Received: 31 March 2022 | Revised: 14 July 2022 | Accepted: 18 July 2022

DOI: 10.1111/cyt.13171

ORIGINAL ARTICLE

WILEY

Performance of breast fine needle aspiration as an initial diagnostic tool: A large academic hospital experience

Zhengshan Chen | Christine Salibay | Wafaa Elatre | Wesley Y. Naritoku | Yanling Ma | Sue Ellen Martin | Tiannan Wang

Department of Pathology and Laboratory Medicine, University of Southern California/LAC-USC Medical Center, Los Angeles, California, USA

Correspondence
Tiannan Wang and Sue Ellen Martin, Department of Pathology and Laboratory Medicine, Keck School of Medicine of the University of Southern California USC/LAC+USC Medical Center Los Angeles, CA 90033, USA.
Email: tiannan.wang@med.usc.edu and sue.martin@med.usc.edu

Abstract

Background: The clinical performance of the Yokohama reporting system for breast cytology remains uncertain.

Methods: In this study, we retrospectively evaluated 318 breast fine needle aspirations (FNABs) from Los Angeles County Hospital over a five-year period, analysing data for breast cytology, histology, and radiology.

Results: Among 318 breast FNAB cases, 78.3% (249/318) were benign and 5.3% (17/318) malignant. Of 83 cases with follow-up histology, 14.5% (12/83) were insufficient, 66.3% (55/83) were benign, and 16.9% (17/83) were malignant. Of 55 benign cases, 61.8% (34/55) were fibroadenoma and 9 (9/55, 16.4%) were fibrocystic changes. Two cases were diagnosed as "atypical" but confirmed "benign" on core needle biopsy (CNB). No "suspicious" cases were found. Seventeen malignant cases were confirmed by CNB, including 70.6% (12/17) invasive ductal carcinoma, 11.8% (2/17) invasive lobular carcinoma, and one malignant phyllodes tumour. Receptor studies on cell blocks of three malignant cases showed concordant results with CNB results. In addition, 82.2% (148/180) of lesions with Breast Imaging-Reporting and Data System (BI-RADS) scores of 2 or 3 were benign and 92.3% (12/13) BI-RADS score 5 lesions were malignant on FNAB. Finally, 90% (67/74) of BI-RADS 4a lesions were benign, and 97% (36/37) of fibroadenomas were BI-RADS score 4a.

Conclusion: This, by far the largest U.S. breast cytology study, showed 93.3% sensitivity, 100% specificity, 100% positive predictive value, and 98.2% negative predictive value for breast FNAB. Women with breast lesions of BI-RADS score 3 or less have a low risk of malignancy; FNAB would contribute to the reduction of excisional biopsies. FNAB can be considered as an initial diagnostic tool for BI-RADS 4 mass/lesions and satellite lesions, as well as for triaging patients.

KEYWORDS
Breast cytology, cytology, histology, and radiology correlation, fine needle aspiration

1 | INTRODUCTION

In the United States, about one in eight women develops breast cancer over the course of the lifetime.[1] Early breast cancer detection and diagnosis are critical for the appropriate treatment and for the survival of breast cancer patients.[1] Both fine needle aspiration biopsy (FNAB) and core needle biopsy (CNB) are widely accepted for the diagnosis of breast lesions[2–5]; however, FNAB is used less frequently due to its inability to evaluate the architecture and occasional inadequacy for performing ancillary studies such as fluorescence in situ hybridisation (FISH).[6] During the COVID-19 pandemic many procedures, in particular CNB, were deferred.[7–9] As a safe and alternative tool, breast FNAB is especially needed at this time to provide accurate and prompt diagnosis.[10]

The International Academy of Cytology Yokohama (IACY) system for reporting breast FNAB cytology results was initiated at the Yokohama International Congress of Cytology Meeting in 2016. Further editing and modifications were made in 2019.[11] In this categorised system, breast FNAB cytology results are stratified into five categories by their risks of malignancy (ROM): 1 = insufficient/inadequate; 2 = benign; 3 = atypical; 4 = suspicious of malignancy; 5 = malignant.[12] A few recent studies have shown this to be a validated as well as reliable system for triaging palpable breast lesions[13–16]; however, given the aforementioned reasons, the system has not yet been widely adopted.

