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Original Research Article

Frozen section evaluation and clinicopathological correlation of sentinel lymph nodes in breast carcinoma: A study at a regional cancer centre in Western India

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ABSTRACT

Axillary lymph-node (ALN) involvement is an important prognostic factor in patients with breast carcinoma. Evaluation of Sentinel Lymph-nodes (SLN) is an accurate procedure for its assessment in the clinically node negative cases. Frozen Section Evaluation (FSE) is more widely used for intra operative evaluation of SLNs. Our study aimed to assess the sensitivity, specificity and accuracy of FSE of SLN and to compare SLN positivity with other clinico-pathological parameters. All breast carcinoma cases having FSE of SLNs were studied for a duration of two years and were compared with permanent sections. SLN positivity was also compared with other clinico-pathological parameters. A total of 281 cases were evaluated. 88 cases were positive in FSE while 92 cases were positive in permanent sections (one false-positive and five false-negatives) with sensitivity, specificity and accuracy of 94.57%, 99.47% and 97.86% respectively. SLN positivity was significantly less in T1 tumors (17.7%; p-0.005), grade I tumors (17%; p-0.040) and in triple negative tumors (15%; p-0.041). In SLN positive cases, T1 tumors showed lesser additional ALN positivity (11.11%) comparing higher T stage tumors (35.71%). FSE of SLNs in breast carcinoma has high sensitivity and accuracy. Even though Micro metastasis and ITCs are the main source of false negative rate, they do not carry much prognostic significance. SLN positivity is significantly less in T1 tumors, grade I tumors and triple negative tumors. T1 tumors with positive SLNs showed lesser additional axillary lymph-node positivity questioning their requirement for further axillary dissection.

1. Introduction

The status of axillary lymph-node (ALN) is a very important prognostic factor and determinant for treatment in patients with breast carcinoma. Axillary Lymph-Node Dissection (ALND) has been adopted as a standard procedure to determine the status of lymph-node, but is associated with significant morbidity.[1] The sentinel lymph-node (SLN) dissection which is defined as the dissection of the first echelon node or nodes receiving lymphatic drainage from the primary lesion has proven to be minimally invasive and its evaluation is an accurate procedure to assess the axillary involvement by metastasis in clinically node negative breast carcinoma.[2] Numerous studies have proven the reliability of SLN dissection (SLND).[1,3–5]

In clinically node-negative (cN0) axilla, SLND has replaced ALND as an accurate staging procedure in breast cancer patients and also total ALND can be avoided in patients with negative SLNs.[4] Evaluating sentinel lymph-nodes intra operatively avoids the need for re-surgery. Several methods for intraoperative evaluation of SLNs have been described which includes Frozen Section Evaluation (FSE), imprint cytology, Immunohistochemistry

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(IHC) stain, serial intraoperative sectioning and rapid molecular technique. FSE is more widely used for this purpose. Freezing introduces artifactual tissue distortion and sectioning of frozen tissue block could potentially lead to the loss of tumor tissue because of which micro metastasis and isolated tumor cells (ITCs) are missed; furthermore, experience of the pathologist plays a very important role in picking up SLN metastasis amidst frozen artifacts. All of these lead to inconsistencies in the SLN diagnosis when results of FSE are compared with permanent sections. The sensitivity of FSE of SLNs in literature is variable ranging from 44 to 94% while the false negative rate has also been highly variable, ranging from 5.5 to 56%.[1,5,6] Even then, frozen section is often the preferred method for intraoperative evaluation of SLNs. FSE of SLNs is used to take immediate intra-operative decision and while ALND is routinely done for all patients with positive SLN having macro metastasis, the significance of the presence of occult metastases (micro metastasis and ITCs) in SLNs and its relationship with prognosis and survival has been assessed by various studies.[7–9] The requirement of ALND with respect to size of the primary tumor in positive SLN cases have also been evaluated.[10,11]

2. Aims

To estimate the sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of FSE of SLN and to compare SLN positivity with tumor stage, histological type, grade, hormonal and HER 2-receptor status

3. Materials and Methods

Ours was a retrospective study conducted at a tertiary care center in west India where all the breast carcinoma cases with FSE of SLNs between January 2018 and February 2020 were studied. All breast carcinoma patients with no clinically hard, palpable nodes (cN0) or clinic-radiologically suspicious axillary lymph nodes which were negative on Fine needle aspiration cytology (FNAC) underwent SLND.

