IAC
Hong Kong Cytology Tutorial 2023

2-3. December 2023 Prince of Wales Hospital Hong Kong

CYTOLOGY OF BREAST

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IAC 1957

RISE Health Research Network From the Lab to the Community

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Official Journal of the IAC
ACTA CYTOLOGICA
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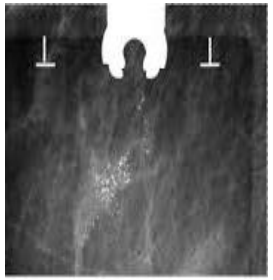
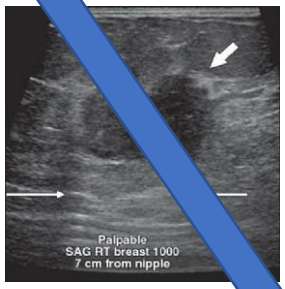
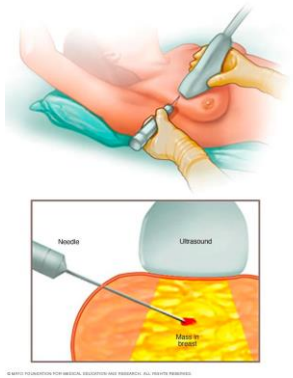
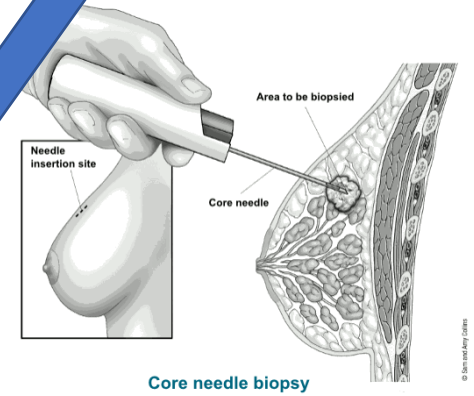
BREAST FNAB in our practice

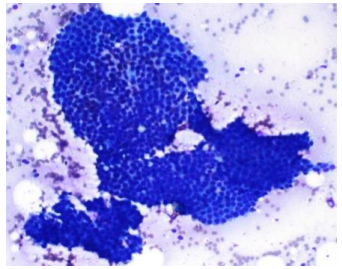


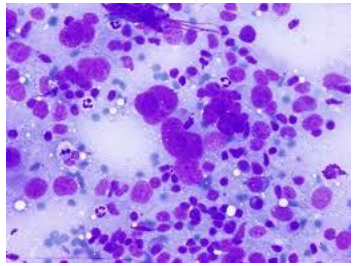






Core needle biopsy





ESMO Open
Cancer Horizons

Check for updates

Breast cancer subtypes: implications for the treatment and survival of patients in Africa—a prospective cohort study from Mozambique

Mariana Brandão ,[1,2] Assucena Guisseve,[3,4] Genoveva Bata,[5] Matos Alberto,[4] Josefo Ferro,[6] Carlos Garcia,[6] Clésio Zaqueu,[7] Cesaltina Lorenzoni,[3,4] Dina Leitão,[8,9] Jotamo Come ,[10] Otília Soares,[5] Alberto Gudo-Morais ,[5,11] Fernando Schmitt ,[9,12] Satish Tulsidás ,[1,5] Carla Carrilho ,[3,4] Nuno Lunet [1,13]

Figure 1 – Implementation of the multidisciplinary tumor board (MTB) at the Maputo Central Hospital

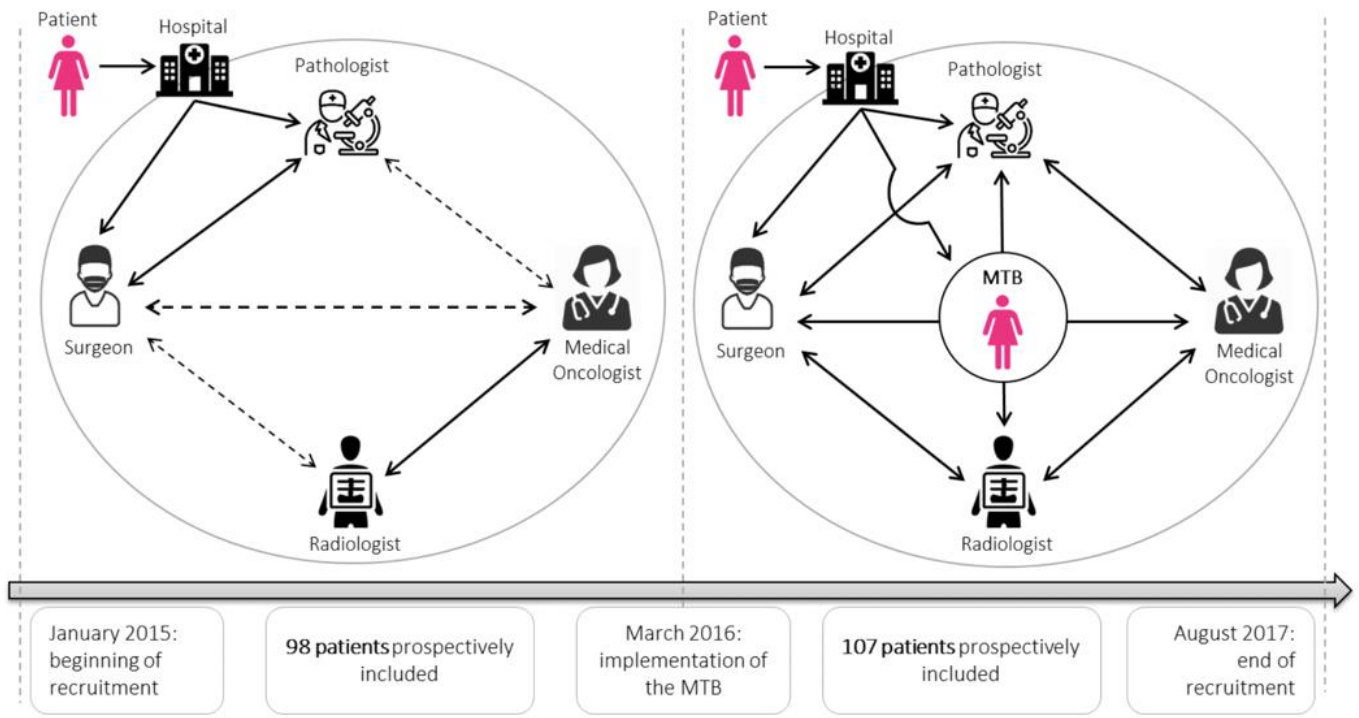
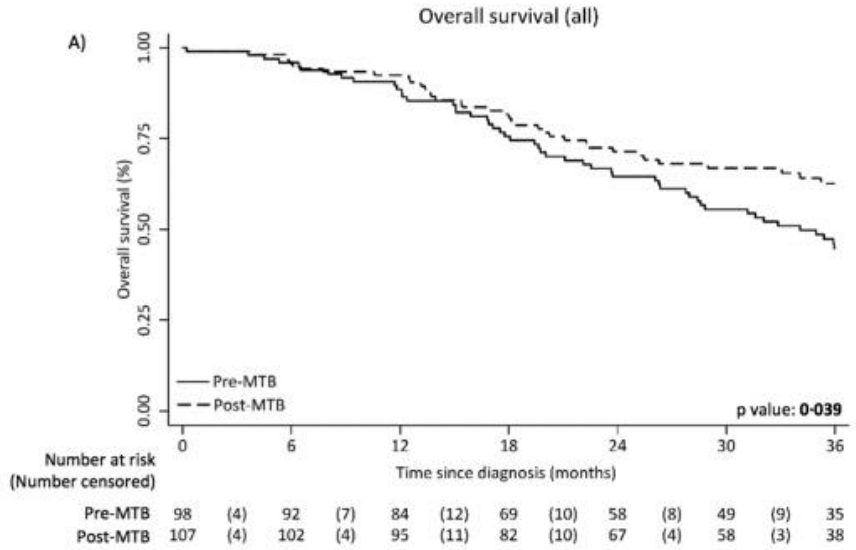
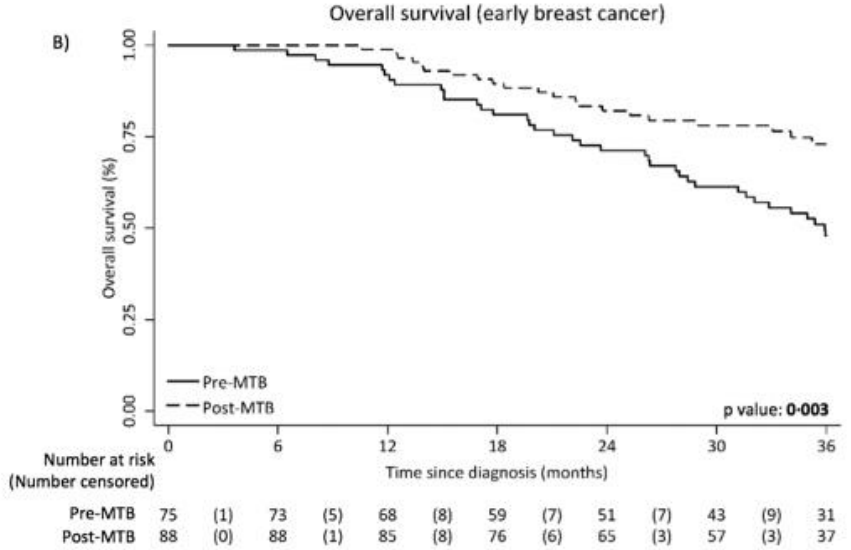
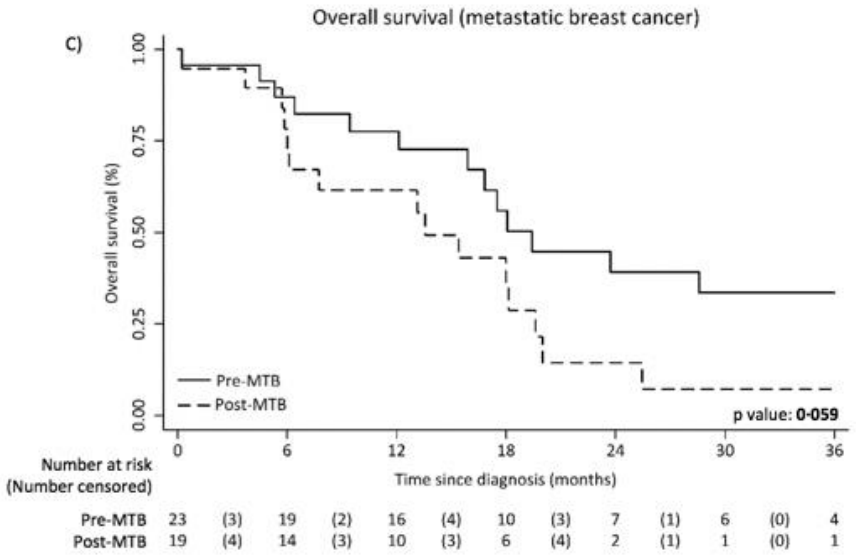
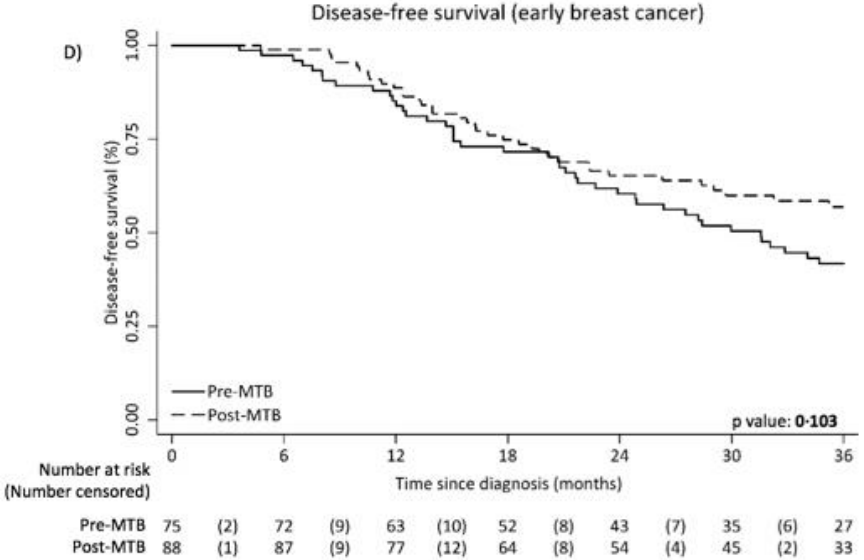


Figure 2 – Kaplan-Meier curves for overall survival among all patients, patients with early breast cancer and patients with metastatic breast cancer; and for disease-free survival among patients with early breast cancer









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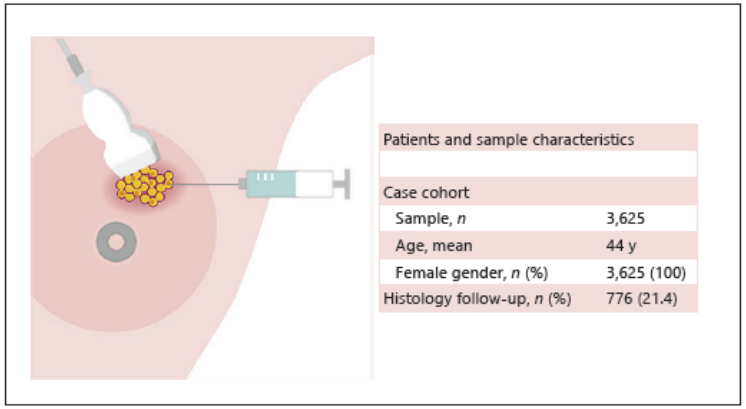
Breast Fine Needle Aspiration Biopsy Cytology Using the Newly Proposed IAC Yokohama System for Reporting Breast Cytopathology: The Experience of a Single Institution

Diana Montezuma[a, c] Daniela Malheiros[b, c] Fernando C. Schmitt[c–e]

[a]Portuguese Institute of Oncology, Porto, Portugal; [b]Faculdade de Ciências Médicas da Santa Casa de São Paulo, São Paulo, Brazil; [c]Institute of Molecular Pathology and Immunology, University of Porto, Porto, Portugal; [d]Instituto de Investigação e Inovação em Saúde, University of Porto, Porto, Portugal; [e]Medical Faculty, University of Porto, Porto, Portugal



Patients and sample characteristics	
Case cohort	
Sample, *n*	3,625
Age, mean	44 y
Female gender, *n* (%)	3,625 (100)
Histology follow-up, *n* (%)	776 (21.4)

Table 3. Sensitivity, specificity, PPV, NPV, and accuracy rate of breast cytology

	Sensitivity	Specificity	PPV	NPV	Accuracy
Category A	97.56%	100%	100%	98.62%	99.11%
Category B	97.98%	99.65%	99.49%	98.62%	98.97%
Category C	98.28%	54.79%	68.21%	98.62%	49.25%

Category A: only malignant cases considered positive; category B: suspicious and malignant cases considered positive; category C: atypical, suspicious, and malignant cases considered positive. NPV, negative predictive value; PPV, positive predictive value.

A sensitivity and specificity comparison of fine needle aspiration cytology and core needle biopsy in evaluation of suspicious breast lesions: A systematic review and meta-analysis

Mei Wang [a], Xiaoning He [b], Yaping Chang [a], Guangwen Sun [c], Lehana Thabane [a, d, e, f, g, h, *]

The Breast 31 (2017) 157–166

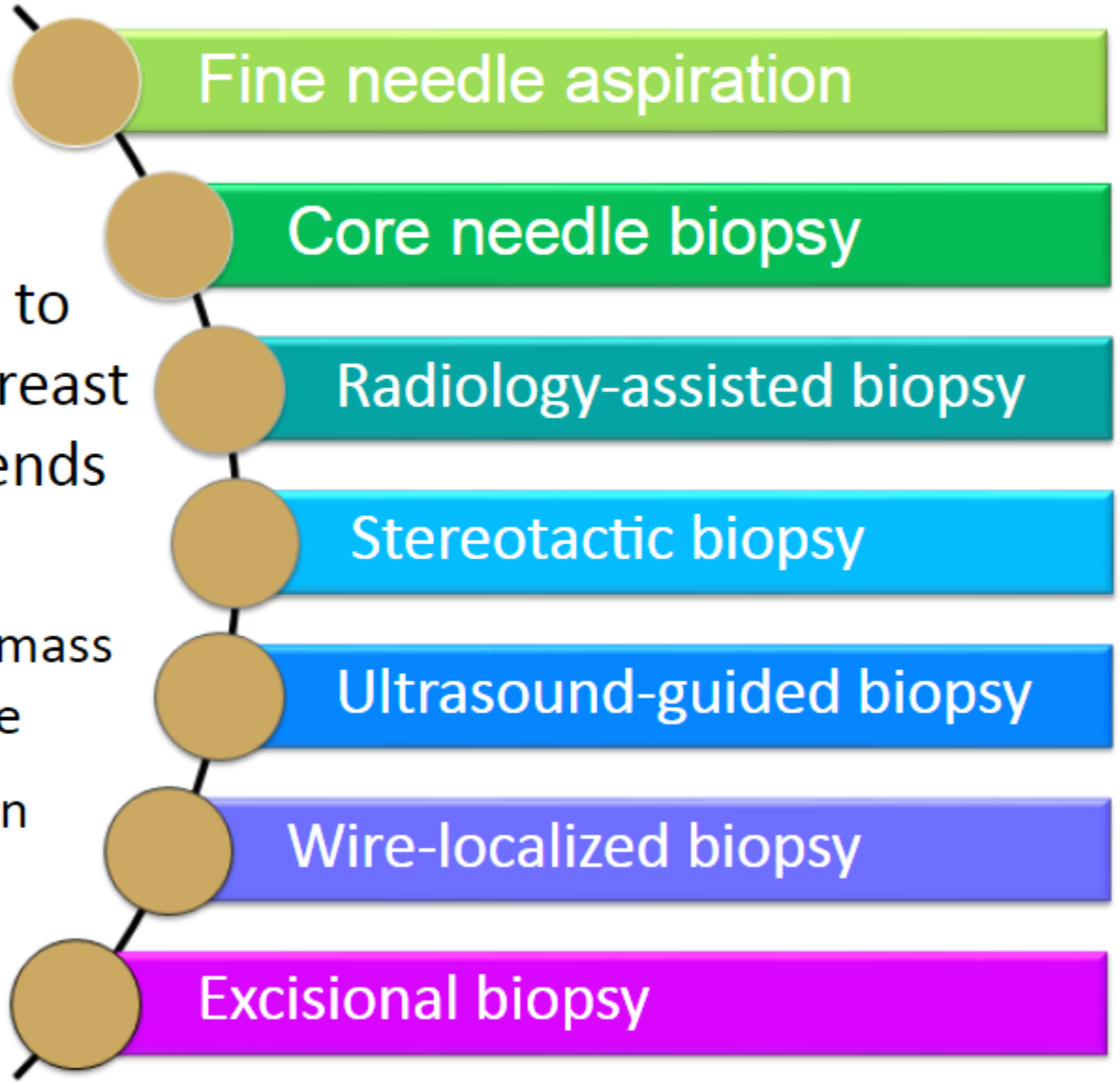
Table 5
Subgroup analysis based on publication year for accuracy of FNAC and CNB.

	Category (prevalence)	# of studies (# of participants)	Sensitivity		Specificity	
			FNAC % (95% CI) (P value), (I^2%)	CNB% (95% CI) (P value), (I^2%)	FNAC% (95% CI) (P value), (I^2%)	CNB% (95% CI) (P value), (I^2%)
Year of publication	2007 or later (69%)	7 (682)	81 (77–84) (<0.001), (84.4)	88 (85–91) (0.079), (47)	99 (97–100) (0.613), (0)	98 (95–99) (0.066), (49.2)
	Before 2007 (60%)	5 (1112)	70 (66–73) (<0.001), (89.6)	86 (83–88) (<0.001), (95.1)	95 (92–97) (<0.001), (86.1)	98 (96–99) (0.184), (35.6)
Pooled estimate	(64%)	12 (1802)	74 (72–77) (<0.001), (88.5)	87 (84–88) (<0.001), (88.3)	96 (94–98) (<0.001), (76.2)	98 (96–99) (0.081), (39)

Conclusion: Our study suggests that both of FNAC and CNB have good clinical performance. In similar circumstances, the sensitivity of CNB is better than that of FNAC, while their specificities are similar. FNAC could be still considered the first choice to evaluate suspicious nonpalpable breast lesions.

