

Diagnosis of Breast Lesions on Frozen Section and it's Cyto- Histopathological Correlation in Jharkhand**Jitendra Singh¹, Amit Vikram Prasad², Kumudini Sardar³, Mukesh Chandra Das⁴**¹Assistant Professor, Blood Bank, Medinirai Medical College and Hospital, Palamu, Jharkhand, India²Assistant Professor, Department of Surgery, Medinirai Medical College and Hospital, Palamu, Jharkhand, India³Medical Officer, Jharkhand, India⁴Assistant Professor, Department of Pharmacology, Medinirai Medical College and Hospital, Palamu, Jharkhand, India

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Corresponding Author: Amit Vikram Prasad

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Abstract:

Introduction: The most common malignant tumour in women is breast cancer. Early breast abnormalities, including cancer, may be curable if properly controlled in the period of breast conservative therapy. For this, various diagnostic techniques are employed. Although aspiration cytology's widespread use, perioperative imprint cytology (IC) and frozen section (FS) are still useful for determining the boundaries of lumpectomies and the nodal status during surgery, as well as when the outcomes of cytological or biopsy cores are unclear. Both IC and FS are reliable intra-operative diagnostic consultation techniques that provide accurate results quickly, enabling the formulation of informed therapy decisions.

Materials and Method: This two-year prospective study was carried out in the Medinirai Medical College and Hospital, Palamu. A total of 63 surgically removed breast specimen cases were examined for IC, FS, and connection with HP diagnostic characteristics. Following the description of the gross features, a representative tissue piece was extracted, followed by the creation of three imprint smears, FS, and regular HP processing. Slides generated by IC and FS were analysed and afterwards connected with the diagnosis of HP.

Results: 33 (52.33%) of the 63 cases were cancerous, whereas 29 (46.03%) were harmless. The sensitivity, specificity, and precision of the IC were 100%, 96.43%, and 98.36% respectively, while those of the FS were 100%, 96.55%, and 98.39%. Both had p-values of 0.001, demonstrating a meaningful association with the HP research.

Conclusions: Where services for FS are unavailable, IC offers a quick, easy, precise, and affordable intra-operative diagnostic technique. It keeps every fine cellular and nuclear distinction. The architecture of FS tissue is very similar to that of permanent HP sections, but freezing artefact is commonly a problem. However, FS can tell harmless breast lesions from cancer in situ and infiltrative lesions. Because IC and FS together provide a more accurate diagnosis, it is always beneficial to prepare both slides during surgery. The gold standard for making a final diagnosis of any breast lesion is still the HP study. An crucial component of surgical pathology's quality control activity is the connection of intraoperative IC and FS diagnoses with the final HP diagnostic.

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Introduction

More than 10 million cases of breast cancer are diagnosed worldwide each year, making it the leading cause of death for women [1, 2]. Breast conservative surgery and early diagnosis increase survival rates. Although advances in imaging technology, the use of IC and FS investigation has been made possible by the requirement for intraoperative consultation of the breast cancer. As a result, the pathologist is essential in the treatment of this illness [2, 3]. Surgery is necessary if there are positive margins in early breast cancer when excision biopsy or lumpectomy is performed without margin assessment.

Breast cancer makes decisions about treatment more difficult and raises anxiety levels as well as concerns about appearance, the loss of a feminine symbol, and cancer-related mortality fears. [4] Apart from clinical inspection, numerous other diagnostic techniques for breast lesions have evolved as a result of this. [4]

1. FNAC
2. Mammography,
3. The freezer
4. Excisional biopsy in tumours less than 2 cm
5. Incisional biopsy for substantial tumours
6. Impedance cytology,
7. Core needle biopsy.

FNAC, despite not being totally specific, is a valuable resource for patients with breast tumours. In particular, it is helpful in designing a surgical approach to the lesion and confidently permits the exclusion of breast cancer and other more prevalent diseases [5]. It is the most typical diagnostic technique for breast lumps that may be felt [6]. The FNAC method has good sensitivity and specificity and is easy, safe, and rapid [7, 8]. Up to 96% of breast cancer diagnoses by FNAC are accurate [9, 10].