SLNs were identified using a combination of both radioactive colloid and methylene blue dye method. In radioactive colloid method, 1millilitre (ml) radioactive sulphur colloid labelled with Technicium-99 (Tc99) was injected in peri-areolar or peri-tumoral region 1 day or 2 hours before surgery. During surgery, gamma probe was used to identify radioactive lymph-nodes (LNs). In methylene blue dye method, 4-5ml of methylene blue was injected in the peri-areolar region 10-15 minutes before surgery. During surgery, the lymphatics were traced to identify blue LNs. On some occasions, any one of the either method was used. Apart from these, any palpable suspicious axillary lymph nodes (ALNs) were also dissected intraoperatively. SLNs found by above mentioned methods were sent for FSE.

Guidelines recommended by the College of American Pathologists (CAP) were used for pathological intraoperative FSE of SLNs. Two millimeter (mm) thin multiple slices were obtained by bisecting the nodes along the long axis.

Imprint cytology of each slice and sections taken from each block were stained with Hematoxylin and Eosin (H&E) and examined by an onco-pathologist and reported accordingly with imprint cytology correlation. Multiple sections were evaluated wherever necessary. The whole procedure took around 20 minutes. Cases reported as positive SLNs on FSE further underwent ALND. The remaining frozen tissue along with further surgical specimen (Breast conservative Surgery/ mastectomy with or without ALND) received were fixed in formalin, grossed and processed according to standard protocol. The SLNs were later reviewed using permanent sections stained with H&E. Sensitivity, specificity, PPV, NPV and accuracy were calculated for FSE of SLNs taking permanent sections as the standard. For statistical evaluation, Isolated Tumor Cells (ITCs) were also considered as positive. Also SLN status in permanent sections were compared with T staging, tumor grade, hormone receptor and HER 2 receptor status. Among cases with positive sentinel lymph-nodes, T stage was compared with number of additional positive axillary lymph-nodes. Chi-square test was done to assess the significance and p value < 0.05 was considered as significant.

4. Results

A total of 281 patients underwent SLND and FSE for breast carcinomas during the study period from whom a total of 1057 lymph-nodes were dissected. The number of SLNs varied from 1 to 8 in each case with a median of 3 SLNs per case. Median and mean age of patients who underwent SLN dissection were 52 and 52.70 years respectively (Range: 24-82 years).

Among the 281 cases, 88 were positive on frozen section evaluation (FSE) while 92 were positive on permanent section evaluation (including ITCs). One case was false positive and five cases were false negative in FSE. Sensitivity, specificity, PPV, NPV and accuracy for FSE evaluation of SLNs for cases were 94.57%, 99.47%, 98.86%, 97.41% and 97.86% respectively (Table 1). Five false negative cases in FSE included two cases each of micro-metastasis (mi), Isolated Tumor Cells (ITCs) and one case of macro-metastasis

From these 281 cases, a total of 1057 SLNs were examined. Among them, 136 were reported as positive in FSE and 139 were given as positive in permanent section evaluation of SLNs. 5 LNs were false negative and 2 LNs were false positive in FSE. Sensitivity, specificity,

Table 1: Frozen and permanent section findings in total cases

Cases	Permanent Positive	Permanent Negative	Total
Frozen positive	87	1	88
Frozen Negative	5	188	193
Total	92	189	281
Sensitivity -94.57%		False Negative rate-5.43%	
Specificity-99.47%		Positive Predictive Value - 98.86%	
Accuracy-97.86%		Negative Predictive Value - 97.41%	

PPV, NPV and accuracy of FSE on SLN for total lymph nodes were 96.40%, 99.78%, 98.53%, 99.46% and 99.34% respectively. (Table 2)