Technique to biopsy a breast mass depends on:

- Whether mass is palpable
- Its location



BREAST FNAB X CNB

- In terms of pathological diagnosis, both methods are accepted to be highly accurate in the assessment of breast lesions.

- CNB is more used in non-palpable screen-detected calcifications, borderline lesions, and when mammography does not show invasion signs.

- Lack of expertise in cytology is one of the main causes of the increased use of CNB.

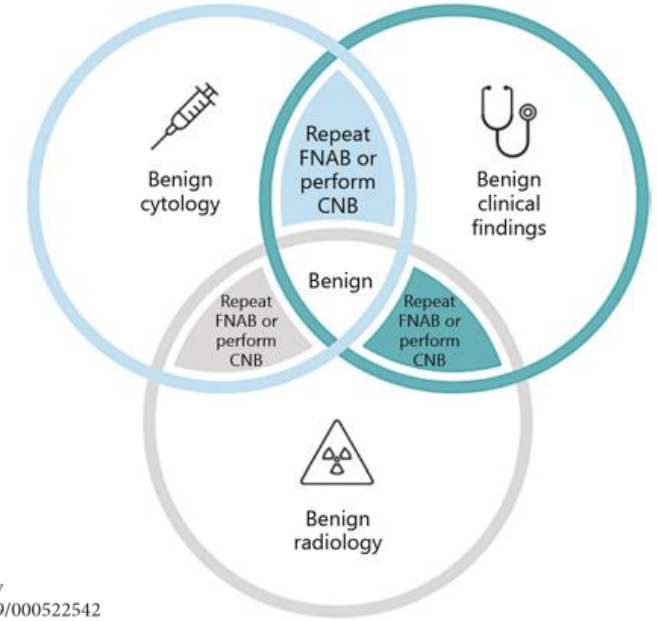
Breast FNAB
Still used in developed countries?

- One day clinic
- Palpable lesions
- Axillary nodes
- Metastatic sites

FNAB
Multistep technique

- Clinical examination
- Image-guided (US)
- Aspiration
- Slide preparation
- Fixation and staining
- Cytological interpretation

TRIPLE ASSESSMENT APPROACH



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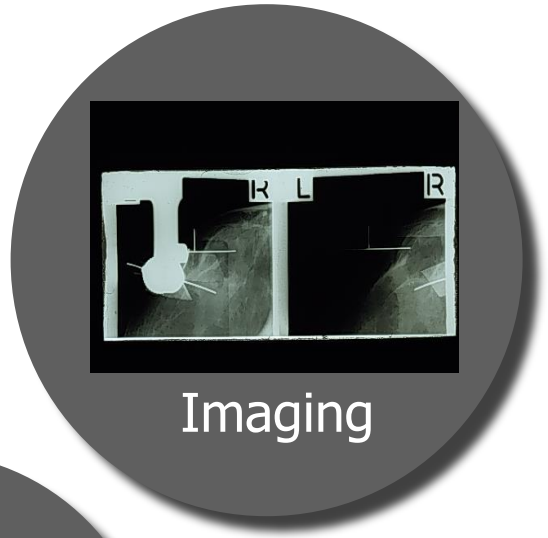
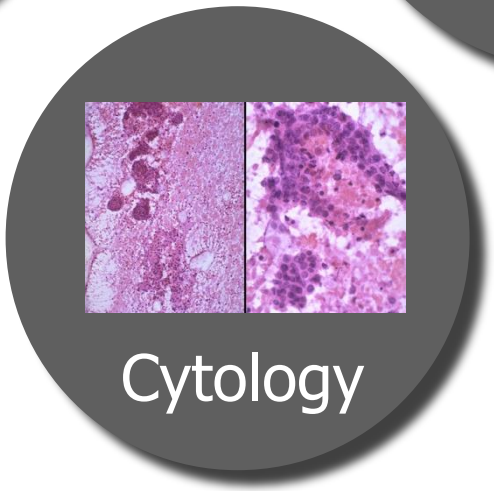


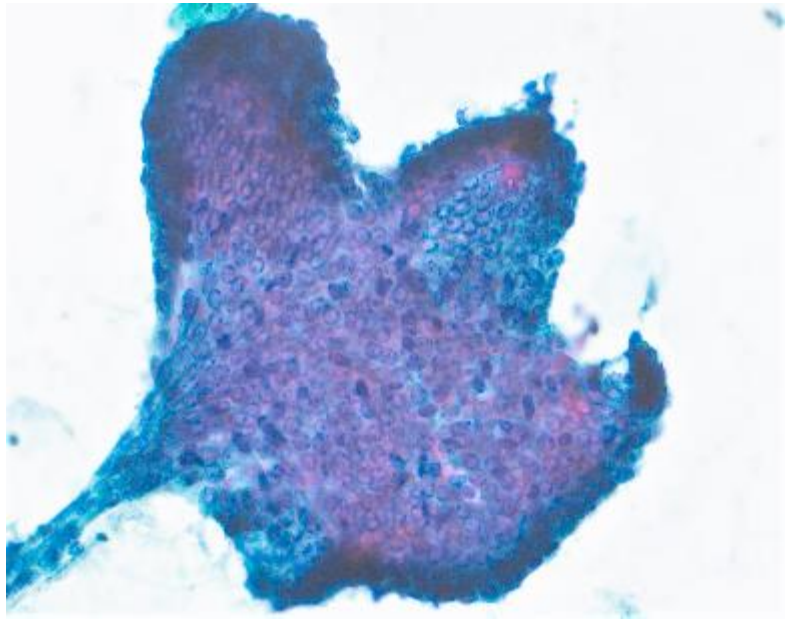


BBB: 98% benign – follow up
MMM: 1% error – surgery
Other: biopsy

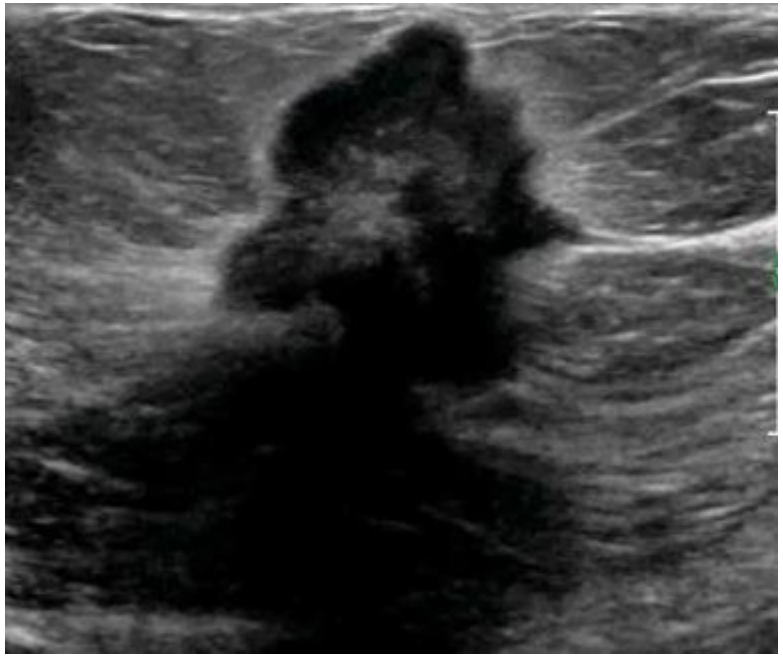
NEEDLE BIOPSY

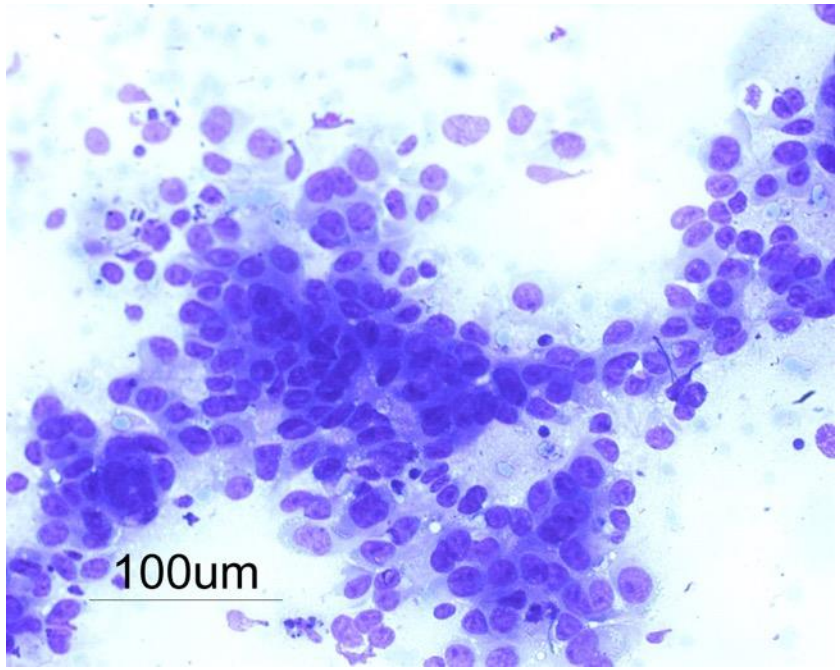
- Knowing clinical history and imaging findings, including radiological differential diagnosis is essential.
- The pathological diagnosis on FNA/CNB must be concordant with the imaging studies.
- Discordant diagnoses must be reconciled; may require repeat sampling or surgical excision.

RADIOLOGY-PATHOLOGY CORRELATION

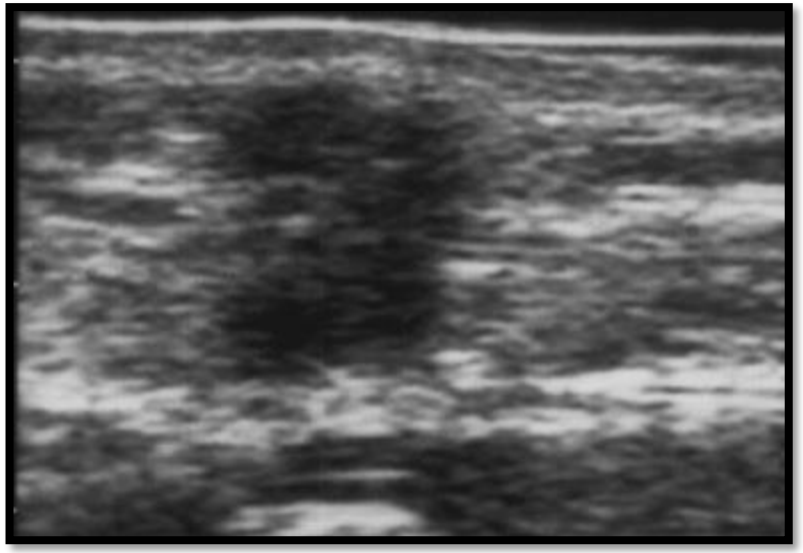


RADIOLOGY-PATHOLOGY CORRELATION

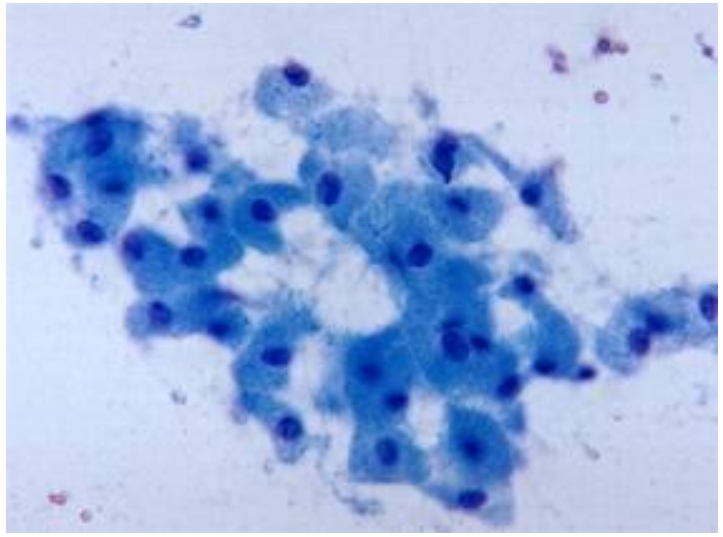


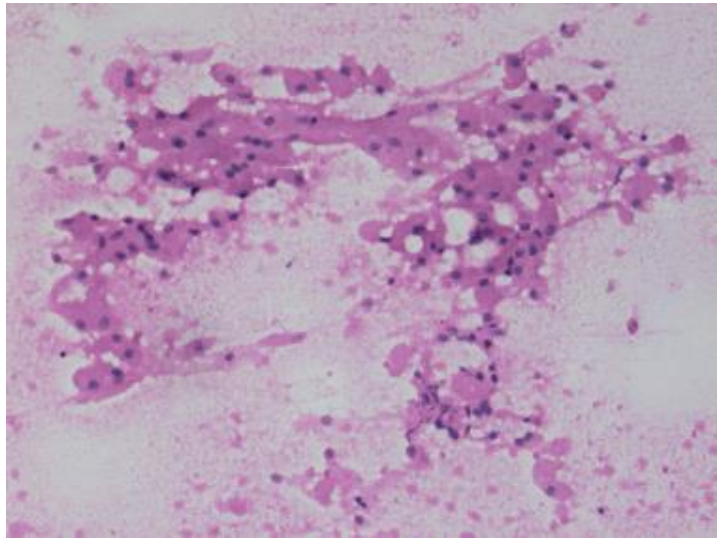


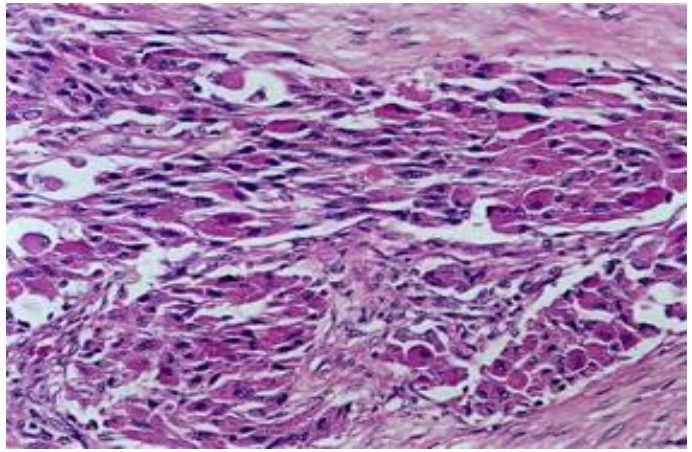
Discordance with imaging

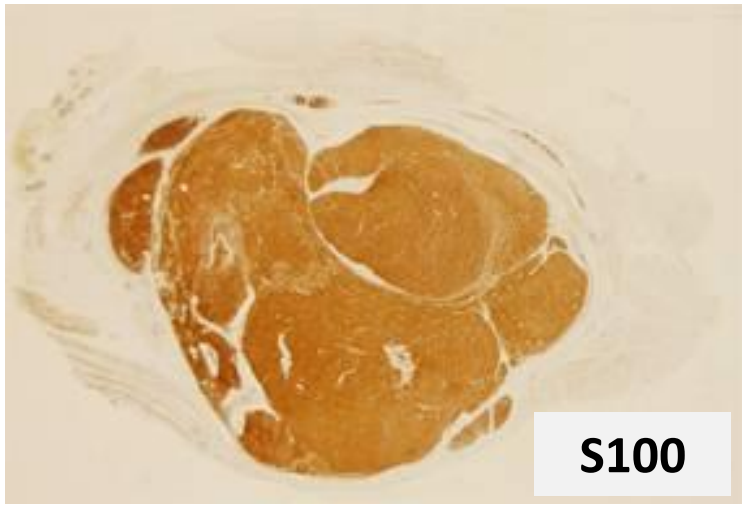


- A 33-year-old female presented with a 15 mm ill-defined nodule in the right breast. Mammography and the US are compatible with carcinoma.





