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# Spectrum of breast diseases with Cyto-Histopathological correlation in a tertiary care hospital of Western Uttar Pradesh

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## Abstract

**Background**: Breast lumps are a cause of concern both for the patients as well as the surgeons because of their turning into malignancy. The most valuable role of cytology in benign lesions is in the identification of proliferative lesions.

**Objectives:** This present study was carried out to evaluate the efficacy of fine needle aspiration cytology (FNAC) in different diseases and its correlation with the histopathological findings.

**Material & Methods:** All the lesions were categorized cytologically into 5 categories ranging from C1 to C5 as per NHS Breast Screening Programme (NHSBSP) reporting criteria.

**Results**: This present study was carried out a total of 220 patients during a 1 year period from January 2015 to December 2015. All patients presenting with lump in the breast and all those who had FNAC of these lumps were included in this study. The age of the patients ranged from 14 to 80 years. The maximum numbers of patients were in the 20-40 year group followed by the 41-60 year group. The upper and outer quadrant was affected in 83 patients (37.7%). Benign lesions were observed in patients of all age groups, but especially the young patients were more affected. The FNAC findings were correlated with the histopathological diagnosis for evaluating the diagnostic accuracy of Cytology. The results obtained were arranged in a tabular manner and after statistical analysis were concluded.

**Conclusion**s: Diagnosis of malignancy by FNAC is a safe and definitive procedure. However, in suspicious or atypical smears it may have some limitations. For diagnosis of these lesions histopathology is considered as a 'Gold standard' for definitive diagnosis. FNAC is an easy, accurate and economical diagnostic procedure possible even in the OPD for palpable breast lumps. It is safe with easy repeatability yielding quick results and even obviating the need for open biopsy.

**Keywords:** Breast, FNAC, Histopathology, Benign, Carcinoma

## Introduction

Cytology has gradually moved from an era of 'positive,' 'negative' and 'suspicious' diagnosis to an era of specific morphological typing of benign and malignant lesions. Breast is no exception. Fine needle aspiration cytology (FNAC) today occupies an extremely important place in the pre-operative evaluation of breast lesions and in deciding the management. The most valuable role of cytology in benign lesions is in the identification of epithelial proliferative lesions.[(1)] Triple test is the combination of clinical evaluation, mammography and cytological findings. Triple diagnosis when used in parallel leads to the improvement of pre-operative diagnosis and thus increasing the diagnostic accuracy rate to 99%.[(2)]

Globally with the exception of Japan, breast cancer incidence is very high in developed countries as compared to the developing countries and is a concern for both patients as well as the surgeons. In Urban India, the age adjusted incidence of breast cancer ranges between 20-30 per 1,00,000 persons. In India the increasing incidence of breast cancer and the possible disease curability if detected early emphasises the need for rapid and reliable diagnostic methods. Reconfirmation of prognostically favourable histological types is necessary to select targeted therapy.[(1)]

The present study was conducted with the aim of identifying the spectrum of cytological evaluation of breast lesions in a tertiary care centre of Western Uttar Pradesh and also to evaluate the diagnostic reliability of cytological findings by comparing them with histopathological observations.

## Material & Methods

All cases that underwent FNAC as advised by the Surgery department were included in this study. Information about the patient's age, sex, radiological findings, and cytological report were recorded. The excised specimens after surgery were subjected to histopathological examination. Aspiration was done under full aseptic precautions using 22 or 23 gauge needle in a 10 ml syringe. Multiple smears were prepared from the aspirate and those immediately fixed in 95% ethanol were stained using Haematoxylin and Eosin (H&E) and Papanicolaou (Pap) stains and air dried smears were stained using Leishman – Giemsa and May Grunwald Giemsa (MGG) stains. Whenever the aspirate yielded fluid, it was cytocentrifuged and the smears were prepared from the sediment and stained using the above mentioned stains. For histopathology the specimens were processed routinely and stained by H&E stains. Immunohistochemistry was applied as and when required.

All the lesions were categorized cytologically into 5 categories C1 – C5 as per the NHSBSP reporting criteria.[3,4]

**Cl (Inadequate):** Aspirates were classified as inadequate if a total of six or more epithelial cell clusters, each comprising of at least five to ten well preserved cells were not present.

