

## Use of Sentinel Lymph Node Biopsy to Detect Metastatic Spread in Axillary Nodes in Primary Breast Carcinoma

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### Abstract

**Objectives:** Although sentinel lymph node (SLN) biopsy is recommended approach in the evaluation of metastatic status of lymph node in breast cancer management, the efficacy of this technique requires validation. In current study, results of patients who underwent sentinel lymph node biopsy by using only methylene blue dye were evaluated.

**Methods:** The study included 17 cases of primary ductal carcinoma with tumor size up to 5.0cm. Patients who had previous breast or axilla surgery and radiation or chemotherapy for any breast lesion were excluded from this study. During operation 3.0 ml of sterilized methylene blue dye was injected in peritumoral area or around the lumpectomy cavity. The axillary sentinel lymph node was removed and later on axillary dissection was done. Imprint cytology, frozen section and routine H&E slides were made from sentinel lymph node.

**Results:** The sentinel lymph node was found in all cases. Among them, eight (47.1%) cases were positive for SLN and axillary lymph node and nine (52.9%) cases were negative for both SLN and axillary lymph node. No false negative result was observed and no complication was recorded due to use of methylene blue dye.

**Conclusion:** Sentinel lymph node biopsy is a safe and accurate method in staging the early breast cancer. This method will reduce the unnecessary axillary lymph node dissection and other morbidity associated with it.

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**Keywords:** Breast cancer, Sentinel lymph node biopsy, Methylene blue dye.

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## Introduction

Breast cancer is the most common cause of cancer death among women (6,26,679 deaths in 2018).<sup>1</sup> In spite of lower incidence rate, the mortality rate is relatively much higher in less developed countries due to lack of early detection and access to the treatment facilities.<sup>2</sup> An urge need in cancer control today is to develop effective and affordable approaches to the early detection, diagnosis and treatment of breast cancer among women living in less developed countries.<sup>3</sup>

Previously, for the management of breast cancer aggressive surgical treatment including axillary lymph node dissection (ALND) were done. But, routine ALND does not benefit the 70-80% of early breast cancer patients who are clinically node negative.<sup>4</sup> The sentinel lymph node biopsy (SLNB) technique is an alternative to ALND for staging breast cancer.<sup>5</sup> The sentinel lymph node biopsy concept suggests removal of the first lymph node/s draining the tumor lymph. If sentinel lymph node is free, it is assumed that there is no metastasis in other lymph node.<sup>6</sup>

As only few lymph nodes need to be removed, SLNB has the potential to be a less invasive method of staging the axilla than ALND, in which many more axillary lymph nodes are removed for pathological testing. SLNB also could help to avoid the morbidities associated with axillary clearance.<sup>7</sup>

Presently, three detection reagents are used for detecting SLNB in clinical setting: (1) blue dye (2) radioactive colloids and (3) indocyanine green (ICG). Among them, Methylene blue dye (MBD) is an accurate dye for sentinel node identification in early breast cancer.<sup>8</sup>

## Methods

The Bangabandhu Sheikh Mujib Medical University Ethics Committee approved this study. A total of seventeen women with T1 and T2

tumors diagnosed as duct cell carcinoma of breast in fine needle aspiration cytology or needle core biopsy were included in the study. Patients with history of previous conservative breast surgery, radiotherapy or chemotherapy for axillary or breast lesion were excluded in this study. Informed written consents were obtained in all patients.

The surgical procedure was performed at operation theater by expert surgeons. At the operation table, prophylactic antibiotics were given at the time of induction to all the patients. Then 3.0ml of sterilized 1% MBD was injected in the peritumoral area of the affected breast. Gentle massage of that region was done for 1-2 minutes. After 5-10 minutes a transverse incision was made in the axilla and searched for blue stained node/s followed by blue colored lymphatic channels. The blue stained lymph node/s was/were identified as sentinel lymph node/s figure 1. The node was then carefully dissected out and after proper labeling, collected fresh for imprint smear or frozen section or both.