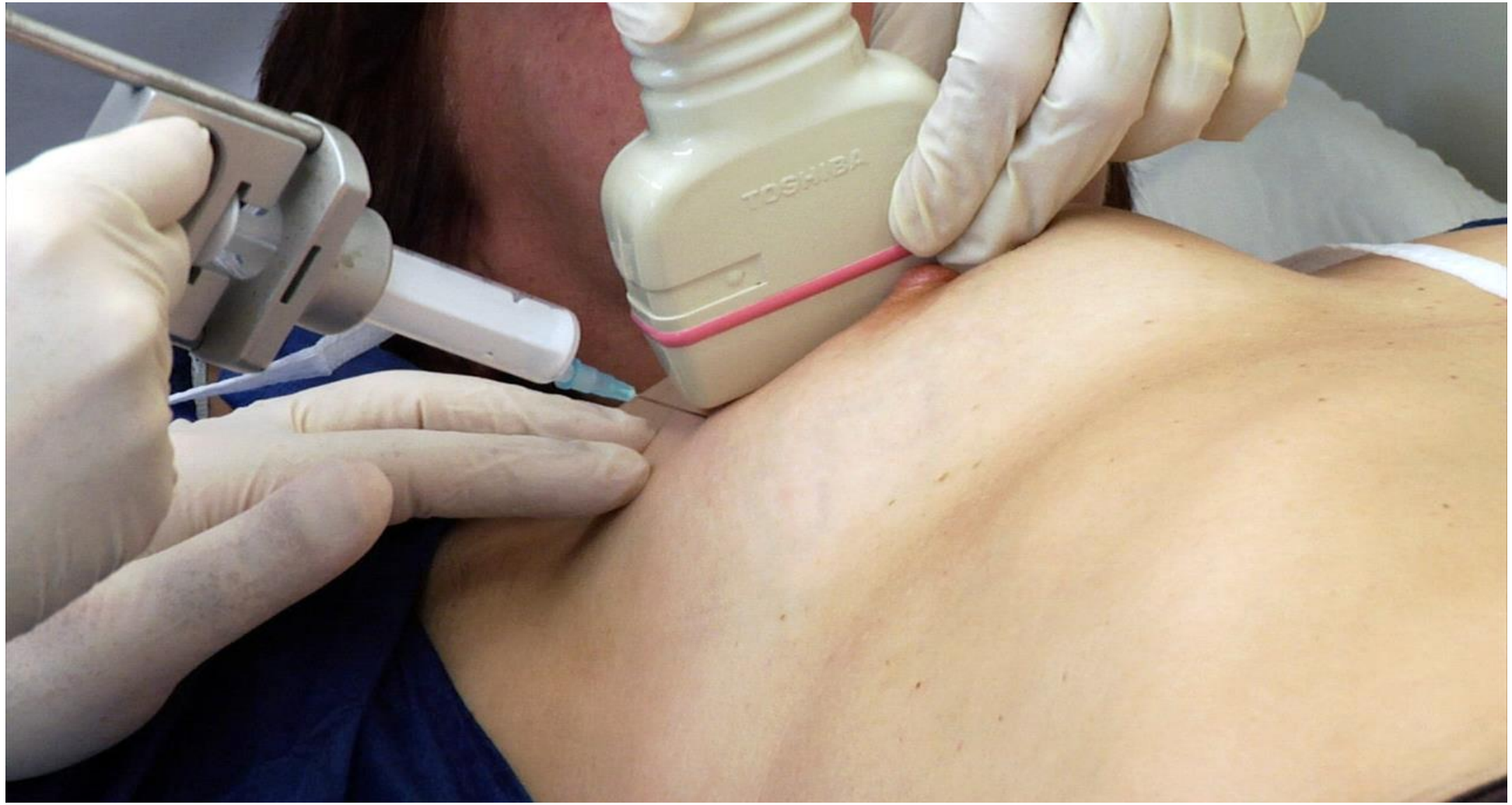




Benign Granular Cell Tumour

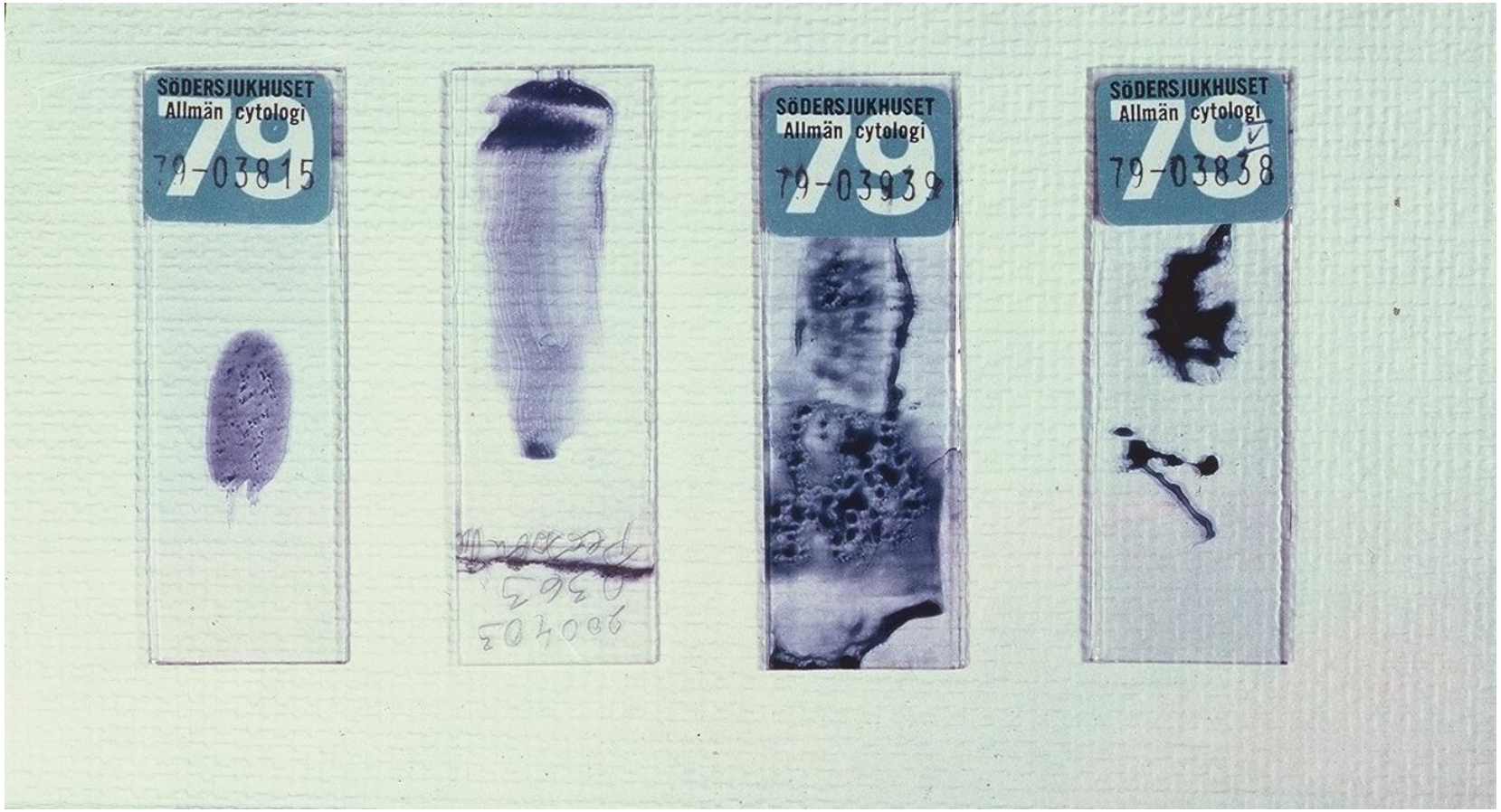
NEEDLE BIOPSY
Be careful when…

IMAGING	PATHOLOGY
SPICULATED MASS	ANY BENIGN DIAGNOSIS (except radial scar, GCT)
CIRCUMSCRIBED MASS	BENIGN, NON-SPECIFIC DIAGNOSIS
“MALIGNANT” CALCIFICATIONS	ANY BENIGN DIAGNOSIS, EVEN IF CALCIFICATIONS ARE PRESENT



The transducer probe locates the lesion in one of the edges of the US field; the aspirator passes the needle through the skin, in parallel with the transducer probe in the edge where the lesion is located in

Quality of the smear



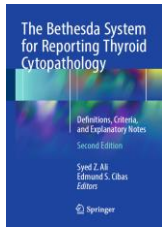
Standardized Pathology Terminology

- Should be uniform among pathologists and universally understood by clinicians
- Must reflect our current understanding of the relevant disease entities
- Provide clinically relevant information to the treating physician to allow for proper patient management

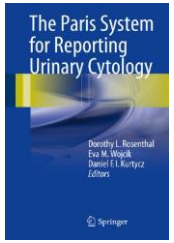
Advantages of Standardized Terminology

- Unifies reporting of disease categories.
- Reduces interobserver variability.
- Improves intra-observer reproducibility.
- Better aligns patient management options with interpretations.
- Improves patient care.

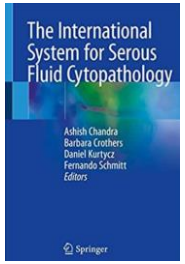
Advantages of Cytology Standardized Terminology
Some examples…



- Improved clinical confidence in a benign cytological diagnosis.
- Reduced unnecessary surgery in 50% of the patients.

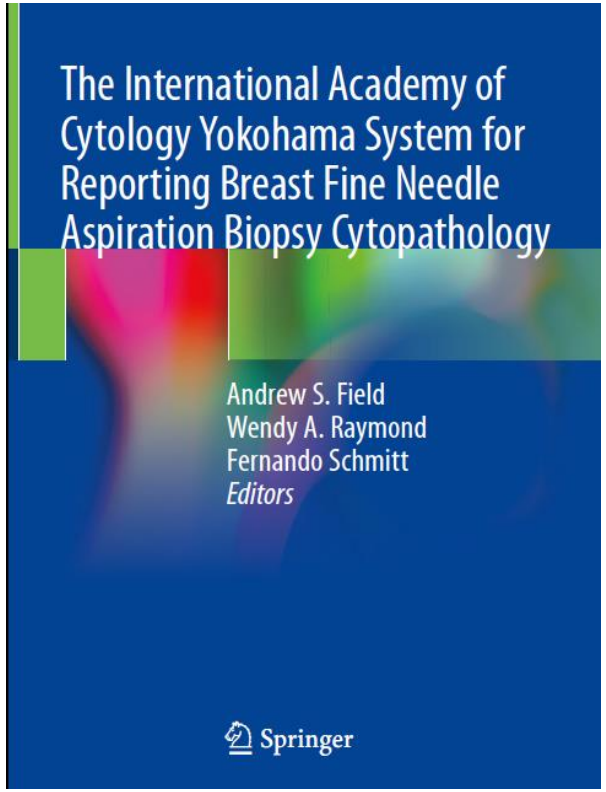


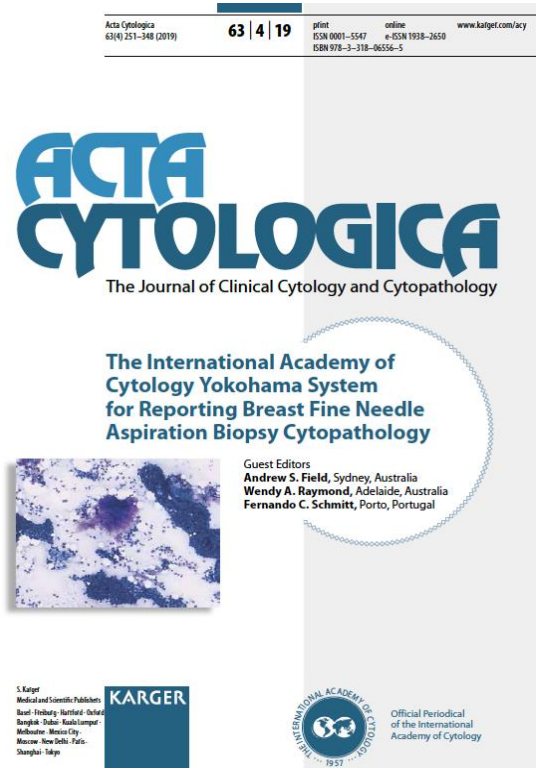
- Focused cytopathologists on that really matters: HGUC.
- Reduced the meaningless “atypical category”.



- Link each category with clear clinical management and use of ancillary techniques.

IAC Yokohama System 2016-2020

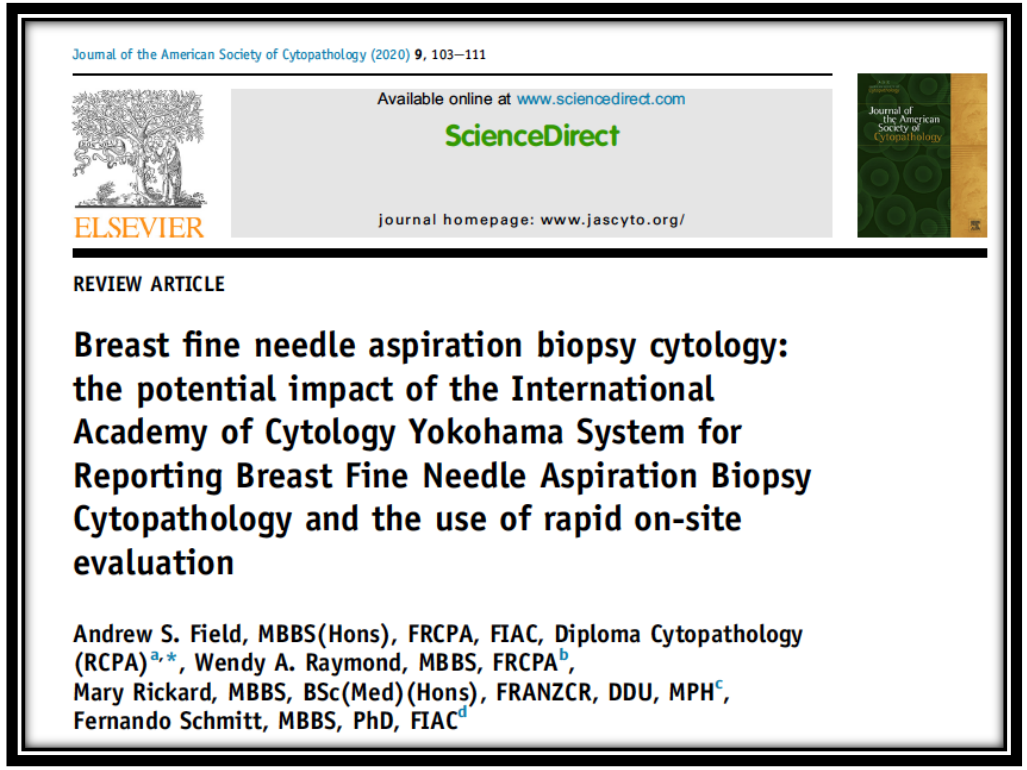




- Standardized approach with best practice guidelines.
- Structured reporting improves quality, clarity, and reproducibility
- Linking cytology reporting to management algorithms will enhance clinicians' use of breast cytology

Table 1.1 Categories, risk of malignancy and summary of management recommendations

Category	ROM[a, b]	Management[c]	LMICMX[d]	Comment
Insufficient	2.6–4.8%	Review clinical & imaging findings: If imaging indeterminate or suspicious, repeat FNAB or proceed to CNB; if imaging benign consider repeat FNAB	Review clinical; if indeterminate or suspicious repeat FNAB	At ROSE, if inadequate due to a technical issue or the material does not explain the clinical or imaging findings, repeat FNAB up to a total of 3 times, ideally using ultrasound guidance. If FNAB still insufficient, proceed to CNB
Benign	1.4–2.3%	Review clinical & imaging; if 'triple test' benign, no further biopsy required and review depends on the nature of the lesion; if clinical &/or imaging indeterminate or suspicious, repeat FNAB or proceed to CNB	Review clinical: if benign nil further; if suspicious repeat FNAB	At ROSE, if the cellular material does not explain the clinical or imaging findings, repeat FNAB, up to a total of 3 times, using ultrasound guidance. Follow-up depends on the nature of the lesion, e.g. abscess, 2 weeks after antibiotics; fibroadenoma, 12 months. Some centres review in line with screening programme policy
Atypical	13–15.7%	Review clinical & imaging: repeat FNAB if atypia considered likely to be due to a technical issue. If good material available and atypical, repeat FNAB or preferably proceed to CNB.[e]	Review clinical and repeat FNAB; manage based on FNAB category. If further FNAB atypical, consider excisional biopsy	At ROSE, if atypia is considered due to a technical issue, repeat FNAB; if cellular material adequate and atypical, proceed to CNB
Suspicious	84.6–97.1%	Review clinical & imaging: CNB is mandatory.[f]	If no CNB available, excision biopsy	At ROSE proceed to CNB
Malignant	99.0–100%	Review clinical & imaging: proceed to CNB if any discrepant findings. If 'triple test' is concordant and malignant, proceed to definitive management.[g, h]	If no CNB available, excision biopsy	At ROSE may proceed to CNB



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REVIEW ARTICLE

Breast fine needle aspiration biopsy cytology: the potential impact of the International Academy of Cytology Yokohama System for Reporting Breast Fine Needle Aspiration Biopsy Cytopathology and the use of rapid on-site evaluation

Andrew S. Field, MBBS(Hons), FRCPA, FIAC, Diploma Cytopathology (RCPA)[a,*], Wendy A. Raymond, MBBS, FRCPA[b], Mary Rickard, MBBS, BSc(Med)(Hons), FRANZCR, DDU, MPH[c], Fernando Schmitt, MBBS, PhD, FIAC[d]

- ROSE reduces the rate of inadequate cases and increases the number of specific benign and malignant diagnoses.
- ROSE performed by a cytopathologist provides a provisional diagnosis, reducing patient anxiety and facilitating management through cost-effective immediate triage and patient selection for ancillary testing.
- Patients can be selected for immediate core biopsy if required

The IAC Yokohama System for Reporting Breast FNAB Cytopathology: recent research findings and the future

- IAC Yokohama System **stimulated interest and research** into its effectiveness in providing clinically relevant information for patient management
- **Problem areas have been identified** and some research has occurred in these areas: intraductal papillomas vs papillary DCIS; cellular fibroadenomas vs low grade phyllodes tumours; proliferative lesions including fibroadenomas vs carcinoma; diagnosis of low and high grade DCIS; diagnosis of low grade carcinomas and invasion
- CAP National Survey, 2019: only 54.5% of 499 laboratories (390 in USA, and 93 international) that report breast FNAB used a standardized system, only 82 (16.8%) aware of the IAC System, and only 7 use the IAC System, none of which are in USA. **If the IAC System is used, significant improvements can be expected in breast FNAB.**

WHO Cytopathology Reporting Systems Sponsored by IARC/WHO and IAC

- The World Health Organization (WHO), the International Agency for Research on Cancer (IARC), and the International Academy of Cytology (IAC) have joined forces to create a series of International Reporting Systems for Cytology.

- These cytopathology reporting systems
  - **mirror the WHO Classification of Tumours (with links between them).**
  - include the key diagnostic cytopathological features, establish a ROM per category, discuss ancillary studies, and recommend subsequent diagnostic procedures and patient management.
  - **Raise the profile and promote the use of FNAB cytopathology by increasing awareness of its current diagnostic role**
  - Emphasize a morphological differential diagnosis for low and middle-income countries (LMIC) with a relative lack of histopathological and ancillary testing services.
  - Organization: Standing Committee, Expert Editorial Board, Editors, Authors and co-authors

World Health Organization

WHO Cytopathology Reporting Systems Sponsored by IARC/WHO and IAC

Standing Committee (Series Editors)

Dr. Andrew Field
Australia

Dr. Ian Cree
IARC/WHO

Dr. Fernando Schmitt
Europe

Dr. Martha Pitman
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Dr Ravi Mehrotra
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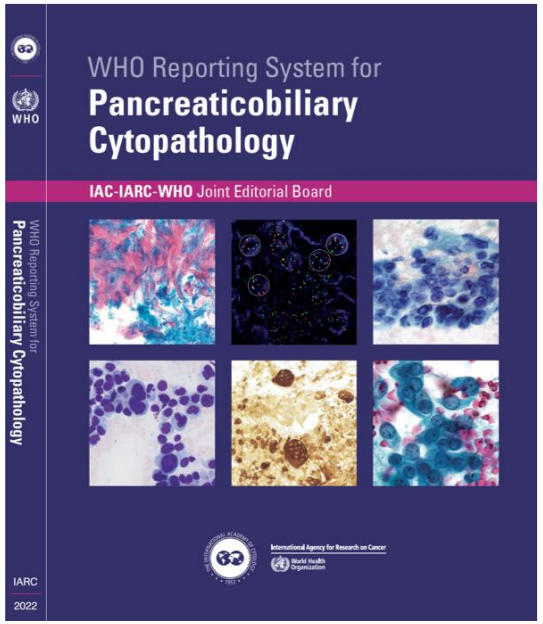
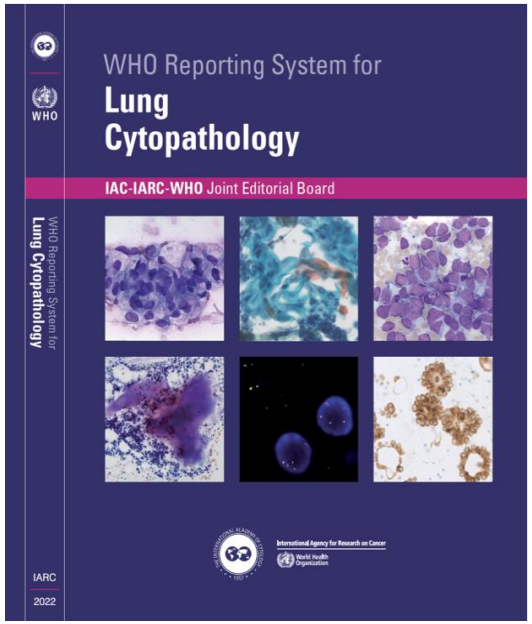
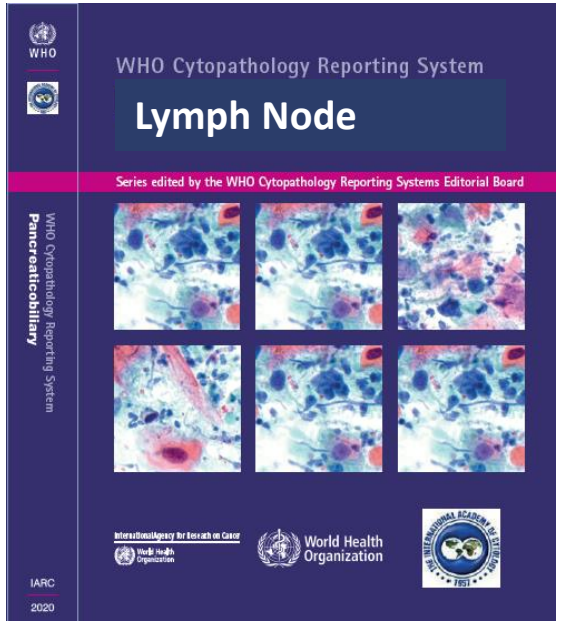
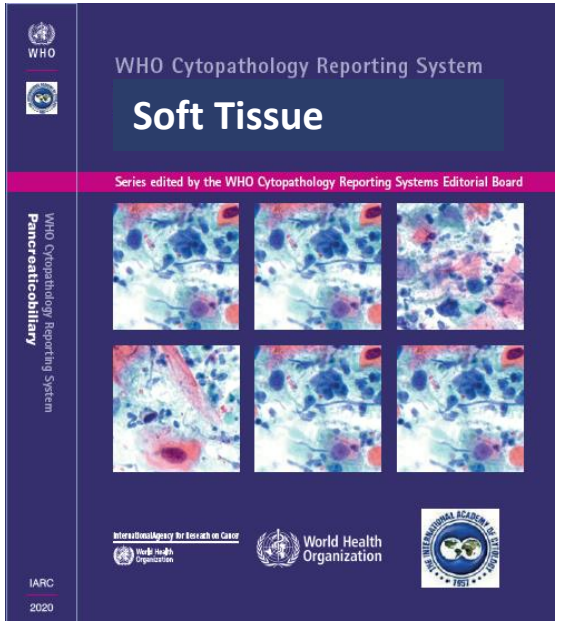




