Value of frozen section and primary tumor factors in determining sentinel lymph node spread in early breast carcinoma

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Abstract

Introduction Sentinel lymph node biopsy (SLNB) is the standard of care to assess the metastasis in breast carcinoma. Accuracy of intraoperative frozen section examination to evaluate SLN in detecting metastasis is important as it determines the further management of axilla. Primary tumor characteristics determining the metastasis to the lymph node will help in predicting the probability of spread and to determine the nature of disease. It also helps in refining selection of patients for SLNB. We evaluated all these criteria on Indian patients for the better management.

Materials and methods Between January 2005 and April 2009, 114 consecutive patients of all age group of both sex, with cytology or biopsy proven carcinoma breast, clinical stage T1/T2 N0 M0 at Manipal Comprehensive Cancer Center, Manipal Hospital, Bangalore were subjected to SLNB and intraoperative frozen examination. First 75 cases had complete axillary clearance irrespective of SLNB result and subsequently, positive cases underwent axillary lymph node dissection (ALND). Age of the patient and primary tumor characteristics like size, grade, lymphovascular invasion (LVI), perineural invasion, ER/PR status, Her2-neu status and histological sub-types were evaluated for predicting the SLN metastasis. Feasibility of SLNB in previously treated patient is also evaluated.

Results The age of the patient ranged from 23 to 87 years and its association with SLN spread is not significant. Frozen section examination had accuracy of 97.37% in determining metastatic sentinel node with sensitivity of 96.15% and specificity of 100% with value $P < 0.001$. SLN remained significant indicator of the status of rest of axilla with value $P < 0.001$. Primary tumor characteristics like histological subtypes, grade ($P = 0.353$), ER/PR status ($P = 0.839$), Her2-neu status ($P = 0.296$) were not significantly associated with SLN metastasis. Size of the primary tumor ($P = 0.002$), LVI ($P < 0.001$), perineural invasion ($P = 0.084$) were significant factors determining the SLN metastasis. SLNB evaluation had no false negative values in previously treated breast.

Conclusion SLNB is a valuable method of determining the axillary nodal metastasis. Intraoperative frozen section examination is highly accurate in detecting nodal metastasis. Primary tumor characteristics like size, LVI and perineural invasion are significant in predicting SLN metastasis. SLNB remains an important method of predicting axillary metastasis even in previously treated breast carcinomas.

Keywords: Sentinel lymph node · Breast carcinoma · Metastasis

Introduction

Axillary nodal status is the most important factor in staging of breast cancer. With improvement in breast cancer screening and awareness, more patients are diagnosed at a stage without nodal involvement. Traditional routine axillary lymph node dissection (ALND) can cause serious morbidity. Therefore, sentinel lymph node biopsy (SLNB) is the standard of care in most centers and has gained acceptance as a predictor of axillary lymph node status with a reported accuracy of 95–100%.^{1–3} Patients with metastatic involvement of the axillary nodes should be offered ALND or radiotherapy for better locoregional control.

Frozen section examination is used to assess the sentinel node status intraoperatively and ALND is done based on this report. The accuracy of frozen section examination remains important for the management of carcinoma breast and its value is assessed in our study on Indian population.

Many studies found that younger age, increasing tumor size, and the presence of lymphovascular invasion (LVI) correlated with a higher incidence of axillary lymph node metastasis.^{4–11} We analyzed characteristics of primary breast tumors in Indian patients predicting positive SLNB results and to determine which patients should undergo SLNB.

Patients and methods

Patients

Between January 2005 and April 2009, 114 consecutive patients of all age groups of both sex, with cytology or biopsy proven carcinoma breast, clinical stage T1/T2 N0 M0 at Manipal Comprehensive Cancer Center, Manipal Hospital, Bangalore were included in the study. All procedures were performed by specialized surgeons with extensive experience in the field of breast cancer surgery. Patients with palpable lymph nodes in the axilla, prior axillary surgery, previous radiotherapy and chemotherapy and pregnant patients were excluded from the study. Institutional review board approval was taken.

