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Research Article

# Optimizing Breast Cancer Diagnosis: Unifying IAC Yokohama System with Imaging and Histopathology in Evaluation of Breast Lesions

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ABSTRACT

***Background:*** Determining the appropriate management for breast lesions relies on a combined approach using clinical examination, imaging techniques, and fine-needle aspiration biopsy (FNAB). This study investigates the effectiveness of integrating the established Breast Imaging-Reporting and Data System (BI-RADS) with the recently introduced International Academy of Cytology (IAC) Yokohama System for reporting FNAC results. ***Material and methods:*** A retrospective analysis was done on all breast FNAC cases from 2018 to 2023, which were recategorized according to IAC Yokohama system. Correlation with BIRADS and histopathology was performed and PPV, NPV, sensitivity, specificity, diagnostic accuracy and ROM for each category was calculated. ***Results:*** The PPV, NPV, sensitivity, specificity and diagnostic accuracy of FNAC with category III assumed as benign were 94.3%, 95.70%, 86.8%, 98.2% and 95.3% respectively and the ROM for categories I to V were 33.4%, 0.0%, 12.5%, 83.4% and 100% respectively. ***Conclusion:*** Study highlights the power of FNAB and IAC Yokohama System for breast lump diagnosis, especially when combined with BI-RADS. This "duo" excels in unclear FNAB cases and specific lesion types, offering valuable insights for treatment decisions. Further refining categories and embracing advancements can further strengthen this approach for improved patient care.

## INTRODUCTION

Breast cancer is now the most common malignancy in Indian women, surpassing cervical cancer. In 2020, there were 178,361 new cases of breast cancer and 90,408 deaths from breast cancer in India, according to GLOBOCAN, accounting for 14% of all cancers in women [1,2]. Triple assessment, which combines clinical examination, imaging, and fine-needle aspiration (FNA) cytology, is essential for evaluating breast lesions. It ensures accurate diagnosis and tailored treatment. In developing countries, where resources are limited, breast FNA remains one of the most important diagnostic tools [3,4]. Core needle biopsies (CNB) are becoming more common and are replacing fine-needle aspiration biopsies (FNAB) in many centres [5]. While core needle biopsy (CNB) can assess additional factors such as invasion and hormone receptor status, it is a time-consuming, expensive, and invasive procedure. In contrast, fine-needle aspiration biopsy (FNAB), which can be guided by palpation or ultrasound, is a safe, fast, and inexpensive way to evaluate breast masses and can be used as a first line of diagnostic procedure and reduce the need for unnecessary surgeries [6]. The accuracy of FNAB depends on several factors, including the size and location of the lesion, the patient's cooperation, the skill and experience of the pathologist performing and interpreting the procedure, and technical factors such as staining [7].

It is essential to regularly evaluate the performance of breast cytopathology using a consistent and reliable system. The IAC Yokohama Breast FNAC Reporting system, developed by expert cytopathologists in collaboration with surgeons, oncologists, and radiologists, standardizes breast cytology reporting to improve interpretation and communication between cytopathologists and clinicians by linking reporting categories with management options. This categorized system for breast FNA cytology results stratifies them into five categories based on their risk of malignancy (ROM): insufficient/inadequate, benign, atypical, suspicious of malignancy, and malignant. [8].

Mammography and/or ultrasound, depending on availability, are used

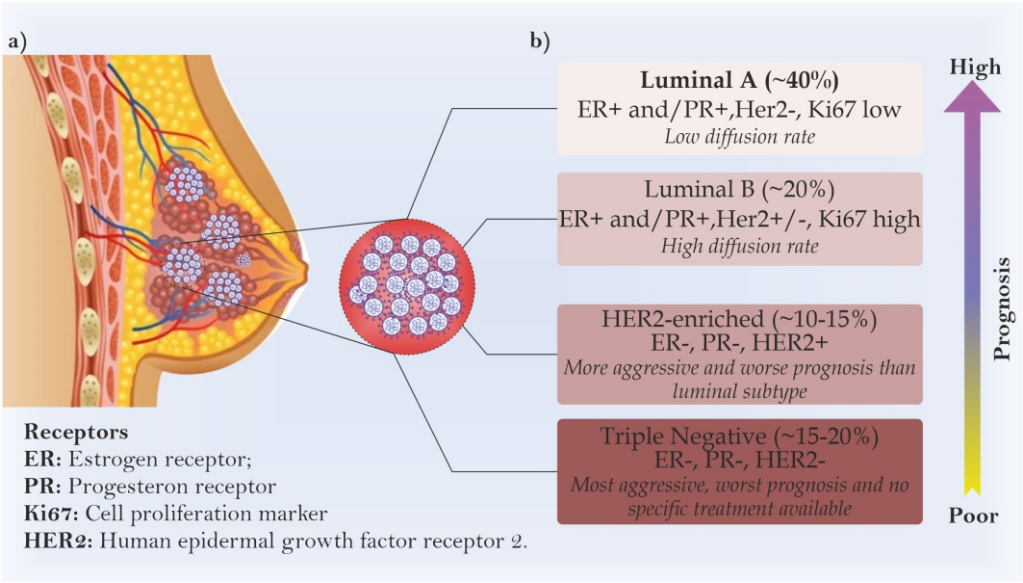


**Figure 1: Classification of breast cancer based on molecular characteristics and their prognosis rate (Image courtesy: D.D. Singh & D.K. Yadav, 2021)**

to image the breast, and the results are reported using the Breast Imaging-Reporting and Data System (BI-RADS) proposed by the American College of Radiology (ACR). BI-RADS has six categories, each with a reported likelihood of cancer and a recommended management approach: normal, benign, probably benign, suspicious, highly suggestive of malignancy, and known biopsy-proven malignancy. Studies have shown that using imaging with FNAB improves the accuracy of malignancy prediction [9,10].

This study aims to assess the clinical performance of breast FNAB using the IAC Yokohama system and correlate the cytological findings with those of BI-RADS, the radiological system. For cases with a subsequent CNB or resection, the cytological, histological, and radiological findings are also correlated.

