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# Diagnostic Accuracy of Fine-Needle Aspiration Cytology Alone and With Cell Block Preparation for Palpable Breast Lesions: A Prospective Study in Central India

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## Abstract

### Background

Fine-needle aspiration cytology (FNAC) is a rapid and minimally invasive test for palpable breast lesions, but limited architecture and sampling variability can reduce sensitivity. Cell block preparation may complement smears by preserving tissue fragments in paraffin sections. This study estimated the diagnostic accuracy of FNAC and the incremental diagnostic yield obtained by adding cell block interpretation in the histologically verified subset, while describing cell block adequacy in the entire enrolled cohort.

### Materials and methods

This prospective observational diagnostic accuracy study enrolled 74 consecutive patients with palpable breast lesions at a tertiary-care center in Bhopal, India, from May 2024 through December 2025. A first dedicated pass was used for conventional smears and a second for plasma-thrombin cell block preparation. FNAC was classified using the International Academy of Cytology Yokohama system. Histopathology was available for 46 clinically biopsied or excised lesions and served as the reference standard. Exact 95% confidence intervals were calculated from the two-by-two counts, and FNAC and combined interpretation were compared using an exact two-sided McNemar test among the 46 verified participants.

### Results

The mean age was 36.4 ± 14.0 years, and 70 participants (94.6%) were female. All FNAC smears were adequate; 58 lesions (78.4%) were benign, 1 (1.4%) atypical, 5 (6.8%) suspicious, and 10 (13.5%) malignant. Ten cell blocks (13.5%) were inadequate or hemorrhagic. Histopathology identified 35 benign and 11 malignant lesions. FNAC yielded 81.82% sensitivity (95% CI, 48.22%-97.72%), 100% specificity (95% CI, 90.00%-100%), and 95.65% accuracy (95% CI, 85.16%-99.47%). Combined interpretation yielded 90.91% sensitivity (95% CI, 58.72%-99.77%), 100% specificity (95% CI, 90.00%-100%), and 97.83% accuracy (95% CI, 88.47%-99.94%). Paired analysis showed one discordant result favoring combined interpretation and none favoring FNAC (exact McNemar p = 1.000).

### Conclusions

Combined interpretation showed numerically higher sensitivity and accuracy than FNAC alone in the histologically verified subset, but the small number of malignant lesions, wide confidence intervals, and partial verification preclude a definitive claim of superiority. Cell blocks are best used as an adjunct within clinical-radiological-pathological correlation; discordant or concerning lesions still require histopathology.

**Categories:** Obstetrics/Gynecology, Pathology
**Keywords:** breast cytopathology, cell-block, diagnostic test accuracy, fine-needle aspiration cytology, yokohama system

## Introduction

Breast cancer is the most frequently diagnosed cancer worldwide, and the burden in India continues to make timely evaluation of breast symptoms a clinical priority [1,2]. A palpable breast lesion may represent a benign, inflammatory, proliferative, or malignant process. Diagnostic strategies must therefore identify malignancy promptly, while avoiding unnecessary invasive procedures for concordant benign disease.

Fine-needle aspiration cytology (FNAC) is rapid, inexpensive, repeatable, and minimally invasive. Although core needle biopsy generally has higher sensitivity in suspicious lesions, FNAC remains useful for palpable masses when it is integrated with clinical examination and imaging and is performed by experienced teams [3,4]. The International Academy of Cytology Yokohama system standardizes reporting into insufficient,

benign, atypical, suspicious for malignancy, and malignant categories, each linked to a progressively increasing risk of malignancy and a recommended management approach [5-7].

The main vulnerabilities of conventional smears are sampling error, limited cellularity, and loss of architectural relationships. These limitations are most consequential in fibroepithelial, papillary, proliferative, and low-grade lesions that occupy a cytological gray zone [8]. Cell block preparation converts aspirated material into formalin-fixed paraffin-embedded sections. When adequately cellular, a cell block can show epithelial-stromal relationships, support serial sectioning, and preserve material for validated ancillary tests; however, methods vary, and poor cellular yield remains a practical limitation [9-13].

An earlier publication reported an interim analysis of 30 participants from this cohort. The present study reports the completed 74-participant cohort, including 44 additional participants, with an expanded diagnostic-accuracy analysis and Standards for Reporting Diagnostic Accuracy (STARD)-aligned reporting [14].