The Breast Imaging-Reporting and Data System (BI-RADS), as one component of the breast lesions triple test, is a radiological reporting system developed by the American College of Radiology, which includes six categories: 1 = negative; 2 = benign; 3 = probably benign; 4 = suspicious abnormality; 5 = highly suggestive of malignancy; 6 = pathologically proven malignancy.[17] Magny et al[17] have shown that BI-RADS category 3 had a very low ROM of <2%, while BI-RADS category 5 has a ROM of >95%. Category 4 is a heterogeneous group divided into three subcategories as 4a, 4b, and 4c, with ROMs ranging from 2%–10% to 50%–95%.[17] The BI-RADS radiological system has been successfully utilised in classifying breast lesions in North America and shows an excellent concordance with pathological findings. On the other hand, it has been reported to have a certain level of subjectivity, which is inevitable, especially in Categories 3 and 4. Therefore, the diagnostic accuracy and specificity of this system are significantly decreased.[18]

The purpose of this study is to assess the clinical performance of breast FNAB by the IACY system, and to correlate the cytological findings with those of BI-RADS, the radiological system. For cases with a follow-up CNB or a resection, correlations among the cytological, histological, and radiological findings are also analysed.

2 | MATERIALS AND METHODS

The laboratory information database at Los Angeles County Hospital was reviewed from June 2015 to June 2020. The FNAB procedure is performed over a five-day FNA clinic by a pathology resident or cytopathology fellow under the supervision of an attending cytopathologist. A breast mass/lesion is aspirated by using ultrasound guidance, targeting areas of notable ultrasonographic features. Aspirate smears are immediately fixed in 95% ethanol for Papanicolaou staining. Air-dried smear with Diff-Quick staining is used to perform rapid on-site evaluation (ROSE). Formalin-fixed, HistoGel (Hardy Diagnostics, Agar deep, 1.5% in 9 ml) liquefied cell blocks are processed routinely for each case. All breast FNAB samples were classified into five diagnostic categories according to the IACY system, comprising insufficient/inadequate, benign, atypical, suspicious for malignancy, and malignant. The demographic information and BI-RADS score of each patient were retrieved for this study from the medical electronic record system. This study was conducted with approval from the institutional review board of the University of Southern California and with the agreement of the Los Angeles County Hospital Laboratory.

2.1 | Immunohistochemistry

Deparaffinised, rehydrated cell block and tissue sections were incubated with 0.3% hydrogen peroxide for 30 min to block endogenous peroxidase. For antigen retrieval, the slides were placed in 1 mmol/L tris-ethylenediamine tetraacetic acid buffer (pH 9.0) and heated at 97°C in a microwave oven for 20 min. The slides were then washed and incubated with primary antibodies, oestrogen receptor (ER, clone EP1, ready to use; Agilent), or progesterone receptor (PR, clone PGR 636, ready to use; Agilent) for 20 minutes at room temperature. The EnVision Flex High pH kit (Agilent) was used for the signal detection. All slides were then counterstained with haematoxylin. Appropriate positive and negative controls were used throughout.

2.2 | FISH Testing

A representative 5-μm thick formalin-fixed, paraffin-embedded cell block section from an individual case and tissue sections of all invasive breast cancers were subjected to FISH assay for human epidermal growth factor receptor 2 (HER2) amplification, and the HER2 FISH results were interpreted by a commercial laboratory (Quest Diagnostics LLC).

2.3 | Statistical analysis

The ROM of each breast FNAB category was calculated and correlated with the available follow-up histology. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for FNAB were calculated. Breast FNAB cytology results with insufficient/inadequate material were not included in this analysis. The categories “benign” and “atypical” were considered together as

benign, and the categories "suspicious" and "malignant" together as malignant. On CNB and resection, atypical ductal hyperplasia (ADH) was considered pre-malignant in the statistical analysis.

The ROM of breast lesions based on BI-RADS scores were calculated and correlated with the results of breast FNAB diagnosis or available histology diagnosis.

3 | RESULTS

Overall, 318 breast FNABs were retrieved from the archived pathology database including 94.0% (299/318) female FNABs and 6.0% (19/318) male FNABs in addition to 5.3% (17/318) females with bilateral FNABs. The median age of female patients was 41 years (range 15 to 78 years). The median age of male patients was 40 years (range 21 to 69 years).

Of 19 male breast FNABs, 63.2% (12/19) cases were diagnosed as gynecomastia, 15.9% (3/19) cases were lipoma, 1 case was inadequate, 1 case was fat necrosis, 1 case was spindle cell lesion (confirmed as cavernous haemangioma on CNB), and 1 case was adenocarcinoma (confirmed as invasive ductal carcinoma on CNB).

3.1 | Cytology-radiology correlation

Of the total 318 breast FNABs, 13.5% (43/318) were in IACY Category 1 ("insufficient"). BI-RADS scores were not available in 5 (11.6%) of these cases. In 2.3% (1/43) of the cases, the BI-RADS score was 5, and in 86.0% (37/43) cases the BI-RADS scores were 1-4. Of 249 (78.3%) FNABs in IACY Category 2 ("benign"), 23 (9.2%) had no BI-RADS score, 152 (61.0%) were BI-RADS score 1-3, and 74 (29.7%) were BI-RADS score 4, including 67 BI-RADS 4a, 5 BI-RADS 4b, and 2 BI-RADS 4c.