**C2 (Benign):** In this category it included an adequate sample with no evidence of significant atypia or malignancy. Alternatively, an aspirate could be poorly to moderately cellular, comprising mainly of uniform benign ductal epithelial cells arranged as monolayer. The background was composed of dispersed individual and paired naked nuclei.

**C3 (Atypia probably benign):** This category has all the characteristics observed in aspirates of benign breast diseases as described in the $C_2$ category. However, there were few features not routinely seen in aspirates of benign breast disease.

**C4 (Suspicious of malignancy):** This category includes aspirates with highly atypical features, such that the pathologist is almost certain that they come from a malignant lesion although a confident diagnosis cannot be made.

**C5 (Malignant):** This category includes adequate smears containing cells characteristic of carcinoma, or other malignancy diagnosed on the basis of a combination of features.

Malignant lesions were cytologically graded using Robinson's criteria based on 6 parameters- cell dissociation, size of nuclei, uniformity of cells, presence of nucleoli, nuclear chromatin and nuclear margins. Each parameter was given a score of 1, 2 or 3.The scores were added up to get the total score used for grading breast carcinomas. Grade I was labeled when the scores were between 6 to 11, Grade II from 12 to 14 and Grade III from 15 to 18.[5] The excised mass was subjected to histopathological examination. All cases of ductal carcinoma (not otherwise specified) were graded as per the modified Scarff Bloom Richardson's scoring system. The scoring system included tubule formation, nuclear pleomorphism and mitotic figures giving each parameter a score ranging from 1 to 3. The scores were added together to give the final grade. Grade I had a score ranging between 3 to 5, Grade II from 6 to 7 and Grade III from 8 to 9.

## Results

The present study was conducted on 220 patients during a 1 year period from January 2015 to December 2015. All patients presenting with lump in the breast underwent FNAC. Of these, 124 patients underwent surgical exploration either in the form of removal of the lump or mastectomy. The aspiration cytology findings were correlated with the histopathology report to estimate the sensitivity, specificity and diagnostic accuracy rates of FNAC as compared to biopsy. The results obtained were tabulated and conclusions drawn based on the statistical test analysis.

In the present study, the age ranged from 14 to 80 years with 6 (2.72%) male and 214 (97.27 %) female patients. The majority of the patients were in the 20-40 (51.4%) year group followed by the 41-60 year (23.6%) group (Table 1). All patients with malignancy were more than 35 years of age. Benign lesions were observed in patients belonging to all the age groups but, more commonly in the younger age groups patients. No case of breast tumour was observed during the first decade of life. No breast lesions were observed below 14 years of age. Right breast was more commonly involved – 114 (51.82%). However, both breasts were affected in 16 (7.27%) patients. The upper and outer quadrant was the commonest site of lump in 83 patients (37.7%). All the patients presented with mass in the breast. 58 (26.36%) patients presented with pain along with breast mass. 9 (7.09%) patients had additional ulceration of the overlying skin. The duration of lump in our study ranged from 2 to 7 months in 187 patients (85.0%) and in the remaining 33 cases (15.0%) the duration was more than 7 months.