The primary objective was to estimate the diagnostic accuracy of conventional FNAC and the incremental diagnostic yield obtained by adding cell block interpretation in the histologically verified subset of 46 participants with palpable breast lesions. The combined strategy incorporated FNAC through the prespecified OR rule described below and was therefore not considered an independent competing diagnostic modality. Secondary objectives were to describe the distribution of FNAC categories and cell block adequacy and diagnostic yield among all 74 enrolled participants, and to summarize histopathological outcomes in the verified subset. Because the comparison was exploratory, no superiority hypothesis or minimum clinically important difference was prespecified.

# Materials And Methods

## Study design and setting

This was a single-center, prospective, observational, diagnostic accuracy study conducted in the Cytology and Histopathology sections of the Department of Pathology, People's College of Medical Sciences & Research Centre, Bhopal, Madhya Pradesh, India. Participants were enrolled from May 2024 through December 2025. Reporting was organized with reference to the Standards for Reporting Diagnostic Accuracy Studies statement [14].

Thirty of the 74 participants had been included in an earlier preliminary publication from the same ongoing study. The remaining 44 participants were enrolled as recruitment continued and were not included in the earlier analysis [15].

A finite-population sample-size calculation used an assumed proportion of 50%, a 95% confidence level, 5% absolute precision, and an estimated eligible population of 90 patients over the recruitment interval, yielding a target of 74 participants. The participant was the unit of analysis, and each participant contributed one paired FNAC-cell block observation. In the eight participants with bilateral breast masses, the mass that underwent paired FNAC and cell block sampling was designated as the index lesion. Only the index lesion contributed to the diagnostic-accuracy analysis, and the contralateral mass did not contribute a separate statistical observation. This calculation estimated a general proportion rather than the precision of sensitivity or specificity; diagnostic accuracy estimates were therefore treated as exploratory. Consecutive patients referred with a palpable breast lesion were eligible. Patients who declined FNAC and those who had received neoadjuvant chemotherapy or radiotherapy were excluded.

Demographic and clinical information, including age, sex, laterality, lesion location, symptoms, and relevant history, was recorded on a structured case-record form. Breast imaging was performed according to clinical indication, and imaging findings were recorded using the Breast Imaging Reporting and Data System (BI-RADS).

## Fine-needle aspiration cytology

After aseptic preparation, palpable lesions were sampled with a 22- or 23-gauge needle attached to a 10-mL syringe. At least two dedicated passes were performed. Material from the first pass was used for conventional smears: air-dried smears were stained with May-Grünwald-Giemsa, and wet-fixed smears were stained by the Papanicolaou method. Rapid on-site evaluation was not routinely performed.

Two cytopathologists independently reviewed the smears while blinded to histopathology and assigned an International Academy of Cytology Yokohama category: C1, inadequate; C2, benign; C3, atypical; C4, suspicious for malignancy; or C5, malignant [5]. Cytological interpretation considered cellularity, epithelial arrangement, nuclear atypia, myoepithelial cells, stromal fragments, necrosis, inflammation, and background elements.

## Cell block preparation and combined interpretation

A separate second needle pass from the same lesion was dedicated to cell block preparation. The aspirated material was expelled directly into 10% neutral buffered formalin and allowed to fix for at least 30 minutes before centrifugation. The material was centrifuged for 10 minutes at 1,500-2,000 rpm in an Eppendorf centrifuge 5420 equipped with the standard FA-24×2 rotor. Based on an effective rotor radius of 8.4 cm, this corresponded to approximately 211-376 ×g. After removal of the supernatant, 0.5 mL of patient plasma and 0.25-0.5 mL of thrombin solution, at a concentration of 1,000-5,000 NIH units/mL reconstituted in saline, were added to form a clot. When required to improve clot visibility, two drops of 3% acetic acid were added to the pellet. The clot was transferred to a tissue cassette and remained in formalin with routine surgical specimens for a total fixation period of 6-24 hours before tissue processing. It was subsequently embedded in paraffin, sectioned at 3-4 µm, and stained with hematoxylin and eosin.