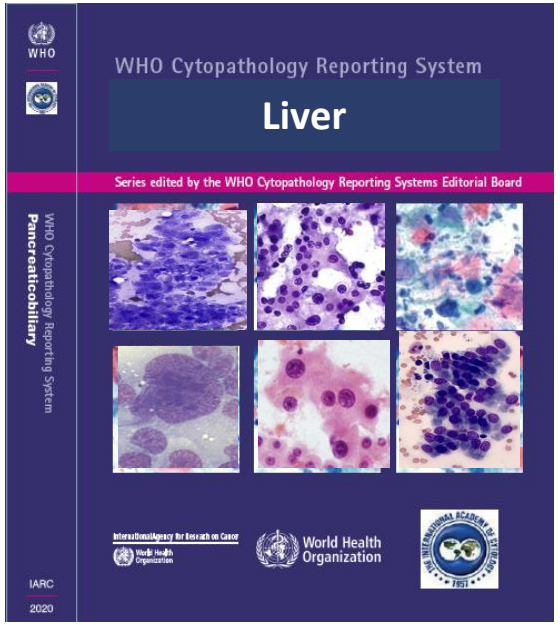


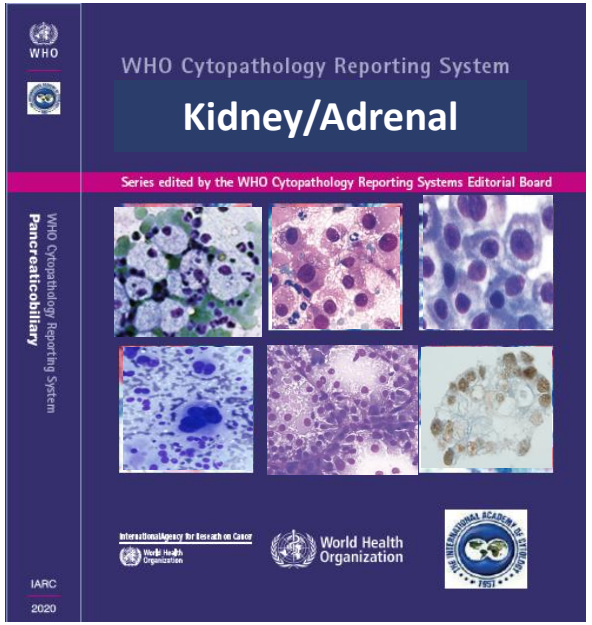


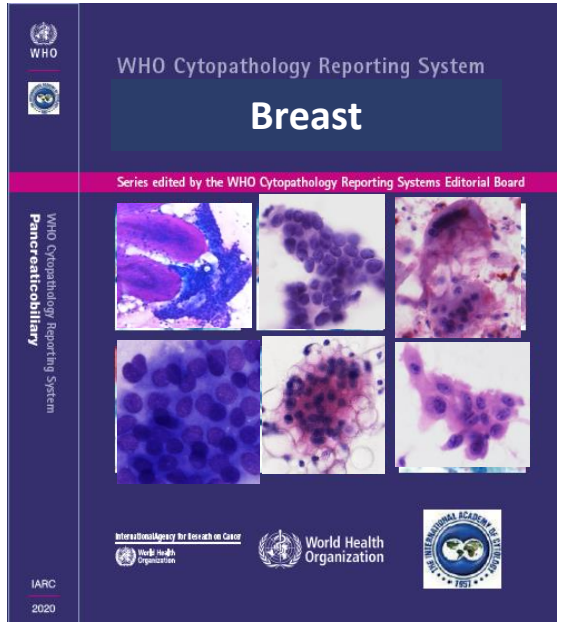
Mock-up of covers

WHO Reporting Systems in Cytopathology

In Development





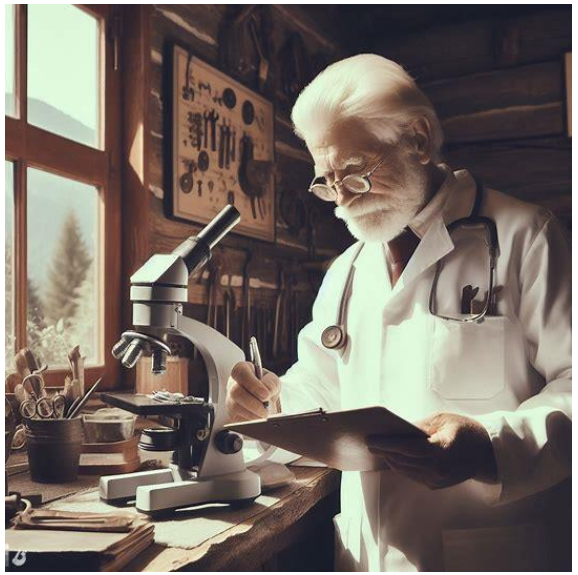


Mock-up of covers

WHO Reporting System for Breast Cytopathology

Five **well defined categories:**

- Insufficient/Inadequate/Non-diagnostic
- Benign
- Atypical
- Suspicious for malignancy
- Malignant



- **Each category has a clear descriptive term** for the category, a definition, a risk of malignancy and a suggested management algorithm
- The **key diagnostic cytopathology features** of each of the lesions within each category have been established by consensus for the first time, and a detailed **differential diagnosis based on cytopathology** is provided and highlighted in the text, so that the System can be used globally
- The authors recognize that the **availability of ancillary tests will vary**, particularly in low- and middle-income countries, and the recommendations for further diagnostic management include options that **can be followed in all settings throughout the world**

WHO Reporting System for Breast Cytopathology
Issues discussed by the EEB2

- Recurring issue with the reporting systems is the "**Insufficient/Inadequate/Non-diagnostic" category.**
- Breast FNAB can yield at least adequate if not **abundant benign components categorized as "Benign**", in cases with indeterminate or even suspicious imaging.
- Broad agreement that in such cases there should be **a multidisciplinary "Triple test" approach** with review of FNAB and the imaging, and that the FNAB should be **categorized as "Benign" with a comment/caveat in the report, "that the FNAB material may not represent the lesion".**
- For example: imaging may show a **stellate lesion** that is suspicious of carcinoma but the FNAB shows fibrocystic change with epithelial hyperplasia **suggestive of a radial scar.**

WHO Reporting System for Breast Cytopathology
Issues discussed by the EEB2

- Benign processes, benign tumours and malignant tumours presented generally in line with 5th Edition WHO Classification of Tumours of the Breast, but **lesions are split into "Benign" and "Malignant" categories** with a discussion of the differential diagnoses when a benign and malignant lesion may share some features.
- **Lesions with low or uncertain malignant potential** are presented alongside their common differential diagnoses **eg. borderline PT** are discussed in the DD with high grade PTs and other malignant spindle cell tumours, **and also** in the section on fibroadenoma and benign PT.
- **No particular lesions or tumours are presented in the "Atypical" and "Suspicious for malignancy" categories**; DD of lesions/tumours that may present in these categoriers are discussed. Different to the IAC Yokohama system

WHO Reporting System for Breast Cytopathology
Issues discussed by the EEB2

- The **DD of epithelial hyperplasia and of intraductal papilloma** are discussed in detail, and similarly the **DD of low and intermediate grade DCIS with papillary carcinoma and the benign proliferative lesions** is emphasized.
- '**Atypical ductal hyperplasia**' **is a surgical pathology diagnosis** with specific criteria, and is not discussed as an entity that can be diagnosed on cytopathology; ADH will usually be categorized as "Atypical" or perhaps "Suspicious for malignancy".
- The aim of **establishing the cytopathological features that suggest low and intermediate grade DCIS** is not to suggest that these diagnoses can be routinely made but rather to try and **avoid under-calling them as benign epithelial hyperplasia and on the other hand overcalling them as carcinoma.**

WHO Reporting System for Breast Cytopathology
Issues discussed by the EEB2

- The EEB agreed that **FNAB cannot diagnose high grade ductal carcinoma in situ definitively excluding invasive carcinoma**
- Features such as necrosis, calcifications and usually sparse cellularity consisting of epithelial cells with high grade nuclei, **can suggest high grade DCIS**
- But **all of these features can be seen with invasive carcinoma and high grade DCIS is frequently found with invasive carcinoma**
- In most cases these lesions will be **categorized as "Malignant**" on FNAB
- **Correlation** is required with imaging and the **management will be very similar**
- In some cases where the triple test is applied, there will be minimal or no clinical or imaging evidence of a mass, casting calcifications will be present, and it can be suggested that **"carcinoma with or without a high grade ductal carcinoma in situ component is present"**
- **Clear communication** with clinicians is essential

WHO Reporting System for Breast Cytopathology
Issues discussed by the EEB2

- The **heading of 'Salivary gland type carcinomas**" of the 5th Edition Breast text was not used but rather acinic cell carcinoma, adenoid cystic carcinoma, muco-epidermoid carcinoma and secretory carcinoma are presented as separate topics, because there is **no common cytopathology** in these lesions to raise a differential diagnosis.
- Lesions and particularly carcinomas that have **not been reported** in the cytopathology literature are not presented as separate topics.
- Lesions and carcinomas that **rarely reported** are not presented as specific sections but are discussed in the DD of more common lesions eg juvenile papillomatous hyperplasia is discussed in DD of intraductal papillomas.

WHO Reporting System for Breast Cytopathology

ROM Studies

- ROM for the diagnostic categories of the WHO Reporting System for Breast Cytopathology are based on publications using and critiquing the IAC Yokohama System for Reporting Breast FNAB Cytopathology (2020) and its five categories similar to the WHO Reporting System.

- The ROM published in the IAC Yokohama System were from two large recent studies, one of which included only cases performed by cytopathologists using ultrasound guidance, and one which included cases performed by well trained radiologists and breast physicians using ultrasound guidance, most of which utilized ROSE

- Insufficient rates very low in both these studies (below 5%)

WHO Reporting System for Breast Cytopathology

Table 1. The WHO Reporting System for Breast Cytopathology on breast FNAB: implied risk of malignancy (ROM) and clinical management options by diagnostic category.

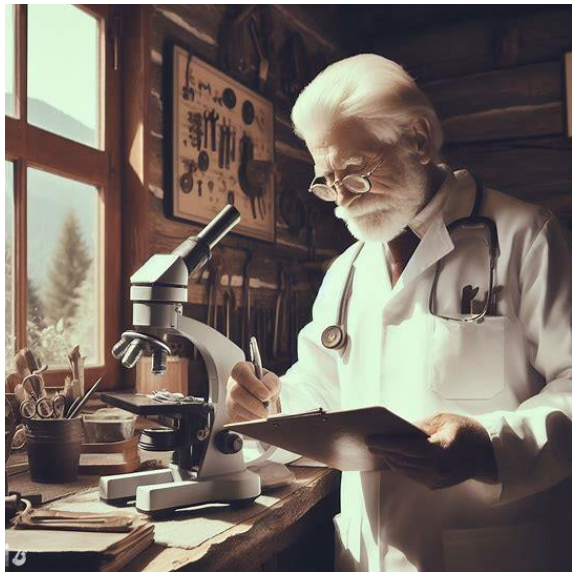
Diagnostic category	Estimated ROM[a]	Clinical management options[b]
Insufficient/Inadequate/Non-diagnostic	0-60.9%	Repeat FNAB or consider CNB. If low clinical suspicion, consider repeat clinical and radiologic examination in 3-6 months.
Benign	0-11.7%	Correlate clinically.
Atypical	13.0-40.0%	Repeat FNAB or consider CNB. If low clinical suspicion, consider repeat clinical and radiologic examination in 3-6 months.
Suspicious	45.8-100%	CNB or surgical management.
Malignant	91.1-100%	If clinical or imaging discordant, CNB; if clinical and imaging concordant, treat per clinical stage.

Abbreviations: CNB, core needle biopsy; FNAB, fine needle aspiration biopsy; ROM, risk of malignancy.

WHO Reporting System for Breast Cytopathology

Five **well defined categories:**

- Insufficient/Inadequate/Non-diagnostic
- Benign
- Atypical
- Suspicious for malignancy
- Malignant



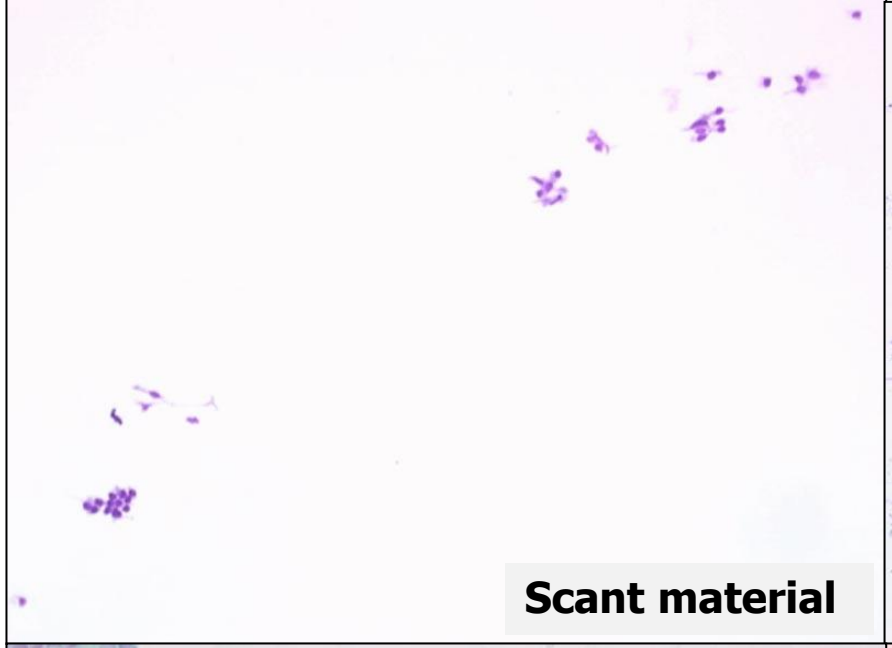
CATEGORIES

- **Each category has a clear descriptive term** for the category, a definition, a risk of malignancy and a suggested management algorithm
- The **key diagnostic cytopathology features** of each of the lesions within each category have been established by consensus for the first time, and a detailed **differential diagnosis based on cytopathology** is provided and highlighted in the text, so that the System can be used globally
- The authors recognize that the **availability of ancillary tests will vary**, particularly in low- and middle-income countries, and the recommendations for further diagnostic management include options that **can be followed in all settings throughout the world**

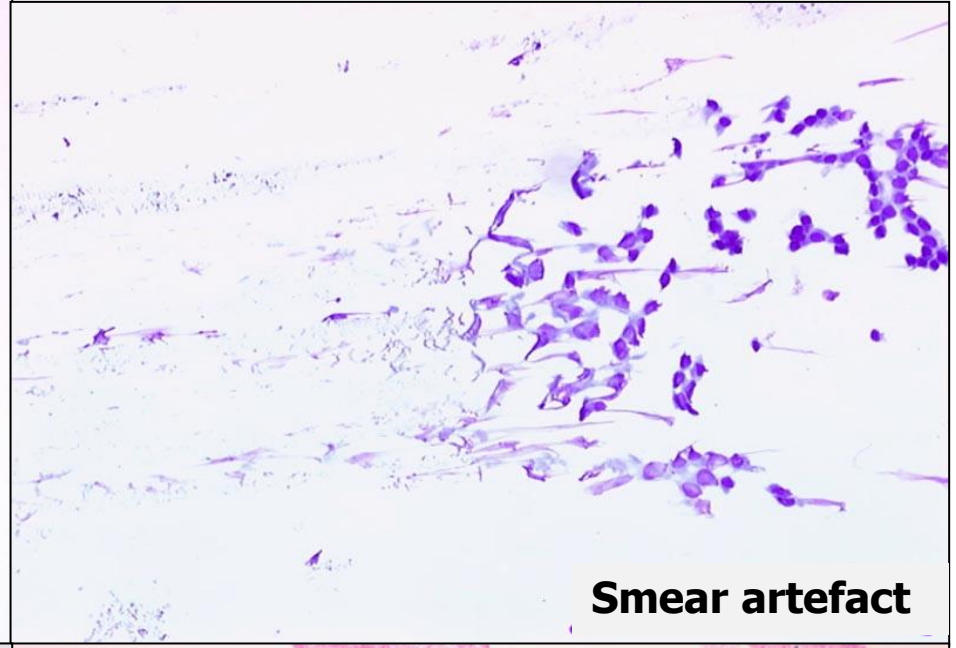
Categories For The WHO Reporting System for Breast Cytopathology

Insufficient/Inadequate/Non diagnostic

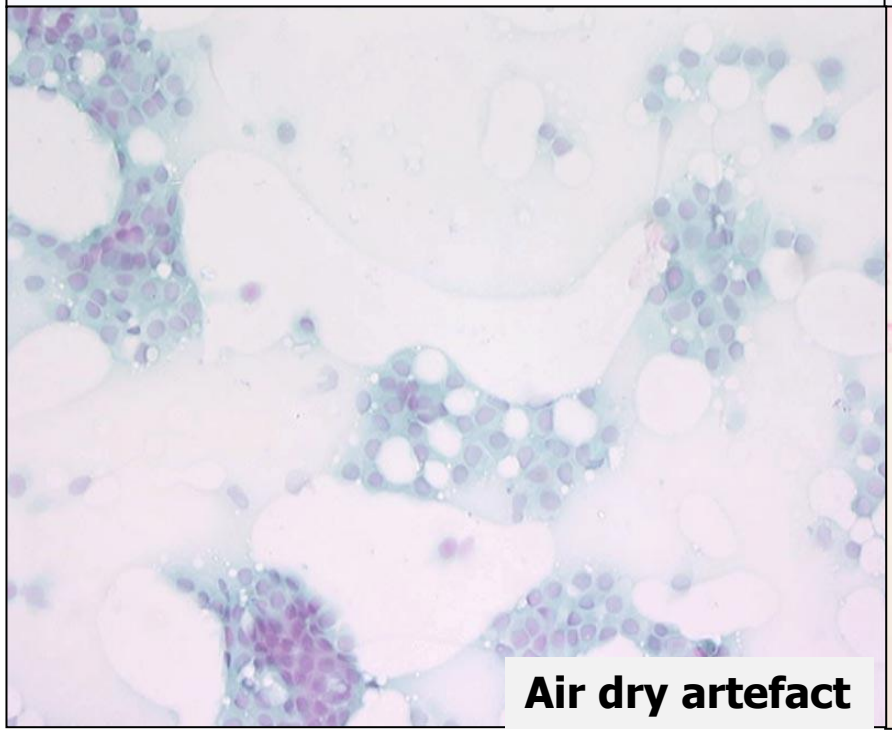
- A specimen categorized as “Insufficient/Inadequate/Non-diagnostic” is one that for qualitative and/or quantitative reasons does not permit a cytomorphological diagnosis for the targeted lesion.
- The reasons that render a FNAB sample in this category should be stated in the report:
  - ✓Paucicellular or acellular sample from a palpable mass or defined solid mass on imaging
  - ✓Cellular degeneration
  - ✓Preparation artifact, including air-dried cells, crush artifact, and/or thick smear preparation.
  - ✓Obscuring elements, such as blood, necrosis, or ultrasound gel.
- Any atypia should be reported as such and put under the atypical or “suspicious” category.
- Incidence: 1-40% (<10%). Our rate: 5.7%
- Reported ROM: ranging from 0.0% to 60.9% (median, 14.8%; mean; 21.2%)
- Management: review of the clinical and radiological findings to determine whether a repeat FNAB or a CNB should be performed.