Table 2: Frozen and permanent section findings in total lymph-nodes

Lymph nodes	Permanent Positive	Permanent Negative	Total
Frozen positive	134	2	136
Frozen Negative	5	916	921
Total	139	918	1057
Sensitivity-96.40%		False Negative rate-4.40%	
Specificity-99.78%		Positive Predictive Value - 98.53%	
Accuracy-99.34%		Negative Predictive Value – 99.46%	

Among the FSE positive SLNs (88 cases) after excluding 9 post lumpectomy cases in which T staging cannot be done, T1 tumors (9 cases) had comparatively less mean positive additional ALNs (0.33) than tumors having T stage greater than T1 (70 cases) (1.46) (p-0.351). Additional ALN positivity was seen only in one of the nine T1 tumors (11.11%), while 25 out of 70 cases (35.71%) with T stage greater than T1 showed additional axillary lymph node positivity (p-0.134). But this difference was not statistically significant.

Out of the total 281 cases, majority (247 cases) were Invasive Breast Carcinoma-no special type (IBC- NST). 34 cases had other specific diagnosis with varying SLN positivity. (Table 3).

After excluding post lumpectomy specimens with no residual tumor, there were a total of 254 breast carcinomas. Among them, SLN positivity was 17% in T1 stage cases while it was 37% in higher T stage cases (p-0.005) (Table 4). Among 281 IBC cases, 35 were grade I, 131 were grade II and 115 were grade III and their SLN positivity were 17%, 38% and 30% respectively (p-0.040). (Table 6)

Based on IHC - hormonal and Her2 receptor status on primary tumor, these cases were classified into 4 groups as only Hormone receptor (HR) positive (Estrogen Receptor (ER) and/or Progesterone Receptor (PR) positive), both HR and HER 2 positive, HR negative and HER2 receptor positive or Triple negative. After excluding equivocal Her2 cases (26 cases) and cases in which IHC was not done (11 cases), SLN positivity in triple negative, only HR positive, both HR and HER 2 positive and only Her2 positive were 15%, 34.78%, 36.67% and 44.83% respectively. (Table 6)

Table 3: Special types of breast carcinoma

Types	Total no. of cases	No. of SLN Positive cases (%)
Invasive Breast carcinoma-NST	247	87(35.2%)
Adenoid cystic carcinoma	1	0(0%)
Cribriform and tubular carcinoma	1	0(0%)
Carcinoma with apocrine differentiation	1	1(100%)
Invasive carcinoma with medullary like features	2	1(50%)
Invasive papillary carcinoma	5	0(0%)
Lobular carcinoma	12	2(16.6%)
Mucinous carcinoma	5	0(0%)
Metaplastic carcinoma	2	0(0%)
Solid papillary carcinoma	3	0(0%)
Solid papillary and mucinous carcinoma	1	0(0%
Tubular carcinoma	1	1(100%)
Total	281	92(32.7%)

Table 4: T stage with SLN positivity

Stage	Total	Positive SLN
T1	62	11(17%)
>T1	192	71(37%)
Total	254	82(32%)
SLN- Sentinel Lymph-node		

Table 5: Grade with SLN positivity

SLN status		Positive	Total
Grade	1	6	35(17%)
	2	51	131(38%)
	3	35	115(30%)
Total		92	281

Table 6: Hormonal receptor and Her 2 status in breast carcinoma with SLN positivity

Hormonal Receptor and Her 2 status	SLN Positivity	Total
HR + and Her2 +	22/60(36.67%)	60
HR +and Her2 -	40/115(34.78%)	115
HR- and Her2 +	13/29(44.83%)	29
Triple negative	6/40(15%)	40
Total	81	244

