

## Comparative Study Between Sentinel Node Biopsy Versus Axillary Sampling in Women with Clinically Node Negative Operable Breast Cancer

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### ABSTRACT

**Background and Objectives-** More recent advance in the field of breast cancer detection at early stage is axillary lymph node sampling, which involves sampling of few lymph nodes removed from axilla for detecting cancerous cells. The aim is to compare the methodologies between sentinel lymph node biopsy and low axillary sampling in predicting status of axillary lymph nodes in clinically node negative operable breast cancer patients.

**Methodology:** A prospective longitudinal study was conducted among 50 breast cancer operable patients with clinically node negative. Axillary sampling was performed first by making a 2 cm incision in the middle third of the proposed axillary clearance incision below the axillary hairline. All axillary fat and tissue in an area of 2cm diameter was dissected out.

**Results-** LAS has a sensitivity of 97.5%, which means it would be able to detect the true positives in 97.5% of the patients and the ability to detect true negatives (specificity) is 64.5%. Similarly, the positive predictive value and the negative predictive value is 91.5% and 89.7% respectively with an accuracy rate of 90%.

**Conclusion-** The results of this study indicate that Sentinel node biopsy and Low axillary sampling are equally accurate. Given the resource and equipment constraints, especially with respect to nuclear medicine facilities, LAS could be the preferred technique in developing countries.

**Keywords:** Node negative breast cancer, sentinel lymph node biopsy, low axillary sampling, validity.

### 1. INTRODUCTION

For more than a century, surgery for cancer breast is adhered to the Halstedian model, which is primarily a loco-regional condition that spreads via lymphatic system, and it is most often curable by performing a extensive surgical resection. As per recent research, it is now clearly evident that breast cancers biological attributes, rather than the extent of surgery, predominantly influences the risk for systemic, local and regional recurrence.<sup>1</sup> The shift had promoted the adoption of using less invasive techniques, thereby enhances the clinical outcomes as well as the quality of life among the patients.<sup>2</sup>

Survival of patients after the treatment for breast cancer has improved tremendously over the past two decades, because of more targeted and personalized management techniques. Though it is advantageous for the cancer survivors but still certain disadvantage like, experiencing long-term adverse consequences arising due to treatment.<sup>3</sup> Before planning the management of breast cancer, staging the cancer is the first and foremost step, for which axillary lymph node dissection (ALND) has been followed for years together. Though following axillary lymph node dissection has a therapeutic role for patients with node positive, whereas it ends up in over treatment for node negative patients.<sup>4</sup> Considering these adverse events it is now suggested that instead of performing an axillary lymph node dissection for diagnosing breast cancer, an alternate procedure like sentinel node biopsy can be planned as it has low failure rate as well as other morbidities that would occur due to ALND could be avoided.<sup>5,6</sup> More recent advance in the field of breast cancer detection at early stage is axillary lymph node sampling

which involves sampling of few lymph nodes removed from axilla for detecting cancerous cells. Currently as per the literature it is shown that for node-negative early stage of breast cancer, limited axillary surgery with sentinel node biopsy (SNB) alone is said to be the standard of care and it is associated with low failure rates.

## 2. MATERIALS AND METHODOLOGY

It was a Prospective longitudinal study conducted at Surgery department of Vinayaka Missions Kirupananda Variyar Medical College for a period of November 2022 to January 2024 among Breast cancer patients with clinically node negative. 50 breast cancer patients through Non – random purposive sampling

### *Inclusion criteria:*

- Clinically node negative operable breast cancer patients
- Patients who haven't undergone prior incision or excision biopsy

### *Exclusion criteria:*

- Patients with palpable axillary lymph nodes
- Patients who have contraindications for isosulphan injection

### *Study procedure:*

Study was started after getting approval from the institutional ethical committee. Informed consent was obtained from all the patients involved in the study. Isosulphan blue dye was then injected subdermally (0.5ml) over the tumor and the intraparenchymal (3-4ml) area towards the axilla about 10-15mins before making the incision.

Axillary sampling was performed first by making a 2 cm incision in the middle third of the proposed axillary clearance incision below the axillary hairline. All axillary fat and tissue in an area of 2cm diameter was dissected out. The following surface marking was considered while performing the axillary sampling, the anterior limit of dissection is the posterior border of pectoralis major, the posterior limit of dissection is the anterior border of latissimus dorsi muscle, upper limit of dissection is the intercostobrachial nerve, and the base is serratus anterior muscle on lateral chest wall. In cases for whom mastectomy is advised, the tissue in the axillary tail was identified first and then it was removed as specified above.

