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Original Research Article

Role of Frozen Section in Breast Lesions in Correlation with Touch Imprint Cytology and Histopathological Examination in a Tertiary Care Hospital

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Abstract:
Background: A reliable intraoperative pathological diagnosis is necessary before a proper surgery of breast lesions. Frozen section and imprint cytology are two most important techniques used for intraoperative diagnosis of breast lesions. When frozen section and touch imprint cytology are widely used together, the sensitivity, specificity and diagnostic accuracy can be very well increased.
Objectives: This study was conducted in GMKMCH, Salem to evaluate the role of frozen section in diagnosing both benign and malignant breast lesions, to find out the diagnostic accuracy of frozen section in breast lesions by correlating it's findings with those of touch imprint cytology and Histopathological examination.
Materials and Methods: This is a prospective study conducted in the department of pathology in Govt. Mohankumaramangalam medical college, Salem for a period of 2 years from November, 2016 to June 2018 after getting approval from the institutional ethical committee with the inclusion criteria being all patients of both genders of all age groups presenting with breast lesions to the department of surgery and referred to the department of Pathology and exclusion criteria being infective pathology. Both frozen section and touch imprint cytology were done from the breast lesions immediately on the day of surgery. Then the results of both the techniques were correlated with one another keeping paraffin section diagnosis as the gold standard. The data collected were analyzed with IBM.SPSS Statistics software 23.0 Version.
Results: In this study, the sensitivity of touch imprint cytology was 93.1 %, specificity was 100 %, positive predictive value was 100%, negative predictive value was 92.3% and accuracy was 96.55%. and the sensitivity , specificity, positive predictive value and negative predictive value of frozen section were 100 % thus proving frozen section is a better technique than touch imprint cytology.
Conclusion: In this study, although the results of Touch imprint cytology correlates with frozen section and paraffin section in terms of benignity and malignancy, the ability of imprint cytology in diagnosing individual lesions is inferior to that of frozen section study and paraffin section examinations. Though the frozen section study had some limitations, it was proved to be a highly accurate diagnostic modality with an accuracy rate of 100%. Thus a judicious and proper selection of these diagnostic modalities is essential for proper management of the patients.
Keywords: Frozen section, Touch imprint cytology, Breast lesions, Histopathological correlation, Diagnostic accuracy, Positive predictive value (PPV), Negative predictive value (NPV).

Introduction

The female breasts being complex glandular structures are under constant threat of hormones predisposing them to a wide range of pathological conditions. The most common benign lesion of breast is Fibroadenoma accounting for about 68 % of all breast masses and its overall incidence being 2.2% worldwide. According to GLOBOCAN 2018, the most common malignancy in women is Breast cancer with an incidence of 20,88,849 new cases with an age standardized incidence rate of 46.3 per 1,00,000 people. There were 6,26,679 deaths because of breast cancer all over the world, in the year 2018. In India, 1,62,468 women were newly diagnosed with breast cancer and 87,090 women died with breast cancer. India has one of the worst breast cancer survival rates in the world. The marked increase in the rate of breast lesions warrants an early and accurate diagnosis which can reduce the morbidity and mortality of the patients giving them a fair survival rate. FNAC, Core needle biopsy, Intraoperative imprint cytology, frozen section are the pathological investigations used for early diagnosis followed by histopathological examination and confirmatory ancillary tests.

Imprint Cytology and frozen section are the most important modes of intraoperative diagnosis of breast lesions [2,3]. Imprint cytology gives crispy cellular details and the sensitivity, specificity and diagnostic accuracy becomes more if we use it along with the frozen section. For more than 100 years, Frozen section is in practice and the introduction of cryostat in 1960 has made it more popular in recent days for its high reliability and accuracy in making on table diagnosis and quick therapeutic decisions Evaluation of margin and sentinel node status avoids further repeated surgeries thereby reducing intraoperative and postoperative risks, poor cosmetic appearance, financial burden and psychological stress to the patients. This study was therefore conducted in GMKMCH, Salem to evaluate the efficiency of frozen section in comparison with touch imprint Cytology and histopathological examination.

Materials and Methods

This is a prospective study conducted in the department of pathology in Govt. Mohankumaramangalam medical college, Salem for a period of 2 years from November 2016 to June 2018 after getting approval from the institutional ethical committee with the inclusion criteria being all patients of both genders of all age groups presenting with breast lesions to the department of surgery and referred to the department of Pathology and exclusion criteria being infective pathology. For touch imprint cytology and frozen section, fresh specimens were collected on the day of surgery. After getting informed consent and thorough clinical examination.