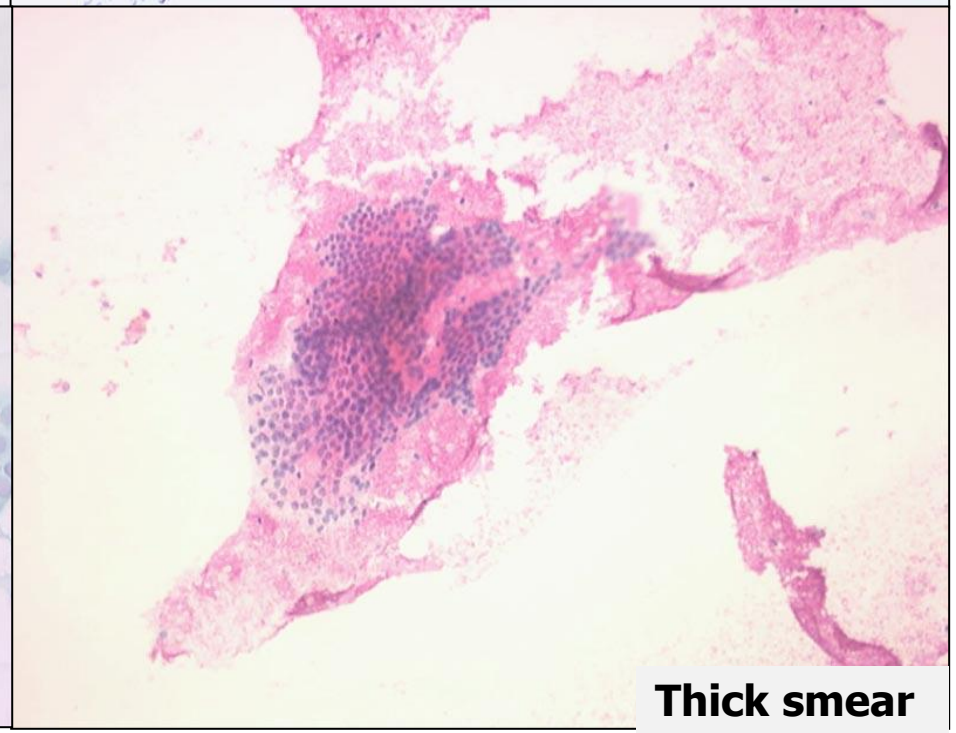
Scant material



Smear artefact



Air dry artefact



Thick smear

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Liquid-Based Cytology in Fine-Needle Aspiration of Breast Lesions: A Review

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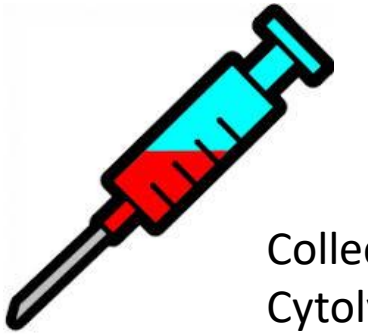
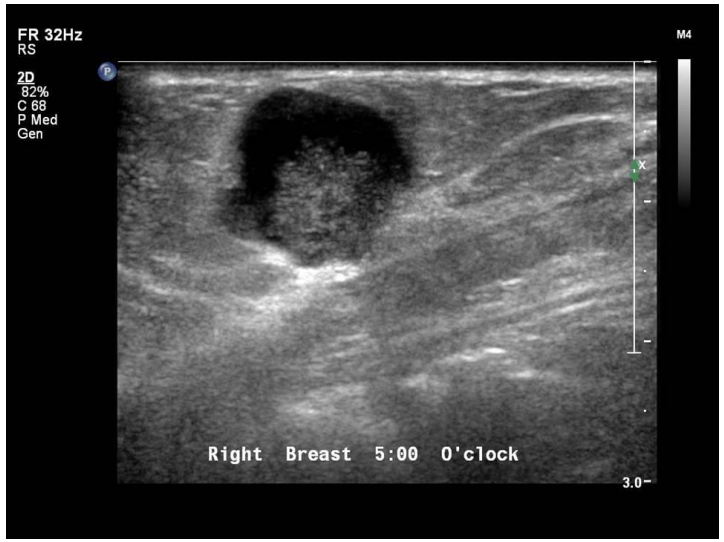


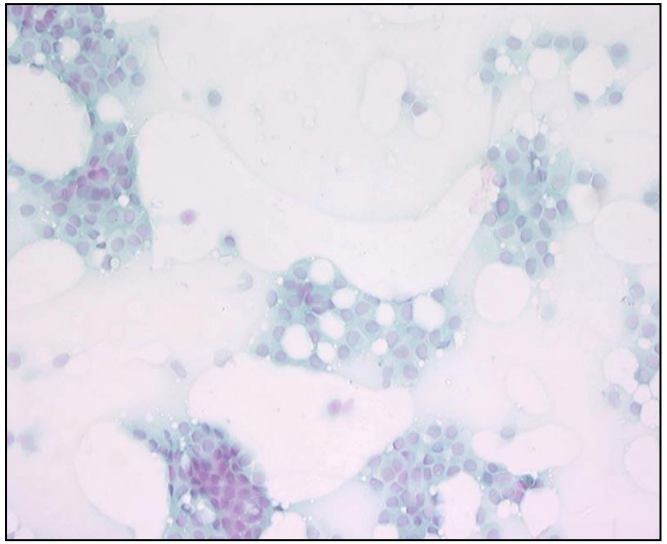
Collect sample directly into prefilled Cytolyt®tubes

Example Report

25 mm solid irregular mass



Specimen adequacy: Evaluation limited by scant cellularity and air-drying artifact.
Category: Non-diagnostic
Diagnosis: Smears display limited ductal epithelial cells with air-drying artifact.



Note: The biopsy does not explain a breast mass.

Categories For The WHO Reporting System for Breast Cytopathology

Insufficient/Inadequate/Non diagnostic

There are clinical situations where a smear may be adequate and diagnostic in the absence of epithelial cells if it correlates with the clinical and imaging findings:

- Cyst contents: proteinaceous background +/- histiocytes; state if no apocrine or other epithelium. Palpable cyst is no longer palpable or the cyst seen on ultrasound is drained by the FNAB with no residual lesion.
- Fat necrosis, lipomas, spindle cell lesions, scar, hyalinized or sclerosed fibroadenomas
- BUT IF a palpable or impalpable mass lesion is seen on imaging it is suggested that a minimum of 7 epithelial tissue fragments of at least 20 cells each is required; look for MEC and ductal ‘bimodal pattern’
- If there are any atypical features present then categorize as “Atypical” not insufficient

Categories For The WHO Reporting System for Breast Cytopathology

Benign

- *A specimen categorized as 'Benign' demonstrates unequivocal benign cytopathological features, which may or may not be diagnostic of a specific process or benign neoplasm.*

- INCIDENCE: 24-77%. Our rate: 70%
- Reported ROM: 0-11.7%.
- MAIN CAUSES: inflammatory/infectious diseases/benign hyperplastic and neoplastic lesions
- MANAGEMENT: A benign cytological diagnosis requires only clinical or image follow-up rather than core biopsy or excision. In practice, a negative clinical and/or radiologic follow-up at 6-12 months is regarded as sufficient to record the original "triple negative" diagnosis incorporating the benign FNA as correct.

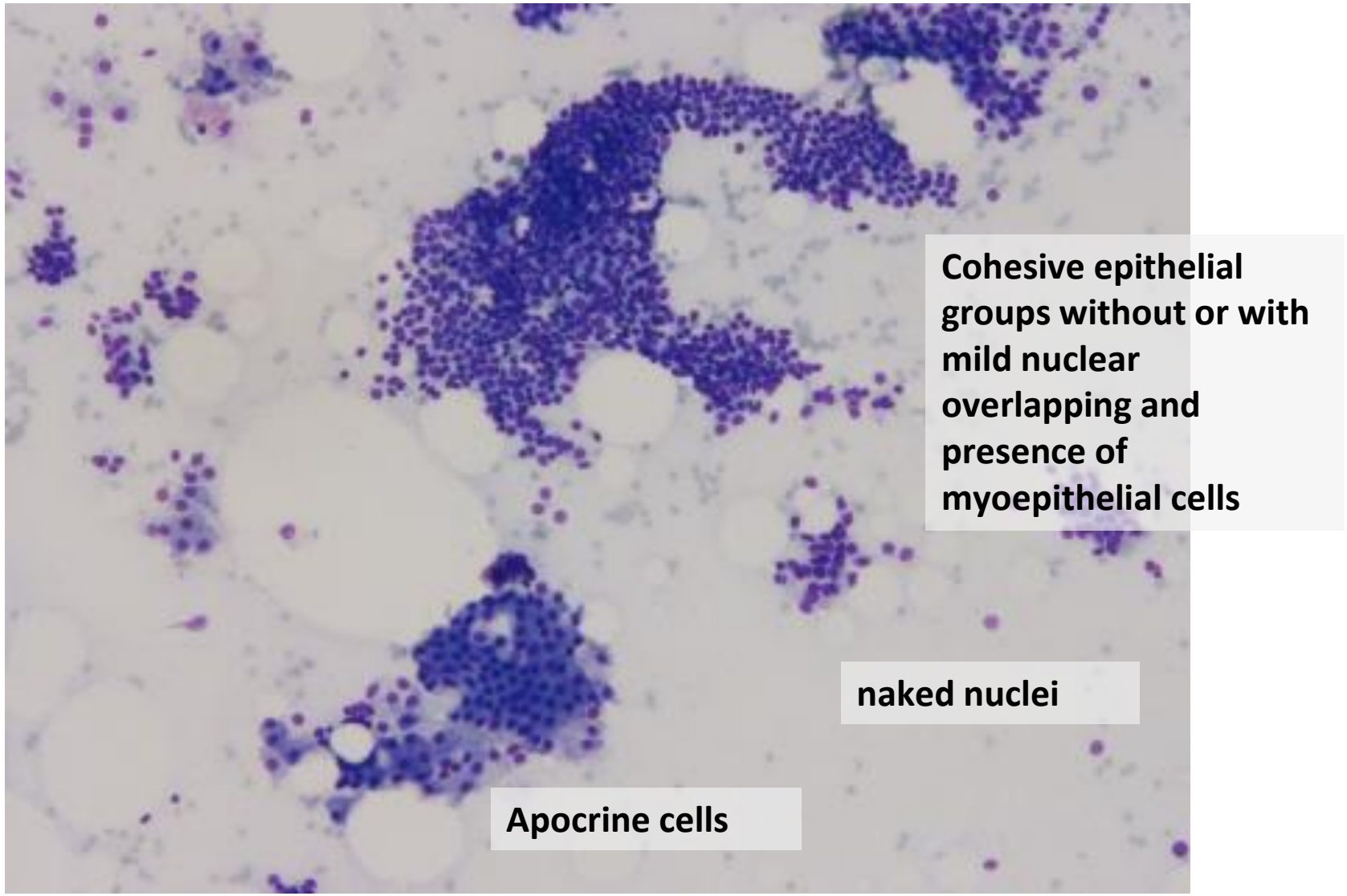
Categories For The WHO Reporting System for Breast Cytopathology

Benign

6.1: Entities in the Benign Category

- 6.1.0.1: Introduction
- 6.1.1: Inflammatory processes
  - 6.1.1.1: Acute inflammation and supparation
  - 6.1.1.2: Granulomatous inflammation
  - 6.1.1.3: Lymphoid hyperplasia and related disorders
  - 6.1.1.4: Fat necrosis
- 6.1.2: Benign epithelial proliferations and neoplasms
  - 6.1.2.1: Hamartoma (Note: include discussion of features of normal breast)
  - 6.1.2.2: Fibrocystic change: adenosis and benign sclerosing lesions including apocrine adenosis, apocrine adenoma, and tubular adenoma.
  - 6.1.2.3: Columnar cell lesions including flat epithelial atypia
  - 6.1.2.4: Epithelial hyperplasias
  - 6.1.2.5: Lactational changes
  - 6.1.2.6: Intraductal papilloma
  - 6.1.2.7: Radial scar/complex sclerosing lesions
  - 6.1.2.8: Gynaecomastia
- 6.1.3: Benign fibroepithelial tumours of the breast
  - 6.1.3.1: Fibroadenoma and benign phyllodes tumour
  - 6.1.3.2: Epithelial-myoepithelial tumours including pleomorphic adenoma and adenomyoepithelioma
- 6.1.7: Epithelial-myoepithelial tumours
- 6.1.4: Mesenchymal tumours
  - 6.1.4.1: Spindle cell tumours including myofibroblastoma, pseudoangiomatous hyperplasia, nodular fasciitis, schwannoma, desmoid fibromatosis
  - 6.1.4.2: Lipoma and angiolipoma
  - 6.1.4.3: Granular cell tumour
- 6.1.5: Tumours of the nipple
  - 6.1.5.1: Nipple adenoma
  - 6.1.5.2: Syringomatous tumour
- 6.1.6: Sample reports

CYTOLOGICAL CRITERIA OF BENIGN LESION



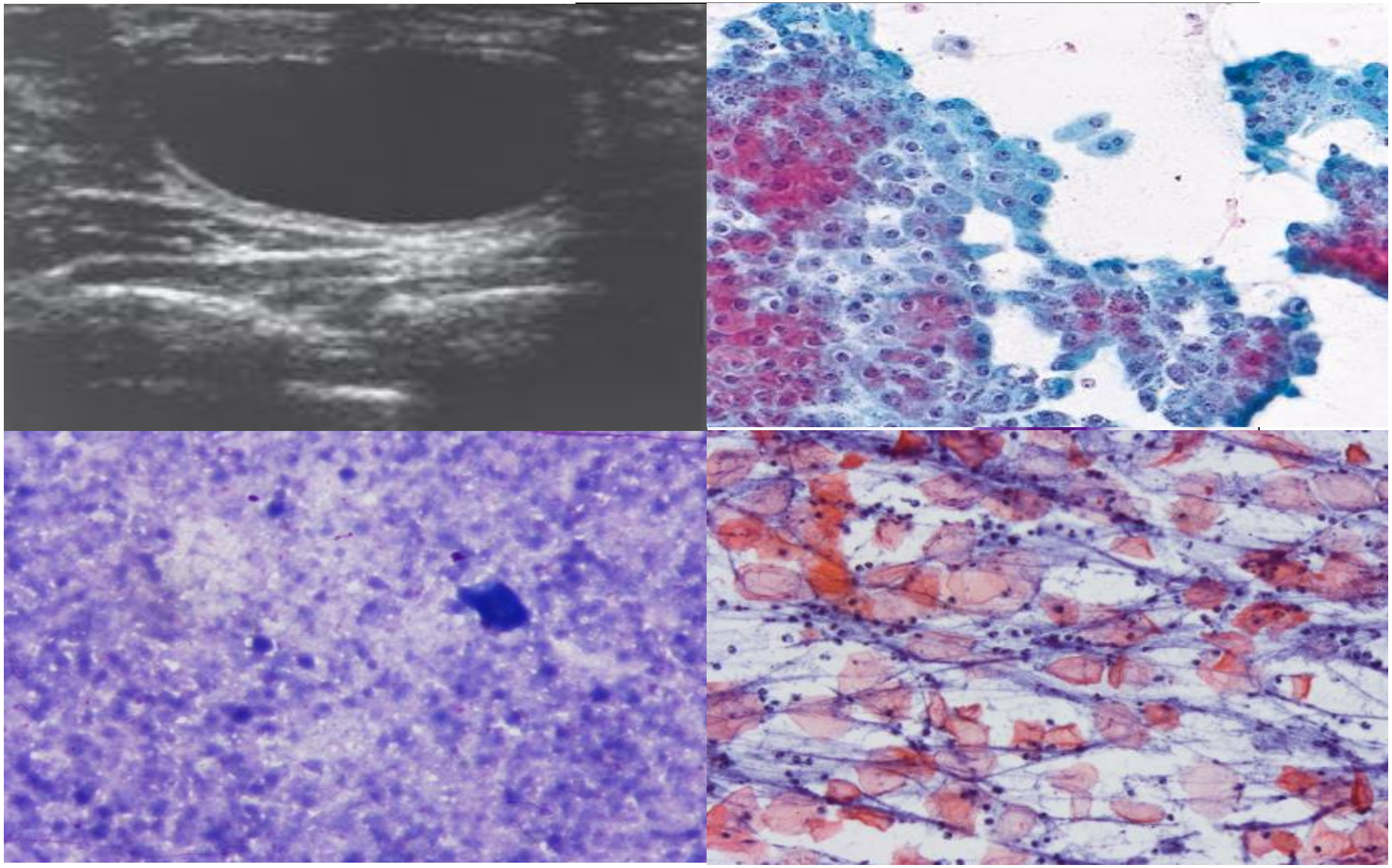
BREAST FNAC: solving problems
Benign Lesions

- FNAC is a useful and reliable tool in the evaluation and management of benign breast lesions, such as:

  - ✓ Cysts
  - ✓ Inflammatory conditions
  - ✓ Fibroadenoma

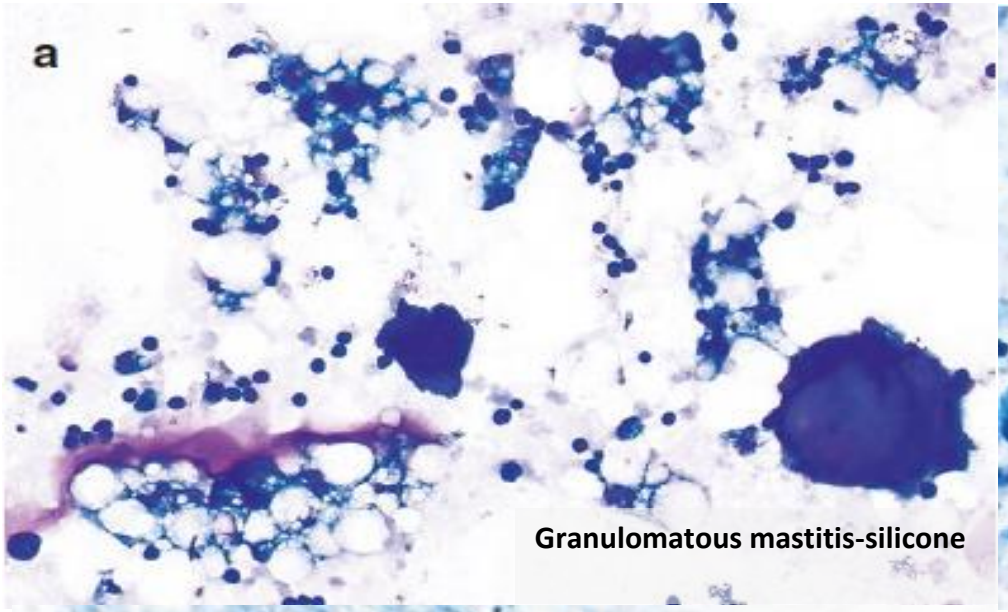
CYTOLOGICAL INTERPRETATION

BENIGN - CYSTS

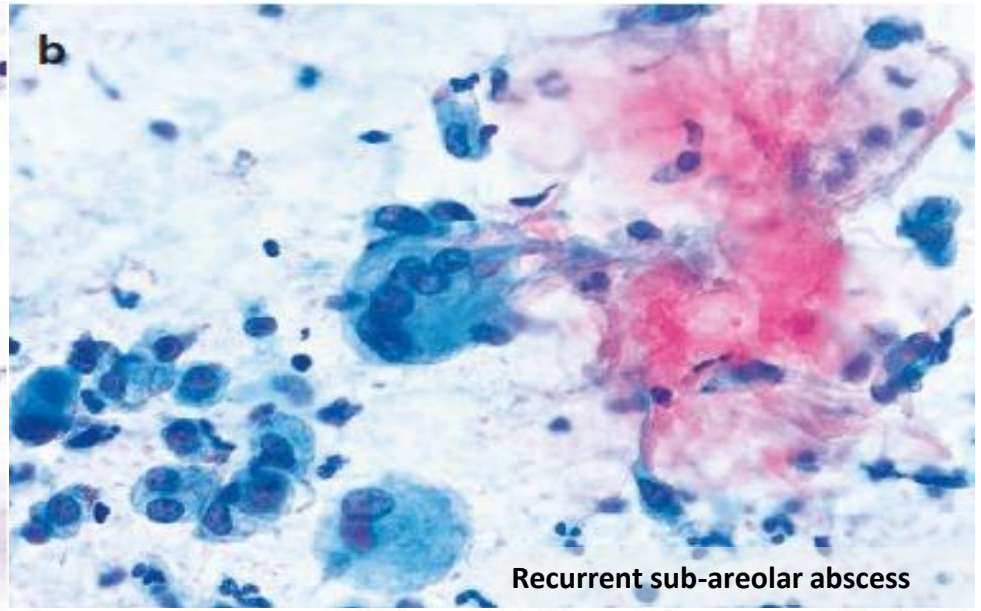


CYTOLOGICAL INTERPRETATION

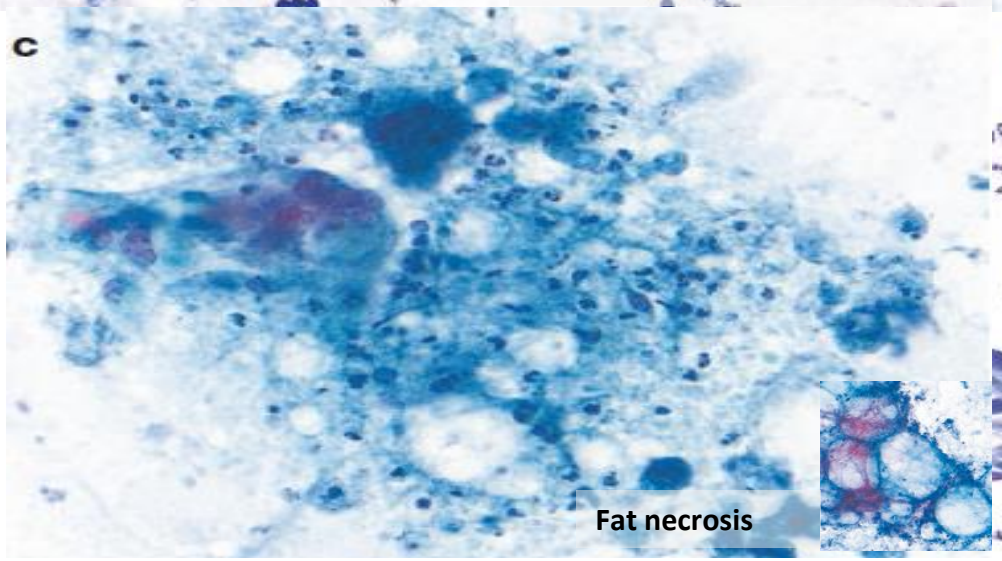
Inflammatory diseases



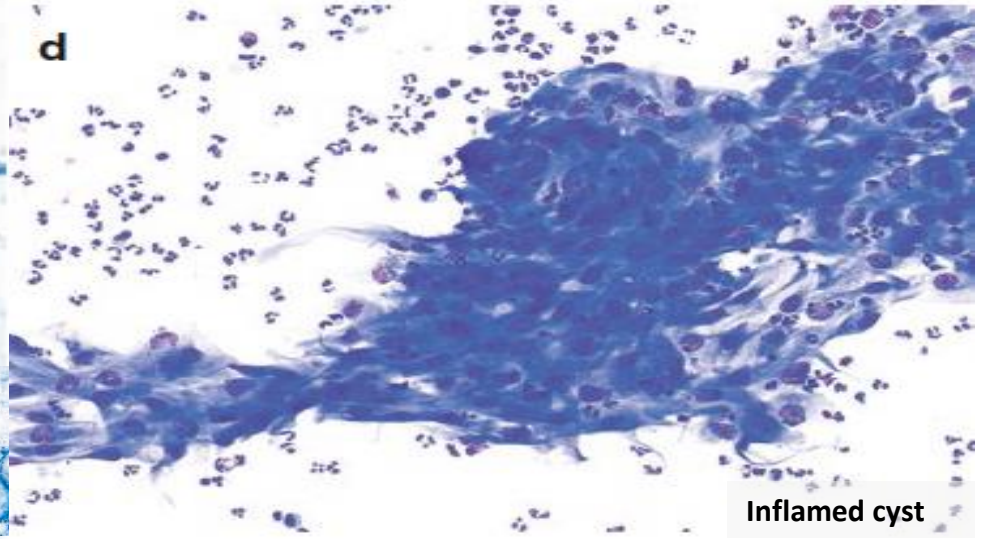
Granulomatous mastitis-silicone



Recurrent sub-areolar abscess

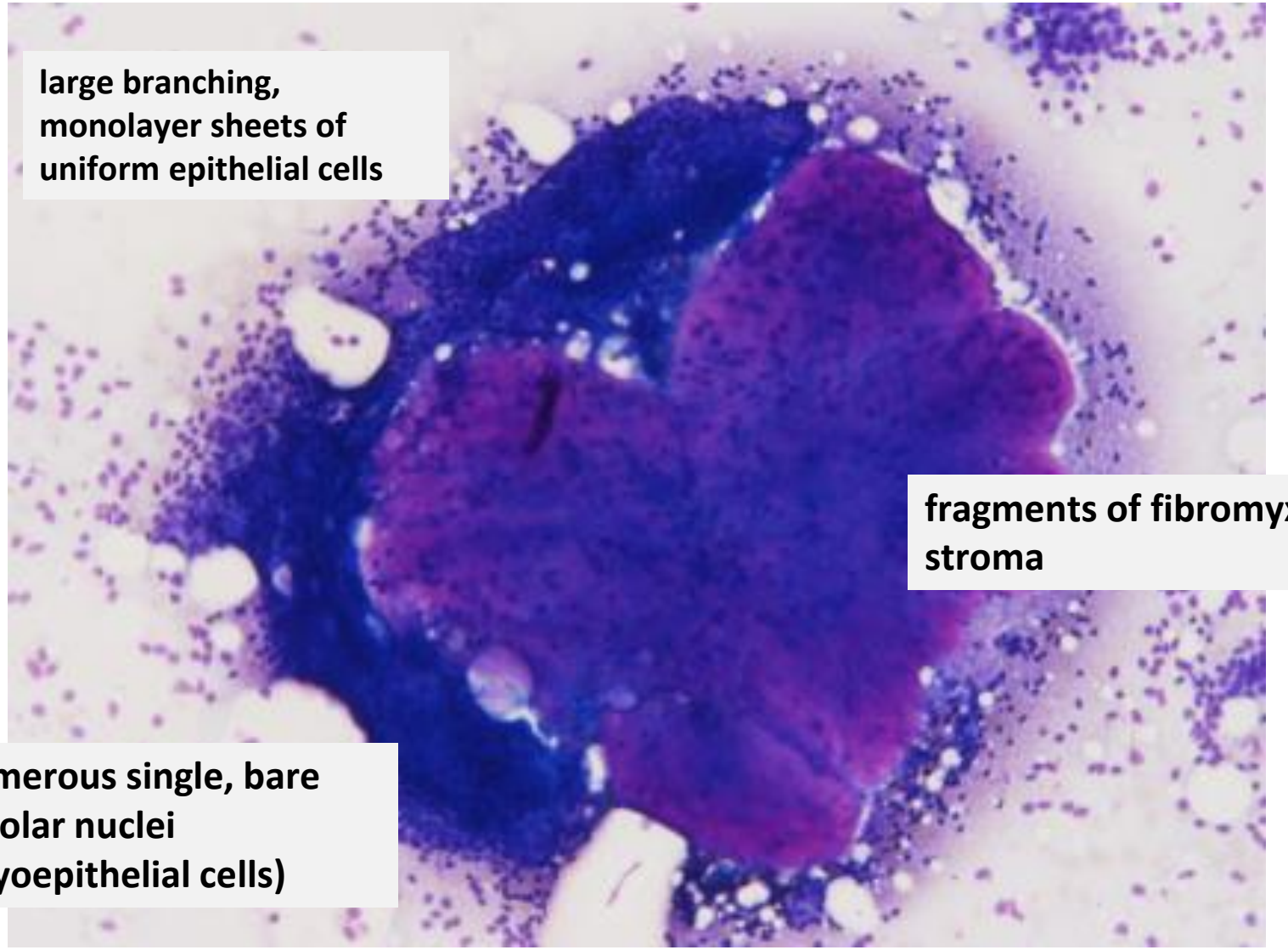


Fat necrosis



Inflamed cyst

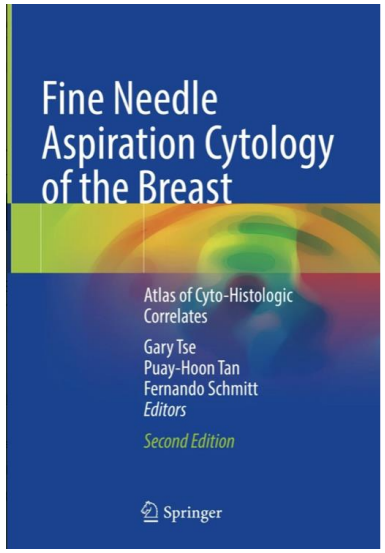
CYTOLOGICAL CRITERIA OF FIBROADENOMA



CYTOLOGICAL INTERPRETATION

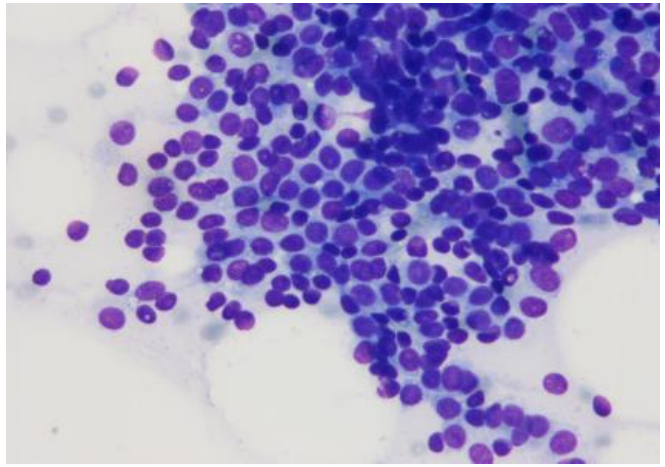
Benign epithelial proliferative lesion

Predominant pattern	
Cystic	Solid
Low cellularity of epithelial cells	Moderate to high cellularity
Foam cells and apocrine metaplasia frequently present	Cohesive epithelial groups without or with mild nuclear overlapping and presence of myoepithelial cells
Fluid background	Heterogeneous cell population: mild variation in the size and shape of the nuclei (oval, round, or spindle)
Inflammatory cells can be present	Bipolar naked nuclei in the background Foam cells, apocrine metaplasia, and stroma fragments can be observed



Fine Needle Aspiration Cytology of the Breast

Gary Tse • Puay Hoon Tan
Fernando Schmitt



Categories For The WHO Reporting System for Breast Cytopathology

Benign

- Benign FNAB diagnosis requires only routine clinical or imaging followup rather than CNB or excision biopsy
- There is a long history of utilizing breast FNAB without necessarily performing imaging, for example:
- A **specific benign FNAB diagnosis that correlates with the clinical findings** eg. abscess yielding pus or a cyst which drains without a residual palpable nodule or a rounded firm mobile nodule with characteristic cytopathological features of a fibroadenoma
- **Recommend correlation** with imaging to achieve ‘triple test’
- FNAB should be repeated if a lesion changes its characteristics.

Categories For The WHO Reporting System for Breast Cytopathology

Atypical

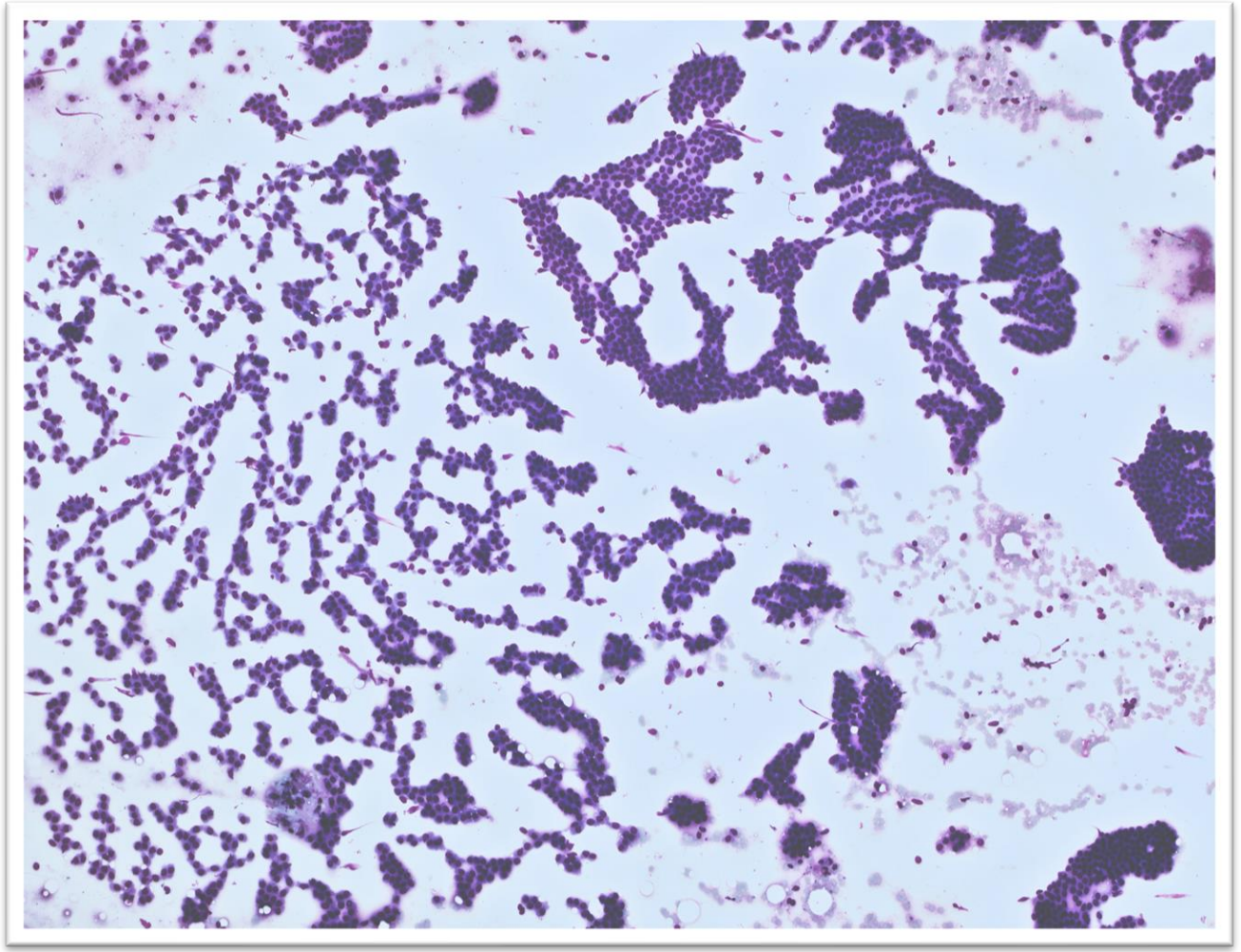
- *A specimen categorized as 'Atypical' demonstrates the presence predominantly of cytopathological features that are seen in benign processes or lesions, but with the addition of some features that are uncommon in benign lesions and which may be seen in malignant lesions.*

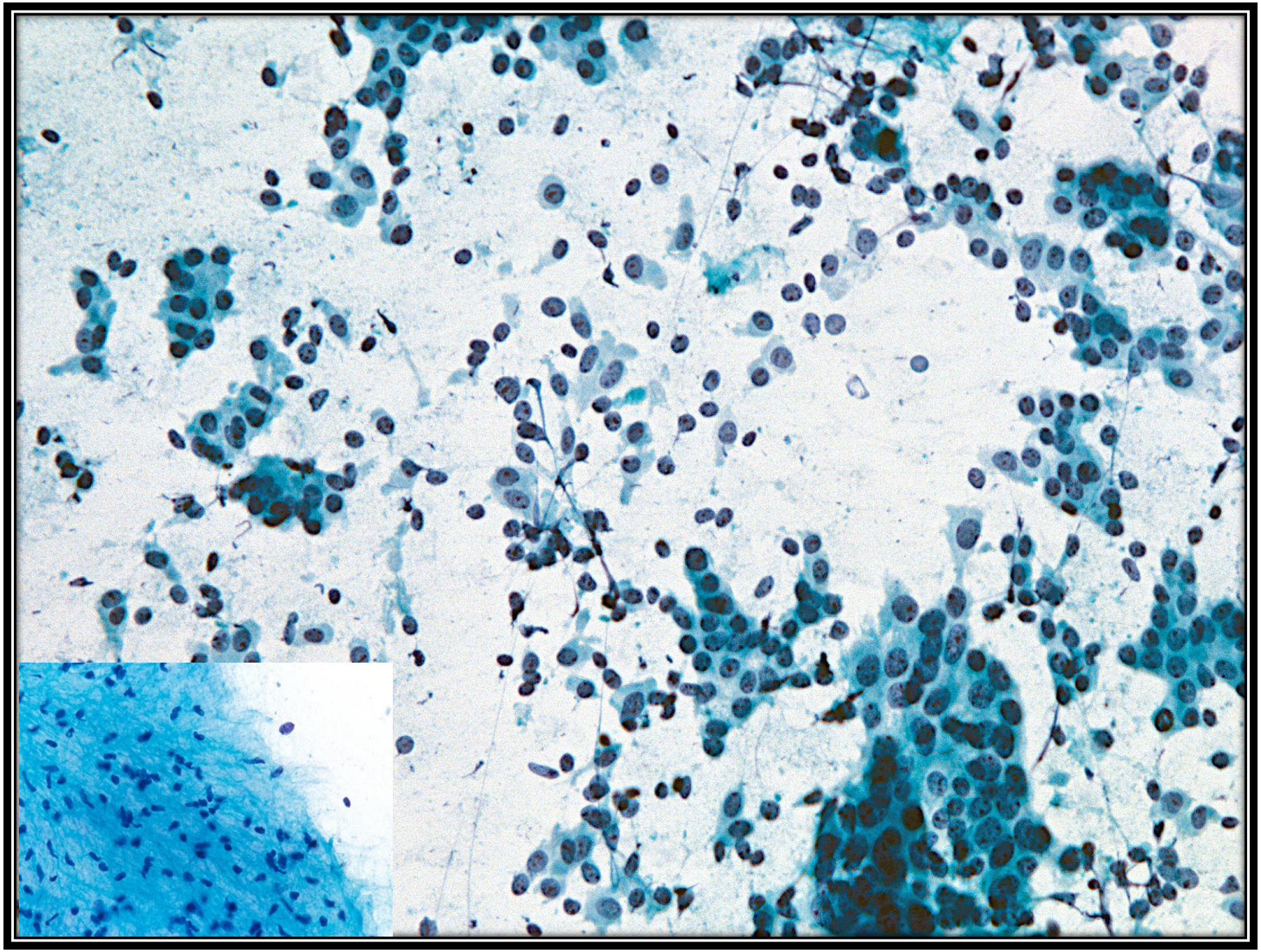
- INCIDENCE: 1.2-24% (mean:9.3%). Our rate: 13%
- Reported ROM: 13.0% to 40.0% (median, 24.1%; mean, 24.0%)
- MAIN CAUSES: Interpretative expertise, technical limitations and type of lesion (fibroadenoma, papillary lesions, epithelial proliferation, fibro-epithelial lesions, rare lesions…)
- Some cytological features: single intact cell dispersal, nuclear enlargement and pleomorphism, high cellularity, necrosis, complex architectural features
- MANAGEMENT: Repeat FNAB or consider CNB. If low clinical suspicion, consider repeat clinical and radiologic examination in 3-6 months.

