

**Original article**

## **Comparison of imprint cytology and histopathology in axillary sentinel lymph node biopsy**

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### **Abstract**

**Introduction-** Varying extent mastectomy along-with axillary lymph node dissection (ALND) is the preferred treatment in early breast cancer. Due to the morbidity of ALND a less extensive but safe method of predicting axillary lymph node involvement is needed. Sentinel lymph node biopsy (SLNB) has emerged as such a modality. It is ideally performed using identification with radio-isotope and blue dye and evaluation by frozen section. However, facilities for the same are not universally available.

**Aims-** To assess the efficacy of imprint cytology in evaluating SLNB.

**Materials and Methods-** This observational prospective study was conducted on 35 patients of early breast carcinoma with clinically node negative axilla. All patients underwent modified radical mastectomy (MRM). SLN isolation was done using Methylene blue dye (2.5% solution) injected 10-15 minutes pre-operatively peri-lesionally. SLNB evaluated by imprint cytology and completion ALND was done in all cases.

**Observation and Results-** In our study, sentinel lymph node was positive in 22.86% of patients and was negative in 71.43% of patients. In 5.71% patients (n=2), sentinel lymph node was not visualized. The sentinel node localization rate was 94.29%. In our study the imprint cytology was positive in 24.24% while biopsy (HPE) was positive in 27.27%. In all cases where imprint cytology was positive HPE was also positive but imprint cytology had one false negative.

**Conclusion -** SLN localization with blue dye alone together with imprint cytology, is a good and universally available alternative to evaluate axillary lymph node status.

**Keywords:** Axillary lymph node dissection, Sentinel lymph node biopsy, Early breast cancer, imprint cytology.

### **INTRODUCTION**

Breast or mammary gland is a modified sweat gland .Carcinoma of breast continues to be one of the most frequent cancers in women all over the world. In Indian women, it is second only to carcinoma of cervix with annual incidence of 17/10000 population. In the past radical mastectomy has been the cornerstone of management of Ca.

breast. For the last few decades, a controversy is raging about the extent of excision. Various methods of predicting axillary lymph node status has been described including clinical assessment, radiological and operative procedures. Axillary lymph node dissection is considered to be the gold standard for evaluating the axillary lymph node status. However, Axillary lymph node dissection (ALND) may be associated with significant morbidities such as post-operative numbness in inner side of arm, local wound complications, seroma formation, infection, limitation of shoulder movements, chronic pain syndrome and lymphedema which can lead to lymphosarcoma in many cases.<sup>(1)</sup> In addition, with increasing awareness and better screening more number early breast carcinomas are being detected. The benefit of ALND is being questioned in these early breast carcinoma patients because these rarely have metastasis and should therefore not to be subjected to the potential of complications of ALND. Thus there is a need of a procedure which can detect axillary lymph node status as accurately as ALND and is free from its attendant complications.

Based on the concept that the lymph from the primary tumor drains into the first regional group of lymph node/nodes defined as SENTINAL LYMPH NODE, the concept of intraoperative lymph node mapping and sentinel lymph node biopsy (SLNB) was developed to identify lymph node metastasis from primary cutaneous melanoma<sup>(2)</sup>. This technique has false negative rate of only 1% in melanoma. The same technique was adopted by Guiliano et al to identify the axillary lymph node metastasis in breast carcinoma. In this study, the sentinel lymph node was identified in 114 of 174 patients and accurately predicted axillary status in 109 of these 114 patients with false negative rate of 5%.<sup>(3)</sup> The technique has a long learning curve. Guiliano et al, had 29% detection rate in their first 87 procedures which increase to 82% in subsequent 87 procedures. In addition all false negative occurred in first 87 cases and two of these occurred in first five cases.<sup>(4)</sup> Subsequent studies showed that false negative rate can be decreased by examining sentinel lymph node by histopathology and immuno-histochemistry.<sup>(5)</sup>

Another method of detection of the sentinel node involves use of filtered technetium labeled sulfur colloid and technetium labeled human serum albumin. In western world, due to easy availability of better facilities and wide coverage under health insurance they can use facilities of sentinel node biopsy using both radioactive colloid and blue dye.

India being a developing country, facilities of radioactive colloid technique and frozen section are only available at the tertiary level. Moreover most patients here are unable to pay for these procedures. So there is a need of less expensive, comprehensive and accessible technique.