Lymph node identification

Combination of isotope labeling and methylene blue dye injection were used to identify the sentinel node. Total of 1 ml (1 mCi/37 MBq) radioactive technetium ^{99m}Tc sulphur colloid was injected in retroareolar space in case of lump being in outer upper, outer lower and central quadrant. When lump was in upper inner and lower inner quadrants 0.2 ml each (0.2 mCi/7.4 MBq) of radioactive ^{99m}Tc sulphur colloid was injected peritumorally in

all four sides and intradermally anterior to lump (total of 1 ml and 1 mCi/37 MBq). Colloid is injected 2 h prior to surgery. Four milliliter methylene blue dye (10%) was injected in similar sites, 20 min prior to surgery. Sterile packed hand held gamma ray detecting probe was used to assess radioactivity of the injected primary tumor area and survey the nodal basins for focal sites of increased counts. While surveying the nodal area, a small lead shield to prevent shine through effect from primary site was used. The area of axillary skin (hot spot) with audible tone (acoustic signal) and high counts as shown by the probe (at least one-tenth of the count at the injected primary area and/or counts of 10 : 1 ratio of SLN to background) was marked over axillary skin just prior to the surgery. Intra-operatively, SLN was searched through a short dedicated incision over the marked axillary skin area along skin crease in cases of breast conservation surgery or after raising upper flap (in cases of mastectomy). Axillary tissue is gently dissected until blue stained nodes and nodes with high count and audible tone (hot and blue node) as identified by hand held gamma probe were excised. Additional radioactive SLNs were removed, if present until back-ground was less than one-tenth the value of the hottest node. Nodes were sent for frozen section examination and 75 patients underwent complete axillary dissection immediately as a part of validation study. In remaining cases, axillary dissection was done only when sentinel node was positive on frozen section.

Pathological examination

Each SLN was examined by means of frozen section by taking six sections in each lymph node and standard hematoxylin and eosin (H&E) analysis. A positive SLN is defined as metastatic breast cancer cells seen on results of frozen section or standard H&E analysis.

Statistical analysis

A prospective correlation clinical study with 114 patients is undertaken. Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on mean $\pm$ SD (min–max) and results on categorical measurements are presented in number (%). Significance is assessed at 5% level of significance. Chi-square/22, 2×3 , 2×5 , 2×6 Fisher exact test have been used to find the significance of study parameters on categorical scale between two groups. Diagnostic statistics namely sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were computed to find the relationship and diagnostic value of various tests. The statistical software namely SPSS 15.0, Stata 8.0, Med-Calc 9.0.1 and Systat 11.0 were used for the analysis of the data and microsoft

word and excel have been used to generate graphs, tables, etc.

Results

Patients

The age of patients ranged from 23 to 87 years with mean age 54.81 years (Table 1). All but one of the 114 patients were female.

Frozen section examination of the SLNB (Table 2)

Frozen section examination accurately diagnosed in 97.37% of the patients. Total 75 cases (65.8% with 95% confidence interval [CI]: 56.69–73.86) had metastasis and 39 cases (34.2% with 95% CI: 26.14–43.31) were negative on frozen section examination. Where as on histopathologic examination 78 cases (68.4% with 95% CI: 59.41–76.23) had metastasis and 36 cases (31.6% with 95% CI: 3.77–40.59) were negative. Among three false negative, two had micrometastasis from infiltrating lobular and medullary carcinoma.

Table 1 Association of age with SLN

Age in years	Number of patients	SLN		Total
		Positive	Negative	
21–30	2	0	2 (2.7%)	2 (1.8%)
31–40	10	4 (10.0%)	6 (8.0%)	10 (8.8%)
41–50	28	14 (35.8%)	14 (18.7%)	28 (24.6%)
51–60	41	14 (35.9%)	27 (36.0%)	41 (35.9%)
61–70	17	4 (10.2%)	13 (17.3%)	17 (14.9%)
>70	16	3 (7.7%)	13 (16.0%)	16 (14.1%)
Total	114	39 (100.0%)	75 (100.0%)	114 (100.0%)

Age is not statistically associated with the SLN positive with $P = 0.265$.

Table 2 Association of frozen section test with histopathology (HPR)

Frozen section test	HPR		Total
	Positive	Negative	
Positive	75 (96.2%)	0	75 (65.8%)
Negative	3 (3.8%)	36 (100.0%)	39 (34.2%)
Total	78 (100.0%)	36 (100.0%)	114 (100.0%)

Frozen section test is significantly associated with HPR with $\chi^2 = 101.18$; $P < 0.001$ with a sensitivity of 96.15%, specificity of 100%, PPV 100% and NPV 92.31%.

Association of SLNB with rest of axilla (Table 3)

As a part of validation study, first 75 cases underwent complete axillary dissection irrespective of results of frozen section examination. Among 37 patients with metastasis, 17 cases had metastasis only in the sentinel nodes and rest of the axilla was free.