## MATERIALS AND METHODS

This study was conducted at Department of Pathology, SGT Medical College, Hospital & Research Institute, Gurugram, Haryana. A retrospective study was conducted where cases of breast FNAC from August 2018 to August 2023 were retrieved from the departmental archives. Only cases with available radiology findings were included in the study.

Radiologists performed ultrasound-guided FNABs and pathologists performed palpation-guided FNABs using 22- to 24-gauge needles with 2 to 3 passes, depending on the cytopathologist's assessment of cellularity. Air-dried slides were stained using Giemsa along with Papanicolaou staining for standard cytopathology reporting.

All breast FNAB samples were re-classified by two cytopathologists into five diagnostic categories using the IACY system: insufficient/inadequate (C1), benign (C2), atypical (C3), suspicious for malignancy (C4), and malignant (C5). The cases that had discordant cytopathologi-c findings between the two cytopathologists, were discussed between the two and were re-classified into either of the five categories. Patient demographic information and BI-RADS scores were retrieved from the requisition forms for this study.

Histopathological reports for core needle/incision and excision biopsies were retrieved for the cases wherever available. For analysis, invasive carcinomas, ductal carcinoma in-situ (DCIS), and malignant phyllodes tumors were considered malignant. All other lesions (benign phyllodes tumour, fibroadenoma, fibrocystic change, and acute/chronic inflammatory disease) were considered benign.

### Statistical Analysis

Data was entered in Microsoft Excel, version 2309, and statistical analysis was performed in IBM SPSS Statistics for Windows, version 20.0, NY.

The risk of malignancy (ROM) was calculated for each breast FNAB and BIRADS category and correlated with the results of follow-up biopsies. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of FNAB and BIRADS were also calculated.

The overall accuracy of fine-needle aspiration biopsy (FNAB) in distinguishing between benign and malignant breast disease was calculated, considering category III of the IAC Yokohama System as negative for malignancy (benign).

## RESULTS

A total of 330 cases were retrieved, reviewed and categorised according to IAC Yokohama reporting system. The majority of patients were in their 20s and 30s, with ages ranging from 13 to 87 **(fig. 2)** with a mean age of 31.5 years. Clinical and demographic details of all the cases is mentioned in table 1.

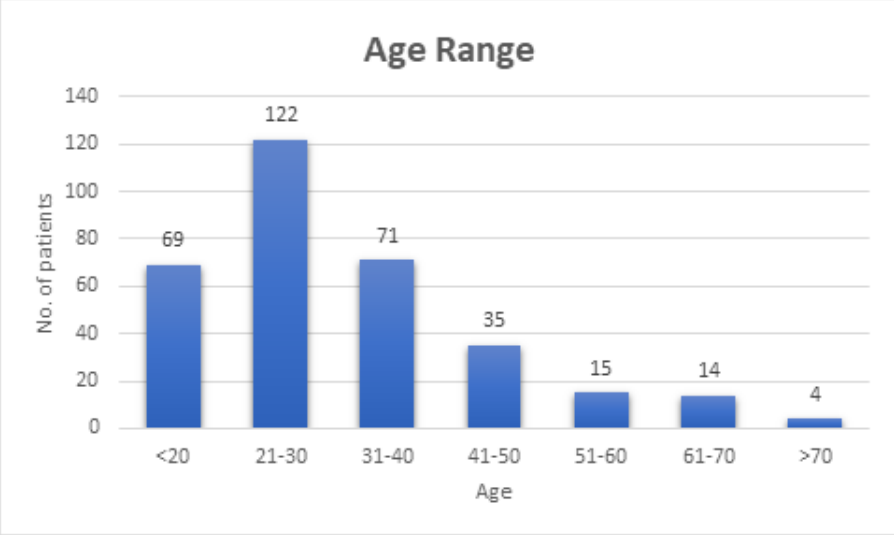


**Figure 2: Age range of patients who underwent Breast FNAC.**

**Table 1: Clinical and demographic details of patients who underwent Breast FNAC.**

| **Gender** | |
|---|---|
| Female | 314 |
| Male | 16 |
| Total | 330 |
| **Axillary Lymphadenopathy** | |
| No | 316 |
| yes | 14 |
| Total | 330 |
| **Laterality** | |
| bilateral | 13 |
| left | 162 |
| right | 155 |
| Total | 330 |
| **Quadrant** | |
| all | 14 |
| center | 13 |
| lower inner | 63 |
| lower outer | 83 |
| upper inner | 37 |
| upper outer | 120 |
| Total | 330 |
| **Single/ Multiple lesion** | |
| Multiple | 10 |
| single | 320 |
| Total | 330 |

The male to female ratio was 1:19.6. Bilaterality was observed in 13 cases where as the rest were unilateral with left side being the most commonly involved. Of all the four quadrants, upper outer (36.4%) was the most commonly involved and all the quadrants was involved only in 4.2% cases. Axilla was involved in 4% of the cases. Majority of the lesions were single (96.9%) while rest were multiple on presentation. A wide range of size distribution was observed, varying from smallest (0.7x1 cm) to largest (8x8 cm).

Radiological findings of all the cases were obtained and categorised according to the BIRADS score. Of all the 330 cases, on radiologic characterisation 260 cases came out to be benign (BIRADS category I, II and III) and rest 70 cases were diagnosed either as suspicious for malignancy (31) (BIRADS category IV) or positive for malignancy (39) (BIRADS category V). Whereas on cytological evaluation 266 cases were categorised as benign (IACY category I, II, III) and remaining 64 turned out to be malignant (IACY category IV and V). Therefore, the concordance between BIRADS and IAC Yokohama system was 97.74% in benign category. Under malignancy 9.3% cases were discordant and were misdiagnosed as false positive on BIRADS evaluation. Radiological evaluation misdiagnosed 16 cases false positively as carcinoma and 7 cases were misdiagnosed as false negative which were later found to be positive for malignancy on histopathological assessment.