In a study done in India at AIIMS, Deos et al, imprint cytology showed sensitivity of 84.2%, specificity of 100% and accuracy of 91.3%, in locally advanced breast cancer.<sup>(6)</sup>

The best method of identification of sentinel lymph node is using both dye and radioactive colloid but such facilities are available only few centers in our country. Results using dye alone are also promising but the sufficient studies not available in our country. The positivity of lymph node is best done intra-operatively by frozen section of sentinel node but this facility is also present only in few specialized centers in India. Imprint cytology can be done at almost all centers without much infrastructure requirement. The purpose of this study is to determine the role of sentinel lymph node biopsy in predicting the axillary lymph node status of patients with early invasive breast cancer using patent V dye and imprint cytology alone.

### **AIMS AND OBJECTIVES**

1. To localize sentinel node by injecting 2.5% Methylene blue dye around the primary tumor.
2. To assess the reliability of imprint cytology technique in evaluating the biopsied sentinel lymph node.

### **MATERIALS AND METHODS**

This observational prospective study was conducted in the department of Surgery, Northern Railways Central Hospital, New Delhi, from July 2016 to October 2018.

#### **Inclusion Criteria:**

Patients with early proven carcinoma breast with clinically negative axillary node

#### **Exclusion Criteria:**

1. Patient with clinically multifocal lesion
2. Prior axillary surgery
3. Inflammatory carcinoma breast
4. Recurrent carcinoma following previous surgery
5. Patient with clinically positive axillary lymph nodes.

#### **Sample size & Sample Technique:**

Assuming the accuracy to be 83% with a margin of error of 14% and the 5% level of significance. The minimum required sample size was 28 patients.

In this study a total no of 35 patients with carcinoma breast diagnosed with core needle biopsy with clinically negative axilla were included. In all these patients, thorough history was taken and detailed clinical examination was performed along with the relevant investigations according to the study proforma.

#### **Study Method:-**

After above investigations clinical staging of disease was done. Patient belonging to stage I (T1 N0 M0) and Stage II (T2 N0 M0, T3 N0 M0) and patient with neo-adjuvant chemotherapy who were included in lymph node negative group were selected for MRM and sentinel lymph node biopsy and ALND.

After preliminary investigations, confirmation of diagnosis and after pre anesthetic checkup, patients were taken up for modified radical mastectomy (MRM). In all patients SLNB was done and evaluated by imprint cytology. However, in the absence of unequivocal guidelines, completion ALND was done in all cases.

3-5 ml of sterilized Methylene blue dye (2.5% solution) was injected 10-15 minutes before surgery into the breast tissue surrounding the primary tumor after cleaning and draping the patient. Standard incision for MRM was made and inferior and superior skin flaps dissected.

Then axilla was explored after 10-20 minutes and sentinel lymph node was detected by its blue color and by tracing the afferent lymphatic vessel and was removed. Modified Radical Mastectomy was completed and whole of the breast tissue along with axillary contents labeled as L1, L2, L3 were sent for histopathology along with sentinel lymph node in a separate container.

Result of sentinel lymph node imprint cytology and histopathology were compared with each other and with histopathology of other axillary lymph nodes.

## **OBSERVATION AND ANALYSIS**

Out of these 35 patients included in the study, maximum were between age groups 46-55(42.86%) and 56-65 age group(31.43%). Most patients in our study were postmenopausal (94.29%) and most attained menopause in age group 45-50 years (69.7%).

Most of our patients attained menarche between 13-15 years of age (51.43%) and 42.86% before 13 years of age. In our study age at first birth was between 19-22 years in maximum no. of patients (62.86%) and only 5.71% has first child above 26 years. Most patients had  $\geq 3$  children (68.57%), and only 28.57% had 2 children. Maximum patients breastfed their children for an average period of 6-12 months (82.86%), and 11.43% for <6 months. Most of our patients presented with painless lump(97.14%), and only 5.71% presented with pain in breast and, 2.85% presented with nipple discharge. Maximum no. of patients presented with a lump in outer quadrant of breast 57.14% and 20% in upper inner quadrant. The size of lump on presentation was between 2-5 cm in 94.29% of patients and 5.71% presented with breast lump size of <2 cm.

Most patients were in clinical staging T2N0M0 (51.43%) and 42.86% in clinical stage T3N0M0.

In our study, sentinel lymph node was positive in 22.86% of patients and was negative in 71.43% of patients. In 5.71% patients(n=2), sentinel lymph node was not visualized. The sentinel node localization rate was 94.29%. In our study the imprint cytology was positive in 24.24% while biopsy (HPE) was positive in 27.27%. In all cases where imprint cytology was positive HPE was also positive but imprint cytology had one false negative.