Grade of tumor and SLN (Table 4, Fig. 1)

Total 31 cases could not be graded due to various reasons like no residual tumor, *in situ* carcinoma and non-infiltrating ductal carcinomas (IDCs). In the remaining 83 cases, most of them were grade III (81.9%).

Histological subtypes with SLN (Table 5)

Pure IDCs were 48 and 29 cases had associated *in situ* (DCIS) component. Result of histological subtypes with SLN is shown in the Table.

LVI and SLN (Table 6, Fig. 2)

Lymphovascular invasion is not reported in 30 cases due to absence of residual tumor or various other reasons.

Table 3 Association of SLNB with rest of axilla

SLN test	Rest of axilla		Total
	Positive	Negative	
Positive	17 (94.4%)	20 (35.1%)	37 (49.3%)
Negative	1 (5.6%)	37 (64.9%)	38 (50.7%)
Total	18 (100.0%)	57 (100.0%)	75 (100.0%)

False negative result (SLN negative in the presence of other positive axillary nodes) is observed in one case. SLN test is significantly associated with rest of axilla with $\chi^2 = 19.282$; $P < 0.001$.

Table 4 Association of grade of tumor with SLN

Grade	SLN		Total
	Positive	Negative	
Grade I	1 (3.2%)	0	1 (1.2%)
Grade II	4 (12.9%)	10 (19.2%)	14 (16.9%)
Grade III	26 (83.9%)	42 (80.8%)	68 (81.9%)
Total	31 (100.0%)	52 (100.0%)	83 (100.0%)

Grade is not statistically associated with SLN with $P = 0.353$. Remaining 83 cases were correlated with SLN metastasis in the Table.

Perineural invasion with SLN (Table 7)

In 47 cases perineural invasion could not be evaluated. Perineural invasion indicates the early spread along the nerve course.

Estrogen receptor (ER)/progesterone receptor (PR) status with SLN (Table 8)

Total 98 cases were studied for hormone receptor study, and 60.2% of the patients had either of the receptors in our study.

Fig. 1

Table 5 Association of histological subtypes with SLN

Histological subtype	SLN positive	SLN negative	Total
IDC	29	48	77
ILC	3	4	7
ILC + IDC	1	0	1
Medullary	1	4	5
IDC + mucinous	3	0	3
DCIS + microinvasion	0	2	2
ILC + DCIS + tubular	1	0	1
DCIS	0	1	1
Mucinous	0	2	2
Papillary + mucinous	0	1	1
Papillary	0	2	2
No residual tumor	2	10	12

Most of the non-IDC and non-ILC (infiltrating lobular carcinoma) cases had no metastasis. Pure IDC was identified in 77 of 114 patients and pure ILC in 7 patients. Positive SLNB findings were detected in 29 (37.66%) of 77 patients with IDC and in 3 (42.85%) of 7 patients with ILC.

Her2-neu status with SLN (Table 9)

Group 3+ is taken as positive for the receptor study and in 24 cases, it couldn't be reported.

Size of the primary tumor and SLN (Table 10, Fig. 3)

Size could not be evaluated in 12 cases because of the absence of residual tumor. Most of the lumps were 1.6–3 cm in size.

Fig. 2 Association of LVI with SLN.

Table 6 Association of LVI with SLN

LVI	SLN		Total
	Positive	Negative	
Present	22 (88.0%)	31 (52.5%)	53 (63.1%)
Absent	3 (12.0%)	28 (47.5%)	31 (36.9%)
Total	25 (100.0%)	59 (100.0%)	84 (100.0%)

Among the 31 cases with absent lymphovascular invasion, only 3 had metastasis to axillary lymph node, indicating that absence of LVI rarely has positive SLN. LVI is significantly associated with SLN spread with $\chi^2 = 9.481$; $P < 0.001$.

Table 7 Association of perineural invasion with SLN

Perineural invasion	SLN		Total
	Positive	Negative	
Present	13 (54.2%)	14 (32.6%)	27 (40.3%)
Absent	11 (45.8%)	29 (67.4%)	40 (59.7%)
Total	24 (100.0%)	43 (100.0%)	67 (100.0%)

Perineural invasion is significantly associated with SLN with $\chi^2 = 2.988$; $P = 0.084+$.

Feasibility of SLN in previously treated breast (Table 11)

Total 13 cases had lumpectomy done elsewhere and reported to us for further management. SLNB of such cases had high accuracy with no false negatives.

In conclusion, the sensitivity, specificity, PPV, NPV and accuracy of different parameters are compared with SLN in Table 12 and Fig. 4.