Only 9 (2.8%) FNABs were in IACY Category 3 ("atypia"), including 2 (22.2%) cases without BI-RADS scores and 7 (77.8%) BI-RADS scores from 1 to 4a. No FNABs were in IACY Category 4 ("suspicious"). Lastly, 5.3% (17/318) FNABs were in IACY Category 5 ("malignant"), with 2 (11.8%) of them without BI-RADS scores, 3 (17.6%) having a BI-RADS score 4 including 2 cases of 4b and 1 case of 4c, and 12 (70.6%) were BI-RADS score 5.

By cytology-radiology correlation, the ROM was 100.0% (12/12) for BI-RADS score 5. ROMs for BI-RADS score 4c, 4b and 4a lesions were 33.3% (1/3), 28.6% (2/7), and 0.0% (0/67), respectively. ROMs for BI-RADS scores 1-3 were all 0.0% (0/156) (Table 1).

3.1.1 | Benign lesions (IACY Category 2) on radiology-cytology correlation

As mentioned above, all the 249 IACY Category 2 cases were BI-RADS score 4 or less on radiology (Table 2). Among them, 32.1% (80/249) of IACY Category 2 cases were diagnosed as fibroadenoma. Thirty-seven (46.3%) of these fibroadenoma were BI-RADS score 4, including 97% (36/37) BI-RADS 4a and one BI-RADS 4b. The remaining fibroadenoma cases were BI-RADS scores 1-3 when the scores were available.

In addition, cystic lesions accounted for 20.9% (52/249) of IACY Category 2 cases; 7 of these were BI-RADS score 4a. Fibrocystic changes (FCC) were identified in 40.4% (21/52) of the cystic lesions and three cases were BI-RADS score 4a. Inflammatory lesions including acute mastitis, abscess, and granulomatous mastitis were seen in 6% (15/249) of IACY Category 2 cases, and all of them were BI-RADS score 4.

In terms of other cases in IACY Category 2, two of 12 gynecomastia on breast FNAB were BI-RADS score 4b. Two of 10 epidermal inclusion cysts (EICs) were BI-RADS score 4a. Eight lipomatous

TABLE 1 Cytology-radiology correlation of breast lesions

Yokohama system for breast FNA cytology		Radiology BI-RADS score					
Category	No. (%)	N/A No. (%)	1 No. (%)	2 No. (%)	3 No. (%)	4 No. (%)	5 No. (%)
Insufficient	43 (13.5)	5 (11.6)	3 (7.0)	16 (37.2)	13 (30.2)	5 (11.6)[a]	1 (2.3)
Benign	249 (78.3)	23 (9.2)	4 (1.6)	93 (37.3)	55 (22.1)	74 (29.7)[b]	0
Atypical	9 (2.8)	2 (22.2)	1 (11.1)	2 (22.2)	1 (11.1)	3 (33.3)[c]	0
Suspicious	0	0	0	0	0	0	0
Malignant	17 (5.3)	2 (11.8)	0	0	0	3 (17.6)[d]	12 (70.6)
Total	318	32 (10.1)	8 (2.5)	111 (34.9)	69 (21.7)	85 (26.7)	13 (4.1)

Note: BI-RADS score: N/A: not available; 1-negative; 2-benign; 3-probably benign; 4-suspicious abnormality, 4a-low suspicion, 4b-moderate suspicion, 4c-high suspicion; 5-highly suggestive of malignancy.Abbreviations: BI-RADS, Breast Imaging-Reporting and Data System; FNA, fine needle aspiration.

[a]Four cases with BI-RADS score 4a and one case with 4c.

[b]Sixty-seven cases with 4a, five cases with 4b and 2 cases with 4c.

[c]All three cases with 4a.

[d]Two cases with 4b and one case with 4c.