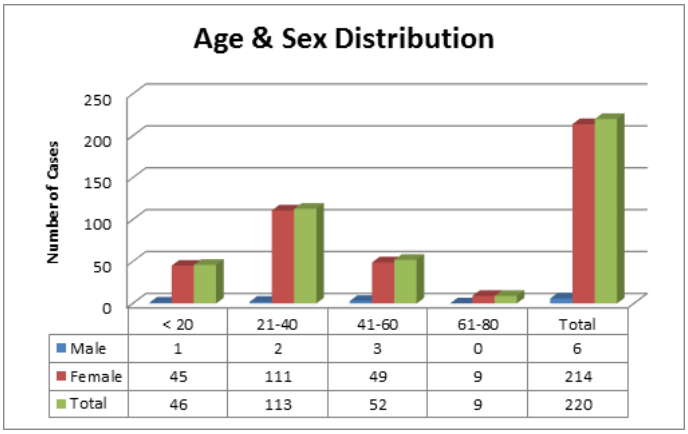


**Fig. 1: Showing age and sex distribution of cases**

**Table 1: Clinical presentations of breast lesions**

| Side | | | Presenting Symptoms | | | Quadrant Location | | |
|---|---|---|---|---|---|---|---|---|
| | n | % | | n | % | | n | % |
| Right | 114 | 51.82 | Mass in the breast | 220 | 100.00 | Upper Outer | 83 | 37.73 |
| Left | 90 | 40.91 | Mass + Pain | 58 | 26.36 | Upper Inner | 44 | 20.00 |
| Bilateral | 16 | 7.27 | Mass+Nipple discharge | 11 | 5.00 | Lower Outer | 32 | 14.55 |
| | | | Mass+ Ulceration of overlying skin | 9 | 4.09 | Lower Inner | 36 | 16.36 |
| | | | | | | Subareolar | 10 | 4.55 |
| | | | | | | Upper & Lower Outer | 1 | 0.45 |
| | | | | | | Upper Inner & Outer | 5 | 2.27 |
| | | | | | | Diffuse | 9 | 4.09 |
| Total | 220 | 100.00 | Total | 220 | 100.00 | Total | 220 | 100.00 |

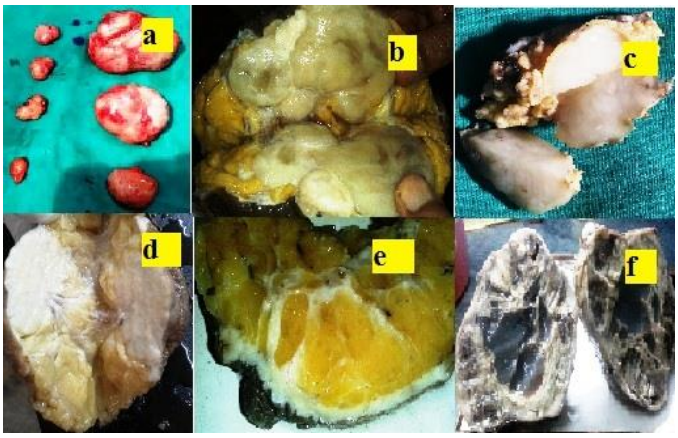


**Fig. 2: Gross photographs showing (a) Multiple bilateral fibroadenoma (b) Myofibroblastoma (c) Myxoma (d) Ductal Carcinoma (e) Pagets' disease nipple with underlying ductal carcinoma (f) Stromal sarcoma**

In our study five aspirates (2.27%) were reported as unsatisfactory. The commonest breast disease observed in our study was fibroadenoma in 100 patients (45.45%), followed by malignancy in 42 (19.09%) and fibrocystic disease in 30 (13.64%) patients. A case of clinical interest was also found in a 40 year old lady who presented with a lump in the right breast. The clinical diagnosis thought of was breast abscess or carcinoma. FNAC showed clusters of microfilariae in the smears (Fig 3c).

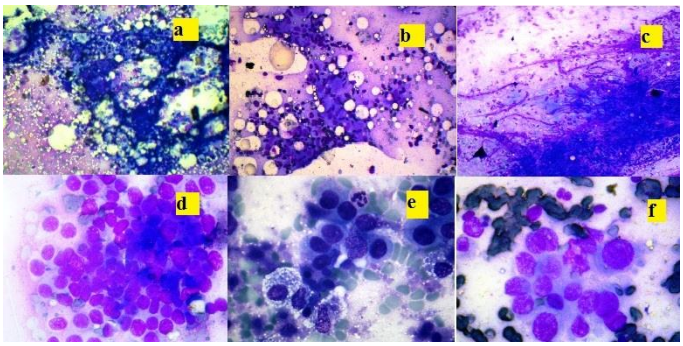


**Fig. 3: Photomicrograph showing cytological picture of (a) Lactating adenoma (b) Granulomatous mastitis (c) Microfilaria (d) Fibroadenoma (e) Intracystic Papillary carcinoma (f) Ductal carcinoma (g) Lobular Carcinoma (h) Medullary Carcinoma (i) Stromal sarcoma**