A cell block was considered diagnostic when sufficiently preserved lesional epithelial, stromal, or inflammatory material was present to permit assignment to a benign, atypical, suspicious, or malignant category. A preparation was classified as inadequate when no lesional material, or insufficient preserved material for diagnostic categorization, was identified after examination of the available hematoxylin and eosin-stained sections. It was classified as predominantly hemorrhagic when blood or clot dominated the sections, and the residual lesional material was insufficient for diagnosis. Inadequate and predominantly hemorrhagic preparations were grouped as non-diagnostic for descriptive analysis.

Cell block findings were recorded as non-diagnostic, benign, atypical, suspicious, or malignant. Combined interpretation integrated the FNAC cytomorphology with the cellular and architectural features preserved in the corresponding cell block. No study-specific immunohistochemical or molecular results contributed to the diagnostic-performance analysis.

### Reference standard and diagnostic thresholds

Histopathology from 26 clinically indicated core biopsies and 20 surgical excisions was available for 46 of the 74 lesions and served as the reference standard. The index-to-reference interval was 1-21 days, and no intervening treatment was recorded. Histopathology readers were blinded to the index-test results. Routine paraffin sections stained with hematoxylin and eosin were classified as benign or malignant, with specific histological diagnoses recorded where available. The remaining 28 lesions did not undergo tissue sampling within the study dataset and were excluded from diagnostic accuracy calculations.

For FNAC, C4 and C5 interpretations were considered positive for malignancy, whereas C2 and C3 interpretations were considered negative. Cell blocks categorized as suspicious or malignant were considered positive; benign and atypical cell blocks were considered negative. Inadequate cell blocks were retained as a separate descriptive category and did not by themselves count as positive. The combined result followed a prespecified OR rule: positive if FNAC was C4 or C5 or if the cell block was suspicious or malignant; otherwise negative. Thus, an inadequate cell block did not override a positive FNAC result and did not itself constitute a positive result. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were calculated against histopathology.

### Statistical analysis

Data were entered in Microsoft Excel 2016 (Microsoft Corporation, Redmond, Washington, United States) and analyzed using IBM SPSS Statistics version 25 (IBM Corporation, Armonk, New York, United States). Continuous variables were summarized by mean, standard deviation, median, and range; categorical variables were summarized by frequencies and percentages. Diagnostic performance estimates are accompanied by exact two-sided 95% binomial confidence intervals reconstructed from the verified two-by-two counts. Participant-level paired results were available for the 46 verified participants, and an exact two-sided McNemar test assessed discordant classifications between FNAC and combined interpretation. A two-sided $p < 0.05$ was considered statistically significant. All analyses were performed at the participant level, with one index-lesion observation per participant.

### Ethical approval and consent

The Institutional Ethics Committee of People's College of Medical Sciences & Research Centre approved the study (Ref no. PCMS/OD/PS/2024/738(9); approval dated March 26, 2024). Written informed consent was obtained from every participant before FNAC. Records were anonymized for analysis, and the study was conducted in accordance with the Declaration of Helsinki.

## Results

### Participant flow and baseline characteristics

Seventy-four consecutive patients with palpable breast lesions were enrolled, and all underwent paired FNAC and cell block sampling. All 74 were included in descriptive analyses. Histopathology was available for 46 participants (62.2%), who formed the diagnostic accuracy population; 28 participants (37.8%) without histopathology were excluded from accuracy calculations (Figure *1*). Histopathological verification was available for all 32 BI-RADS 4 lesions and the single BI-RADS 5 lesion, corresponding to a verification rate

of 100% in both categories. Among the 41 participants with BI-RADS 2 or 3 lesions, 13 underwent histopathological verification, corresponding to a combined verification rate of 31.7%. These lower-category lesions underwent tissue examination because of lesion size, persistent symptoms, or patient preference. Participant flow is shown in Figure *1*. No adverse events were recorded.