For touch imprint cytology, fresh specimens collected on the day of surgery were grossed and the cut surface of the lesions were exposed and blot by a clean filter paper and a clean slide was pressed gently against the cut surface of the lesion, fixed with isopropyl alcohol and stained by rapid H&E staining method. The lesions were categorized as inadequate (no epithelial cells), Benign (Cohesive clusters, bimodal population, bare nuclei, small stromal fragments, no atypical features), Suspicious of malignancy (smears are with benign pattern but few cells show high N:C ratio), positive for malignancy (rich in cellularity, nuclear pleomorphism, irregular nuclear membrane, irregular coarse chromatin and necrosis). After taking touch imprint cytology, bits were taken from the representative areas of the lesions and given for the frozen section.

For the frozen section we used Leica CM 1510 Cryostat with the desired temperature of -24 degree Celsius approximately. The tissue was kept in a chuck and frozen inside the cryobar, mounted and trimmed (20 µm) until a flat surface of the lesion was obtained and uncurled sections of 5 µm thickness were taken with the help of the anti-rolling plate. The top side of a clean slide is held above the section so that it gets adhered to the slide by electrostatic attraction. The sections are then fixed in 95% alcohol and stained by rapid H&E Staining method and studied immediately. Then the results of both the techniques were correlated with one another keeping paraffin section diagnosis as the gold standard. The data collected were analyzed with IBM.SPSS Statistics software 23.0 Version.

Results

During the study period of November 2016 to June 2018, 54 cases, who turned for surgery after FNAC were taken for study. Imprint cytology and frozen section study were done in these cases. Of the 54 cases studied, only one was male and the remaining 53 were females. Of the 54 cases, maximum cases fell between the age group 31-40 years (27.77%). Of the 54 cases, frequency of breast lumps in the left breast was found to be higher (53.74%) that the right breast and 40.74% of the total breast lesions were seen in the upper outer quadrant. The most common presentation was isolated breast lump only (68.51%). 70.37% of the specimens received were less than 5 cm.

In touch imprint cytology 27 cases were reported as benign lesions, 2 cases showed features suspicious of malignancy and 25 smears were positive for malignancy.

In Frozen section study 19 cases (35.18%) were reported as fibroadenoma, 1 as Gynaecomastia, 3 cases were diagnosed as benign phyllodes,3 cases were diagnosed as borderline phyllodes and 1 as malignant phyllodes. 2 cases were diagnosed as Ductal carcinoma in situ. About 18 cases (33.33%) were diagnosed as IDC-NST type. Two of the cases showed sentinel node positivity followed by which axillary clearance was done. There was margin positivity in two of the cases followed by which excess clearance of margin was given. 1 case was diagnosed as a papillary lesion on the frozen section but we couldn't arrive at a diagnosis whether it is benign or malignant and was diagnosed as a malignant lesion by Immunohistochemistry. We had each 1 case of mucinous, medullary, lobular and papillary carcinoma.

Following paraffin sections 17 (31.4%) cases were diagnosed as fibroadenoma, 1 as fibroadenosis, 1 as fibroadenoma with usual epithelial hyperplasia, 1 as fibroadenoma with fibrocystic disease, 1 as gynaecomastia, 3 cases were reported as benign phyllodes, 3 as borderline phyllodes and 1 as malignant phyllodes, 2 cases were reported DCIS with focal invasion. About 17 cases were detected as IDC- NST and 1 was reported with IDC with medullary features. Two cases of Invasive papillary carcinoma were reported and we had 1 case of mucinous, medullary and papillary carcinoma. Paraffin sections also confirmed that fibroadenoma is the most common benign lesion and Invasive ductal carcinoma is the most common malignant lesion. 18 cases fell under grade II and 1 case under grade 1 by modified Bloom Richardson's grading system. ER, PR done in some of the cases turned out to be positive. 24 benign cases (44.44%), 3 borderline phyllodes (5.55%) and 26 malignant lesions (48.14%) were reported. Lymphovascular invasion was seen in 26 cases, nodal metastasis in 12 cases, and skin infiltration in 1 case and margin involvement in 5 cases. For statistical analysis, suspicious for malignancy category reported by touch imprint cytology was clubbed with malignant lesions and the borderline phyllodes cases are clubbed with malignant lesions 1 Case in which there was no residual tumour was not taken for statistical analysis. Out of the 26 benign by Imprint cytology 24 cases were proved to be benign lesions, 2 were diagnosed as malignant lesions by paraffin sections. All the 27 malignant cases were proved to be malignant by paraffin sections.