All the 330 cases were reassessed and categorised as per the International Academy of Cytology Yokohama System as outlined in table 2. 3.9% cases of breast FNA were falling under IAC category I (Insufficient). Category II (Benign) was the most frequent interpretation amongst all the cases, amounting upto 67.9%, in which fibroadenoma was the most common diagnosis followed by fibrocystic disease. 8.8% cases were categorised as atypical (Category III). Under cat--egory IV (Suspicious for malignancy) 24 cases were interpreted and 40 cases were classified under category V (Malignant) of IAC Yokohama System under which Invasive ductal carcinoma was the most common malignancy encountered. Spectrum of lesions diagnosed according to IAC Yokohama system are listed in table 3.

**Table 2: Categorisation of cases according the International Academy of Cytology Yokohama System (n = 330)**

| | Yokohama category grading | Percentage |
|---|---|---|
| Insufficient | 13 | 3.9 |
| Benign | 224 | 67.9 |
| Atypical | 29 | 8.8 |
| Suspicious | 24 | 7.3 |
| Malignant | 40 | 12.1 |
| Total | 330 | 100 |

**Table 3: Spectrum of lesions on IAC Yokohama categorization.**

| Category | No. of cases | Subcategories | |
|---|---|---|---|
| I (Insufficient) | 13 (3.9%) | | |
| II (Benign) | 224 (67.9%) | Fibroadenoma | 108 (48.2%) |
| | | Gynaecomastia | 10 (4.5%) |
| | | Fat necrosis | 04 (1.8%) |
| | | Fibrocystic disease | 15 (6.7%) |
| | | Mastitis/Breast abscess | 12 (5.4%) |
| | | Duct ectasia | 08 (3.6%) |
| | | Granulomatous mastitis | 08 (3.6%) |
| | | Phyllodes | 12 (5.4%) |
| | | Lactational change | 20 (8.9%) |
| | | Benign breast disease | 27 (11.9%) |
| III (Atypical) | 29 (8.8%) | Fibroadenosis | 04 (13.8%) |
| | | Phyllodes | 02 (6.9%) |
| | | Proliferative breast disease with atypia | 23 (79.3%) |
| IV (Suspicious) | 24 (7.3%) | Atypical ductal hyperplasia | 24 (100%) |
| V (Malignant) | 40 (12.1%) | Medullary carcinoma | 02 (5%) |
| | | Ductal carcinoma | 38 (95%) |

Histopathologic follow up was available only for 151 cases of all the 330 cases. 113 cases were reported as benign on histopathologic evaluation and rest 38 cases were malignant which were majorly in concordance with the cytology report. 5 cases were misdiagnosed false negatively as benign on cytology evaluation (category I, II, III) but were later revealed to be malignant on histopathology. On the other hand, histopathology revealed 2 cases confirmed as benign, that were under malignant category (category IV and V) on FNA smears. Hence, the concordance between IAC Yokohama system and histopathology was 95.7% in benign category and 5.7% cases were discordant under the malignant category and were miss diagnosed and false positive on IAC Yokohama system. Table 4 tabulates the spectrum of lesions encountered on histology.

**Table 4: Spectrum of lesions on histopathological evaluation of the cases.**

| IAC Yokohama Category | Benign Histology | Malignant histology |
|---|---|---|
| **I (Insufficient)** | Gynaecomastia (1) | Invasive Ductal carcinoma (1) |
| | Fibroadenoma (3) | Mucinous carcinoma (1) |
| **II (Benign)** | Fibroadenoma (61) | |
| | Phyllodes (03) | |
| | Gynaecomastia (02) | |
| | Granulomatous Mastitis (02) | |
| | Fat necrosis (04) | |
| | Galactocele (2) | |
| | Fibrocystic disease (5) | |
| | Fibro adenomatoid hyperplasia (05) | |
| | Duct papilloma (02) | |
| **III (Atypical)** | Phyllodes (07) | DCIS (1)<br>Invasive Ductal carcinoma (2) |
| | Gynaecomastia (3) | |
| | Fibroadenoma (02) | |
| | Fibrocystic change (06) | |
| | Galactocele (03) | |
| **IV (Suspicious)** | Atypical Ductal Hyperplasia (2) | Invasive ductal carcinoma (10) |
| **V (Malignant)** | | Invasive ductal cancer (22) |
| | | Medullary carcinoma (1) |

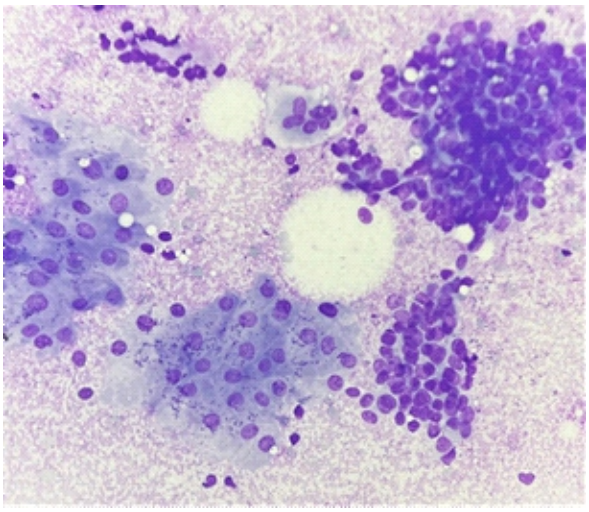

**Figure 3: Benign breast disease- Cluster of benign ductal epithelial and myoepithelial cells. Some ductal cells showing apocrine changes.**