Discussion

Sentinel lymph node is the standard method of assessing axillary nodal spread in many centers. Accurate analysis will prevent patients from unnecessary morbidity of axillary surgery. Primary tumor factors which determine the probability of positive SLN will help in deciding the category of patients in whom SLNB can be avoided.

Most common age group in our study was 51–60 years. Caywood et al.¹² observed that overall, SLN metastasis is more common in younger patients (≤ 66 years) than in older patients. Many studies predicted age as an independent predictor of risk of SLN metastasis, but we did not observe the same in our patients, though older age had more negative SLN results.

Intraoperative frozen section examination allows immediate ALND for patients with positive SLNs. The sensitivity and accuracy of frozen section examination of

the SLN has been reported to range from 36.0 to 93.3% and 83.2 to 96.0%, respectively.^{1,13–19} However, these studies differ considerably in size, tumor characteristics, number of nodes sampled, number of frozen section slides taken and the staining procedure utilized for the pathological examination.

In our study, only H&E staining was used for all paraffin sections with sensitivity, specificity and overall accuracy of 96.2, 100 and 97.4%, respectively. Therefore, frozen section examination remains the accurate intraoperative diagnostic method for sentinel node assessment. Among the false negative cases, two had micrometastasis

Fig. 3

Table 8 Association of ER/PR status with SLN

ER/PR status	SLN		Total
	Positive	Negative	
Present	20 (58.8%)	39 (60.9%)	59 (60.2%)
Absent	14 (41.2%)	25 (39.1%)	39 (39.8%)
Total	34 (100.0%)	64 (100.0%)	98 (100.0%)

ER/PR status is not statistically associated with SLN status with $\chi^2 = 0.041$; $P = 0.839$.

Table 9 Association of Her2-neu status with SLN

Her2-neu	SLN		Total
	Positive	Negative	
Negative	8 (25.8%)	26 (44.1%)	34 (37.8%)
1+	2 (6.5%)	2 (3.4%)	4 (4.4%)
2+	6 (19.4%)	7 (11.9%)	13 (14.4%)
3+	15 (48.4%)	24 (40.7%)	39 (43.3%)
Total	31 (100.0%)	59 (100.0%)	90 (100.0%)

Her2-neu is not statistically associated with SLN status with $P = 0.296$ (2×4 fisher exact test).

Table 10 Association of size of primary tumor and SLN

Size of tumor	SLN		Total
	Positive	Negative	
≤ 1 cm	1 (2.7%)	5 (7.8%)	6 (5.9%)
1.1–1.5 cm	0	5 (7.8%)	5 (4.9%)
1.6–2.0 cm	9 (24.3%)	16 (25.0%)	25 (24.7%)
2.1–3.0 cm	9 (24.3%)	29 (45.3%)	38 (37.6%)
3.1–4.0 cm	7 (18.9%)	6 (9.4%)	13 (12.8%)
4.1–5.0 cm	8 (21.6%)	3 (4.7%)	11 (10.9%)
> 5.0 cm	3 (8.1%)	0	3 (2.9%)
Total	37 (100.0%)	64 (100.0%)	101 (100.0%)

Tumor with a size of < 1.5 cm, rarely have metastasis in the axillary lymph node. Larger size of tumor is significantly associated with SLN positivity with $P = 0.002$.

Table 11 Association of SLN in previously treated breast

SLN	Rest of axilla positive	Rest of axilla negative	Total
Positive	1	1	2
Negative	0	11	11

Table 12 Diagnostic statistics

Comparison	Sensitivity	Specificity	PPV	NPV	Accuracy
1. Frozen section test vs HPR	96.2	100.0	100.0	92.3	97.4
2. SLN vs rest of axilla	85.0	63.6	45.9	92.1	69.3
3. Lymphovascular	88.0	47.5	41.5	90.3	59.5
4. Perineural invasion vs SLN	54.2	67.4	48.2	72.5	62.7
5. ER/PR status vs SLN	58.8	39.1	33.9	64.1	45.9
6. Her2-neu vs SLN	48.4	59.2	38.5	68.6	55.6

Fig. 4

which probably would have been detected by IHC (immunohistochemistry). Celebioglu and colleagues reported an improvement in sensitivity from 73.5% to 83.7% when H&E staining was coalesced with IHC staining. However, the sensitivity for macrometastases was already 100% for H&E staining. Combining H&E with IHC staining raised the sensitivity from 45 to 55% for micrometastases. Yet, almost half of the cases with micrometastases were not found during intraoperative frozen section examination.²⁰

