

Mean age of patients was 54 years and 77.14% patients were in postmenopausal age group. 88.58% patients were having T2 size tumor and upper outer quadrant (37.14%) was the commonest tumor location.

Invasive ductal carcinoma (88.58%) was found to be most common type of cancer after pathological examination. Modified radical mastectomy (94.29%) was performed in most of the patients and in these patients SLN was identified. SLN could not be identified in 2 cases (Table 1). Further study is restricted to 33 patients in which SLN was identified. SLN (96.97%) was most commonly identified at level I and it was at level II in only one case (3.03%). Mean numbers of sentinel node and axillary node were 1.52 and 16.11 respectively. Results of histopathology are shown in Table 2.

**Table 2: Results of histopathology.** 

Sentinel lymph node	No. of patients (%)
Positive	13 (37.14)
Negative	22 (62.86)
Axillary lymph node	
Positive	16 (45.71)
Negative	19 (54.29)
SLN was the only positive node	03 (8.57)
SLN negative; rest of axilla positive	03 (8.57)

Table 3: Comparison of present study with previous studies for examining sentinel lymph node.

Study	Identification rate	Accuracy	False negative rate	Mean no. of nodes	Location of injection	Prior excision biopsy	Tracer / dye
Krag et al <sup>13</sup>	91%	97%	11%	2.6	PT	Included	TC Sulfur colloid
Borgstein et al <sup>18</sup>	94%	98%	2.3%	1.2	PT	Included	Nano coil
Veronesi et al <sup>19</sup>	98%	98%	4.7%	1.4	SD	Excluded	Nano coil
Guenther et al <sup>20</sup>	71%	97%	10%	1.6	PT	Included	Isosulfan blue
Giuliano et al <sup>15</sup>	93%	100%	0%	1.8	PT	Excluded	Isosulfan blue
McMasters et al <sup>14</sup> (single agent)	86%	95.7%	11.8%	1.5	PT	Included	Isosulfan blue or TC sulfur coil
McMasters et al <sup>14</sup> (dual agent)	90%	98.2%	5.8%	2.10	РТ	Included	Both
McMasters et al <sup>14</sup> (all technique)	88%	97.5%	7.2%	1.95	PT	Included	All technique
Simmons et al <sup>21</sup>	95.5 % (combined) 92% (methylene blue only)	-	-	-	PT+SD	Included	Methylene blue + TC Sulfur colloid
Present study	93.7%	96.64%	7.2%	1.375	PT	Included	Methylene blue

PT = Peritumoral SD = Subdermal.

Table 4: Comparison of present study with previous studies for diagnostic value of sentinel lymph node.

Study	SLN Identificat ion rate	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Overall accuracy	Tracer /dye
Veronesi et al <sup>19</sup>	98%	93.3%	100%	100%	94%	96.8%	TC - colloid
Giuliano et al <sup>15</sup>	96%	88%	100%	100%	93.5%	95.6%	Isosulfan blue
McMasters et al <sup>14</sup> (single agent)	86%	89%	100%	100%	93.7%	95.7%	Isosulfan blue
McMasters et al <sup>14</sup> (dual agent)	90%	94.2%	100%	100%	97.5%	98.2%	Both TC- colloid and isosulfan blue
McMasters et al <sup>14</sup> (all technique)	88%	92.2%	100%	100%	96.4%	97.5%	All technique
Present study	93.7%	92.8%	100%	100%	94.11%	96.64%	Methylene blue

Study of SLN biopsy with methylene blue for staging the axilla was done with a sensitivity of 81.25%, specificity of 100%. Positive predictive value was 100% and was able to negatively predict the axilla in 86.36% of the patients with an overall accuracy of staging of 96.97% and false negative rate of 18.75% (Table 3 and 4).