TABLE 2 Cytology-radiology correlation of benign breast lesions

Breast FNA cytology diagnosis	No. (%)	Radiology BI-RADS score N/A No. (%)	1 No. (%)	2 No. (%)	3 No. (%)	4 No. (%)
FA	80 (32.1)	1 (1.3)	0	16 (20.0)	26 (32.5)	37 (46.3)[a]
Cystic lesion	52 (20.9)	2 (3.8)	1 (1.9)	39 (75.0)	3 (5.8)	7 (13.5)
Benign ductal cells	34 (13.7)	6 (17.6)	1 (2.9)	4 (11.8)	10 (29.4)	13 (38.2)[b]
FCC	21 (8.4)	3 (14.3)	0	13 (61.9)	2 (9.5)	3 (14.3)
Inflammation	15 (6.0)	2 (13.3)	0	4 (26.7)	5 (33.3)	4 (26.7)[c]
Gynecomastia	12 (4.8)	8 (66.7)	0	2 (16.7)	0	2 (16.7)[d]
EIC	10 (4.0)	0	0	4 (40.0)	4 (40.0)	2 (20.0)
Lipomatous neoplasm	8 (3.2)	1 (12.5)	0	5 (62.5)	2 (25.0)	0
Fat necrosis	7 (2.8)	0	0	4 (57.1)	2 (28.6)	1 (14.3)[e]
Fibroadipose tissue	6 (2.4)	0	2 (33.3)	2 (33.3)	1 (16.7)	1 (16.7)
Lactational change	3 (1.2)	0	0	0	0	3 (100.0)
Spindle cell lesion	1 (0.4)	0	0	0	0	1 (100.0)
Total	249	23 (9.2)	4 (1.6)	93 (37.3)	55 (22.1)	74 (29.7)

Note: BI-RADS score: N/A: not available; 1-negative; 2-benign; 3-probably benign; 4-suspicious abnormality, 4a-low suspicion, 4b-moderate suspicion, 4c-high suspicion.

Abbreviations: BI-RADS, Breast Imaging-Reporting and Data System; EIC, epidermal inclusion cyst; FA, fibroadenoma; FCC, fibrocystic change; FNA, fine needle aspiration.

[a]Thirty-six cases with BI-RADS score 4a and one case with 4b.

[b]Twelve cases with BI-RADS score 4a and one case with 4b.

[c]Two cases with BI-RADS score 4a, one case with 4b and one case with 4c.

[d]Two cases with BI-RADS score 4b.

[e]One case with BI-RADS score 4c; all other cases in this category had score 4a.

TABLE 3 Correlation of breast lesions classified by the Yokohama system

Yokohama system categories	No. (%)	Biopsy or resection No. (%) Benign	Atypical	Malignant	Radiology BI-RADS score No. (%) N/A	2	3	4	5
Insufficient	12 (14.5)	10 (83.3)	1 (8.3)	1 (8.3)	0	2 (16.7)	6 (50.0)	3 (25.0)[a]	1 (8.3)
Benign	55 (66.3)	54 (98.2)	1 (1.8)	0	0	10 (18.2)	9 (16.4)	36 (65.5)[b]	0
Atypical	2 (2.4)	2 (100.0)	0	0	0	0	0	2 (100.0)[c]	0
Suspicious	0	0	0	0	0	0	0	0	0
Malignant	14 (16.9)	0	0	14 (100.0)	2 (14.3)	0	0	1 (7.0)[d]	11 (78.6)
Total	83	66 (79.5)	2 (2.4)	15 (18.1)	2 (2.4)	12 (14.5)	15 (18.1)	42 (50.6)	12 (14.5)

Note: BI-RADS score: 2-benign; 3-probably benign; 4-suspicious abnormality, 4a-low suspicion, 4b-moderate suspicion, 4c-high suspicion; 5-highly suggestive of malignancy.Abbreviation: BI-RADS, Breast Imaging-Reporting and Data System.

[a]Two cases with BI-RADS score 4a and one case with 4c.

[b]Thirty-two cases with 4a, three cases with 4b and one case with 4c.

[c]All two cases with 4a.

[d]One case with 4c.

neoplasms on breast FNAB were BI-RADS scores ranging from 3 or less. Only one of seven fat necrosis (14.3%) cases was BI-RADS score 4c. It should be noted that the diagnosis of "fibroadipose tissue" was only applied to superficial and small lesions (less than 1 cm) for which a lipomatous neoplasm was favoured but the criteria were not met. This diagnosis was seen in 6 (2.4%) cases and 1 of them was BI-RADS score 4a. All three lactational change cases were BI-RADS score 4a. One spindle cell lesion was BI-RADS score 4a as well.

Finally, the diagnosis of "benign ductal cells" was applied when only benign ductal cells were found, but a definitive diagnosis could not be rendered. A total of 13.7% (34/249) cases had the diagnosis of "benign ductal cells" and 13 (38.2%) of these were rated BI-RADS score 4, with 4b in one case.

3.2 | Cytology-histology correlation

In total, 83 of 318 breast FNAB cases (83/318; 26.1%) had an in-house follow-up histology (Table 3). Of these, there were 12 (14.5%) cases in IACY Category 1 ("insufficient"), 55 cases (66.3%) in IACY Category 2 ("benign"), and 14 cases (16.9%) in IACY Category 5 ("malignant").