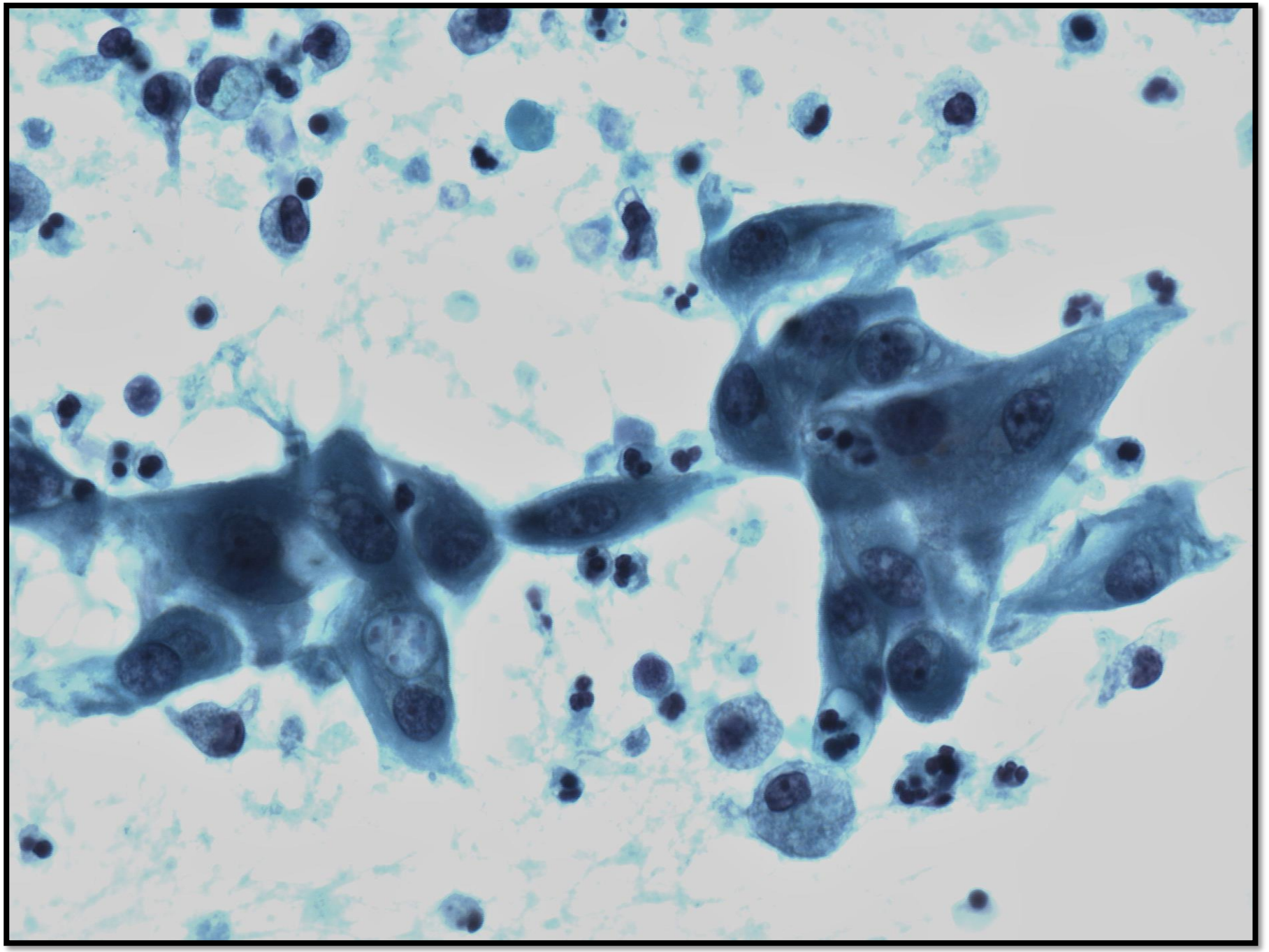
Atypical: lesions that may produce an “Atypical” categorisation

- Fibroadenoma: epithelial hypercellularity or sclerotic low cellularity
- Fibroadenoma with stromal hypercellularity Vs low grade phyllodes
- Intraductal papillomas with epithelial hyperplasia
- Fibrocystic change with epithelial hyperplasia including radial scars
- Spectrum of proliferative lesions: columnar cell change, flat epithelial atypia, ‘usual’ epithelial hyperplasia, sclerosing adenosis
- Lobular neoplasia: often associated with low cellularity
- Extensive necrosis or presence of mucin
- Adenomyoepithelioma
- Spindle Cell Lesions

Atypical: pre-analytical causes related to technique: smears and fixation

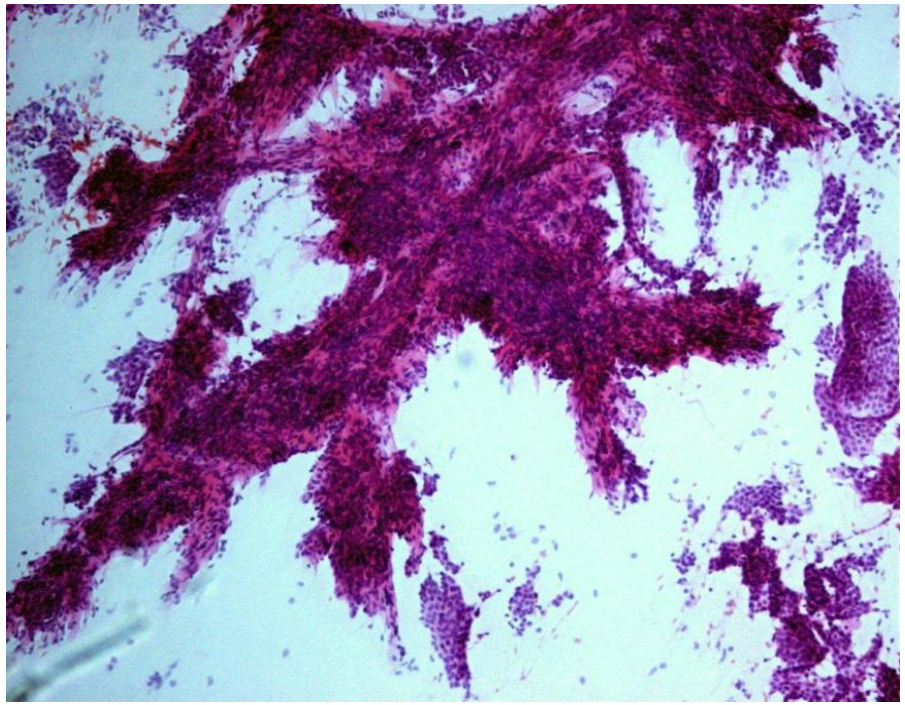


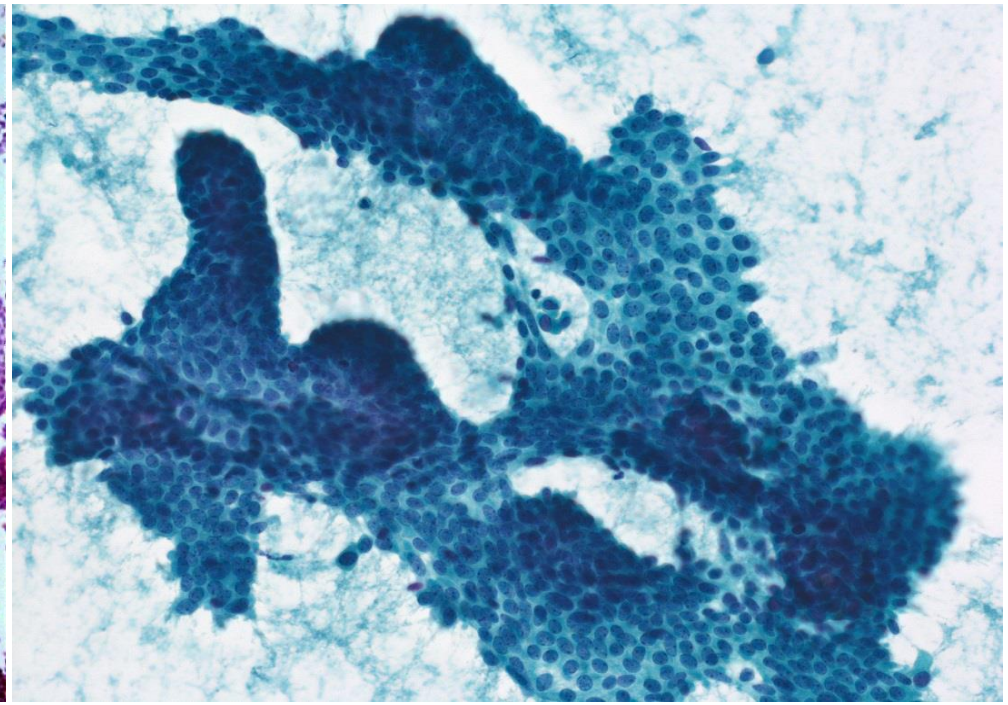




CYTOLOGICAL INTERPRETATION

Papillary Lesions

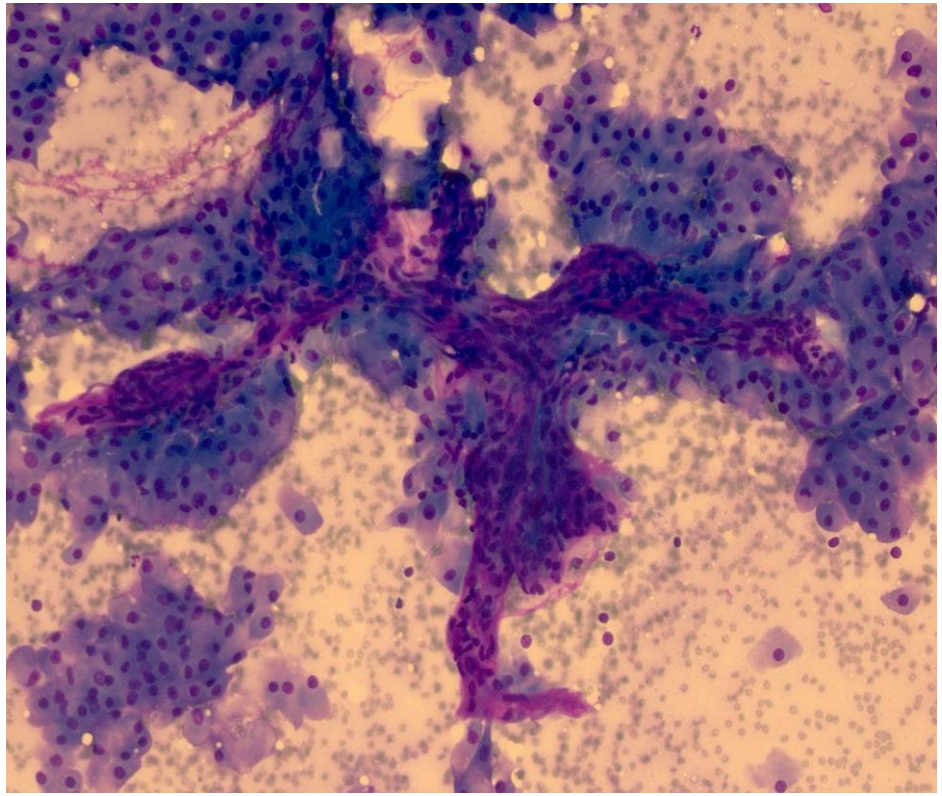


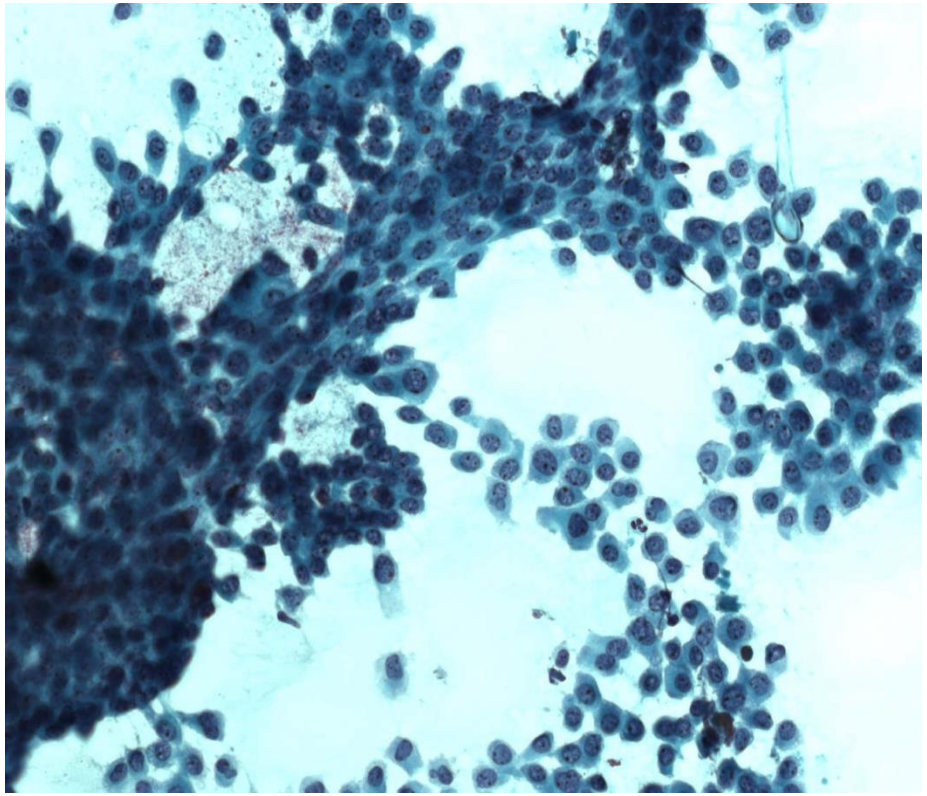


- Papillary three-dimensional arrangements.
- Columnar cells in rows, palisades, and single.
- Complex folded and branching sheets of epithelial cells.

CYTOLOGICAL INTERPRETATION

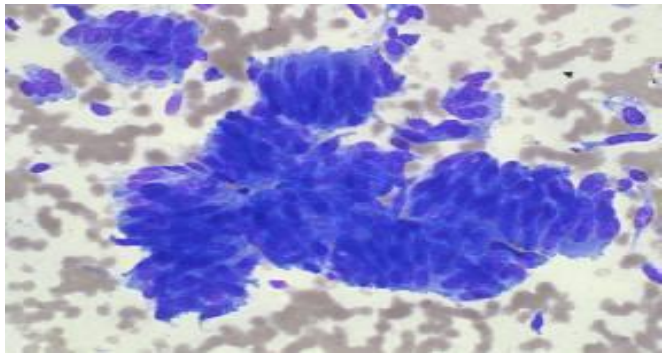
Papillary Lesions

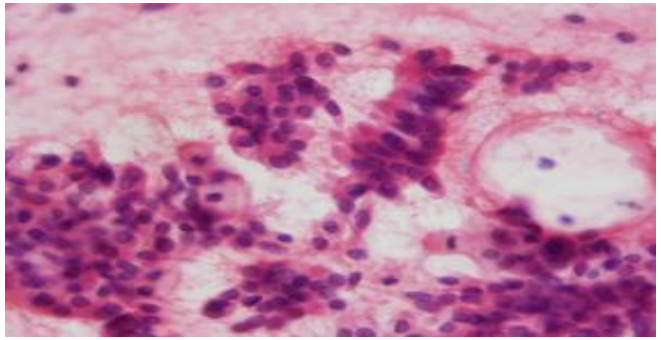




CYTOLOGICAL INTERPRETATION

Is it possible to distinguish benign and malignant Papillary breast tumors on FNA?





Cytological findings favouring malignant

- Higher cellularity
- Papillary three-dimensional arrangements without a central fibrovascular core (cell balls)
- Tall columnar cells frequent.
- Isolated cells with cytoplasm.
- Absence of bare nuclei, apocrine metaplasia, and rare macrophages.

Papillary lesion on CNB

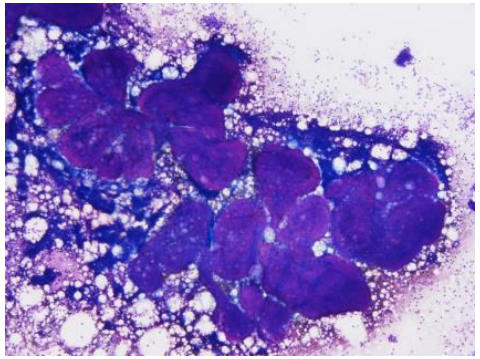
- The excision of all papillary lesions (PL) is being challenged. The option of prolonged follow-up with imaging has been suggested as an alternative approach, but all palpable or symptomatic PL or any PL with atypia must be excised.

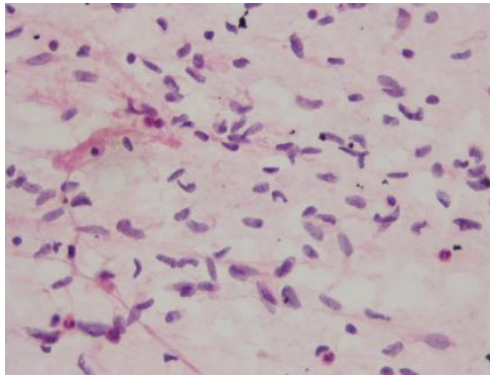
- However, after the diagnosis of intraduct papilloma at CNB, 14% of the incidence of carcinoma and 17% of high-risk lesions had been reported in the excision.

- **There appears to be insufficient evidence to support a general change to the current protocol of excision of intraduct papilloma with the exception of small papillomas with no atypia generously sampled by VACB and with no residual lesion in post-core imaging**.

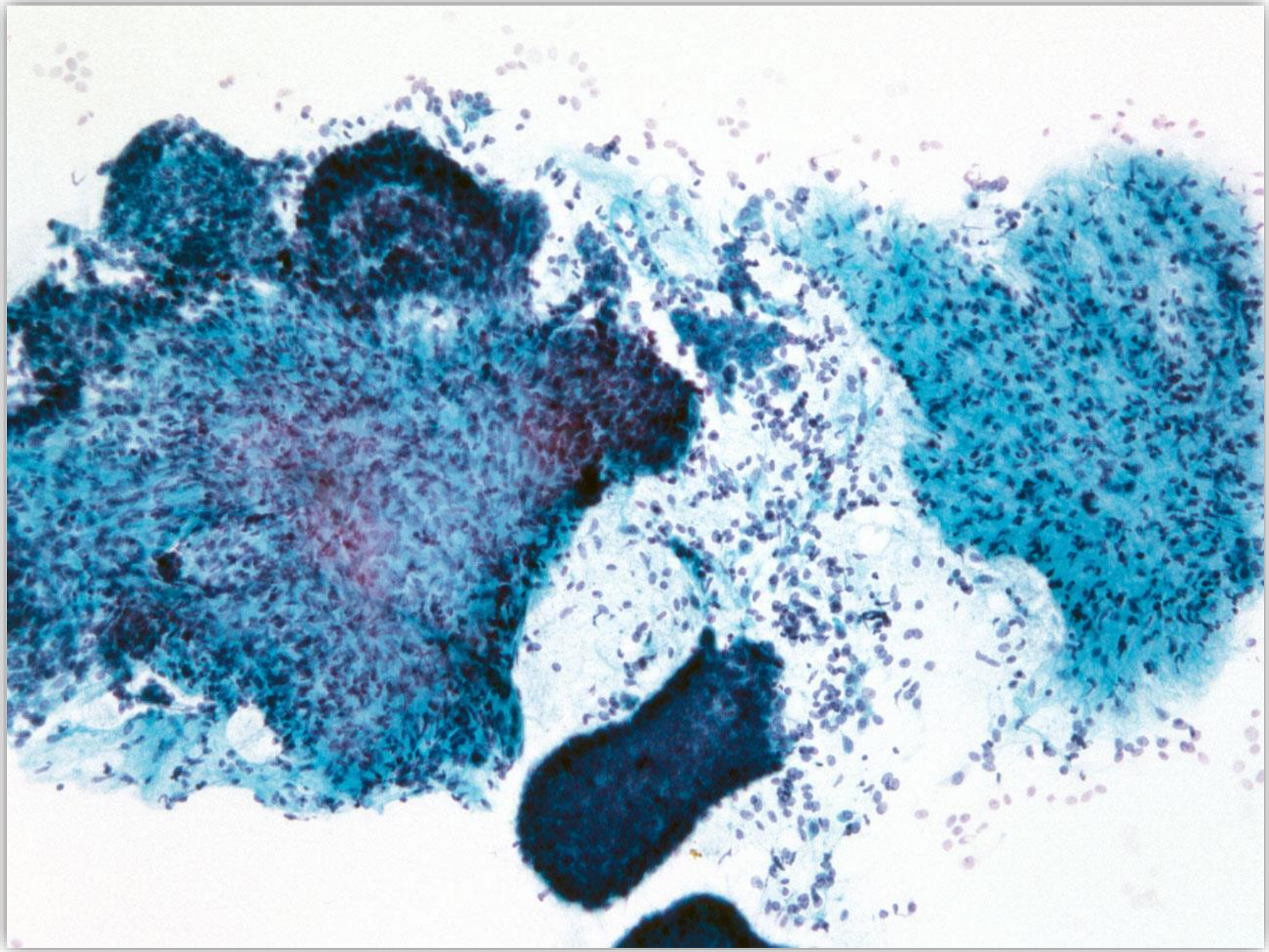
CYTOLOGICAL INTERPRETATION
Fibroepithelial lesions