After that, mastectomy and axillary dissection was done in all cases irrespective of sentinel lymph node status. These specimens were collected in 10% neutral buffered formalin. These were histopathologically evaluated according to standard procedure<sup>9</sup> and metastatic status was compared with respective sentinel node status.

## Results

A total 17 cases were included in this study (according to the exclusion criteria). Patients' age varied between 31-65 years (mean:  $49.8 \pm 9.9$ ). Fine needle aspiration cytology (FNAC) was done in all of the 17 cases and core needle biopsy was performed in three cases. In FNAC, out of 17 cases 15 cases were positive for malignant cell and two were suspicious for malignant cells (Figure 2). The later cases were diagnosed by frozen section biopsy followed by lumpectomy.

Table I: Tumor location by USG finding

USG Finding	Number of patients	Percentage (%)
Right breast	10	58.8
Left breast	7	41.2
Upper outer quadrant	7	36.8
Upper inner quadrant	2	10.5
Lower outer quadrant	6	31.6
Lower inner quadrant	1	5.3
Central	1	5.3

Table II: Comparison between frozen section histopathology, imprint cytology and routine H&amp;E diagnosis in assessment of sentinel lymph node status

Frozen section diagnosis		Imprint cytology diagnosis		Routine H&E diagnosis	
Positive	Negative	Positive	Negative	Positive	Negative
7 (41.2%)	10 (58.8%)	8 (47.1%)	9 (52.9%)	8 (47.1%)	9 (52.9%)

The largest positive sentinel node was 2.0 cm in maximum diameter and the smallest one was 0.6 cm. Again, the largest negative sentinel node was 1.2 cm in maximum diameter and the smallest one was 0.4 cm. Among the 8 SLN positive cases, in one case malignant cells were detected in imprint smear but the frozen sections failed to reveal tumor focus, but metastasis was confirmed in routine section of the same node. This may be due to frozen artifact. However, no association between sentinel lymph node size with lymph node status was found (Table III).

Table III: Association between sentinel lymph node size with sentinel lymph node status

Lymph node size (cm)	No of SLN				P value
	Positive (n=8)		Negative (n=9)		
	n	%	n	%	
Up to 0.4	0	0.0	4	44.4	0.08
>0.4-1.0	5	62.5	4	44.4	
>1.0-2.0	3	37.5	1	11.2	
>2.0	0	0.0	0	0.0	

P value reached from chi square test.

Table IV: Association between distances from nipple/skin with sentinel lymph node

Distance from skin/nipple (cm)	n	SLN status				P value
		Positive (n=8)		Negative (n=9)		
		n	%	n	%	
0-2	6	5	83.3	1	16.7	0.027s
2-5	4	0	0.0	4	100.0	
>5	6	2	33.3	4	66.6	
Mean ± SD		2.8±2.9		5.0±3.0		
Range (min, max)		1, 7.0		1.5, 9.0		

S= significant



Figure 1. Photograph showing partly blue stained cut surface of sentinel lymph node

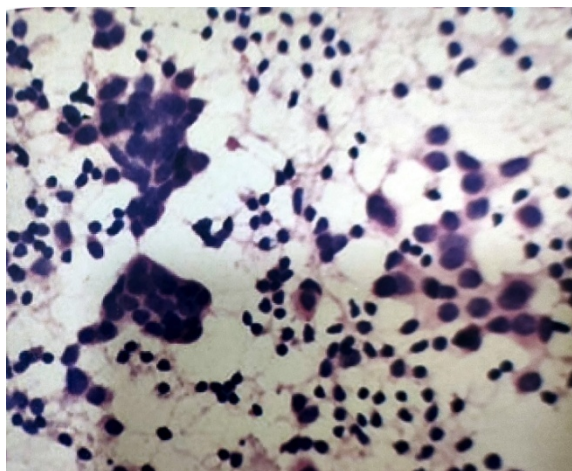


Figure 2. Photomicrograph showing positive imprint cytology of sentinel lymph node