Sentinel node being the first lymph node to contain metastatic cancer within a tumor's lymphatic basin guides the management of rest of axilla. In our study, in only one case, rest of axilla was positive when sentinel node was negative. All studies in the literature on SLNB report variable rates of false negative rates, which in most series are between 5% and 10%.²¹ The constant occurrence of false negative results has given rise to concern, because its impact on the prognosis is still unclear. A false negative SLNB is not an uncommon event, especially in the presence of a small primary tumor with a single metastatic node and if the surgeons involved have gained little experience with this procedure. False negative results can lead to less than optimal adjuvant treatment, however the clinical impact of false negative in terms of axillary

recurrence at 56 months was minimal.²² Currently, however, the role of axillary status has been reduced, as most decisions regarding adjuvant therapies are based on the histopathologic features of the primary tumor.²³ Therefore, it is widely believed that understanding due to false negative SLN leads to under treatment in very few cases, specifically those for whom only the missed positive nodes would have indicated treatment.^{24,25} In a series of 285 patients who underwent SLNB associated with ANLD, Nano et al.²⁶ considered eight patients with false negative SLN and 1–11 positive lymph nodes in the ALND specimen and assessed whether adjuvant treatment would have been different if only the false negative SLN had been considered. The authors concluded that only 2/8 patients would not have received the correct adjuvant therapy, which means that <1% of the patients who underwent SLNB (2/285) would have been under-treated with a potentially negative impact on their prognosis.

Many times, SLN is the only positive node in the axilla raising the question for need of ALND. In our series, among 37 positive SLNB, 20 cases had SLN as the only positive node. The current guidelines of the American Society of Clinical Oncology (ASCO) and the German Society of Senology (GSS) recommend complete ALND or irradiation for the presence of micrometastasis MIC (>0.2 mm, but <2 mm),^{27,28} whereas no axillary treatment is recommended for patients with isolated tumor cells (ITC) in the SLN, although the current evidence is controversial. Approximately 50% of patients with positive SLNs are found to have no other nodal metastases.^{1,3,29–32} Therefore, many patients are undergoing unnecessary ALND, with no additional therapeutic benefit or further staging information provided. It is also argued that because patients with SLN metastases will generally receive systemic therapy, regardless of the presence of any additional nodal metastases, any residual disease does not influence choice of therapy and may itself be eradicated by the systemic therapy. In addition, radiation therapy after breast-conserving surgery may contribute to control of any additional nodal disease. To assist in the estimation of risk of residual disease in non-SLNs of a woman with sentinel node positive breast cancer, a nomogram was developed taking variables of tumor type,

nuclear grade, LVI, multifocality of primary tumor, ER status, number of negative SLNs, number of positive SLNs, pathological size, and method of detection of SLN metastasis.³³ To predict non-SLN metastases (NSLNM) in patients with a positive SLNB, four different nomograms developed by Memorial Sloan-Kettering Cancer Center, Tenon Hospital, Cambridge University, and Stanford University were used.

Although no model is perfect, MSKCC nomogram provides an estimate of the likelihood of finding additional disease detectable by H&E staining of the specimen taken by completion axillary dissection. The model has been validated in several other populations,^{34–40} showing it to be robust in its application to groups of women that vary greatly from the population in which it was developed.

Certain primary breast tumor characteristics can be used to predict positive SLNB results and thus determine which patients should undergo SLNB. Many studies have shown that age,^{41–44} grade,^{41,45–47} LVI,^{41,42,45–50} and tumor size^{41–43,45–49,51}, predicted positive ALND findings. Grade I breast cancer is likely to have positive nodes in 10% of patients, while 39% of patients with grade III tumors are likely to have positive nodes.⁵²

In our study though grade III lesions were the most, but were not statistically correlated with positive SLN, as was found by Chen et al.⁵³ The breast cancer favourable histological subtypes present challenges to both the pathologist in accurate diagnosis and to the treating physician because of their unclear metastatic potential and unknown response to adjuvant treatment. Clear pathologic definition of these sub-types is important, because the favorable histological subtypes are defined as tumors that are less likely to metastasize to nodes and distant sites. Rosen et al.⁵⁴ previously determined that the 10-year survival rate for node negative patients with tumors <3 cm of breast cancer with favorable histological subtypes was equal to the survival rate of patients with node negative IDC measuring <1 cm, a group that traditionally has not received adjuvant systemic treatment. The favorable breast cancer histological subtypes include tubular, mucinous (colloid), papillary, medullary, adenoid cystic and secretory cancers. Favorable subtypes are defined as ‘pure’ when they have the characteristic histological features in at least 90% of the tumor. Wide variations have been reported in the pathologic diagnosis of these tumors. These have a lower frequency of lymph node metastases compared with infiltrating ductal (IDC) and lobular cancers.^{55,56}