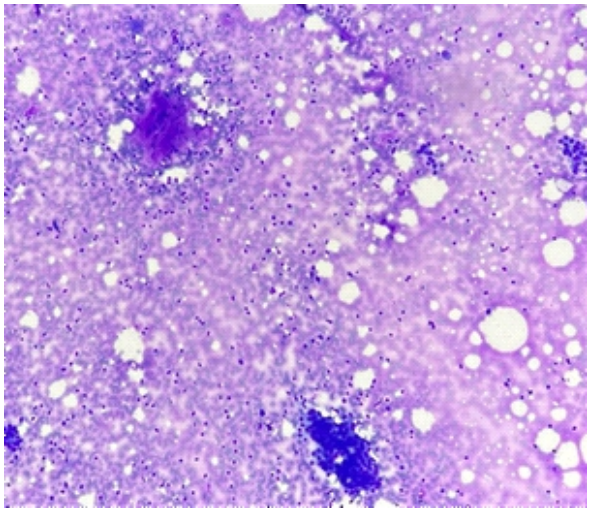

**Figure 4: Fibroadenoma with fibroadenosis- Clusters of benign ductal and myoepithelial cells along with fibromyxoid stroma. Some benign ductal cells showing acinar arrangement.**

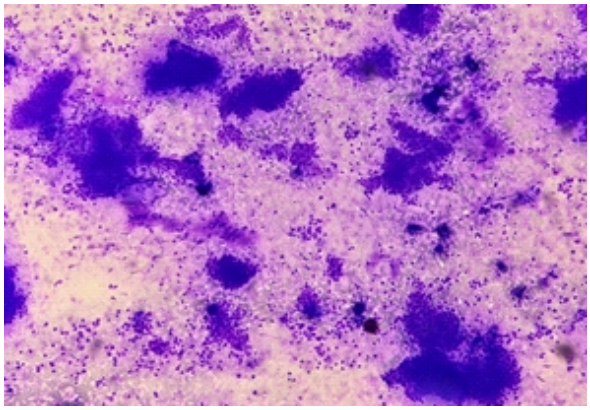

**Figure 5: Phyllode's tumour- Proliferation of stromal (spindle) cells. No mitosis or atypia seen.**

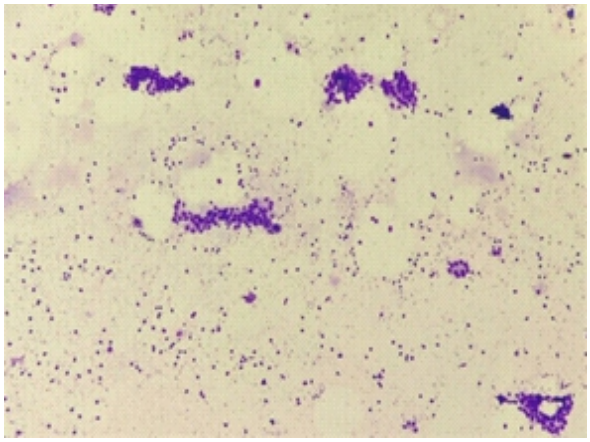

**Figure 6: Gynaecomastia showing loosely cohesive sheets and variable pleomorphism.**

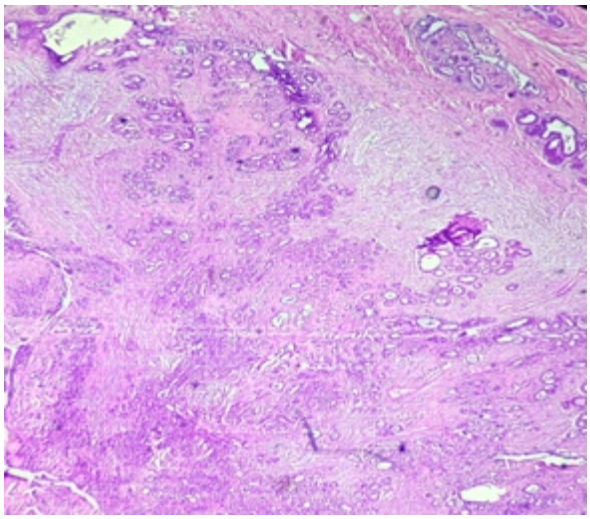

**Figure 7: Proliferation of intralobular stroma containing epithelial elements against a loose stroma.**

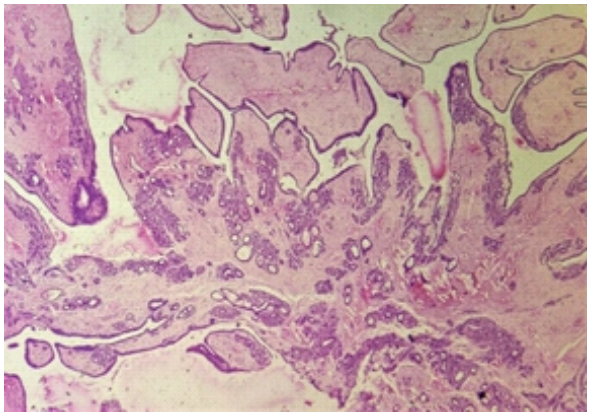

**Figure 8: Benign phyllodes tumour with leaf-like epithelial pattern.**

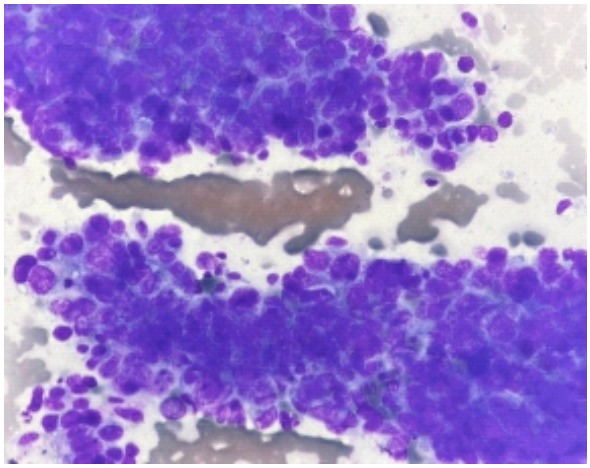

**Figure 9: Ductal carcinoma - Clusters of tumour cells with high N:C ratio, pleomorphic hyperchromatic nucleus and moderate amount of cytoplasm.**