After completion of the axillary sampling procedure, the remaining axillary tissue was checked for any other node showing a blue discoloration and the same was documented as found outside of axillary sampling. Axillary clearance was planned for all those patients by following the standard technique, extending the incision without waiting for the frozen section report.

Once the axillary sampling procedure is completed then for all the patients, Isosulphan blue dye will be injected subdermal (0.5ml) over the tumor and intraparenchymal (3-4ml) towards the axilla 10- 15mins before incision. The lymph node with maximum dye is then removed and sent for histopathological examination.

### *Statistical analysis:*

All data were entered and analysed using SPSS version 24. Mean and SD were calculated for all parametric variables and percentage for all frequency variables. Chi-square test was used to derive the statistical inference. Sensitivity, specificity, positive predictive value and negative predictive value was calculated for low axillary sampling in comparison with sentinel lymph node biopsy.

## 3. RESULTS

**Table 1: Age wise distribution of the study subjects**

Age group	Frequency	Percentage	Mean	SD
30 – 35	3	6%	49.7	8.4
36 – 40	7	14%		
41 – 45	4	8%		
46 – 50	13	26%		
51 – 55	4	8%		
56 – 60	16	32%		
61 - 65	3	6%		
Total	50	100%		

Table 1 shows the age wise distribution of the study subjects. It is seen from the table that majority of the study subjects were in the age group between 56 and 60 years with a minimum age of 30 and the maximum age was 60 and the mean age was

49.7 years.

**Table 2 : Distribution of the study subjects based on the diagnosis**

Diagnosis	Frequency	Percentage
Left sided breast cancer	20	40%
Right sided breast cancer	30	60%
Total	50	100%

Table 2 shows the distribution of the study subjects based on the diagnosis made by histo pathological examination. It is seen from the table that 60% of the patients were diagnosed as right sided breast cancer and the remaining 40% are left sided breast cancer.

**Table 3 : Distribution of the study subjects based on their pre-op staging of breast cancer**

Pre-op staging	Frequency	Percentage
T1aN0M0	9	18%
T1bN0M0	10	20%
T1cN0M0	14	28%
T2N0M0	17	34%
Total	50	100%

Table 3 shows the distribution of the study subjects based on the pre-op staging of breast cancer. It is depicted from that table that majority (34%) of the patients staging of breast cancer was T2N0M0 and the remaining of the patients had T1 staging with a, b or c.

**Table 4 : Distribution of the study subjects based on the histopathological diagnosis**

HPE diagnosis	Frequency	Percentage
Ductular carcinoma	26	56%
Lobular carcinoma	24	54%
Total	50	100%

Table 4 shows distribution of the study subjects based on the histo-pathological report. It is seen from the table that 56% had ductular carcinoma and 54% had lobular carcinoma.

**Table 5 : Distribution of the study subjects based on sentinel node HPE positivity**

SN – HPE	Frequency	Percentage
Positive	38	76%
Negative	12	24%
Total	50	100%

Table 5 shows distribution of the study subjects based on sentinel node HPE positivity. It is depicted from the table that HPE positivity was found to be 76% in sentinel node biopsy specimen.

**Table 6 : Distribution of the study subjects based on low axillary sampling –HPE positivity**

LAS – HPE	Frequency	Percentage
Positive	43	86%
Negative	7	14%
Total	50	100%

Table 6 shows the distribution of the study subjects based on low axillary sampling HPE positivity. It is depicted from the table that LAS-HPE detected 86% positivity among the study sample.

**Table 7 : Association between LAS and SNB in detecting positivity in HPE**

Type of procedure	HPE report		Chi-square value	P value
	Positive	Negative		
SNB	38	12	1.624	0.202
LAS	43	7		

Table 7 shows the association between sentinel node biopsy and low axillary sampling in detecting the positivity rate in histopathological examination. It is inferred from the table that there is no statistical significant difference between sentinel lymph node and low axillary sampling in detecting lymph node positivity (>.05).

**Table 8 : Validity of LAS in comparison with SNB**

Test	Disease		Total
	Present	Absent	
Positive	38	5	43
Negative	1	6	7
Total	39	11	50

Statistic	Value
Sensitivity	97.5%
Specificity	64.5%
Positive predictive value	91.5%
Negative predictive value	89.7%
Accuracy	90%

Table 8 shows the validity of low axillary sampling in detecting lymph node positivity in comparison with sentinel lymph node biopsy, which is considered as gold standard technique. It is inferred from the table that LAS has a sensitivity of 97.5%, which means it would be able to detect the true positives in 97.5% of the patients and the ability to detect true negatives (specificity) is 64.5%. Similarly the positive predictive value and the negative predictive value is 91.5% and 89.7% respectively with an accuracy rate of 90%. This highlights that low axillary sampling can be substituted for sentinel node biopsy for testing the status of the lymph node in clinically node negative patients with breast cancer in resource limited settings.