FNAC is a difficult diagnostic procedure that is carried out prior to surgery, and studies have shown that it is effective. Another diagnostic procedure that is frequently carried out during surgery and is likewise regarded as a therapeutic process of decision-making is FS. [11] Another intraoperative diagnostic technique that is thought to be superior to FNAC is IC. [11] Combining IC with FS is advised to improve diagnosis accuracy. [11] Depending on who is assessing the case, a different diagnostic approach is chosen. The goal of the current investigation is to determine the diagnostic precision of frozen sections and imprint cytology (IC), which differs from centre to centre.

In terms of breast oncology, intra-operative frozen section diagnosis has been crucial in helping to choose the best course of treatment [12, 13]. Before undergoing major radical surgery, the two main indications for frozen section are 1) to confirm the diagnosis of carcinoma in cases where FNAC or core needle biopsies have yielded inconclusive results, and 2) to assess the resection margins and completeness of excision in carcinoma [14, 15].

Materials and Methods

Study Design: A prospective study was carried out for two years and comprised all cases clinically presenting with lesions of the breast sent to the Medinirai Medical College and Hospital, Palamu for FNAC, frozen section, and histological assessment.

Data Collection and Analysis: The FNAC technique was carried out according to the accepted protocol and in accordance with international best practises [16]. The study only covered diagnosed instances. Cases that did not have surgery or lacked appropriate patient information were not included in the study. According to Boerner S et al., aspirates were categorised as adequate if there were six or more epithelial cell clusters overall, each cluster containing at least five to ten excellently preserved cells, or as insufficient if there were fewer than six epithelial cell clusters [17].

1. Malignant
2. Unsatisfactory
3. Suspicious of malignancy
4. Atypia probably benign

All breast samples that were taken directly from the operating room in normal saline (0.9%) solution before being fixed in formalin were subjected to frozen section. After that, they were processed for H&E staining for histological inspection and fixed in 10% formalin for 24 hours.

Results:

63 cases in the current study had a history of breast lumps. All of these cases underwent FNAC following a comprehensive clinical assessment. All cases involved intraoperative frozen sections, after which the tissues were transferred for sections of paraffin. Finally, using wax section as the standard of excellence, a link between frozen section and FNAC was established.

No case of a male patient was discovered in the current study's cases, which all involved female patients. 21 cases, or 33.33% of the total, of breast lesions were discovered in people between the ages of 41-50. Following this, there were 14 instances (22.22%) in the 31-40 year period and 12 cases (19.04%) in the 21-30 year period. 7 instances (11.11%) were found in the age group of 11 to 10 years, while 6 cases (9.52%) were found in the age group of 51 to 60 years. The age ranges of 61-70 years and those over 70 years each had only 3 cases (4.76%). In the age range of 0 to 10 years, no lesions were discovered.

Lumps of the breast occurred more frequently on the left side (56.71% of instances), while the opposite side was affected in 43.29% of cases. When looking at the breast quadrants afflicted, the upper outer quadrant had 41% of the cases and the lower inner quadrant had just 8.14% of the cases. The patient with the breast lesion was 15 years old at the youngest point in time and 71 years old at the oldest. The diagnosis of fibroadenoma was later confirmed by frozen and paraffin sections in the youngest instance, a 15-year-old.

Out of the entire 63 cases, 28 (44.44%) were benign lesions and 35 (55.55%) were malignant according to FNAC. Fibroadenoma (14 cases) was the most prevalent among the 28 benign lesions (C2, C3) in this study, followed by fibrocystic disease (6 cases), epithelial hyperplasia (4 cases), benign phyllodes (2 case), and granulomatous mastitis (2 case). The most frequent malignant breast lesions were infiltrating duct carcinoma (27 cases), followed by malignant phyllodes (2 case). 6 instances (17.14%) had a few clusters of abnormal cells and were thought to be malignant.