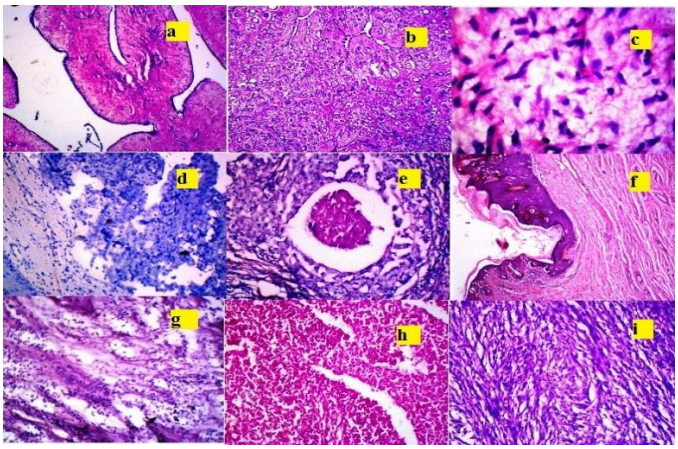


**Fig. 4: Photomicrograph showing histopathological picture of (a) Phyllode's (b) Tubular Adenoma (c) Myofibroblastoma (d) Intracystic Papillary Carcinoma (e) Ductal Carcinoma Comedo pattern (f) Paget's disease nipple**

Two of the four cases which were diagnosed on cytopathology as fibroadenoma on cytology were diagnosed as phyllodes tumour, one of lobular hyperplasia and one as infiltrating ductal carcinoma on microscopic examination. One case (0.45%) each of the uncommon tumours like Intracystic papillary carcinoma and infiltrating ductal carcinoma with Paget's disease of nipple were observed in our study. Of the 42 cases diagnosed as malignant on cytology, 38 cases were diagnosed as infiltrating ductal carcinoma, 3 as lobular carcinoma and 1 as medullary carcinoma on histopathology (Table 2).

**Table 2: Category-wise Cyto-Histological correlation**

| Cytological Category | FNAC Result | n | % | No Biopsied | * Histopathological Examination |
|---|---|---|---|---|---|
| **C1** | Inadequate | 5 | 2.27 | - | |
| **C2** | Acute Mastitis | 4 | 1.82 | - | |
| | Breast Abscess | 6 | 2.73 | - | |
| | Galactocoele | 3 | 1.36 | 1 | Galactocoele (1) |
| | Chronic Mastitis | 1 | 0.45 | 1 | Chronic Mastitis (1) |
| | Granulomatous Mastitis | 5 | 2.27 | 1 | Tuberculous mastitis (1) |
| | Lactational Adenoma | 3 | 1.36 | 1 | Lactational Adenoma (1) |
| | Fibrocystic disease | 30 | 13.64 | 10 | - Fibrocystic disease (7)<br>- Fibroadenoma (3) |
| | Epithelial cyst with secondary inflammation | 1 | 0.45 | 1 | Epithelial cyst with secondaryinflammation (1) |
| | Gynaecomastia | 6 | 2.73 | 5 | Gynaecomastia (5) |
| | Microfilaria Breast | 1 | 0.45 | - | |
| | Fibroadenoma | 100 | 45.45 | 58 | - Fibroadenoma (54)<br>- Phyllodes tumour (2)<br>- Lobular hyperplasia (1)<br>- Infiltrating ductal carcinoma (1) |
| | Phyllodes Tumour | 4 | 1.82 | 3 | - Phyllodes Tumour (2)<br>- Myofibroblastoma (1) |
| **C3** | Atypical ductal hyperplasia | 7 | 3.18 | - | |
| | Atypical Ductal Cells | 1 | 0.45 | - | |
| **C4** | Suspicious of carcinoma | 1 | 0.45 | 1 | Ductal Carcinoma (1) |
| **C5** | Ductal carcinoma | 38 | 17.27 | 32 | - Infiltrating ductal carcinoma (31) |

| | | | | | |
|---|---|---|---|---|---|
| | | | | | - Stromal sarcoma (1) |
| | Lobular carcinoma | 3 | 1.36 | 3 | Lobular carcinoma(3) |
| | Medullary carcinoma | 1 | 0.45 | 1 | Medullary carcinoma (1) |
| Total | | 220 | 100 | 124 | |

The cyto-histologic concordance was 89.7% for fibroadenoma, 65.2% for fibrocystic disease, 60% for benign phyllodes tumour, 57.1% for fibroadenosis and 33.3% for breast abscess. Out of 19 cases reported as fibroadenoma on FNAC, 14 were confirmed histologically as fibroadenoma, 3 as fibrocystic diseases, 1 case as fibroadenosis and 1 as phyllodes tumour. Cyto-histologic concordance rate was 94.44% for ductal carcinoma. One case diagnosed as infiltrating ductal carcinoma turned out to be medullary carcinoma on histopathology.