#### 4. DISCUSSION:

Our study was conducted with an objective of comparing the methodologies in predicting status of axillary lymph nodes in clinically node negative operable breast cancer patients. The two methods which were followed for predicting the lymph node status were sentinel lymph node biopsy and lower axillary sampling. Our study found that the node positivity rate as

76% through sentinel biopsy and 86% through lower axillary sampling.

In our study we have taken sentinel lymph node biopsy as the gold standard for detecting axillary lymph nodes in clinically node negative breast cancer. As most of the previous studies that were conducted had proven that SLN biopsy is quite effective in detecting clinically node negative breast cancer. The landmark study for SLN is the B32 trial. The B-32 trial supports that when the sentinel nodes are negative, there is no significant difference in regional node recurrence between axillary node dissection and sentinel node resection. There is a little increase in extremity edoema above baseline following sentinel node surgery, along with functional and neurological impairments.<sup>7,8</sup>

Our study reports show that the sensitivity rate for LAS in comparison with SLNB is 97.5% and the positive predictive value is 91.5% with a accuracy rate of 90% for detecting lymph node positivity in clinically node negative breast cancer patients. The results of the study done by Vani Parmar showed that LAS investigation in 676 (91.3%) of the 740 patients were able to identify three or more sampled LNs. When three or more nodes were sampled using LAS, the false negativity rate was decreased to 8.8%, with a sensitivity of 83% and a high NPV of 94.4%.<sup>9</sup> Parmar et al in 2013 conducted a study on Sentinel node biopsy versus low axillary sampling in women with clinically node negative operable breast cancer, where he quoted that, when it comes to predicting axillary nodal status, LAS and SNB are equally effective.<sup>9</sup>

In the present study we found the false negative rate for LAS is 2.5% in comparison with sentinel node biopsy False negative rate was found to be 29% in a meta-analysis of 69 studies involving 8059 participants. The findings of Parwar et al in 2013 had also indicated that the FNRs of SNB (12.7%, 95% CI 8.1e19.4) and LAS (10.5%, 95% CI 6.6e16.2%) were similar to those of SNB as reported in the NSABP B32.<sup>9</sup>

However, our study also support the use of blue dye directed SNB alone because to its high identification rate (97%) and low false negative rate (2.5%), as it is in par with the published meta-analysis<sup>11</sup> suggesting that "those surgeons who have mastered the technique of blue dye and have procured reliable, high identification rates and low FNR" may be able to achieve this. When comparing the 99m-Tc labelled radiocolloid guided SNB with four node axillary sampling (4-NAS), the Nottingham Study found a decreased false negative outcome.<sup>12</sup>

It is known that there is an upstaging of axillary node positive by up to 15% with an increase in the number of histological sections analysed.<sup>13</sup> Without any information on FNR, a different big study<sup>14</sup> sampled the largest or firmest lymph nodes in the lower axilla and reported that this method was a dependable substitute for full axillary clearing.

It is clear that there is a great deal of variation in the patient selection, methods, and reported outcomes among these research. The use of dye versus radiocolloid, the amount and kind of radiocolloid, the injection site, the timing of operation, the use of lymphoscintigraphy, and intraoperative versus histopathologic examination were among the often mentioned distinctions.

The proportion of patients who were effectively mapped increased when studies using radiocolloid and blue dye were compared to those using blue dye alone (92% vs. 83%;  $P = 0.006$ ). In multivariate analysis, however, neither comparison was demonstrated to be an independent predictor of decreased FNR or PVN. Up to now, results from the literature have supported using either blue dye alone<sup>15</sup>

A better understanding of these techniques may result from systematic reviews of diagnostic and prognostic studies, which can summarise test accuracy results from multiple investigations, pinpoint some of the causes of variation in individual study results, and possibly improve future study quality by outlining the methodological shortcomings of earlier reports.

## 5. CONCLUSION:

The validity of low axillary sampling in detecting node positivity among clinically node negative breast cancer patients is more than 90%. The results of this study indicate that Sentinel node biopsy and Low axillary sampling are equally accurate in predicting axillary nodal status in clinically node negative patients. Given the resource and equipment constraints, especially with respect to nuclear medicine facilities, LAS could be the preferred technique in developing countries. LAS has a low false-negative rate and is a dependable method for axilla assessment upfront in node-negative axilla.

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