One fibroadenoma instance in our investigation exhibited an insufficient smear pattern on aspiration for the first time. On a later aspiration, however, the smear displayed characteristics indicative of a fibroadenoma. This resulted from a needle aspiration

from an unrepresentative spot and the tumor's reduced size.

Out of the entire 63 cases after frozen section, 28 cases (44.44%) were harmless and 35 instances (55.55%) were malignant. The 28 harmless lesions included in this study were fibroadenoma (13 instances), fibrocystic disease (8 cases), epithelial hyperplasia (3 cases), benign phyllodes (2 case), and granulomatous mastitis (2 case). The most frequent malignant breast lesions were infiltrating duct carcinoma (35 instances), infiltrating lobular carcinoma (2 case), and malignant phyllodes (5.71%), in that order. No cases were put on hold.

37 cases of breast cancer were observed in this study's 63 cases, according to the histopathological findings. The most frequent type of breast cancer among them, accounting for 92.74% of cases, was infiltrating duct carcinoma, followed by infiltrating lobular carcinoma and malignant phyllodes with 3.63% and 3.63% of cases, respectively. One case of cancerous phyllodes was identified in the current study in a patient who was 49 years old.

In one FNAC tests, there was a false positive result that showed a few clusters of atypical cells and was labelled as possibly malignant. Two cases of in-situ ductal carcinoma and one case of invasive lobular carcinoma were the three erroneous negative diagnoses made by FNAC. On FNAC, one instance of DCIS was incorrectly identified as atypical ductal hyperplasia. The patient had a frozen section done during surgery and a carcinoma of the ducts in-situ diagnosis was performed. After a straightforward a mastectomy, the tissue went out for biopsy. The biopsy result later revealed DCIS. unusually ductal hyperplasia was the cause of the second false negative case discovered by FNAC. Despite doing an intraoperative frozen section, the incorrect diagnosis of atypical ductal hyperplasia was established. The

tissue was sent for permanent section after the patient had a lumpectomy. The diagnosis of DCIS was made after a biopsy.

An incurable carcinoma of the lobes was the FNAC's third incorrect diagnosis. Smear tests from the carcinoma of the lobe revealed sporadic bare nuclei with bland shape, harmless epithelium and myoepithelial cell clusters, and a few aberrant, detached cells with intact cytoplasm and nuclear atypia. Small and tightly packed epithelial cells led to the incorrect diagnosis of fibroadenoma. Invasive lobular cancer was identified during an intraoperative frozen sections. Finally, the biopsy of the tissue verified the diagnosis of a frozen portion.

In our investigation, out of 63 cases, three fine needle aspiration cytology diagnoses were falsely negative and one was falsely positive. After statistical analysis, the sensitivity was determined to be 93.11%, the specificity to be 95.88%, the accuracy to be 97.29%, the positive predictive value to be 96.22%, and the negative predictive value to be 91.18%. The current investigation did not identify any frozen section false positive diagnoses.

In the current study on frozen sections, an intraductal carcinoma misdiagnosed as atypical ductal hyperplasia was the lone false negative item. It is characterised as an intraluminal lesion that exhibits some, but not all, of the characteristics of ductal carcinoma in-situ. It is not surprising that it may be challenging or impossible to identify atypical ductal hyperplasia from carcinoma of the ducts in-situ cytologically given how challenging it can be to do so histologically. Analysis of the current study showed accuracy rates of 97.57%, false positivity rates of 1%, false negativity rates of 0%, and deferral rates of 1%, all of which were well within the bounds of what has been previously reported in the literature.