5. Discussion

5.1. Methods of intraoperative sentinel lymph-node evaluation

Intraoperative evaluation of SLNs allows immediate axillary dissection in patients with metastatic disease avoiding the need for another surgery and also prevents axillary dissection in sentinel lymph nodes negative patients. Hence, the intraoperative diagnosis of SLNs must be performed with accuracy and efficiency. Several methods of intra operative evaluation have been discussed including FSE, imprint cytology, IHC stain, serial intraoperative sectioning and rapid molecular technique. Imprint cytology technique is faster than FSE and does not cause significant loss of nodal tissue, but it has lesser sensitivity compared to FSE.[2] Veronesi et aldiscussed serial intraoperative sectioning for SLN evaluation and found that it correctly predicts a metastasis-free sentinel node in 95.4% of cases (NPV).[12] Salem et al, in their study used IHC staining of touch imprints of axillary SLNs and concluded that intra-operative IHC is a reliable method for evaluating axillary nodes with sensitivity of 91.4% and accuracy of 99.3%.[13] Santaballa et al described one step nucleic acid amplification molecular assay for intraoperative evaluation of SLNs measuring cytokeratin 19 mRNA in homogenized SLN tissue and showed high sensitivity for detection of metastasis.[14] Even though all these are appealing with increased identification of micro metastasis and ITCs, it is not practical to implement due to man power and financial constraints in most centers in India

FSE is still a reliable and preferred method for intra operative evaluation of SLNs. Among FSE, lymph-nodes are one of the more frequent tissues for a discordant diagnosis(10%) following skin (17.1%) and breast (16%).[15] The possible sources of discrepancy include technical issues (including cauterization during surgery, over freezing, mounting and processing artifacts during processing), sampling error (where the lesion is present on permanents of the frozen block or in fresh block from left over frozen tissue, but was not present in the actual cryostat).and finally diagnostic error (where disease process is missed in which the experience of the pathologist comes to play).[15,16] The sensitivity of intraoperative evaluation in the literature is variable ranging from 44 to 94% with false negative rate ranging from 5.5 to 54%.[1,3–5] This large variation is probably due to different histopathological techniques used, the number of serial sections taken and the use of immunohistochemistry.

In our study, FSE of SLNs had a higher sensitivity (94.57%), specificity (99.47%), PPV (98.86%), NPV (97.41%) comparing other studies with a false negative rate of 5.43% and an accuracy of 97.86%. Systemic grossing of each SLNs with 2mm thin slices, imprint cytology of each slice and detailed microscopic examination with multiple serial sections whenever required have contributed to higher sensitivity, specificity and accuracy compared to other studies.[1,3–5] Also, ours being a tertiary care centre, majority of the patients present with advanced disease with larger tumor increasing the chance of macrometastasis[17] contributing to the higher PPV in our study.

5.2. False negatives

Our study revealed 5 false negatives out of which 1 was macro-metastasis, 2 were micro-metastasis (Figure 1) and 2 were ITCs (Figure 2). The macro-metastasis (one case) which was evident on permanent section was not picked up in the initial FSE; while re-evaluation of FS revealed the presence of tumor cells which apparently got missed due to the folds in the section (Figure 3). This highlights the importance of taking proper sections for FSE and trimming of the excess fat present around the lymph-nodes while grossing which can cause difficulty while sectioning causing problems during interpretation. Also experience of the pathologist in reporting FS is vital in picking up small foci of tumor cells amidst frozen artifacts. These results suggest that intra operative FS technique is highly accurate for detecting macro metastasis but the sensitivity reduces in detecting micro metastasis and ITCs.

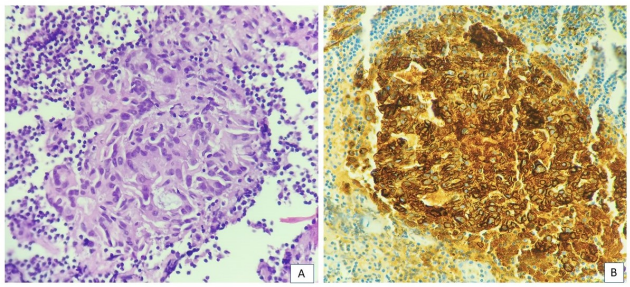

Fig. 1: A: Sentinel lymph node showing micrometastasis with focal glandular pattern in permanent section (40X) (H and E); **B:** IHC shows AE1 positivity (400x)

5.3. Significance of micro metastasis and ITCs

The micro-metastasis and ITCs (2 cases each) that were not picked up on FSE, were identified in permanent sections (deeper levels). Guidelines suggest that while grossing SLN