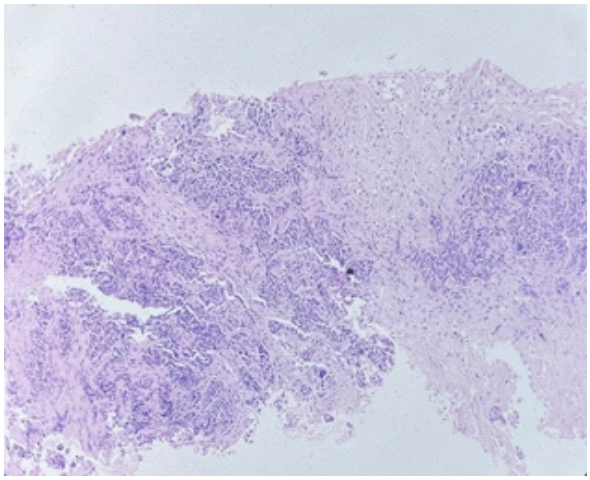

**Figure 10: Invasive breast carcinoma showing tumour in nests and cords with moderate nuclear pleomorphism.**

Figure 2-7: Benign lesions (FNAC + Histopathology)

Figure 8 and 9: under malignant lesions (FNAC + Histopa--thology)

We investigated the correlation between FNAC and ultrasound diagnoses of breast lesions with definitive histological confirmation as tabulated in table 5. The concor--dance and discordance of IAC Yokohama system with BIRADS on radiology and final histopathological diagnosis in mentioned in table 6.

**Table 5: Correlation of IAC Yokohama category with radiological and histopathological findings.**

| Yokohama Category | No. of cases FNAC | Radiological findings | | Histopathological findings | | |
|---|---|---|---|---|---|---|
| | | BIRADS I, II, III | BIRADS IV, V | Benign | Malignant | Total |
| **1 - Insufficient** | 13 (3.9%) | 11 (4.3%) | 2 (2.9%) | 4 (3.5%) | 2 (5.4%) | 6 (4%) |
| **2 – Benign** | 224 (67.9%) | 212 (81.5%) | 12 (17.1%) | 86 (76.1%) | 0 (0.0%) | 86 (57%) |
| **3 - Atypical probably benign** | 29 (8.8%) | 25 (9.6%) | 4 (5.7%) | 21 (18.6%) | 3 (7.9%) | 24 (15.9%) |
| **4 - Suspicious of malignancy** | 24 (7.3%) | 10 (3.8%) | 14 (20%) | 2 (1.8%) | 10 (26.2%) | 12 (7.9%) |
| **5 - Malignant** | 40 (12.1%) | 2 (0.8%) | 38 (54.3%) | 0 (0.0%) | 23 (60.5%) | 23 (15.2%) |
| **Total** | 330 (100%) | 260 (100%) | 70 (100%) | 113 (100%) | 38 (100%) | 151 (100%) |

**Table 6: Concordance and discordance of IAC Yokohama system with BIRADS and histopathology.**

| Concordance/Discordance | With Radiology (%) | With histopathology (%) |
|---|---|---|
| **Concordance in Malignant lesions** | 90.7% | 94.3% |
| **Concordance in Benign lesions** | 97.4% | 95.7% |
| **Discordance in Malignant lesions** | 9.3% | 5.7% |
| **Discordance in Benign lesion** | 2.6% | 4.3% |

Radiologic evaluation of category I (Insufficient) cases showed 11 (4.3%) cases under benign category and 2 (2.9%) cases under malignancy. Follow up on histopathology was available for 6 (4%) out of 13 cases under this category, 2 out of which were diagnosed as epithelial malignancy (invasive ductal carcinoma and Mucinous carcinoma of the breast) and the overall calculate ROM for this category turned out to be 33.4%.

Amongst the category II (Benign) lesions radiology categori--sed 212 (81.5%) lesions as benign while the rest 17.1% (12) of the cases were either suspicious for malignancy or positive for malignancy (BIRADS IV and V respectively). 86 cases were followed up on histology under this category and revealed all the cases to have a benign pathology with fibroadenoma being the most common lesion followed by fibrocystic disease and fibro adenomatoid hyperplasia. IAC category II accounted for a ROM of 0%.

Out of 29 cases categorised as atypical (category III) on cytology, radiologic findings put 25 (9.6%) cases under benign and the remaining 4 (5.7%) cases under malignant category. 24 (15.9%) out of 29 cases were followed up with histopathological evaluation and a benign diagnosis was given to 21 (18.6%) cases and a malignant diagnosis to 3 (7.9%) cases, accounting for a ROM of 12.5%. The most common lesions observed under this category were benign with the commonest being phyllodes followed by fibrocystic change. Under the malignant category both the lesions were diagnosed as epithelial malignancy (DCIS and invasive ductal carcinoma).

Suspicious for malignancy (category IV) comprised of 24 cases on cytology. BIRADS category I, II and III was given to 10 (3.8%) cases which were considered benign, while the rest 14 (20%) cases came under malignancy (category IV and V). Histopathological follow up was available for 12 (7.9%) cases. Majority of these were positive for malignancy on histopathology with invasive ductal carcinoma being the most commonly encountered lesion, while 2 (1.8%) cases were benign. The ROM was calculated to be 83.4% for this category.

Cytopathological evaluation categorised 40 cases out of 330 as positive for malignancy (category V). 38 cases out of these 40 were diagnosed as malignant on radiology while the rest were given a benign diagnosis. 23 of these 40 cases were followed up with histopathological investigation and all turned out to be positive for malignancy on histopathology, making the ROM of this category to be 100%.

The PPV, NPV, sensitivity, specificity and accuracy of diagnoses of IAC Yokohama system keeping category III under benign category is tabulated in table 7 and the test and the gold standard agree on 144 out of 151 having a diagnostic accuracy of 95.36%. The ROM of each category of IAC Yokohama system is tabulated in table 8. The concordance between malignant cytology (category IV and V) and histopathology was 94.3%.