Table 1: Prior FNAC diagnosis of breast lesion sent for frozen section (n=63)

FNAC Result	Frequency	Percentage
Benign		
Inflammatory	02	7.14%
Fibroadenoma	14	14.50%
Benign phyllodes	02	7.14%
Fibrocystic disease	06	21.42%
Epithelial hyperplasia	04	14.28%
Total	28	44.44%
Malignant(C4,5)		
Malignant phyllodes	02	5.71%
Ductal carcinoma	27	77.14%
Suspicious for malignancy	06	17.14%
Total	35	55.55%
Inadequate(C1)	0	0
Inadequate smear		
Grand Total	63	100

Table 2: Frozen section diagnosis of the breast lesions(n=63)

FS Dx	Frequency	Percentage
Benign		
Inflammatory	02	7.14%
Fibroadenoma	13	46.42%
Benign phyllodes	02	7.14%
Fibrocystic disease	08	28.57%
Epithelial hyperplasia	03	10.71%
Total	28	44.44%
Malignant		
Malignant phyllodes	02	5.71%
Ductal carcinoma in-situ	01	2.85%
Infiltrating lobular carcinoma	02	5.71%
Infiltrating duct carcinoma	30	85.71%
Total	35	55.55%
Grand Total	63	100

Table 3. FNAC diagnosis in relation to paraffin section diagnosis

Sl.No.	FNAC	Total No.	PSDx		FP	FN	Accuracy
			Benign	Malignant			
01	Malignant	35	02	32	02	00	
02	Benign	28	26	03	00	03	98.69%
	Total	63	28	35	02	03	

Discussion:

Only cancer of the cervical cavity occurs more frequently among females in India than breast carcinoma [16,17]. The majority of breast lesions are benign, according to numerous studies, and merely need comfort [18]. Early detection and diagnosis of breast lesions can help with preventive and precise patient care, reducing the discomfort of patients and worry throughout the process [19,20].

32 cases (45.71%) of benign breast lesions and 38 cases (54.29%) of malignant breast lesions were detected in our study. Niu Yun et al. noted a similar outcome. In 4754 instances (36 percent, 4754/13196), benign breast lesions were discovered, while 8442 cases (64 percent, 8442/13196) had malignant breast lesions [21]. The age range of 21 to 30 years had the most benign breast lesions, with 12 cases (80%), followed by the age range of 31 to 40 years with 10 instances (55.5%). Malignant breast lesions were more prevalent in women aged 41 to 50, with 17 cases (85%) and eight instances (44.4%), respectively.

Breast cancer was most prevalent in the 31–50 age group, followed by 51–65 and 66 years and older, according to Shrestha HG [22]. Breast cancer cases were not found in people under the age of 10 or in those between the ages of 11 and 30. Breast cancer is most frequently diagnosed in women in their middle to late-fifties, according to Rosen PP [23].

According to research by Rakhshindah Bajwa et al., of the 232 cases of benign breast lesions, fibroadenoma accounted for 161 cases (69.39%), followed by fibrocystic disease in 60 cases (25.85%), intraductal cancer in 2 instances (0.86%), and

abnormal ductal hyperplasia in 2 instances (0.86%) [24]. Rosen examined 857 cases of invasive breast cancer and discovered that 75% of cases were ductal carcinoma, 10% were lobular carcinoma, and 9% were medullary carcinoma. There were 32 benign lesions (45.71%) in the current investigation, fibroadenoma. The most prevalent benign lesion, with 18 instances (56.25%), was accompanied by fibrocystic diseases. Epithelial hyperplasia was seen in 9 instances (28.12%), as well as 3 cases (9.37%), 1 case (3.13%) of benign phyllodes, and 1 case (3.13%) of granulomatous mastitis. Invading duct cancer was the most prevalent malignancy among the 38 cases (54.29%) of cancerous breast lesions; it was followed by cancerous phyllodes in 1 instance (2.63%) and invading carcinoma of the lobe in 36 cases (94.74%).

One case of cancerous phyllodes was identified in the current study in a patient who was 48 years old. This is in accordance with the findings of Niu Yun et al., who discovered that borderline and malignant phyllodes usually occur in people aged 40 to 49 [21].