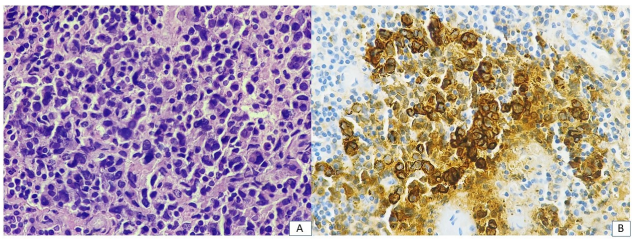

Fig. 2: A: Sentinel lymph node showing isolated tumorcells (ITCs) having hyperchromatic nuceli in permanent section (40X) (H and E); **B:** IHC shows AE1 positivity(400x)

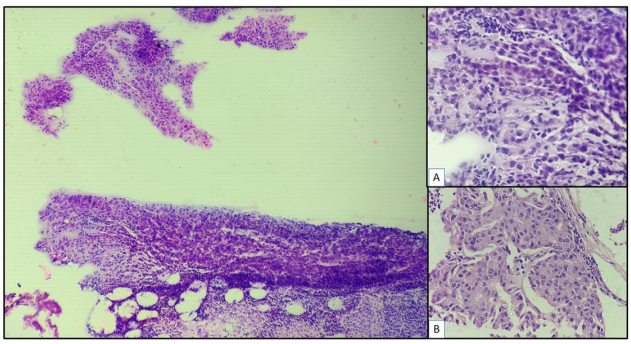

Fig. 3: Tumor cells hid between folds in frozen section (100X) which was apparent in subsequent permanent sections (Inset A-frozen section; Inset B- permanent section) (400X) (H and E)

for FSE, it is vital to take 2mm thin slices of each LNs and examining each of these sections to avoid missing any macro-metastasis.[18] This standard method has the disadvantage of missing micro metastasis and ITC as by definition they are < 2mm.[6]

Various studies have been done to find out the clinical significance of micro-metastasis and isolated tumor cells (ITCs). In a 23-01 trial done by The International Breast Carcinoma Study Group (IBCSG) on T1 and T2 patients with 1 or more micro metastasis(<2mm), metastatic carcinoma was identified in non-SLNs in 13% of patients who underwent ALND, but there was no significant difference in Disease Free Survival(DFS) between patients with and without ALND at a median follow-up of 5 years.[9]

National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) national cancer database did an analysis of population-based data and went on to conclude that there is very little expected detrimental impact associated with the presence of micro-metastasis and ITCs in axillary lymph nodes.[7]

A trial by The National Surgical Adjuvant Breast and Bowel Project B-32 (NSABP B-32) found out that there was no significant difference in Overall Survival (OS) (94.6% vs. 95.8%), DFS (86.4% vs. 89.2%) and distant disease free interval (89.7% vs. 92.5%) going on to conclude that the use of enhanced pathology techniques to identify micro-metastasis and ITCs in initially negative SLNs does not appear to translate into additional clinical benefit.[8] So even though the use of serial intraoperative sectioning and IHC increases the chances of finding ITCs and micro metastasis in SLNs, identifying them does not have much prognostic and therapeutic significance. All these observations support the recommendations by CAP, The American Society of Clinical Oncology (ASCO) and National Comprehensive Carcinoma Network (NCCN); none of them recommend the use of routine multistep level sections and/or CK-IHC in the histologic evaluation of SLNs for identifying micrometastasis and ITCs.[6]

5.4. False positives

In our study we had one false positive case and two false positive lymph-nodes and the specificity of FSE of SLNs for cases and lymph-nodes were 99.47% and 99.78% respectively.

One of the false positive LN had a single cluster of 10-15 cells in the sinusoidal region which were large having moderate cytoplasm, vesicular nuclei and prominent nucleoli and was interpreted as ITCs on FSE (Figure 4). However, permanent sections taken after further trimming of the corresponding FS did not reveal the presence of ITCs due to its exhaustion in deeper cuts. Since permanent sections are considered as gold standard, this case was considered as false positive as there was no way to confirm the ITC.