### Discussion

In current study, among 17 cases, in 9 (52.9%) cases both SLNs and axillary nodes were negative in 7 (47.1%) cases both SLNs and axillary nodes were positive, in only one (05.8%) case only SLNs were positive and none of the cases were false positive. Rida and Hendawy used MBD alone to detect SLN in 30 patients, where in 16 (53.3%) cases both SLNs and axillary nodes were negative, in 5 (16.5%) cases both SLNs and axillary nodes were positive, in 3 (10%) cases only SLNs were positive and 2 (6.6%) cases were false negative.<sup>10</sup> In Turkey, another author and his team used MBD alone to detect SLNs in 32 patients, where SLNs were not identified in two

cases. In rest of the 30 cases, 17(56.6%) cases were both SLNs and axillary node positive, 11 (36.6%) cases were both SLNs and axillary nodes negative and 2 (6.6%) cases were false negative.<sup>11</sup> In this study, no false negative node was found which correspond with the study of another author who also found 100% success rate in his study using MBD alone to detect SLNs from axilla in breast cancer patients.<sup>12</sup> 100% accuracy in this study may be due to- small sample size and not taking the concern about the SLN located other than axillary basin such as internal mammary and supraclavicular nodal basin. However, among the 9 SLN negative cases none of the imprint cytology, frozen section or routine histologic preparation showed suspicious focus of metastasis or micrometastasis.

Among 17 cases, only two cases were in T1 (tumor  $\leq 2.0$ cm) and 100% of these tumors showed lymph node positivity which does not support the other studies. In 2012, Wong and his team included 56 T1 tumors, among them only 33(58.9%) cases revealed positive sentinel node.<sup>13</sup> Ozdemir et al. Found only 5% positive SLN tumor was in T1 stage.<sup>11</sup> In this study, the unusual rate of 100% positivity of T1 tumor maybe due to small sample size and location of tumor (upper outer quadrant and very close to the nipple). Among the 15 T2 (tumor  $> 2-5.0$ cm) tumors 6 (40%) cases were positive for sentinel node metastasis which support the other studies. Wong and his team mentioned that, 36(75.0%) cases of T2 tumor revealed positive sentinel node.<sup>13</sup> In 2014, another study was conducted by Ozdemir and his colleagues and the reported that axillary node metastasis in T2 tumor ranges between 33-48%.<sup>11</sup>

The finding of current study suggests an association between sentinel lymph node positivity with the distance of the tumor from the nipple (Table III). The sentinel lymph node positivity was maximum (83%) with breast tumor that are located within 2.0 cm of nipple, 33% with tumor that are  $> 5.0$  cm from the nipple. It appears

that, discohesive malignant cells invade lymphatics preferentially when the tumor is within 2.0cm of nipple, where they involve the plexus of Sappy and therefore metastasis to the SLN.

After injection of methylene blue dye minor complications were observed in various studies. Zakaria et al.<sup>14</sup> found local inflammation in 21 cases and wheal and flare in 2 cases. Govaert and his team reported blue staining in 33 cases.<sup>15</sup> Another author found skin necrosis in 5 cases.<sup>16</sup> In 2009, Komenaka and his colleagues found palpable mass at the site of injection in 10 cases.<sup>17</sup> However, no such complications were observed in current study.

Previously, there was a fear that the axillary sentinel lymph node biopsy policy would result in a high rate of overt axillary metastases during follow-up, with all of the associated problems. For that reason, in Italy Veronesi and his colleagues conducted a randomized controlled study for 10 years on patients with primary breast cancer in their early stage. They reported that, SLN biopsy can obviate the need for total axillary dissection in patients with a negative sentinel node. Therefore, the post operative side effects were much less frequent and disease-free survival was slightly better in those patients who underwent sentinel-node biopsy only than in those who underwent complete axillary dissection.<sup>18,19</sup>

### Conclusion

Sentinel lymph node biopsy is a safe and accurate method of screening the axillary nodes for metastasis in women with primary breast tumor in T1-T2 stage. It reduces unnecessary removal of axillary lymph nodes and morbidity associated with it.

*Ethics Committee Approval:* Approval was taken.

*Conflict of Interest:* No conflict of interest was declared by authors.

*Informed consent:* Written informed consent was obtained from patients who participated in this study.

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