In one FNAC examination, there was a false positive result that showed a few clusters of atypical cells and was labelled as possibly malignant. Following a frozen section and biopsy, "Fibrocystic disease of the breast" was discovered. The overall rate of false positives was less than 1%, whereas the rate of false negatives among 1158 cases was 9%, according to Ariga R et al. [25]. Two (1,7%) false positive and two (1,7%) false negative results were found among 115 patients in the study by Khaky MP [26]. Interpretive mistake was the main contributor to erroneous positive diagnoses, according to Choi YD et al. [27] Due to the wide diversity of breast lesions'

appearances, Pandey JS et al. came to the conclusion that there was a chance of receiving false positive results [28].

Two cases of in-situ ductal carcinoma and one case of invasive lobular carcinoma were the three erroneous negative diagnoses made by FNAC. On FNAC, two instances of DCIS were incorrectly identified as atypical ductal hyperplasia. A invasive lobular carcinoma was the FNAC's third false negative diagnosis. In contrast to the benign clusters of epithelial and myoepithelial cells, the smears from the lobular carcinoma had minimal cellularity with aberrant, dispersed cells that had intact cytoplasm and nuclear atypia. Small and tightly packed epithelial cells led to the incorrect diagnosis of fibroadenoma. Invasive lobular cancer was identified during an intraoperative frozen section. When the tissue was finally sent for a biopsy, it verified the frozen section diagnostic.

In our investigation, out of 70 cases, three fine needle aspiration cytology diagnoses were falsely negative and one was falsely positive. Also, the accuracy is 94.29%, positive predictive value is 97.22%, negative predictive value is 91.18%, sensitivity is 92.11%, and specificity is 96.88%. The degree of sensitivity, specificity, and precision revealed in this study are statistically comparable to those reported in the majority of previous investigations conducted in various regions of the world.

Analysis of the current study's results regarding frozen section indicated accuracy rates of 98.57%, false positivity rates of 0%, false negativity rates of 1%, and deferral rates of 0%, all of which were well within the range stated in the literature.

The following benign lesions were frequently misdiagnosed as malignancies on frozen sections, according to various sources of literature: microglandular adenosis [29], epithelial proliferations [30], sclerosing adenosis [31], radial scar [32], intracystic papilloma [33], juvenile papillomatosis, and fat necrosis.

There were no false positive diagnoses on freezing in the current investigation. In the current study on frozen sections, an intraductal carcinoma misdiagnosed as abnormal ductal proliferation was the lone false negative item.

The list includes the cancerous tumours that are frequently misdiagnosed as harmless (literature study). 19 of the 40 false negatives mentioned in (out of an aggregate of 40) were intraductal carcinomas.

The table emphasises that the two most frequently misdiagnosed lesions on frozen sections are invasive lobular carcinoma and intraductal carcinoma. Pagetoid development in the affected ducts and intracytoplasmic lumina in the cells that proliferate both favour a diagnosis of lobular malignancy [34]. On the other hand, intraductal proliferation of monotonous

cells with hyperchromatic, round or oval nuclei producing regular gaps and rigid geometric structure without swirls or streams supports intraductal cancer [35]. With decreasing lesion size, the likelihood of false negative on frozen tissues rises [33]. because of artificial deformation during freezing and concern over a lack of sufficient tissue for a paraffin slice. Because of this, the Association of Directors of Anatomic Surgical Pathology advises against freezing lesions smaller than 1 cm [36].

Conclusion

To conclude, even if FNAC is becoming more and more common and has undeniable benefits, there are some situations when frozen section is still the best option for a quick diagnosis. When it comes to quickly assessing the resection margins of a lesion and the extent of metastasis in the case of a malignant lesion to guarantee there is no remaining tumour mass, frozen sections play a very important function. The intra operational frozen section is a vital tool for minimising the need for a second operation and may be useful for starting to arrange future care with the patient. Final paraffin section is necessary to accurately reach a definitive diagnosis only in the select few circumstances where frozen section fails to deliver such a diagnosis. Therefore, it is crucial to choose one or more of these techniques wisely for every patient who presents with a worrisome breast mass.

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