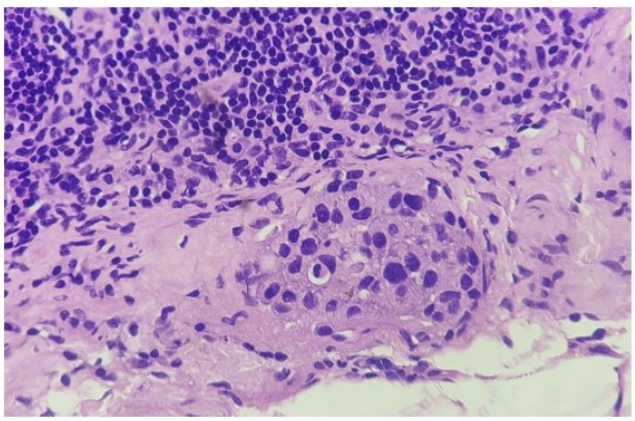

Fig. 4: Frozen section showing ITCs which got exhausted in subsequent permanent section (400X) (H and E)

The other false positive LN on initial FSE showed an apparent glandular pattern of atypical cells with moderate cytoplasm and vesicular nuclei which on permanent section turned out to be an aggregate of histiocytes (Figure 5). This emphasizes the importance of experience of the pathologist in assessing individual cyto-morphology in addition to the architectural pattern amidst frozen tissue artifacts. But in this case, there was another SLN which was frank positive

on both FSE and permanent sections because of which there was no discrepancy in further management.

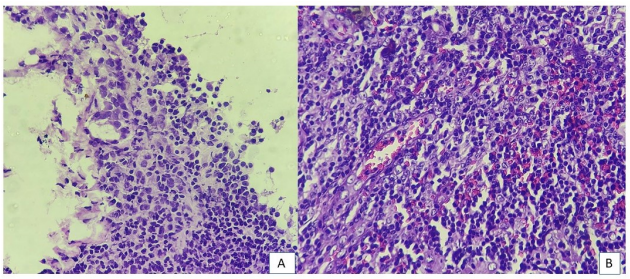

Fig. 5: A: Frozen section showing pseudo glandular pattern (Arrow) formed by histiocytes which was seen in permanent section (**B**) (400X) (H and E)

5.5. Comparison of additional axillary LN status with T stage in positive SLN cases

The American College of Surgeons Oncology Group (ACOSOG) Z0011 prospective randomized trial compared two randomly assigned groups of ALND and no further axillary treatment in T1 or T2 cN0 patients with 1 or 2 positive sentinel LNs and found no significant difference in OS and DFS and axillary recurrence rate. [11,19,20] Similarly The AMAROS (After Mapping of the Axilla: Radiotherapy or Surgery?) trial found out that in patients with T1 or T2 breast carcinoma and with 1 or 2 sentinel lymph-node positivity, there was no significant difference between patients undergoing only axillary radiotherapy or only ALND in DFS, OS and recurrence which was low in both the groups. [10,20]

In our study, on assessing the additional axillary lymph-node status of FSE positive SLNs, we found out that among the FSE positive SLNs, additional axillary lymph-node positivity was 11.11%(1/9 cases) and mean number of additional positive axillary lymph-nodes were 0.33 in T1 stage tumors while in tumors with T stage greater than T1, additional axillary lymph-node positivity was 35.71% (25/70 cases) and mean number of additional positive axillary lymph-nodes was 1.46. Even though this was not statistically significant (p-0.134), additional axillary lymph-node positivity was comparatively less in T1 tumors.

Even though ACOSOG Z0011 trial and AMAROS trial have documented the differences in axillary LN positivity and follow-up with or without axillary nodal dissection in T1 or T2 cN0 patients, [10,19] our study have explored SLN positivity, additional axillary LN positivity and their differences based on T stage in Indian population which to the best of our knowledge was not analyzed and documented before.