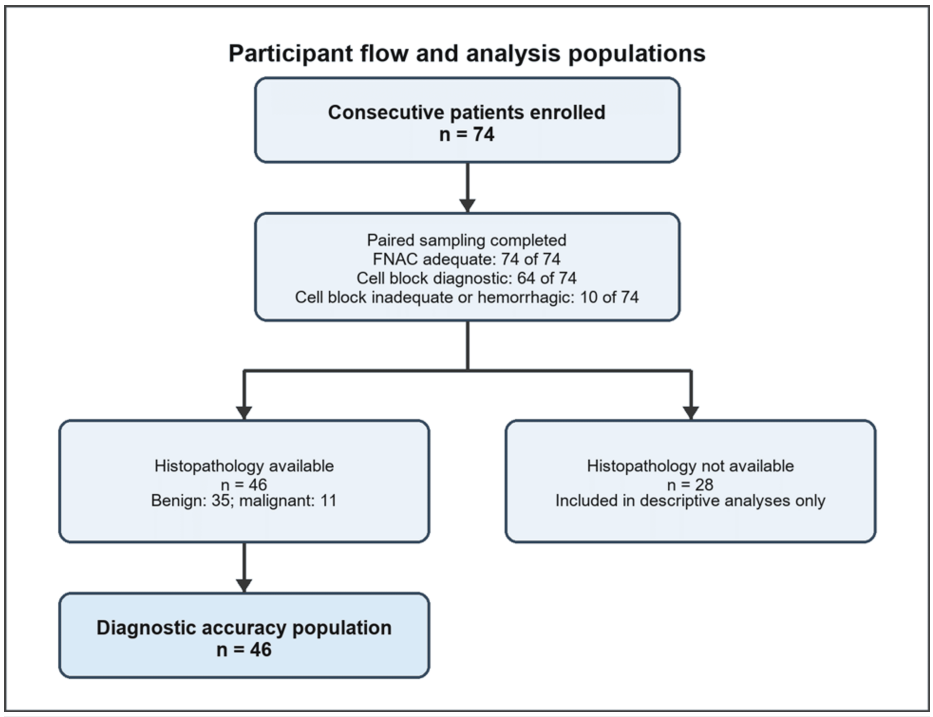


**FIGURE 1: Participant flow and analysis populations**

All 74 participants contributed to descriptive analyses. The 46 participants with histopathology contributed to diagnostic accuracy analyses.

FNAC: fine-needle aspiration cytology

Age ranged from 14 to 73 years, with a mean of 36.4 ± 14.0 years and a median of 35.5 years. Seventy participants (94.6%) were female, and 4 (5.4%) were male. Lesions were left-sided in 34 participants (45.9%), right-sided in 32 (43.2%), and bilateral in 8 (10.8%). Baseline characteristics are summarized in Table *1*.

| Characteristic | Category or summary | Value |
|---|---|---|
| Age, years | Mean ± SD | 36.4 ± 14.0 |
| Age, years | Median (range) | 35.5 (14-73) |
| Sex | Female | 70 (94.6) |
| Sex | Male | 4 (5.4) |
| Laterality | Left | 34 (45.9) |
| Laterality | Right | 32 (43.2) |
| Laterality | Bilateral | 8 (10.8) |
| BI-RADS | Category 2 | 21 (28.4) |
| BI-RADS | Category 3 | 20 (27.0) |
| BI-RADS | Category 4/4A/4B/4C | 32 (43.2) |
| BI-RADS | Category 5 | 1 (1.4) |

**TABLE 1: Baseline participant and lesion characteristics**

BI-RADS: Breast Imaging Reporting and Data System

BI-RADS category 2 accounted for 21 lesions (28.4%). Twenty lesions (27.0%) were category 3, 32 lesions (43.2%) were category 4, and 1 lesion (1.4%) was category 5.

## Cytological and cell block findings

All 74 conventional FNAC preparations were adequate. The predominant Yokohama category was C2 (benign), comprising 58 lesions (78.4%). One lesion (1.4%) was C3 (atypical), five (6.8%) were C4 (suspicious for malignancy), and 10 (13.5%) were C5 (malignant).

Cell block evaluation categorized 54 lesions (73.0%) as benign, 1 (1.4%) as atypical, 4 (5.4%) as suspicious, and 5 (6.8%) as malignant. Ten cell blocks (13.5%) were inadequate or predominantly hemorrhagic. Thus, the cell block provided a diagnostic category in 64 of 74 lesions (86.5%), but adequacy was lower than that of conventional smears. Method-specific diagnostic categories are summarized in Table *2*. Figure *2* shows the smear and cell block morphology in fibroadenoma.