Wong et al.⁵⁷ demonstrated the incidence of axillary metastases found on SLNB with serial sectioning of the lymph nodes to be higher than expected for these special subtypes: 17% for tubular cancers, 6% for mucinous cancers and 21% for pure medullary cancers. The authors believed that these high risks of lymph node metastases

justified the use of SLNB in these patients. However, the number of patients in this study of these rare tumors was relatively small, and the incidence of lymph node metastases was higher than previously reported with axillary dissection. Although the good prognosis for these favorable types is well known, the prognosis of favorable histological subtypes with positive nodes are not well documented. These tumors are rare, and, with the possible exception of tubular and mucinous cancers, most studies are too small to draw conclusions about their natural history and the benefits of treatment. In deciding whether to perform an SLNB, the treating physician must decide whether the results of the sentinel node biopsy will alter treatment. If so, individualized use of SLNB in patients with favorable-histology breast cancer, taking into account the 4% incidence of lymph node metastases and the risks and benefits associated with SLNB in the individual patient is better.⁵⁸ There was no difference in frequency of SLN metastases between ductal and lobular tumor types ($P > 0.25$).⁵⁹

Lymphovascular invasion is an important predictor of spread and has been consistently proved in many studies including the present one. Breast cancers showing LVI on microscopy have a 57% chance of being node positive compared with 23% for tumors without LVI.⁶⁰ Perineural invasion as an independent factor predicting the spread in carcinoma breast is not widely evaluated. In our study, we found that absence of perineural invasion rarely has lymph node metastasis. Though the association is not marked, nevertheless it is significant. ER and PR status was not significant in predicting positive SLN status in our study, as was reported by Chen et al.⁵³ In contrast, some studies report higher frequencies of SLN metastases in ER/PR-positive tumors than those for ER/PR-negative tumors, corresponding to a small, but significant, increase of 2.0% for ER and 4.6% for PR.⁵⁹ Although this observation seems counter-intuitive, it actually is in agreement with the findings of other large studies.

Studies on the association of Her2-neu with the axillary lymph node metastasis are controversial. In our study, Her2-neu status association in predicting positive SLNB was not significant. Chen et al.⁵³ reported similar findings, but Nathanson et al.⁶¹ reported significant association in predicting SLN metastasis, as an independent predictor. Some studies have also suggested adoption of a more conservative surgical approach in the Her2 negative group as larger number of patients in the Her2 negative group showed micrometastasis as the only metastasis in the involved single sentinel node when compared with the Her2 positive group.^{62,63}

Very few patients reported when the lesion was <1 cm, probably because of lack of awareness and mass screening. Size of the primary tumor is an important independent predictive factor for SLN metastasis. In the larger studies, the frequency is 10% in T1mic,⁶⁴ 9–13% in T1a,^{65–70}

13–19% in T1b,^{65–71} 26–29% in T1c,^{65,66,69,71} 39–50% in T2 ≤3 cm,^{65,66,69,71} 48 to 59% in T2 >3 cm,^{69,71} and 71–80% in T3.^{66,69} As the size increases, capacity of the tumor to spread increases which is also the finding in our study. SLNB can also be used as a standard procedure when patient reports after excision biopsy of the primary lesion.⁷² Among the 13 cases of previous lumpectomy,¹¹ were negative for SLN metastasis which was validated by subsequent axillary clearance.

Conclusion

Frozen section examination has very high accuracy of 97.37% in diagnosing SLN metastasis and used as the standard method of investigation intraoperatively. Asso-

ciation of SLN status with rest of axilla being significant, it is used as the guide for further management of axilla. Complete ALND in patients with positive SLN with minimal risk of rest of axilla being positive, is individualized against the risk and benefits in each patient. Grade, ER/PR status and Her2-neu status are not statistically significant in assessing the SLN status. Histological subtypes could not clearly define patients with risk of lymph node spread and further study needs to clarify regarding avoidance of SLNB in favorable histological subtypes. LVI, perineural invasion and size of the tumor remained significant primary tumor characteristics in determining the SLN status. Detection of lymph node metastasis in patients with previous lumpectomies is highly accurate with SLNB.

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