In IACY Category 1, 10 of the 12 cases were benign, one case turned out to be ADH, and one case was found an invasive ductal carcinoma (IDC) on follow-up histology. In IACY Category 2, 54 of 55 cases (98.2%) were confirmed benign on histology and one case (1.8%) was diagnosed a fibroadenoma with focal ADH on the final resection (Figure 1A,B). In addition, two cases (2.4%) diagnosed as IACY Category 3 by FNAB were found to be fibroadenoma on CNB (Figure 1C). Finally, all 14 cases in IACY Category 5 were confirmed malignant by histology, including 11 (78.6%) IDC, 2 (14.3%) invasive lobular carcinoma (ILC), and one recurrent malignant phyllodes tumour (Figure 1D–I).

In summary, IACY Category 1 had a ROM of 16.7% (2/12). The ROMs of IACY Category 2 and IACY Category 3 were 1.8% (1/55) and 0.0% (0/2), respectively, and the ROM for IACY Category 5 was 100.0% (14/14). Therefore, breast FNAB had a sensitivity of 93.3% (14/15), a specificity of 100.0% (56/56), a PPV of 100.0% (14/14), and a NPV of 98.2% (56/57) for the palpable breast lesions.

3.2.1 | Benign lesions (IACY Category 2) on cytology-histology correlation

Fibroadenoma was the most common breast FNAB diagnosis in a total 55 IACY Category 2 cases, accounting for 45.4% (25/55)