5.6. Comparison of SLN status with histologic type, T stage, grade, and hormonal and HER 2 receptor subtypes

Among histologic types, maximum axillary lymph-node positivity was recorded in Invasive breast carcinoma- No special type (IBC-NST) which was 35.2% (87/247 cases). Our study showed a positivity of 16.6% (2 cases; both - T2) in 12 cases of lobular carcinoma. In literature, invasive lobular carcinomas have 3-10% of axillary lymph-node metastasis. [21] None of the invasive papillary(5 cases), mucinous carcinomas(5 cases), metaplastic carcinomas(2 cases) and solid papillary carcinoma(3 cases) showed SLN positivity irrespective of their T stage which correlates with their overall better prognosis. [21]

Comparing Axillary lymph-node status with T stage and histologic grade. [17,22] A study done by Mattes et al found that Independent predictors of nodal positivity include tumor size ($p<0.001$) and tumor grade ($p<0.001$). [17] Supporting this, we too found SLNs to be significantly less positive in T1 tumors (11/67 cases) (17.7%) and in grade 1 tumors (6/35 cases) (17%) compared to higher T category (71/192) (36.9%) (p-0.005) and higher grades of IBC (p-0.040) indicating that both increasing tumor size and tumor grade are positively associated with SLN positivity.

The impact of hormonal and HER 2-receptor status of breast carcinoma on lymph-node metastasis is not well studied. In the study done by Mattes et al, Triple-negative cancers had a significantly lower nodal positivity than the HR+/HER2- subtype (odds ratio, 0.686; p-0.004). [17] Similarly in our study, Triple negative breast cancers had significantly less SLN positivity (15%) compared to other groups (p value of 0.041).

6. Conclusion

To the best of our knowledge, ours is the largest study in Indian population to have compared FSE of SLNs in invasive carcinoma of breast with permanent sections; The study has also analyzed axillary lymph-node positivity with respect to tumor stage, histological type, grade, hormonal and HER 2-receptor status and additional axillary LN positivity with respect to T stage which was not done in such a large scale in Indian population.

Our study concludes that FSE of SLNs in breast carcinoma is a highly reliable procedure showing high sensitivity, accuracy and low false negative rate when systemic grossing and microscopic examination are instilled and even though micro metastasis and ITCs are the main source of false negative rate, they do not carry much prognostic significance and do not require further ALND.

7. Source of Funding

None.

8. Conflict of Interest

The authors declare no conflict of interest.