| Method | Category | n | % |
|---|---|---|---|
| FNAC | C1 — inadequate | 0 | 0 |
| FNAC | C2 — benign | 58 | 78.4 |
| FNAC | C3 — atypical | 1 | 1.4 |
| FNAC | C4 — suspicious | 5 | 6.8 |
| FNAC | C5 — malignant | 10 | 13.5 |
| Cell block | Inadequate/hemorrhagic | 10 | 13.5 |
| Cell block | Benign | 54 | 73 |
| Cell block | Atypical | 1 | 1.4 |
| Cell block | Suspicious | 4 | 5.4 |
| Cell block | Malignant | 5 | 6.8 |

**TABLE 2: Distribution of fine-needle aspiration cytology and cell block categories**

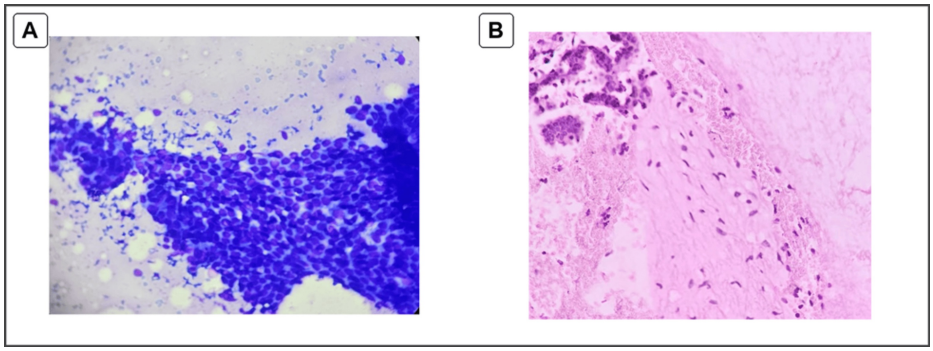


**FIGURE 2: Correlative smear and cell block morphology in fibroadenoma**

(A) Giemsa-stained FNAC smear at 40× showing cohesive benign ductal epithelial cells with myoepithelial cells. (B) Hematoxylin and eosin-stained cell block section showing epithelial and stromal components.

FNAC: fine-needle aspiration cytology

## Histopathological findings

Histopathological examination was available for 46 lesions. Thirty-five (76.1%) were benign, and 11 (23.9%) were malignant. The malignant diagnoses comprised six invasive ductal carcinomas, including three with ductal carcinoma in situ; three mucinous carcinomas; and two papillary carcinomas. Histopathological outcomes are summarized in Table 3.

| Outcome | Diagnosis | n (% of 46) |
|---|---|---|
| Benign | All benign histological diagnoses | 35 (76.1) |
| Malignant | Invasive ductal carcinoma (including three with DCIS) | 6 (13.0) |
| Malignant | Mucinous carcinoma | 3 (6.5) |
| Malignant | Papillary carcinoma | 2 (4.3) |

**TABLE 3: Histopathological outcomes in the reference-standard subset**

Morphological correlation was most informative when smear and cell block findings were interpreted together. In mucinous carcinoma, cohesive tumor clusters in a mucinous background on FNAC were complemented by cell block architecture and confirmed by histopathology (Figure 3).