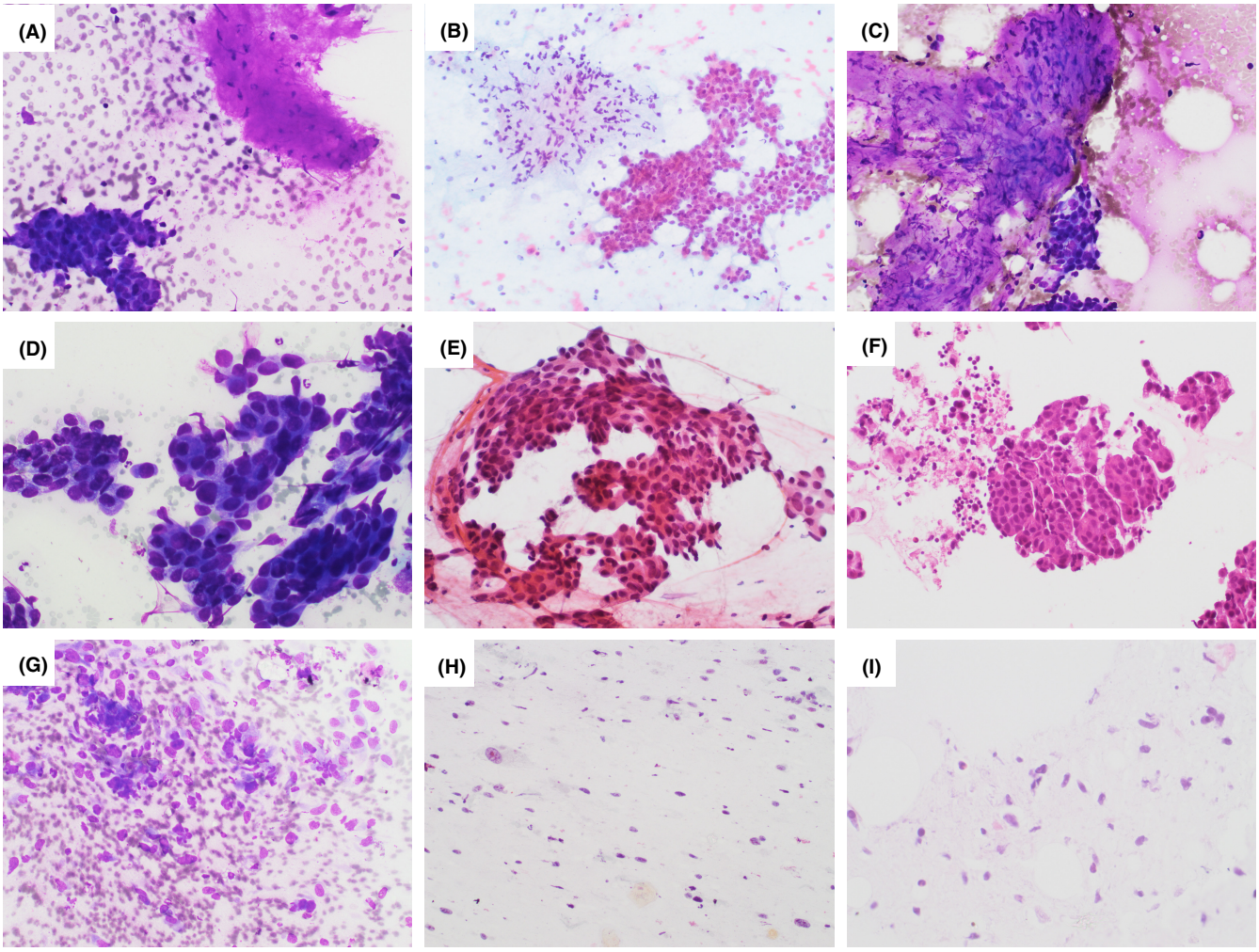

FIGURE 1 Examples of cases reported in the benign, atypical, and malignant categories. (A,B) A case with bland ductal epithelial cells, myoepithelial nuclei, and stromal fragments. This case was reported as benign-fibroadenoma on cytology and confirmed by histology (A: Diff-Quick, ×200; B: Pap, 200×). (C) An atypical stromal fragment with mild hypercellularity, mild nuclear enlargement, and atypia, raising the possibility of a low-grade phyllodes tumour. This case was reported as atypia on cytology, and histology showed a cellular fibroadenoma (Diff-Quick, 200×). (D-F) Clusters of glandular cells with enlarged, pleomorphic, hyperchromatic nuclei, and high N/C ratio. This case was reported as malignant on cytology, and histology showed invasive ductal carcinoma D: (Diff-Quick, 200×; E: Pap, 200×; F: H&E on cell block, 200×). (G-I) Discohesive spindle cells with enlarged, pleomorphic, hyperchromatic nuclei, conspicuous nucleoli, and high N/C ratio. This case was reported as malignant on cytology, and histology showed malignant phyllodes tumour (G: Diff-Quick, 200×; H: Pap, 200×; I: H&E on cell block, 200×)

TABLE 4 Cytology-histology correlation of benign breast lesions

	CNB or resection									
Breast FNAB diagnosis	Total	FA	UDH	IF	FCC	GMA	LP	EIC	HG	Fibrosis
FA	25 (45.5)	25[a]								
Benign ductal cells	9 (16.4)	7	1		1					
Cystic lesion	7 (12.7)		2		5					
Inflammation	5 (9.1)	1		3						1
FCC	4 (7.3)	1			3					
Gynecomastia	2 (3.6)					2				
LP	1 (1.8)						1			
EIC	1 (1.8)							1		
Spindle cell lesion	1 (1.8)								1	
Total No. (%)	55	34 (61.8)	3 (5.5)	3 (5.5)	9 (16.4)	2 (3.6)	1 (1.8)	1 (1.8)	1 (1.8)	1 (1.8)

Abbreviations: CNB, core needle biopsy; EIC, epidermal inclusion cyst; FA, fibroadenoma; FCC, fibrocystic change; FNAB, fine needle aspiration biopsy; GMA, gynecomastia; HG, haemangioma; IF, inflammation; LP, Lipoma; UDH, usual ductal hyperplasia.

[a]There is focal atypical ductal hyperplasia (ADH) present in the resection sample from one case.

TABLE 5 Ancillary studies of malignant lesions in FNAB and CNB

	Ancillary studies	
Case No.	FNAB	CNB
1	IHC: ER –, PR –; FISH: Her2 amplified	IHC: ER –, PR –; FISH: Her2 amplified
2	IHC: ER –, PR –	IHC: ER –, PR –
3	IHC: ER strong + in 90% cells, PR strong + in 90% cells	IHC: ER strong + in 90% cells, PR strong + in 90% cells
4	IHC: ER strong + in 80% cells; PR –	Not available

Abbreviations: CNB, core needle biopsy; ER, oestrogen response; FNAB, fine needle aspiration biopsy; IHC, immunohistochemistry; PR, progesterone response.

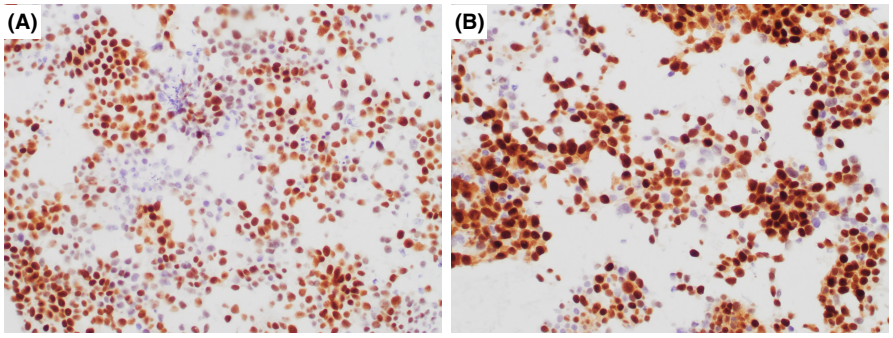

FIGURE 2 Immunohistochemistry of oestrogen receptor (ER) and progesterone receptor (PR) performed on the cell block. (A) ER was strongly positive in about 90% of tumour cells (200×). (B) PR was strongly positive in about 90% of tumour cells (200×)

(Table 4; Figure 1A,B). Twenty-four cases were confirmed and concordant with histologic findings, except for focal ADH found on one case.