References

1. Somashekhar SP, Naikoo ZA, Zaveri SS, Holla S, Chandra S, Mishra S, et al. Intraoperative Frozen Section Evaluation of Sentinel Lymph Nodes in Breast Carcinoma: Single-Institution Indian Experience. *Indian J Surg*. 2015;77(2):335–40.
2. Safai A, Razeghi A, Monabati A, Azarpira N, Talei A. Comparing Touch Imprint Cytology, Frozen Section Analysis, and Cytokeratin Immunostaining for Intraoperative Evaluation of Axillary Sentinel Lymph Nodes in Breast Cancer. *Indian J Pathol Microbiol*. 2012;55(2):183–6.
3. Veronesi U, Paganelli G, Viale G, Luini A, Zurrida S, Galimberti V, et al. A Randomized Comparison of Sentinel-Node Biopsy with Routine Axillary Dissection in Breast Cancer. *N Engl J Med*. 2003;349(6):546–53.
4. Veronesi U, Paganelli G, Viale G, Luini A, Zurrida S, Galimberti V, et al. Sentinel-Lymph-Node Biopsy as a Staging Procedure in Breast Cancer: Update of a Randomised Controlled Study. *Lancet Oncol*. 2006;7(12):983–990.
5. Wada N, Imoto S, Hasebe T, Ochiai A, Ebihara S, Moriyama N. Evaluation of Intraoperative Frozen Section Diagnosis of Sentinel Lymph Nodes in Breast Cancer. *Jpn J Clin Oncol*. 2004;34(3):113–117.
6. Maguire A, Brogi E. Sentinel Lymph Nodes for Breast Carcinoma: An Update on Current Practice. *Histopathology*. 2016;68(1):152–167.
7. Chen SL, Hoehne FM, Giuliano AE. The Prognostic Significance of Micrometastases in Breast Cancer: A SEER Population-Based Analysis. *Ann Surg Oncol*. 2007;14(12):3378–3384.
8. Krag DN, Anderson SJ, Julian TB, Brown AM, Harlow SP, Costantino JP, et al. Sentinel-Lymph-Node Resection Compared with Conventional Axillary-Lymph-Node Dissection in Clinically Node-Negative Patients with Breast Cancer: Overall Survival Findings from the NSABP B-32 Randomised Phase 3 Trial. *Lancet Oncol*. 2010;11(10):927–33.
9. Galimberti V, Cole BF, Zurrida S, Viale G, Luini A, Veronesi P, et al. International Breast Cancer Study Group Trial 23-01 investigators. Axillary Dissection versus No Axillary Dissection in Patients with Sentinel-Node Micrometastases (IBCSG 23-01): A Phase 3 Randomised Controlled Trial. *Lancet Oncol*. 2013;14(4):297–305.
10. Donker M, Tienhoven GV, Straver ME, Meijnen P, Velde CJHVD, Mansel RE, et al. Radiotherapy or Surgery of the Axilla after a Positive Sentinel Node in Breast Cancer (EORTC 10981-22023 AMAROS):A Randomised, Multicentre, Open-Label, Phase 3 Non-Inferiority Trial. *Lancet Oncol*. 2014;15(12):70460–70467.
11. Giuliano AE, Mccall L, Beitsch P, Whitworth PW, Blumencranz P, Leitch AM, et al. Locoregional Recurrence after Sentinel Lymph Node Dissection with or without Axillary Dissection in Patients with Sentinel Lymph Node Metastases: The American College of Surgeons Oncology Group Z0011 Randomized Trial. *Ann Surg*;2010(3):426–432.
12. Veronesi U, Zurrida S, Mazzarol G, Viale G. Extensive Frozen Section Examination of Axillary Sentinel Nodes to Determine Selective Axillary Dissection. *World J Surg*. 2001;25(6):806–808.
13. Salem A, Douglas-Jones AG, Sweetland HM, Mansel R. Intraoperative evaluation of axillary sentinel lymph nodes using touch imprint cytology and immunohistochemistry. Part II. Results. *Euro J Surg Oncol Br Assoc*. 2006;32(5):484–7.
14. Santaballa A, Cueva HL, Salvador C, García-Martínez AM, Guarín MJ, Lorente D, et al. Advantages of one step nucleic acid amplification (OSNA) whole node assay in sentinel lymph node (SLN) analysis in breast cancer. *Springerplus*. 2013;2:542. doi:10.1186/2193-1801-2-542.
15. Biopsy Interpretation. In: The Frozen Section. Philadelphia: Wolters Kluwer; 2013.
16. Desciak EB, Maloney ME. Artifacts in Frozen Section Preparation. *Dermatol Surg*. 2000;26(5):500–4.
17. Mattes M, Bhatia J, Metzger D, Ashamalla H, Katsoulakis E. Breast Cancer Subtype as a Predictor of Lymph Node Metastasis According to the SEER Registry. *J Breast Cancer*. 2015;18(2):143–8.
18. Amin MB, Edge S, Greene F, Byrd DR, Brookland RK, Washington MK, editors. AJCC Cancer Staging Manual. 8th ed. Cham: Springer International Publishing; 2017.
19. Giuliano AE, Hunt KK, Ballman KV, Beitsch PD, Whitworth PW, Blumencranz PW, et al. Axillary Dissection vs No Axillary Dissection in Women with Invasive Breast Cancer and Sentinel Node Metastasis: A Randomized Clinical Trial. *JAMA*. 2011;305(6):569–75.
20. Zahoor S, Haji A, Battoo A, Qurieshi M, Mir W, Shah M. Sentinel Lymph Node Biopsy in Breast Cancer: A Clinical Review and Update. *J Breast Cancer*. 2017;20(3):217–27.
21. WHO Classification of Tumours of the Breast. 5th ed. IARC; 2019.
22. Oluogun WA, Adedokun KA, Oyenike MA, Adeyeba OA. Histological Classification, Grading, Staging, and Prognostic Indexing of Female Breast Cancer in an African Population: A 10-Year Retrospective Study. *Int J Health Sci (Qassim)*. 2019;13(4):3–9.

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