Only those cases were included in this study who's pre-FNAC breast ultrasound or mammography data were available, of whom 151 patients underwent either core biopsy excision or surgery. Out of 47 cases in category IV and V of BIRADS who had a histopathologic follow up, 31 had a malignant histology and 16 cases were miss diagnosed as false positive in BIRADS. 7 cases out of 104 in BIRADS category I, II and III were false negative and were diagnosed

**Table 7: Statistical parameters of IAC Yokohama system in our study.**

| Statistical parameters | Percentage (%) |
|---|---|
| Sensitivity | 86.80% |
| Specificity | 98.20% |
| Positive predictive value | 94.30% |
| Negative predictive value | 95.70% |
| Diagnostic accuracy | 95.39% |

**Table 8: ROM of each IAC Yokohama Category.**

| IAC Yokohama Category | ROM |
|---|---|
| I (Insufficient) | 33.4% |
| II (Benign) | 0.0% |
| III (Atypical) | 12.5% |
| IV (Suspicious of malignancy) | 83.4% |
| V (Malignant) | 100% |

as malignant on histopathology. The concordance between histopathology and radiology is as depicted in table 9. PPV, NPV, sensitivity, specificity and accuracy of diagnosis of the BIRADS are tabulated in table 10 and the ROM of each of the BIRADS category is as listed in table 11.

**Table 9: Concordance and discordance of BIRADS with histopathology.**

| Concordance/Discordance | BIRADS with Histopathology |
|---|---|
| **Concordance in Malignant lesions** | 65.9% |
| **Concordance in Benign lesions** | 93.3% |
| **Discordance in Malignant lesions** | 34.1% |
| **Discordance in Benign lesion** | 6.7% |

**Table 10: Statistical parameters of BIRADS.**

| Statistical parameters | Percentage (%) |
|---|---|
| Sensitivity | 81.60% |
| Specificity | 85.80% |
| Positive predictive value | 66.00% |
| Negative predictive value | 93.30% |
| Diagnostic accuracy | 84.77% |

**Table 11: ROM of each BIRADS category.**

| BIRADS category | ROM |
|---|---|
| I (Normal) | 0.0% |
| II (Benign) | 4.3% |
| III (Probably benign) | 27.3% |
| IV (Suspicious of malignancy) | 50% |
| V (Highly suggestive of malignancy) | 82.6% |

## DISCUSSION

From concerning growths to harmless lumps, the term "breast lesions" encompasses a vast range. Reassuringly, most women experiencing these changes will receive a benign diagnosis [11]. To ensure accurate diagnosis and optimal care, many countries utilize a three-pronged approach: clinical examination, imaging, and pathology. This "triple assessment" offers benefits like simplicity and cost-effectiveness, but concerns have emerged regarding its limitations [12-16]. Some healthcare settings grapple with higher rates of inconclusive results and inconsistent accuracy, raising questions about the method's effectiveness in certain situations. Therefore, incorporating both clinical and radiological findings alongside pathological evaluation, as per the established triple assessment protocol, demonstrably increases the accuracy of breast cancer diagnoses, achieving a rate of approximately 99% [17].

FNAC plays a vital role, particularly in tertiary care settings like ours, where resource limitations often hinder performing adequate core needle biopsies for every breast lump. Time constraints and cost considerations necessitate a more streamlined approach. Fortunately, FNAC shines in these scenarios. Its ease of execution in skilled hands, coupled with its cost-effectiveness compared to core biopsies, makes it a valuable tool. Furthermore, its rapid nature, with the potential for even quicker turnaround time through on-site evaluation, makes it ideal for timely diagnosis.

Established in 2016, the Yokohama system by the IAC revolutionized breast cytology reporting with its standardized five-tier code (C1-C5). This innovative approach brought a multitude of benefits. Firstly, it streamlined reporting, promoting clarity and consistency in breast cytology diagnoses. This, in turn, enhanced the training and performance of FNA techniques, smear preparation, and material handling – crucial aspects for accurate diagnoses. Secondly, the Yokohama system elevated the quality and reproducibility of cytological report-s, minimizing ambiguity and discrepancies. This fostered improved communication with clinicians, enabling them to make informed decisions regarding patient management. Finally, the system optimized the utilization of ancillary tests for prognostic assessments, providing valuable insights for personalized treatment plans. In essence, the Yokohama system transformed breast cytology reporting, fostering accuracy, communication, and ultimately, improved patient care [8].

The present study was studied in a tertiary care set up in North India, extending over a period of five years from August 2018 till August 2023. The study included 330 breast FNA cases. Our study found that more commonly involved side was left with the upper outer quadrant of the breast being the most frequently involved area, which aligns with the findings of Mohanty et al. (2018) [10]. The IAC Yokohama System recommends that the rate of inadequate specimens (category I) should be less than 5%. The reported proportion of category I cases in published studies varies widely, from 5.7% to 40%. The findings in our study were in accordance with the suggested values and was 3.9% (13) of all cases. Mirroring trends observed in the wider literature, our category II diagnoses were dominated by fibroadenoma (48.2%), followed by benign breast disease without atypia (12%). The most frequent lesion in category III was proliferative breast disease with atypia (79.3%) and was 8.8% of all the cases comfortably within the expected range (0.6%-13.74). The range reported in previous studies for category IV cases is 0.7%-4.7% and we reported a higher percent of suspicious cases (7.3%) which is slightly higher as compared to other studies. In category V we observed 12.1% of cases to be positive for malignancy and the most common diagnosis was ductal carcinoma. This is well within the range of 1.6%-28.4% as documented in other studies [6,7,18-22]. The breakdown of our samples under the IAC Yokohama system aligned well with observations in existing research as documented in table 12.