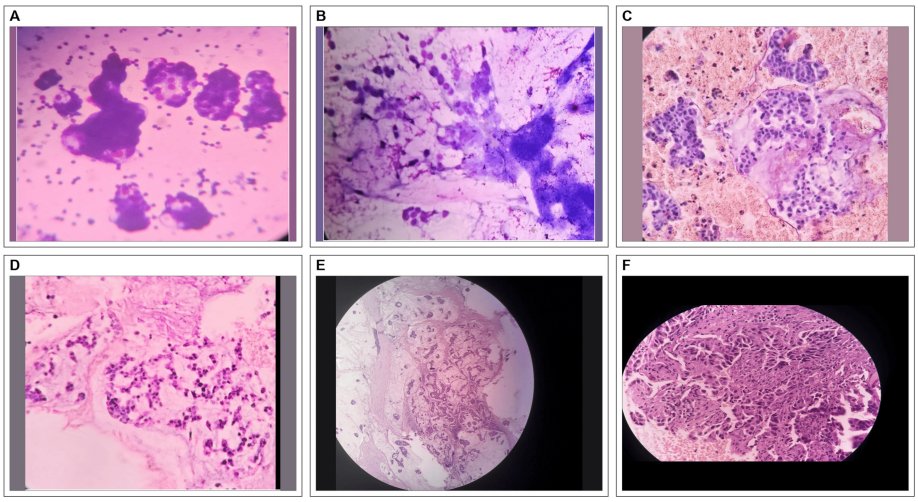


**FIGURE 3: Cytological, cell block, and histopathological correlation in mucinous carcinoma**

(A-B) Giemsa-stained FNAC smears showing cohesive epithelial clusters in a mucinous background. (C-D) Hematoxylin and eosin-stained cell block sections showing atypical ductal epithelial clusters in fibrinous and mucinous material. (E) Histopathology showing tumor-cell clusters in pools of mucin. (F) Histopathology showing infiltrating pleomorphic tumor cells in desmoplastic stroma.

FNAC: fine-needle aspiration cytology

Cross-tabulation of FNAC categories against histopathology showed that all 35 histologically benign lesions were classified as C2. Among the 11 histologically malignant lesions, one was classified as C2, one as C3, three as C4, and six as C5. Two unique histologically malignant lesions were classified as negative by FNAC. The first occurred in a 66-year-old woman with a BI-RADS 4C lesion. FNAC was categorized as C2 and interpreted as proliferative breast disease, while the cell block was categorized as C3 because of atypical architecture. Histopathology demonstrated intracystic papillary ductal carcinoma with foci of infiltrating ductal carcinoma. Because neither the C2 FNAC result nor the C3 cell block result met the prespecified threshold for positivity, this lesion remained false-negative after combined interpretation.

The second lesion occurred in a 35-year-old woman with a BI-RADS 4A lesion. FNAC was categorized as C3 and interpreted as atypia with features suggesting nipple adenoma. The corresponding cell block was categorized as C4, suspicious for malignancy. Histopathology demonstrated apocrine encapsulated papillary carcinoma. Under the prespecified OR rule, the positive cell block result upgraded the combined interpretation and corrected the FNAC false-negative classification.

Thus, the two FNAC false-negative results and the single remaining combined false-negative result represented two unique lesions rather than three separate lesions. One FNAC false-negative was corrected by the cell block component, while the other remained false-negative after combined interpretation (Table *4*).

| FNAC Yokohama category | Histologically benign, n | Histologically malignant, n | Total, n |
|---|---|---|---|
| C1 — inadequate | 0 | 0 | 0 |
| C2 — benign | 35 | 1 | 36 |
| C3 — atypical | 0 | 1 | 1 |
| C4 — suspicious for malignancy | 0 | 3 | 3 |
| C5 — malignant | 0 | 6 | 6 |
| Total | 35 | 11 | 46 |

**TABLE 4: Cross-tabulation of FNAC Yokohama categories against final histopathological outcomes in the verified subset**

FNAC: fine-needle aspiration cytology

### Diagnostic performance

Among the 46 participants with histopathological verification, FNAC yielded 9 true-positive, 35 true-negative, 2 false-negative, and no false-positive results. Combined FNAC-cell block interpretation yielded 10 true-positive, 35 true-negative, 1 false-negative, and no false-positive results.

FNAC sensitivity was 81.82% (95% CI, 48.22%-97.72%), specificity was 100% (95% CI, 90.00%-100%), positive predictive value was 100% (95% CI, 66.37%-100%), negative predictive value was 94.59% (95% CI, 81.81%-99.34%), and accuracy was 95.65% (95% CI, 85.16%-99.47%). Combined interpretation had numerically higher sensitivity at 90.91% (95% CI, 58.72%-99.77%), negative predictive value at 97.22% (95% CI, 85.47%-99.93%), and accuracy at 97.83% (95% CI, 88.47%-99.94%); specificity and positive predictive value remained 100%.