Nine IACY Category 2 cases (9/55; 16.4%) were called benign ductal cells on breast FNAB and were found to be seven fibroadenomas, one usual ductal hyperplasia (UDH), and one FCC on follow-up histology. Of seven cystic lesions (7/55; 12.7%) in IACY Category 2, five were FCC and two were UDH on histology. Additionally, three of the five inflammatory lesions in IACY Category 2 were in concordance with histologic diagnosis. The other two inflammatory lesions were found to be one fibroadenoma and one stromal fibrosis. Of four FCC cases (4/55; 7.3%) in IACY Category 2, in addition to one fibroadenoma, 3 cases were consistent with FCC diagnosis on histology. The remaining cases were two gynecomastia (3.6%), one lipoma, and one EIC, all of which were consistent with histologic diagnosis. Lastly, there was one spindle cell lesion identified in IACY Category 2, and a diagnosis of cavernous haemangioma was made on histology.

3.3 | Malignant lesions by FNA cytology

A total 17 malignant lesions were diagnosed by breast FNAB cytology, comprising 12 IDC, two ILC, one recurrent malignant phyllodes

tumour, and two metastatic pancreatic adenocarcinomas in a single patient (Figure 1D-I). However, one IDC patient was lost to follow-up.

Receptor studies for ER and PR were available in four malignant breast FNAB cases (Table 5). Three of them had concordant histological diagnoses and receptor study results (Figure 2A,B). An HER2 FISH assay was performed on a cell block for one case diagnosed as malignant on breast FNAB, and the result was consistent with that from CNB.

4 | DISCUSSION

This is by far the largest retrospective study in the United States to analyse breast FNAB cytology with correlation on radiology as well as histology to evaluate breast FNAB performance. In our study, breast FNAB is proved to be a reliable sampling technique for the diagnosis of most palpable breast lesions, with 100% specificity and 100% PPV. Furthermore, cell blocks from breast FNABs are also valuable for ancillary studies. To meet the growing demand of breast lesion diagnosis, breast FNAB can be considered as the frontline diagnostic tool.

Breast cancer is the most commonly diagnosed cancer and the leading cause of cancer death among women. However, there are substantial differences depending on the region in breast cancer incidence, screening programs, and therapeutics. In developing countries, breast FNAB still remains the mainstay diagnostic tool for most breast lesions. However, in Western and some developed countries, the utilisation of breast FNAB is limited.[6] In the mid-1990s, CNB was introduced and emerged as the more reliable technique for diagnosis of a palpable breast mass in United States because of its higher sensitivity, and its ability to offer the best possible histological sampling and to make a distinction between in situ carcinoma versus invasive lesion.[6] However, the procedure has drawbacks including high procedure cost, patient anxiety, and complications such as pain and bleeding during the procedure, post-procedural haematoma, and possible seeding of tumour cells.[19–21] Besides, CNB still failed to obtain a sufficient amount of tissue or targeted incorrectly in 5–10% of non-palpable lesions.[23]

Therefore, we might see a resurgence in the use of breast FNAB in the United States due to easy availability, speed of procedure, and cost-effectiveness. Lesions that are palpable and clearly benign on imaging such as fibrocystic changes or a fibroadenoma may be better sampled with FNAB before CNB or even without CNB. Besides, breast FNAB was reported safer for chest wall lesions of the patient with implants or satellite lesions during staging work-up of biopsy-proven carcinoma. As known, the fundamental consideration in the diagnosis of breast disease is to distinguish benign from malignant lesions. Thus, a standardised breast FNAB reporting system such as the IACY categories is an important addition for the cytopathology community to allow the cytopathologist to provide structured information and an integrated report. To validate and further optimise this system, we retrospectively studied and analysed 318 breast FNAB cases from Los Angeles County Hospital over the past 5 years. We found that by using the IACY system, most breast lesions could be classified either into a benign or a malignant category, or for triaging the patient to provide critical information for appropriate management. In our study, the sensitivity of breast FNAB was 93.3% and its specificity was 100%. In the newly updated breast cancer classification from the World Health Organization (2020 version), the importance of hormonal receptors status (ER, PR, HER2) is further emphasised alongside TNM staging factors and the Nottingham grading system. Therefore, the biomarker status of breast cancer can sufficiently predict its biological behaviour. Several studies have shown that cytological materials from breast FNABs including cytological smears and cell blocks can provide good and reliable materials for ancillary studies.[23–27] Likewise, in our study, three malignant breast FNAB cases had concordant ER/PR results on CNB and one had a concordant HER2 FISH result on CNB.