## **DISCUSSION**

Studies have utilized SLN biopsy and compared its ability to correctly identify that a patient had breast cancer lymph node metastasis against the results of ALND. In order to minimize complications related to ALND, surgical oncologists developed this SLN biopsy to evaluate the axillary lymph nodes for cancer spread without having to remove all of the lymph nodes.<sup>8</sup>

In present study, sentinel lymph node was identified in 94.29% of patients, which is similar to the study done by Simmons et al with methylene blue (92%). In reference to other studies as mentioned in Table 3, the SLN identification rate varies from 65% to 93% with isosulfan blue, 91-98% with radiocolloid and 90% with combined method, but many other studies have shown identification rate of 90-97% with combined method. 10-14 It should be noted that the amount of methylene blue dye administered and the technique used to administer the dye were similar to that which would be used for isosulfan blue dye. The sentinel lymph node was distinctively deep blue stained and it was easily possible to follow the stained lymphatic vessels and Sentinel lymph nodes. In most part of India, the SLNB after methylene blue dye injection has become a common practice for early breast cancer surgery due to its simplicity and cost effectiveness. Use of radioactive isotope is not commonly seen due to the scarcity of the resources but the dual technique is followed in few centres where the facilities for nuclear medicine are available.

Sentinel lymph node was most commonly identified at level I position in 96.97% patients and mean number of SLNs was 1.52 which is similar to the other studies (Table 3) but slightly less; compared to studies using dual methods. Sentinel lymph node was positive for metastasis in 37.14% and in 3 cases SLN was the only positive node. This value is comparable to those of other studies which have shown rates of 17-42% in identifying positive sentinel nodes in T1 to T3 breast cancer patients with clinically No axillary nodes.<sup>7,14,15</sup> Axilla was positive for malignancy in 45.71% cases and negative in 54.29% cases and there were 3 patients with negative sentinel node but had positive axilla. Study of SLN biopsy with methylene blue for staging the axilla was done with 81.25% sensitivity and 100% specificity. Positive predictive value was 100% and was able to negatively predict the axilla in 86.36% with an overall accuracy of staging of 96.97% and false negative rate of 18.75%. All these results are compared with other studies in Table 3 and 4 and findings are reasonably similar. But the false negative rate which is 18.75% in our study, varies from

0% to 12% in others, and is lower when TC colloid or a dual technique is used, but Giuliano et al in their study had 0% false negative rate with isosulfan blue. The reason for higher false negative rate in this study may be due to small number of cases, early learning curve, multiple surgeons involved and previous lumpectomies in patients. Previous studies have reported hypersensitivity to isosulfan blue dye at rates of 1-2%. 16,17 Most of the reported hypersensitivity reactions were manifested in the form of anaphylaxis with cardiovascular collapse and hypotension; requiring vigorous resuscitation. Other manifestations include erythema, perioral edema, urticaria, uvular edema and blue hives. Albo et al reported that hospital stay was prolonged by a mean of 1.6 days in patients with anaphylaxis. 16 In our study, none of the patients developed a hypersensitivity reaction to the methylene blue dye. To our knowledge, there have been no studies documenting hypersensitivity reactions, particularly anaphylaxis with the use of methylene blue dye. Comparison of the data presented in this study with the various other earlier studies have shown the high accuracy of the SNB in staging the early breast cancer and thus altering the previous concept ALND in every patient with early breast cancer by preventing the unnecessary axillary dissection and its associated hazards.

## **CONCLUSION**

In conclusion our data indicate that sentinel lymph node biopsy can stage axilla with high accuracy, reasonable sensitivity, specificity and false negative rate; and it can be a better alternative to axillary lymph node dissection. Methylene blue in comparison with other dyes is not only cost effective but also free from the health hazards of radiation and it is easily available. So it is convenient to use this dye in developing countries like India. Sentinel lymph node biopsy without axillary lymph node dissection in sentinel lymph node negative breast cancers appears to be safe and reliable procedure for determining the nodal status and ensuring the loco-regional control.

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