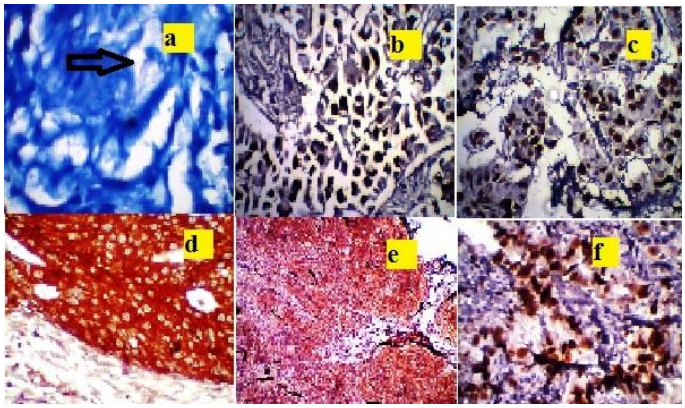


**Fig. 5: Photomicrograph showing special stains and Immunohistochemical markers in (a) AFB Positivity in Tuberculous Mastitis (b) ER Positivity in Ductal Carcinoma (c) PR Positivity in Ductal Carcinoma (d) Her 2 neu Positivity in Ductal carcinoma (e) S-100 Positivity in Stromal sarcoma (f) Ki-67 Proliferative marker**

## Discussion

Benign lesions are more common in the younger age group as compared to the malignant lesions. The commonest age group for malignant breast lesions was 31 to 50 years. Other authors also reported similar age group.[6-9] Breast carcinomas occur at an older age in males than in females.[10] Mass in the breast was the most common presenting complaint in all the patients followed by mass and pain in 26.36%. Other workers have reported mass and pain as the presenting chief complaint.[11] In the present study right breast was more commonly involved than the left breast, however, previous reports of left sided breast to be commonly involved are published.[5] Upper outer quadrant was the commonest site to be affected as observed in the present study also.[7,10,11]

Majority of the patients present with a short duration of complaints. Previous authors have reported duration ranging from 1 month to 2 years.[7] Earlier consultation by the patients was probably due to the location of our hospital in an urban city with a large population aware of an early necessity of medical consultation reflecting increased awareness among general public regarding lump in the breast.

Inadequate sampling rate was about 2% in this study.[12,13] Results are often influenced by the individual performing the aspiration technique and also on the one who interprets the aspirate smears.[13,14] The other probable reason for unsuccessful aspiration could be due to fibrous or cystic changes in the lump.[15] Our experience is that the aspirates taken and smears prepared by the pathologists are of good quality and usually devoid of false negative or false positive results. Diagnostic errors were more in the elderly pateints. In benign lesions, the overall agreement of cytology with histology was 82.4%. In this study, 5 inadequate cases were observed. Histopathology of all the 5 cases showed benign lesions, 2 as fibroadenoma and 3 as fibrocystic disease. Poor cellularity was the main cause of inadequate smears, which could be due to aspiration of fibrocystic lesions, fibroadenoma with hyalinisation or deeply located tumours. The false negative and false positive rates varied from 1% to 10% in various studies.[12-15] In the present study, the rate of false positives was 7.14%. False negativity is usually due to technical reasons, misinterpretation, smears showing an overlapping cellular pattern, needle out of focus, bloody aspiration, scanty cellularity or drying or cell disruption artefacts.[2,13] False positives reports were noticed in proliferative or suspicious lesions. The observations of the present study are thus comparable to the results of the previous studies.[9,12,13]

The commonest benign lesion observed in this study was fibroadenoma (45.45%). Other important conditions such as, invasive ductal carcinoma and fibrocystic disease followed next. Similar results have been observed in previous studies also.[8,11] In our study we found one case of myofibroblastoma which was not observed in any previous study. Some authors have reported fibrocystic disease as the commonest benign

pathology.[2,3,9] Among the male patients, gynaecomastia was the commonest breast lesion as observed by previous authors also.[11,16,17]