Like other studies,[13–16] the present study supports the IACY categories as a standardised FNAB reporting system to facilitate communication between various specialties caring for patients with breast disease and to avoid unwarranted biopsies. As much has been discussed about BI-RADS scores, the risk of malignancy for BI-RADS 1 to 4a was found very low. We found that 90% (67/74) BI-RADS 4a lesions were benign. BI-RADS 4b had a ROM of 33.3%, BI-RADS 4c had a ROM of 66.7%, and BI-RADS 5 had a ROM of 100.0%. These findings are consistent with the established ROM for the BI-RADS system.[17,18]

Nevertheless, there are instances when there is a paucity in the specimen sampling and a high "insufficient/inadequate" rate compared to CNB. In fact, the adequacy of breast FNAB is dependent on multiple factors including the experience of the aspirator, the nature of the lesion (most common cause, accounting for 68%), the location of the tumour (i.e. if its deeply seated, small in size, or sclerotic). A study by Wong et al[13] showed that ROSE dramatically decreased the insufficient rate from 17.1% to 4%, suggesting ROSE should be performed when available. In our study, the insufficient rate was much lower than that from two other studies[15,16] although unanimous definition of specimen adequacy in breast FNAB has not been reached so far. Therefore, we recommend that a review of the BI-RADS score should be combined for cases in IACY Category 1, and a referral to CNB considered if necessary. The cytological features for differentiating invasive carcinoma from in-situ carcinoma on breast FNA have not been established, which limits current utilisation of breast FNA in breast cancer diagnosis. However, in certain situations, including the presence of a main mass and a satellite lesion or nodule, breast FNA can be very valuable for clinical decision-making and treatment.

In addition, we believe that ultrasound-guided FNAB by pathologists or other specialties can play a unique role in breast lesion diagnosis and in triaging the patient, for providing rapid assessment as well as for treatment, and is especially beneficial for patients with a palpable mass.

We realise the limitations of the current study, which include the retrospective nature which is inherently associated with selection bias. In our study, the number of breast FNAB cases with BI-RADS

score 4b and above was low, reflecting that most women with high BI-RADS scores might have undergone CNB directly.

5 | CONCLUSION

In summary, our study demonstrated that breast FNAB had a sensitivity of 93.3%, a specificity of 100.0%, a PPV of 100.0%, and a NPV of 98.2%, based on analysis of five years of experience at the Los Angeles County Hospital. Women with breast lesions of BI-RADS score 3 or less have a very low risk of malignancy, therefore, breast FNAB would significantly contribute to the reduction of excisional biopsies in the assessment of these lesions. Breast FNAB would be also beneficial for BI-RADS score 4 masses and lesions, satellite lesions, as well as for triaging cancer patients.

AUTHOR CONTRIBUTIONS

Zhengshan Chen, MD, PhD: data acquisition, data analysis, writing the manuscript, revising the manuscript. Christine Salibay, DO: data analysis, writing the manuscript, revising the manuscript. Wafaa Elatre, MD: data acquisition and revising the manuscript. Wesley Naritoku, MD, PhD: data acquisition, writing the manuscript, revising the manuscript. Yanling Ma, MD: data acquisition and revising the manuscript. Sue Ellen Martin, MD, PhD: study design and revising the manuscript. Tiannan Wang, MD, PhD: study design, data analysis, writing the manuscript, revising the manuscript.

ACKNOWLEDGMENTS

We would like to thank Thelma Chow, cytology supervisor ASCP, and Jane Minami, Los Angeles County laboratory information staff for assisting the data search.

CONFLICT OF INTEREST

None as it pertains to this manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

IRB APPROVAL

The study was conducted with approval from the institutional review board of the University of Southern California, and had an approved Laboratory Agreement at Los Angeles County Hospital and University of Southern California Medical Center.

ORCID

Tiannan Wang https://orcid.org/0000-0002-2983-7168

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How to cite this article: Chen Z, Salibay C, Elatre W, et al. Performance of breast fine needle aspiration as an initial diagnostic tool: A large academic hospital experience. *Cytopathology*. 2022;33:707-715. doi: 10.1111/cyt.13171