**Table 12: The distribution of our cases according to IAC Yokohama system as compared to other studies.**

| First Author | Wong et al [18] | Montezuma et al [7] | Agarwal et al [19] | McHugh et al [20] | De Rosa et al [21] | Oosthuizen et al [22] | Sundar et al [6] | Present study |
|---|---|---|---|---|---|---|---|---|
| **Country** | Australia | Portugal | India | Kenya | Italy | South Africa | India | India |
| **Year of publication** | 2019 | 2019 | 2021 | 2019 | 2020 | 2021 | 2022 | 2023 |
| **No. of cases (follow up with histopathology)** | 2696 (579) | 3625 (776) | 1205 (321) | 695 (219) | 4624 (1745) | 1532 (1532) | 663 (288) | 330(151) |
| **I** | 11% | 5.77% | 19% | 9% | 19.2% | 40% | 9.3% | 3.9% |
| **II** | 72% | 73.38% | 50.2% | 47% | 36.9% | 57% | 65.7% | 67.3% |
| **III** | 4.3% | 13.74% | 6.6% | 7% | 10.8% | 0.6% | 6.2% | 8.8% |
| **IV** | 2.2% | 1.57% | 3.8% | 11% | 4.7% | 0.7% | 3.9% | 7.3% |
| **V** | 10% | 5.54% | 20.4% | 36% | 28.4% | 1.6% | 14.8% | 12.1% |

Among the 330 cases in our study, 13 FNACs were insufficient for diagnosis (category I). Histopathology follow-up was available for 6 of these cases. While radiological evaluation indicated 11 benign (BIRADS I, II, III) and 2 malignant (BIRADS IV, V) lesions, histopathological examination revealed 4 benign and 2 malignant cases. The probable causes for the insufficient aspirates included small lesion size, deep location, or ill-defined margins leading to scant material despite repeated attempts.

Further histopathological examination was conducted for 86 of the 224 cytologically benign (category II) cases. While radiological assessment initially classified 212 lesions as benign (BIRADS I, II, III) and 12 as malignant (BIRADS IV, V), subsequent histopathological analysis confirmed no malignancy in any of the cases studied.

Among the 29 cases classified as atypical (category III), 24 underwent further histopathological evaluation. While initial radiological assessment categorized 4 lesions as malignant (BIRADS IV, V) and 25 as benign (BIRADS I, II, III), histopathology revealed a more nuanced picture. Six cases were diagnosed with benign conditions like fibrocystic change, galactocele, and fibroadenoma, despite initial cytological concerns due to high cellularity, nuclear atypia, and apocrine metaplasia. Seven cases were confirmed as phyllodes tumors, with five categorized as borderline and two as benign. Three cases diagnosed as gynecomastia were included due to cytological features of loosely cohesive sheets and variable pleomorphism. Notably, two cases were ultimately diagnosed with invasive ductal carcinoma, and one with ductal carcinoma in-situ, highlighting the importance of histopathological confirmation in this category.

Among the cases categorized as suspicious for malignancy (category IV) on cytology, 14 were flagged as malignant by radiology (BIRADS IV and V), while the remaining 10 were initially assessed as benign. Of these, we further evaluated 12 cases through histopathology. Notably, 10 cases were confirmed as invasive ductal carcinoma, highlighting the suspicion raised by cytology. However, the remaining 2 cases despite moderate cytological and nuclear atypia and the presence of necrotic debris on cytological smears, were diagnosed as atypical ductal hyperplasia, demonstrating the importance of definitive histopathological analysis.

Cytology classified 40 cases as malignant ( category V ), a diagnosis largely supported by radiological findings. Only two cases showed discrepancy, appearing atypical on imaging. Subsequent histopathological evaluation further categorized these cases. The majority, 22, were confirmed as invasive ductal carcinoma, while one exhibited carcinoma with medullary features.

Multiple criteria were employed in various studies for statistical analysis and calculation of sensitivity, specificity, PPV, NPV, and diagnostic accuracy related to malignancy assessment. Montezuma et al. [7], Agarwal et al. [19], and Oosthuizen et al. [22] utilized three scenarios:

1. Positive malignancy: IAC Yokohama categories III, IV, and V.
2. Positive: Suspicious and malignant lesions.
3. Positive: Category V lesions only.

The remaining four studies [6,18,20,21] adopted two scenarios:

1. Malignant: Suspicious and category V lesions.
2. Positive: Category V lesions only.

For consistency and comparability, we adopted the single scenario common to all studies, defining category IV and V lesions as positive for malignancy. This decision ensured reliable comparison with the results reported in these studies presented in table 13. Upon comparison, we observed that our findings aligned with prior research, even exhibiting a slightly higher negative predictive value (NPV) compared to others. Our study reported ROM values for all IAC Yokohama System categories except I, where the ROM was significantly higher at 33.4%. This potentially inflated value may be due to the pre-selection of suspicious lesions for biopsy in this category, introducing a bias towards malignancy and impacting the accuracy of the ROM calculation. The risk of malignancy (ROM) values for atypical, suspicious and malignant categories aligned perfectly with the recommended ranges outlined by the IAC Yokohama System [8]. Compared to existing literature [6,7,18-22], our results paint a different picture with no documented instances of benign lesions mistakenly classified as suspicious for malignancy within the category II of IAC Yokohama system. Table 14 provides a comprehensive comparison of the malignancy rates (ROM) observed in our study for each diagnostic category, alongside the recommended range from established guidelines and findings from other research.

Breast imaging plays a vital role in assessing the risk associated with breast lumps, with ACR BI-RADS guiding crucial management decisions based on radiological findings. BI-RADS dictates follow-up strategies, ranging from routine screening for low-risk categories (I and II) to further imaging, short-interval monitoring for suspicious lesions (III), and ultimately, tissue sampling for high-risk categories (IV and V). Furthermore, the risk of malignancy (ROM), sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) associated with BI-RADS categories in our study aligned with findings from previous research [26-29]. Among IAC Yokohama category I malignancies, a notable majority previously fell under the BI-RADS 4 or 5 category on ultrasound. This emphasizes the critical role of core needle biopsy in cases with high-risk ultrasound profiles, irrespective of any inconclusive cytolog-

-y results, to maximize the chances of early cancer detection and prompt intervention. Given the relatively high rate of malignancy (27.3%) observed in category III lesions, our findings suggest that CNB should be strongly considered for patients with a BI-RADS score of 3 or above. This approach, utilizing both BI-RADS and FNAB, can significantly improve the risk stratification of patients, leading to more informed clinical decisions.