In the paired analysis, both strategies were correct in 44 cases and incorrect in 1 case. Combined interpretation corrected one FNAC false-negative result, and no FNAC-correct classification became incorrect after combination. The exact two-sided McNemar p-value was 1.000. Diagnostic performance estimates are summarized in Table *5*.

| Metric | FNAC, n/N | FNAC, % (95% CI) | Combined, n/N | Combined, % (95% CI) |
|---|---|---|---|---|
| Sensitivity | 9/11 | 81.82 (48.22-97.72) | 10/11 | 90.91 (58.72-99.77) |
| Specificity | 35/35 | 100.00 (90.00-100.00) | 35/35 | 100.00 (90.00-100.00) |
| PPV | 9/9 | 100.00 (66.37-100.00) | 10/10 | 100.00 (69.15-100.00) |
| NPV | 35/37 | 94.59 (81.81-99.34) | 35/36 | 97.22 (85.47-99.93) |
| Accuracy | 44/46 | 95.65 (85.16-99.47) | 45/46 | 97.83 (88.47-99.94) |

**TABLE 5: Diagnostic performance against histopathology**

FNAC: fine-needle aspiration cytology

## Discussion

This prospective study provides three clinically relevant observations. First, conventional FNAC was adequate in all 74 palpable lesions and showed high specificity and accuracy in the histologically verified subset. Second, 10 cell blocks were inadequate or predominantly hemorrhagic, showing that a dedicated second pass does not guarantee a diagnostic paraffin section. Third, combined interpretation produced numerically higher sensitivity, NPV, and accuracy than FNAC alone while preserving the observed specificity and PPV. The magnitude and certainty of that difference must be judged in the context of only 11 malignant reference-standard cases and partial histological verification.

The performance of FNAC in this study is plausible within the broader literature. A meta-analysis of 46

studies reported a pooled sensitivity of 92.7% and specificity of 94.8% after excluding unsatisfactory specimens, while emphasizing the clinical risk associated with inadequate samples [16]. More recent analyses focused on the Yokohama system have reported approximately 91% sensitivity when suspicious and malignant categories are considered positive, with high overall discriminatory performance [7,17]. Our sensitivity estimate was lower at 81.82%, but its 95% confidence interval was wide because it was based on nine true-positive results among 11 malignant lesions. Conversely, the observed 100% specificity had a lower confidence bound of 90.00% and should not be interpreted as proof of perfect performance.

Standardized categorical reporting is particularly important because the clinical meaning of a breast aspirate is not binary at the time of microscopy. The Yokohama system links insufficient, benign, atypical, suspicious, and malignant categories to increasing risks of malignancy and management recommendations [5-7]. Marabi et al. found that applying the system improved diagnostic performance compared with original unstandardized diagnoses [18]. In the present study, treating C4 and C5 as positive prioritized specificity, but two malignancies remained false-negative by FNAC alone. This reinforces the principle that a benign cytological label cannot override discordant clinical or imaging findings.

Cell blocks offer a different type of information rather than simply a second reading of the same preparation. Paraffin sections may better display epithelial cohesion, stromal fragments, fibrovascular cores, and other tissue-like relationships, while also allowing serial sections and selected ancillary studies [9,10,13]. In a prospective study of palpable breast lesions, Obiajulu et al. reported additional malignant diagnostic yield and fewer equivocal diagnoses after adding cell blocks [11]. Noda et al. likewise found that cell block morphology and immunocytochemistry reduced atypical classifications in a retrospective breast series [12]. A recent prospective study from India also reported a numerical gain when cell block findings were combined with FNAC, although differences in case selection, preparation, thresholds, and reference-standard verification limit direct comparison [19].

The present study also demonstrates the practical counterweight to those benefits: 13.5% of cell blocks were inadequate or hemorrhagic. Pre-analytical factors, including lesion targeting, distribution of material between preparations, clot formation, fixation, and processing, can determine whether a cell block adds information [9,10]. An inadequate cell block is not a negative test and should not reassure the clinical team. Where feasible, rapid adequacy assessment and deliberate triage of additional passes may improve yield, but rapid on-site evaluation was not routinely used here.

The numerical gain associated with combined interpretation was concentrated in sensitivity: false-negative classifications decreased from 2 to 1, sensitivity increased by 9.09 percentage points, and accuracy increased by 2.18 percentage points. However, the combined strategy used an inclusive OR rule under which every FNAC-positive result remained positive after combination. Therefore, when applied to the same verified participants, the sensitivity of the combined strategy was structurally unable to be lower than that of FNAC alone, although false-positive cell block findings could potentially reduce specificity. The observed increase should consequently be interpreted as the incremental diagnostic yield of adding cell block findings rather than evidence that cell block preparation was independently superior to FNAC.