In our study, sentinel node imprint cytology was positive in 8 cases out of 35, with sensitivity of 72.7%, specificity 100% with diagnostic accuracy of 91.43% and p-value (Fisher's exact test) is <0.001. However, on HPE, the sentinel lymph node was positive in 9 patients and other axillary nodes were positive in 11 patients with sensitivity of 81.8%, specificity of 100% with diagnostic accuracy of 94.29%. p-value of test is <0.001 using Fisher's exact test and kappa value of test is 81.8%, with false negative rate of 18.18%. The other axillary nodes beside sentinel lymph nodes were also positive in all cases where sentinel lymph node were positive. There are 2 cases[post NACT] where sentinel lymph node was negative, but other axillary nodes were positive. In cases in stage T1-T2, sentinel lymph node biopsy sensitivity, specificity and accuracy is 100%

## **DISCUSSION**

The status of axillary lymph node remains the most important predictor of survival in women with invasive breast cancer and this status is used for enrollment in adjuvant protocol and to make treatment decision.

Bassi et al used combined technique of iso-sulphan blue and Tc 99 sulfur colloid for mapping SLN in 40 patients of early breast cancer. The study showed localization in 98%, with accuracy of 92%. Rama et al's done study on 96 patients with early breast cancer shows sensitivity 85.5% and accuracy of 68.8% by using methylene blue dye.<sup>(7)</sup> Cox et al used a combination of isosulfan blue and <sup>99m</sup>Tc labeled sulfur colloid, both injected intraparenchymally. SN was successfully identified in 440/466 (94.4%) patients.<sup>(8)</sup>

A review of the National Cancer Data Base (NCDB) data from 1998 to 2005 revealed that there were no difference seen in axillary recurrence rates or survival for patients who had sentinel node surgery only versus those who underwent ALND.<sup>(9)</sup> Thus the available literature shows that SLND is a new, minimally invasive procedure to assess axillary lymph node status in operable breast carcinoma. It enables accurate prediction of the axillary lymph node

status and improves histopathological staging by enabling pathologist to perform focused analysis of one or two lymph nodes.

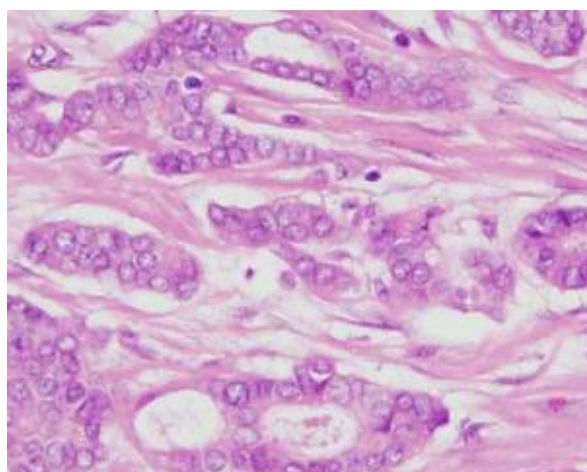
The ACOSOG Z0011 prospective randomized trial revealed that ALND may be safely omitted in patient with clinically negative disease who have sentinel node positive as local recurrence was 3.6% in ALND versus 1.8% in sentinel node only group. Axillary recurrence were reported in 0.5% of ALND group versus 0.9% in sentinel node only group, there was no difference in overall survival (91.9% after ALND versus 92.5% after sentinel node only;  $P=0.24$ ) or disease-free survival at 5 years (82.2% after ALND versus 83.8% after sentinel node only).<sup>(10)</sup>

In our study, 35 patients of carcinoma breast underwent sentinel lymph node biopsy after injecting 2.5% Blue dye at the periphery of lesion before starting the procedure. Sentinel node was localized in 33 patients (94.29%). There were two false negative. So localization of sentinel lymph node is 94.29% (33/35) and it accurately predicted axillary lymph node status in 94.26%. In this study false negative rate for sentinel lymph node biopsy is 18.18%. The sensitivity of the sentinel lymph node biopsy is 81.18% and the specificity is 100% with diagnostic accuracy of 94.29%. The p value of the study using Fischer's Exact Test is  $<0.001$  which is statically significant. The imprint cytology was positive in 24.24% while biopsy (HPE) was positive in 27.27%. In all cases where imprint cytology was positive HPE was also positive.

#### CONCLUSION

SLNB is a safe and effective predictor of axillary lymph node involvement and in patients of early breast cancer with negative SLNB axillary dissection can be omitted. Use of radio-isotope and gamma camera together with blue dye can further improve the yield and frozen section can improve diagnostic accuracy. However, in their absence, localization with blue dye alone together with imprint cytology, is a good and universally available alternative to evaluate sentinel Lymph node and its accuracy is likely to increase as more cases are done.

#### HPE - Infiltrating Duct Carcinoma ( High Power )



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