Table 1: Touch imprint diagnosis in relation to paraffin section diagnosis (n=53)

Imprint	No Of Cases	Paraffin Section		False Positivity	False Negativity	Sensitivity	Specificity	PPV	NPV	Accuracy
		Benign	**Malignant**			93.1 %	100%	100%	92.3%	96.55%
Benign	26	24	2	-	4					
Malignant	27	-	27	-	-					
Total	53	24	29	-	4					

As per table no.1, The sensitivity of touch imprint cytology was 93.1 %, specificity was 100 %, positive predictive value was 100%, negative predictive value was 92.3% and accuracy was 96.55%.

Table 2: Frozen section diagnosis in relation to Paraffin section diagnosis (n=50)

Frozen Section	No of cases	Paraffin Section		False Positivity	False Negativity	Sensitivity	Specificity	PPV	NPV	Accuracy
		Benign	**Malignant**			100%	100%	100%	100%	100%
Benign	24	24	-	-	-					
Malignant	26	-	26	-	-					
Total	50	24	26	-	-					

The analysis of these cases involved a thorough examination of both frozen and paraffin sections to ensure accurate diagnoses. The deferred cases, requiring additional sampling, underscore the importance of comprehensive evaluation to rule out invasive characteristics.

In this study, following frozen section examination, we deferred the diagnosis of three cases to paraffin section study. 2 of them were Ductal carcinoma in situ and 1 was a papillary lesion. These cases were ruled out because extensive sampling was needed to rule out invasion. All the 24 benign cases diagnosed in frozen sections were proved to be benign and 26 malignant cases were reported as malignant in paraffin sections also. Hence as in table No.2, the sensitivity, specificity, positive predictive value, negative predictive value and accuracy of frozen section turned out to be 100% thereby proving that it is better than touch imprint cytology in terms of sensitivity, specificity and diagnostic accuracy.

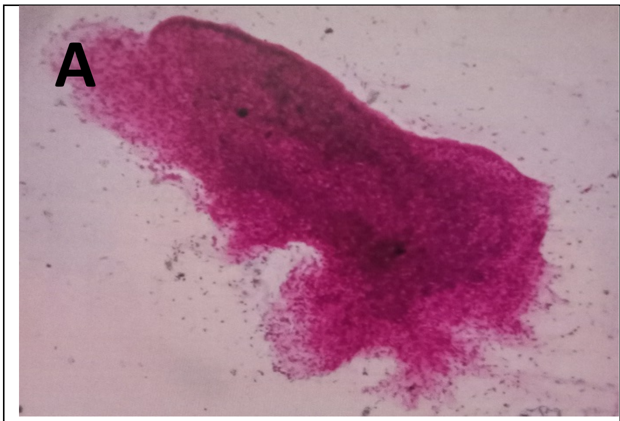

Fig. 1A : Imprint of Phyllodes tumour showing large stromal fragments (H&E, 10X)

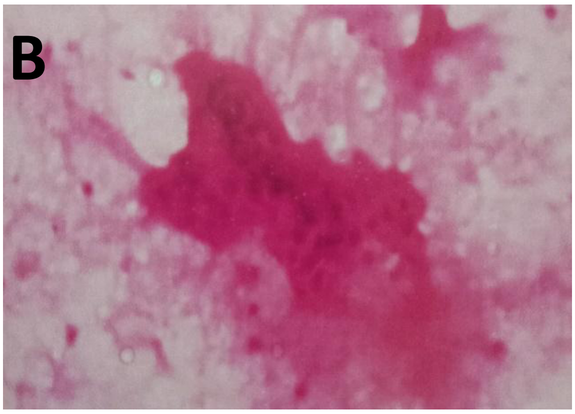

Fig. 1B: Imprint smear positive for malignancy (H&E), 10X)

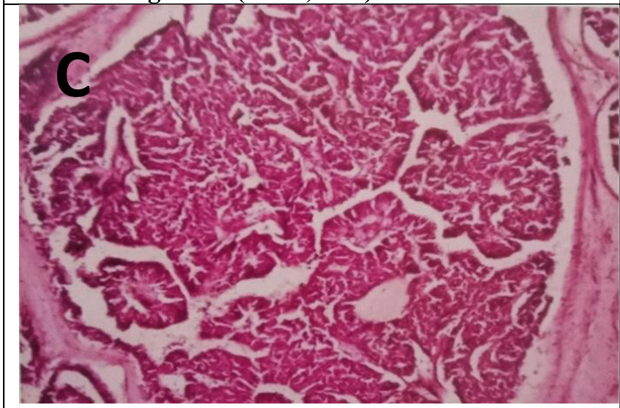

Fig. 1C: Frozen section of Invasive papillary carcinoma showing papillary fronds invading the stroma (H&E, 10X)