**Table 13: Comparison of statistical parameters of FNAC in the present study and other studies**

| First Author | Montezuma et al [7] | McHugh et al [20] | Wong et al [18] | De Rosa et al [21] | Agarwal et al [19] | Oosthuizen et al [22] | Sundar et al [6] | Present study |
|---|---|---|---|---|---|---|---|---|
| **Country** | Portugal | Kenya | Australia | Italy | India | South Africa | India | India |
| **Year of publication** | 2019 | 2019 | 2019 | 2020 | 2021 | 2021 | 2022 | 2023 |
| **Sensitivity (%)** | 88.3 | 79.5 | 92.0 | 93.7 | 96.0 | 81.5 | 96.0 | 86.8 |
| **Specificity (%)** | 99.8 | 85.1 | 97.8 | 90.8 | 91.9 | 92.7 | 91.9 | 98.2 |
| **PPV (%)** | 99.5 | 77.5 | 97.6 | 95.8 | 97.3 | 84.6 | 97.3 | 94.3 |
| **NPV (%)** | 99.3 | 86.6 | 92.7 | 86.6 | 88.3 | 91.1 | 88.3 | 95.7 |
| **Diagnostic accuracy (%)** | 94.7 | 82.9 | 95.0 | 92.8 | 95.0 | 76.8 | 95.0 | 95.4 |

**Table 14: Comparison of the ROM for diagnostic categories in the present study with other studies**

| First Author | Recommended ROM % | Wong et al [18] | Montezuma et al [7] | Agarwal et al [19] | McHugh et al [20] | De Rosa et al [21] | Oosthuizen et al [22] | Sundar et al [6] | Present study |
|---|---|---|---|---|---|---|---|---|---|
| **Country** | | **Australia** | **Portugal** | **India** | **Kenya** | **Italy** | **South Africa** | **India** | **India** |
| **Year of publication** | | 2019 | 2019 | 2021 | 2019 | 2020 | 2021 | 2022 | 2023 |
| **No. of cases (follow up with histopathology)** | | 2696 (579) | 3625 (776) | 1205 (321) | 695 (219) | 4624 (1745) | 1532 (1532) | 663 (288) | 330(151) |
| **I** | 2.6-4.8 | 2.6 | 4.8 | - | 0 | - | 11 | 38 | 33.4 |
| **II** | 1.4-2.3 | 1.7 | 1.4 | 8.3 | 12 | 4.9 | 3 | 0.6 | 0 |
| **III** | 13-15.7 | 15.7 | 13 | 17.2 | 25 | 20.7 | 28 | 21.9 | 12.5 |
| **IV** | 84.6-97.1 | 84.6 | 97.1 | 77.8 | 46 | 78.7 | 56 | 100 | 83.4 |
| **V** | 99.0-100 | 99.5 | 100 | 100 | 91 | 98.8 | 100 | 97 | 100 |

When discordance appears in two out of three "triple test" parameters, a core needle biopsy (CNB) is warranted for definitive diagnosis. [30] The Yokohama System's "atypical" and "suspicious" categories effectively capture borderline lesions like atypical ductal hyperplasia (ADH), which harbour a higher risk of malignancy than benign lesions. [19] However, controversies surround the precise diagnosis of these "grey zone" lesions. Debate within the IAC reporting system mainly revolves around classifying them as C3 or C4. [4,31,32] Our study found a higher accuracy in identifying malignant cases within the C4 category compared to C3. This suggests that further investigations like CNB or trucut biopsy are advisable for grey zone lesions to ensure accurate diagnosis. While maintaining the C3 and C4 categories in the Yokohama System sparks debate, their proponents argue they can refine prognosis and minimize unnecessary interve-ntions. These categories identify patients with a higher likelihood of either benign (C3) or malignant outcomes. For C3 lesions with reassuring clinical and radiologic features, surgical biopsies might be avoided. Repeat FNAC or core needle biopsies after a month (allowing inflammation to subside) offer further clarity. If repeat biopsies confirm benignity, close follow-up or even no further intervention may be sufficient for some C3 patients, reducing anxiety and resource burden. However, C4 lesions with a significantly higher malignancy rate require mandatory histopathological examination to ensure timely diagnosis and optimal treatment planning [33,34].

Ultimately, ongoing research and refinement of the system are crucial to strike the right balance between risk stratification and minimizing unnecessary procedures while ensuring accurate diagnosis and improved patient outcomes.

While our study provided valuable insights, it's important to acknowledge its limitations. The relatively small sample size, retrospective design, and incomplete follow-up on histopathological data may limit the generalizability and conclusiveness of our findings. These limitations underscore the need for further research with larger, prospective cohorts and comprehensive follow-up data to validate our observations and draw more definitive conclusions [35].

## CONCLUSION

Standardizing communication across radiology and cytology is crucial for optimal breast lump diagnosis. Our study strengthens the case for FNAB and the IAC Yokohama System in this process. They synergistically act as a powerful pre-operative duo, with FNAB offering cellular insights and BI-RADS revealing the lump's radiological behavior. This teamwork becomes particularly valuable in inconclusive FNAB cases (category III), where BI-RADS guides crucial treatment decisions. FNAB shines further for BI-RADS 4 lesions, satellite lesions, and even cancer patient triage. While CNB may be preferred in some centers, especially with resource constraints, FNAB remains an indispensable tool. Ultimately, refining indeterminate categories with objective criteria and harnessing advances like immunocytochemistry, imaging-guided FNAB, and Doppler sonomammography can further strengthen this dynamic duo, leading to even more precise risk assessment and improved patient management.

## ETHICS APPROVAL

All necessary approval including ethical approval has been taken before conducting this study.

## AVAILABILITY OF DATA AND MATERIAL

Not Applicable.

## CONFLICT OF INTERESTS

Authors declared that there is no conflict of interest.

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