In the present study 1 case which was cytologically diagnosed as suspicious of malignancy was confirmed as malignant on histopathology. Other authors have also reported an increase in the rate of malignancy on histopathology in lesions which were previously diagnosed under the category of "suspicious of malignancy".[9] Definitive therapeutic surgery should not be undertaken as a result of a C3 or C4 diagnosis. Few authors suggested the use of a single term, such as equivocal, to describe inconclusive diagnosis on breast FNAC.[18] Other authors suggested C3 and C4 lesions as a "gray zone" and observed that about 89% cases turn out to be malignant on histopathological correlation.[19]

Infiltrating ductal carcinoma was the commonest malignant lesion as reported in the previous studies also.[4,8,9,11,12,20] Among these cases we also found one case of Pagets' disease of breast along with infiltrating ductal carcinoma which was not observed in other previous studies. Malignant lesions were not observed in patients less than the 2nd decade. Suspicious smears were mainly observed in the 4th and 5th decade.

Various parameters of estimating the efficacy of FNAC such as specificity, sensitivity, positive predictive and negative predictive value are almost at par with those reported in the literature. The comparative analysis is depicted in Table 3. The sensitivity of FNAC as a diagnostic tool in the present study was observed to be 98.36%, which correlates well with the results of the previous studies.[21,22] The specificity rate previously reported ranged from 98 to 100%; whereas in our study the rate was 100%.[21,22] The diagnostic accuracy of FNAC in various studies ranged from 90 to 100%; as compared to 99.33% in the present study. The best approach clinically to the diagnosis and the management of patients with breast lesions includes combination of all three tests-Physical examination, radiological imaging and pathology (FNAC/ Biopsy) termed Triple test. Diagnostic efficacy of these three tests taken together approaches to nearly 100%.[18,20] It is imperative to note that negative FNAC results do not rule out an underlying malignancy. Occasional complications include the formation of a hematoma, and a rare chance of tumour seeding along the needle tract. Use of fine needles has considerably reduced these chances. However, it includes few limitations as regarding the inability to diagnose lesions if the aspirate is scanty either due to an inexperienced person aspirating the lumps or if the lesions are very small or deeply located. Diagnosis is also not possible if the aspirate is from the centre of a tumour with necrosis. Diagnosis by FNAC may be presumptive in some cases. The final diagnosis in such cases is achieved by histopathology of the excised tissue.[21-24]

**Table 3: Comparison of present study with previous available studies**

| Authors | Year | Sensitivity | Specificity | Positive Predictive value | Negative Predictive Value |
|---|---|---|---|---|---|
| Jayaram G[1] | 1996 | 97.4% | 92% | - | - |
| Sri Lakshmi HP.[2] | 2013 | 95.2% | 100% | 100% | 95.2% |
| Hussain MT[7] | 2005 | 90.9% | 100% | - | - |
| Tiwari M.[8] | 2007 | 83% | 100% | - | - |
| Ariga et al.[9] | 2002 | 99% | 99% | 99% | 99% |
| Hebbar A.[12] | 2013 | 93.10% | 100% | 100% | 90.47% |
| Yeoh GPS.[13] | 1998 | 79% | 98% | 92% | 94% |
| Khemka A.[22] | | 96% | 100% | 100% | 95.12% |
| Choi Y.[23] | 2004 | 77.7% | 99.2% | 98.4% | - |
| Mahajan NA.[24] | | 96.77% | 98.66% | 96.77% | 98.66% |
| Bajaj Petal.[46] | 2013 | 98.2% | 100% | 100% | 93.2% |
| Present Study | 2015 | 89.5% | 100% | 100% | 94.2% |

## Conclusion

The present study concluded that a diagnosis of malignancy by FNAC could be safely used for definitive treatment but the same was not true for non-malignant, suspicious or atypical smears. In these situations surgical biopsy was considered to be essential for definitive diagnosis. FNAC procedure carried out by a well-trained cytopathologist is an easy, accurate and economical diagnostic test for palpable breast lumps. It can be used as an OPD procedure without the need to hospitalise the patient. It is safe and can be repeated easily and the result can become available during patient's first visit to the hospital and it may even obviate the need for open biopsy.

Considering the comfort of the patients, lack of anaesthesia requirement, quick results and almost absence of false positive results makes FNAC an ideal initial diagnostic modality when applied to breast lumps. However, at times it may be difficult to subcategorise the lesions on cytology without available clinical or mammography findings. As per the principle of Triple diagnostic test, acquiring technical, observational and interpretative skills

further enhance the diagnostic accuracy of breast pathologies.

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