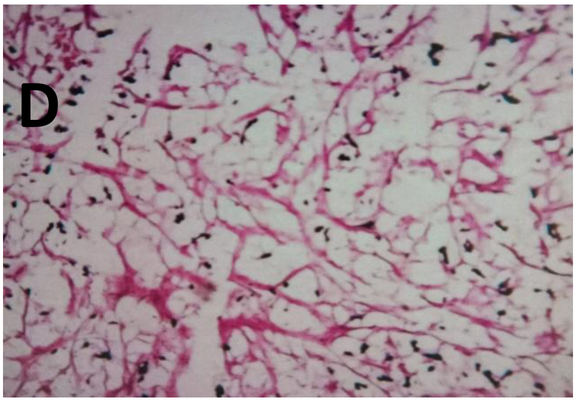

Fig. 1D: Frozen section of Mucinous carcinoma showing tumour cells floating in pools of Mucin (H&E, 10X)

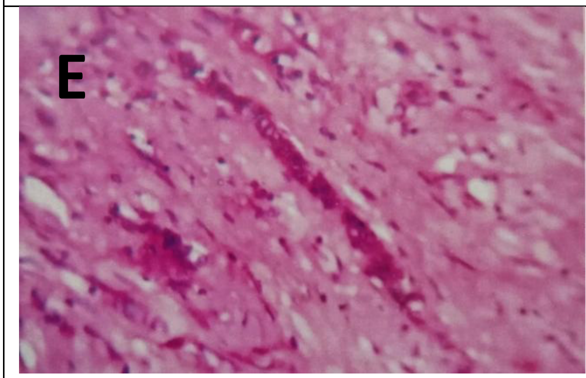

Fig. 1E: Frozen section of Invasive lobular carcinoma showing Indian file pattern (H&E, 10X)

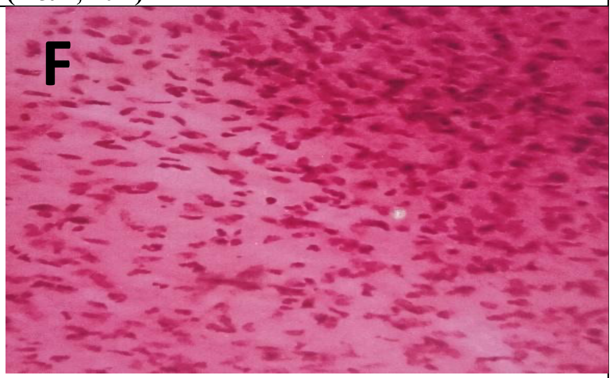

Fig. 1F: Frozen section of malignant phyllodes tumour (H&E, 10X)

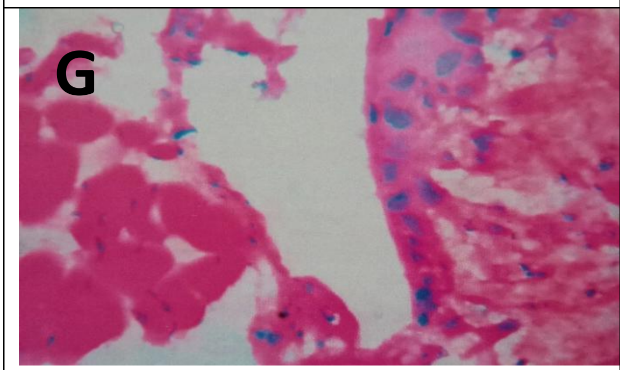

Fig. 1G: Frozen section showing tumour cells infiltrating the posterior margin(H&E, 10X)

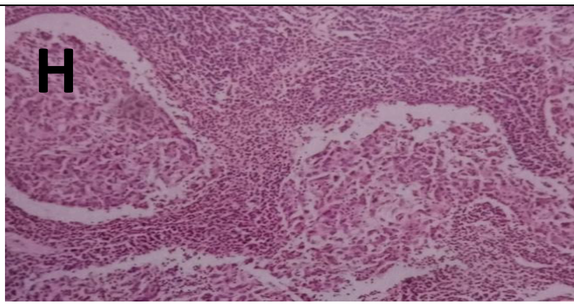

Fig. 1H :Paraffin section of Medullary carcinoma showing tumour cells arranged in syncytium surrounded by stroma having dense lymphocytic infiltration (H&E, 10X)

Figure 1:

Discussion

This study was conducted to evaluate the efficacy of the frozen section in diagnosing breast lesions by correlating the results with Touch imprint cytology and histopathological examination. In our study there was a female preponderance. The percentage of female patients was about 98% and male was only 2%. The studies conducted by Charusheela Gore et al [4], Shah alam sheikh et al [5], David E ibukine et al [6], Ashamahadevappa et al [7] also showed a female preponderance. The most common age group affected in the present study was the premenopausal age group of 31-40 years. This is in concordance with the study conducted by Ashamahadevappaet al [7] in which the overall breast lesions were common in the 4th decade constituting about 4%. But in the study conducted by Shah alam sheikh et al5, the most common age group affected was 41-50 %.

In both the studies benign lesions were common in the age group 20-30% and malignant lesions were common above 40 years. In our study 53.8% of the patients showed lesions in the left breast which is in concordance with Shah alam sheikh et al [5] study which showed 55.7% of left sided breast lesions. In this study outer quadrant was the most common quadrant affected (59.25%). This is in concordance with the study conducted by Meena et al [8] in which 58% of the lesions were found in the outer quadrant. In our study tumours less than 5 cm were more common constituting about 70%. The study conducted by Navneet et al [9] showed concordant results. Our study reported fibroadenoma as the most common benign lesion (52%) and ductal carcinoma as the most common malignant lesion (50%). The study conducted by Pinto et al [10], Ashwin et al [11] and Shoba et al [12] also showed concordant results.

In the study conducted by Ashamahadevappa et al [7] in the year 2017, 1.6% of the smears were found inadequate, 43.4% were benign, 55% of smears were positive for malignancy. Saritha karre et als [13] study reported 62% of benign lesions, 8% smears showed features suspicious of malignancy and 30% of smears were positive for malignancy. In this study also, there were no inadequate smears, 52% of the smears were reported benign, 3,7% of the smears showed features suspicious of malignancy and 44.5% of smears were found to be positive for malignancy. In the study conducted by Safina et al [14] in the year 2016, the sensitivity, specificity, PPV, NPV and accuracy of touch imprint cytology was 96.72%, 100%, 100%, 88.24% and 96.72% respectively. These results are concordant with the present study.

In Our study, all the benign and malignant lesions reported in the frozen section were proved to be the same in paraffin section diagnosis. The sensitivity, specificity, PPV, NPV and accuracy were 100% in the present study. This result is very well concordant with the studies conducted by Shah alamsheilkh et al [5] in the year 2012, Nuzhat sultana [15] in the year 2003, PV karve et al [16] in the year 2005, Ashamahadevappa et al [7] in the year 2013 and H. Haeri et al [17] in the year 2012.

Table 3: Comparison of accuracy of frozen section in other studies

	Sensitivity	Specificity	PPV	NPV	Accuracy
H.Haeri et al	95.4%	92.4%	-	-	100%
Nuzhat Sultana et al(2003)	99.6%	93%	99.3%	96.6%	99%
PV karve et al(2005)	99.36%	100%	100%	98.77%	99.82%
Shah Alam sheikh et al	97.37%	100%	100%	96.97%	98.57%
Ashamahadevappa et al	100%	96.55%	-	-	98.39%
This study	100%	100%	100%	100%	100%

Conclusion

In this study, although the results of Touch imprint cytology correlates with frozen section and paraffin section in terms of benignity and malignancy, the ability of imprint cytology in diagnosing individual lesions is inferior to that of frozen section study and paraffin section examinations. Despite the increasing popularity and utility of touch imprint cytology, there are some cases where frozen section is essential for accurate and rapid diagnosis of the lesion. The utility of frozen section is highly appreciated as it is used as a rapid tool in determining the tumour infiltration in the resection margins, extent of metastasis and sentinel node positivity to decide further axillary dissection. It stands as an unique method in reducing the need of second surgery and in planning further treatment. Only a few cases needed the help of paraffin section study to arrive at a conclusive diagnosis and reporting additional features where the frozen section didn't provide the same. In this study 2 cases of DCIS diagnosed by frozen section showed focal minimal invasion in paraffin sections.

One case diagnosed as papillary lesion was reported as invasive papillary carcinoma in paraffin sections. One case of fibroadenoma had features of usual epithelial hyperplasia and another one case of fibroadenoma showed features of fibrocystic changes in paraffin sections in this study. Though the frozen section study had the above limitations, it was proved to be a highly accurate diagnostic modality with an accuracy rate of 100%. Thus a judicious and proper selection of these diagnostic modalities is essential for proper management of the patients.

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