In addition, cell block material was obtained through a separate second needle pass. The single FNAC false-negative corrected by combined interpretation may therefore reflect increased total tissue sampling, the architectural information provided by cell block processing, or both. Because the study did not include a control in which material from a comparable second pass was prepared as additional conventional smears, the contribution of increased sampling could not be separated from the contribution of the cell block technique itself. Only one discordant pair was observed, and the exact two-sided McNemar p-value was 1.000; therefore, these findings remain descriptive and do not establish statistical superiority.

Clinically, the most defensible application is an adjunctive workflow. FNAC can provide rapid initial categorization; a diagnostic cell block may add architectural context or preserve material for validated immunocytochemistry. Concordant benign clinical, imaging, and cytological findings may support conservative management according to local protocols. Atypical, suspicious, malignant, radiologically discordant, or persistently concerning lesions require repeat sampling or tissue biopsy. Neither FNAC nor a cell block can replace histopathology when invasion, tumor grade, receptor status, or definitive classification will determine treatment.

This study has important limitations. Histopathology was available for 46 of 74 participants and was obtained according to clinical indication, creating partial verification bias; the diagnostic accuracy estimates therefore apply to the verified subset rather than the whole cohort. Because verification was not uniform across FNAC categories, false-positive and false-negative results may be underrepresented. The single-center design and only 11 malignant lesions produced imprecise sensitivity and PPV estimates. Ten cell blocks were non-diagnostic, and procedural predictors of inadequacy were not evaluated. Although paired classifications were available for all 46 verified participants, only 1 discordant pair limited the informativeness of the McNemar test. Separate reader-level classifications were not retained, precluding formal assessment of interobserver agreement, and the process used to resolve initial interpretive differences was not prospectively standardized or documented. These factors limit assessment of

interpretive reproducibility. Reference-standard verification was strongly associated with the imaging category: all BI-RADS 4 and 5 lesions underwent histopathological verification, compared with 31.7% of BI-RADS 2 and 3 lesions. This differential verification increases the possibility of partial verification bias and limits application of the diagnostic-accuracy estimates to the entire enrolled cohort.

Strengths include prospective consecutive recruitment, paired collection of smear and cell block material from the same palpable lesion, standardized Yokohama reporting, explicit diagnostic thresholds, transparent participant flow, complete paired classifications in the verified subset, and exact confidence intervals for the confirmed two-by-two results. A future multicenter study should prespecify a uniform reference-standard pathway, document reader experience and blinding, use standardized cell block adequacy criteria, and evaluate whether any gain changes management rather than only classification.

## Conclusions

Fine-needle aspiration cytology showed high observed accuracy in the histologically verified subset of this cohort. Combined FNAC-cell block interpretation produced numerically higher sensitivity, negative predictive value, and accuracy than FNAC alone, while observed specificity remained high. The small number of malignant cases and non-uniform reference-standard verification mean that these findings support feasibility and potential added value rather than definitive superiority. Because combined interpretation incorporated FNAC by construction and cell block material was obtained through an additional needle pass, the numerical improvement should be understood as the incremental yield of the overall paired-sampling workflow rather than proof of the independent superiority of cell block processing.

Cell block preparation should be regarded as an adjunct whose usefulness depends on adequate cellular material and correlation with imaging and clinical findings. Histopathological confirmation remains necessary for discordant, atypical, suspicious, malignant, or otherwise concerning lesions. The paired analysis did not establish statistical superiority because only one discordant pair was observed (exact p = 1.000).

## Additional Information

### Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

**Concept and design:** Khushboo Shukla, Tarun Kant Tripathi, Sushil Kumar Sharma

**Acquisition, analysis, or interpretation of data:** Khushboo Shukla, Swalaha Sadaf Siddiqui, Sushil Kumar Sharma

**Drafting of the manuscript:** Khushboo Shukla, Swalaha Sadaf Siddiqui

**Critical review of the manuscript for important intellectual content:** Khushboo Shukla, Tarun Kant Tripathi, Sushil Kumar Sharma

**Supervision:** Swalaha Sadaf Siddiqui, Sushil Kumar Sharma

### Disclosures

**Human subjects:** Informed consent for treatment and open access publication was obtained or waived by all participants in this study. Institutional Ethics Committee of People's College of Medical Sciences & Research Centre issued approval PCMS/OD/PS/2024/738(9), dated March 26, 2024. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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