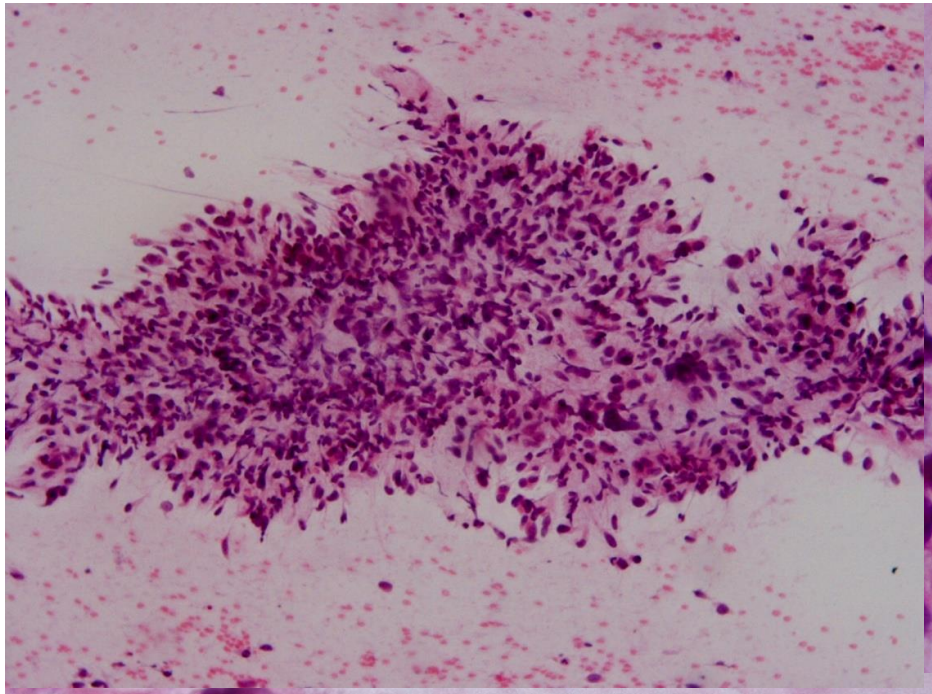
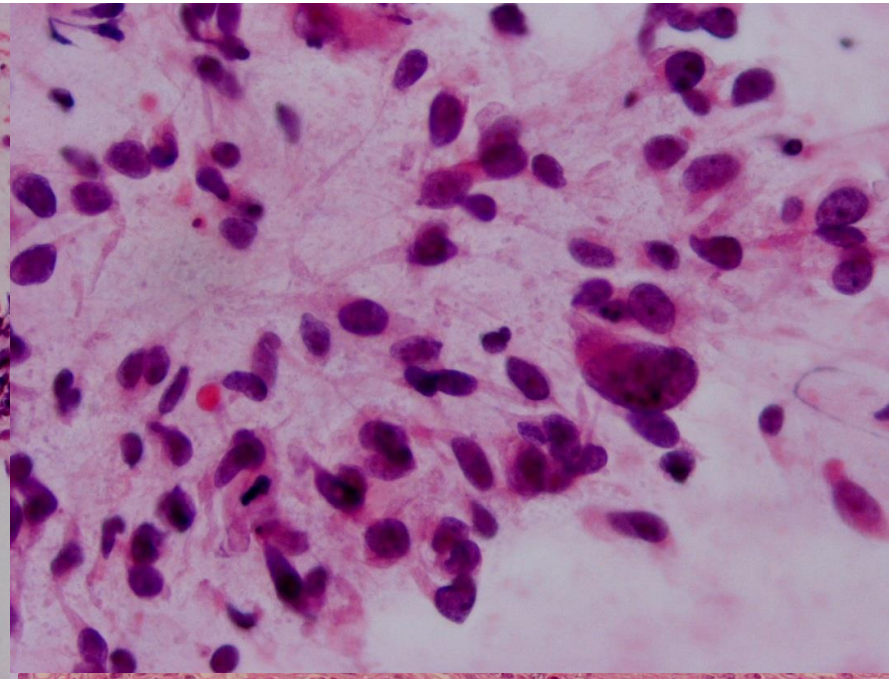
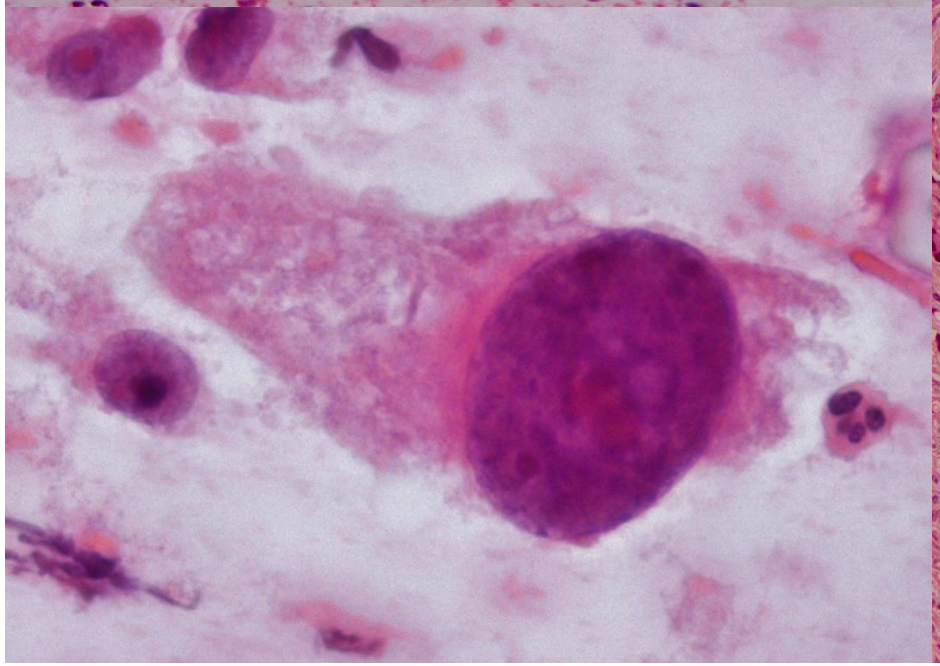
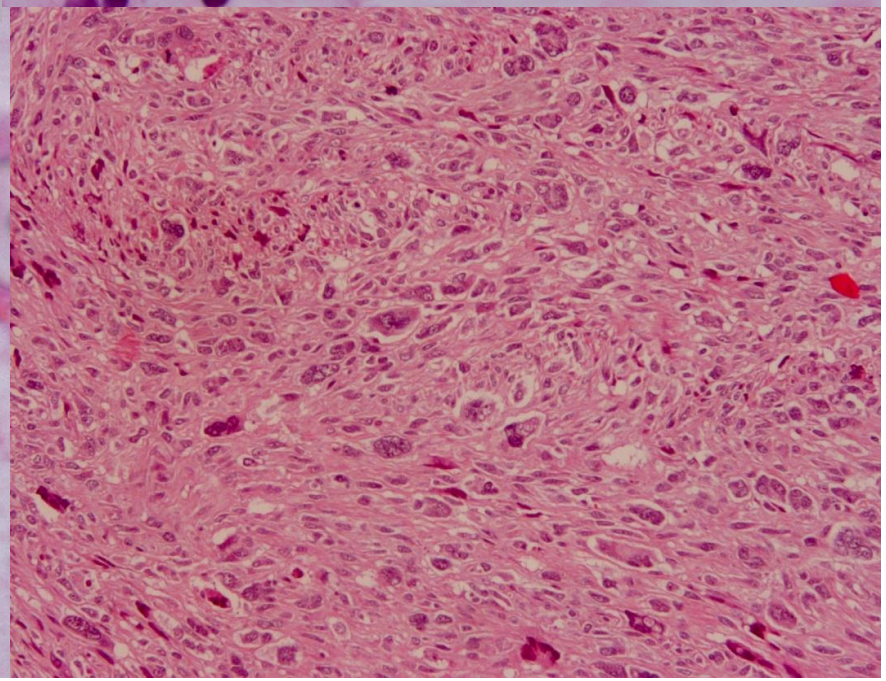
PHYLLODES TUMOUR





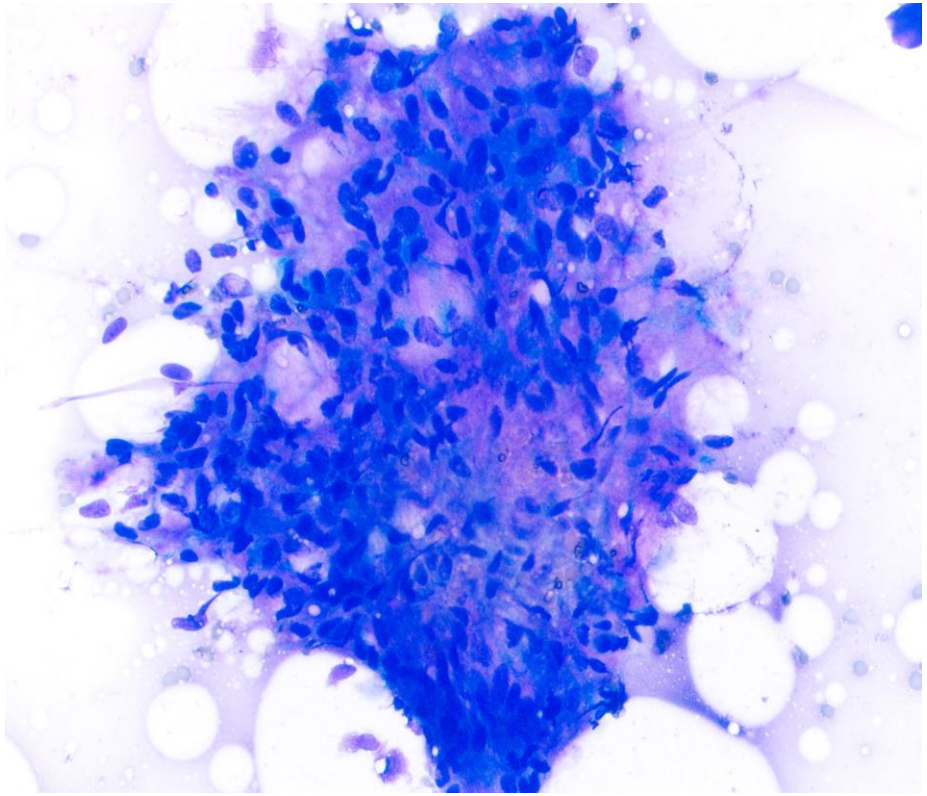
- Biphasic proliferative lesion (epithelial and stromal elements) similar to fibroadenoma but with predominance of the stroma over the epithelium
- Fibromyxoid stromal fragments are larger than those seen in fibroadenomas and are highly cellular with fibroblastic spindle cells.
- The presence of isolated stromal cells with spindle nuclei and abundant pale cytoplasm
- is suggestive of PT.

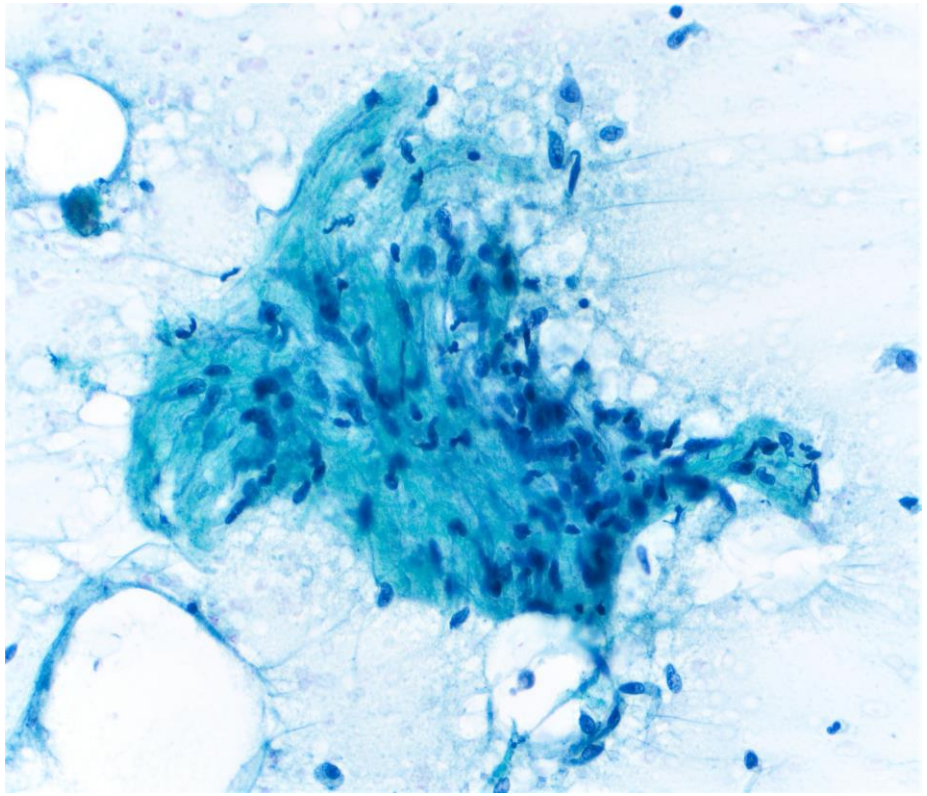


CYTOLOGICAL INTERPRETATION

Spindle-cell Lesions





Categories For The WHO Reporting System for Breast Cytopathology

Atypical

- **Management requires correlation with clinical and imaging findings, in 'Triple test'** (which has a very high PPV and NPV)
- If imaging or clinical findings are indeterminate or suspicious, CNB is recommended; if no CNB is available then repeat the FNAB or go to simple excision biopsy
- If imaging and clinical findings are not atypical/indeterminate, review the patient at 3 -6 months with or without FNAB
- If no CNB or imaging available repeat FNAB recommended

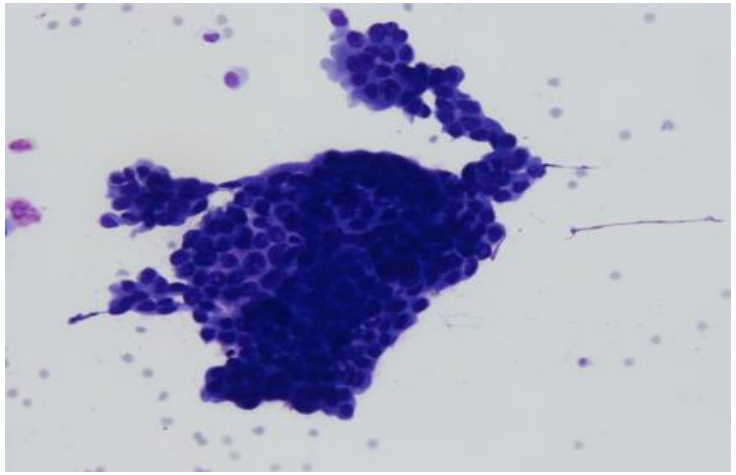
Categories For The WHO Reporting System for Breast Cytopathology

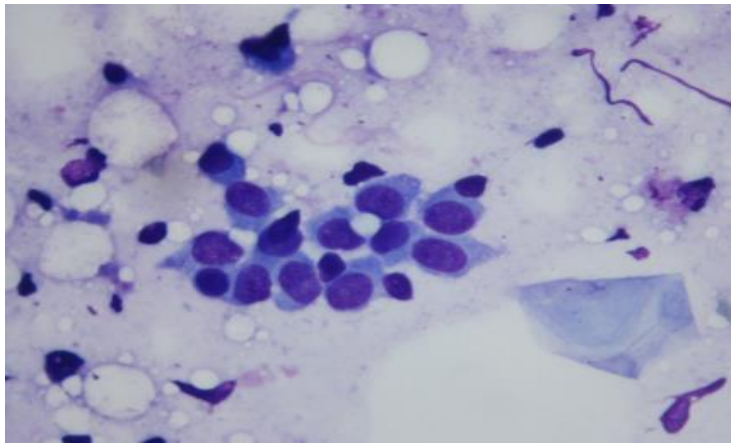
Suspicious for Malignancy

- *This diagnostic category is defined as the presence of some cytopathological features which are usually found in malignant lesions, but with insufficient malignant features, either in number or quality, to make a definitive diagnosis of malignancy. The type of malignancy suspected should always be stated if at all possible, or a differential diagnosis provided.*

- INCIDENCE: 2-20%. Our rate: 2%
- Reported ROM: 45.8% to 100% (median, 85.2%; mean, 85.2%)
- MAIN CAUSES: Interpretative expertise, technical limitations and type of lesion (DCIS, lobular carcinoma, rare lesions…)
- MANAGEMENT: CNB or surgical management.

CYTOLOGICAL INTERPRETATION
Epithelial proliferative lesions



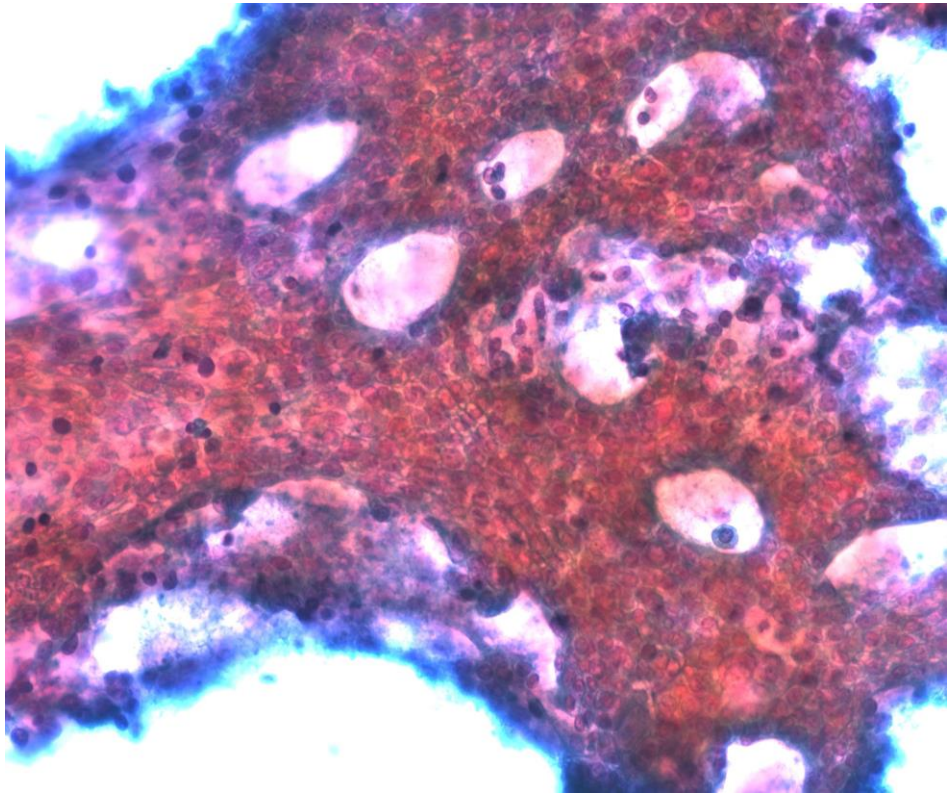


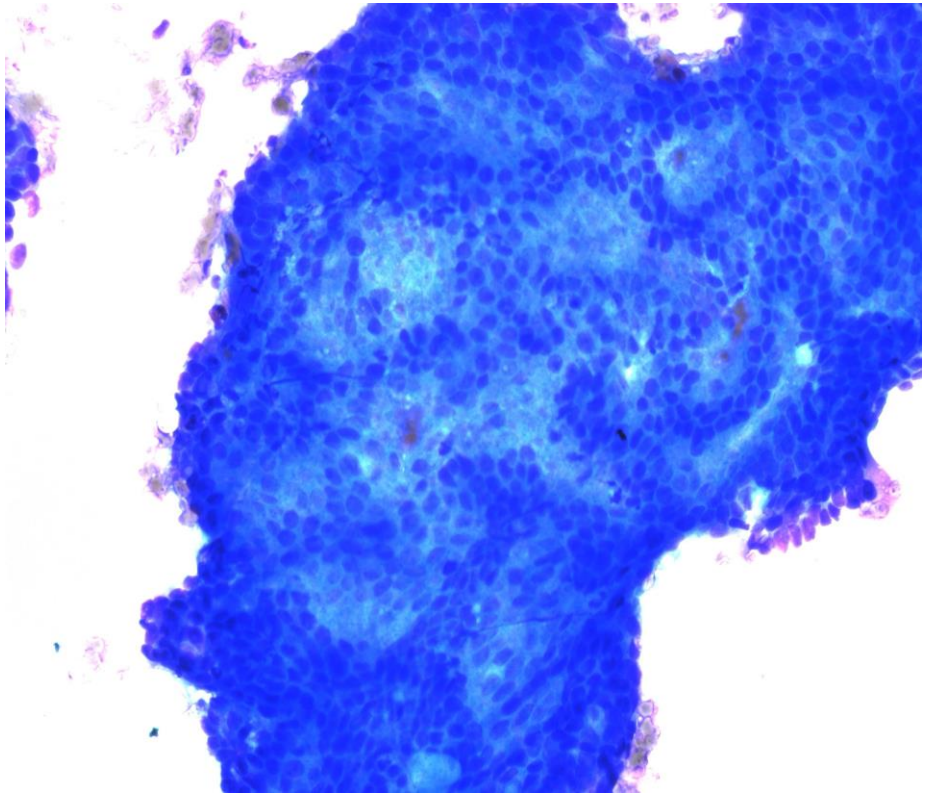
- Moderate to high cellularity.
- Epithelial cell groups with overlapping and without or w/ few myoepithelial cells.
- Bipolar naked nuclei in the background absent or in few numbers.
- Less cell cohesively in the borders of the cell groups with occasional isolated epithelial cells with preserved cytoplasm.
- 20% are malignant at biopsy

Low/intermediate Grade Ductal Carcinoma in Situ

- Cytopathological DD between proliferative disease and LGDCIS is challenging with **overlapping diagnostic criteria.**
- LGDCIS usually presents as calcifications, rarely presents as clinical mass and is an **uncommon FNAB diagnosis.**
- **When features suggest LGDCIS, should recognize them to avoid over-diagnosis of malignancy and under-calling of DCIS as proliferative breast disease**
- Recommended that in cases suspicious of LGDCIS on cytopathological criteria, give a diagnosis of **'suspicious of malignancy', raise the 'possibility of LGDCIS'** and avoid a false positive malignant diagnosis
- **CNB or excision biopsy should be recommended**

CYTOLOGICAL INTERPRETATION

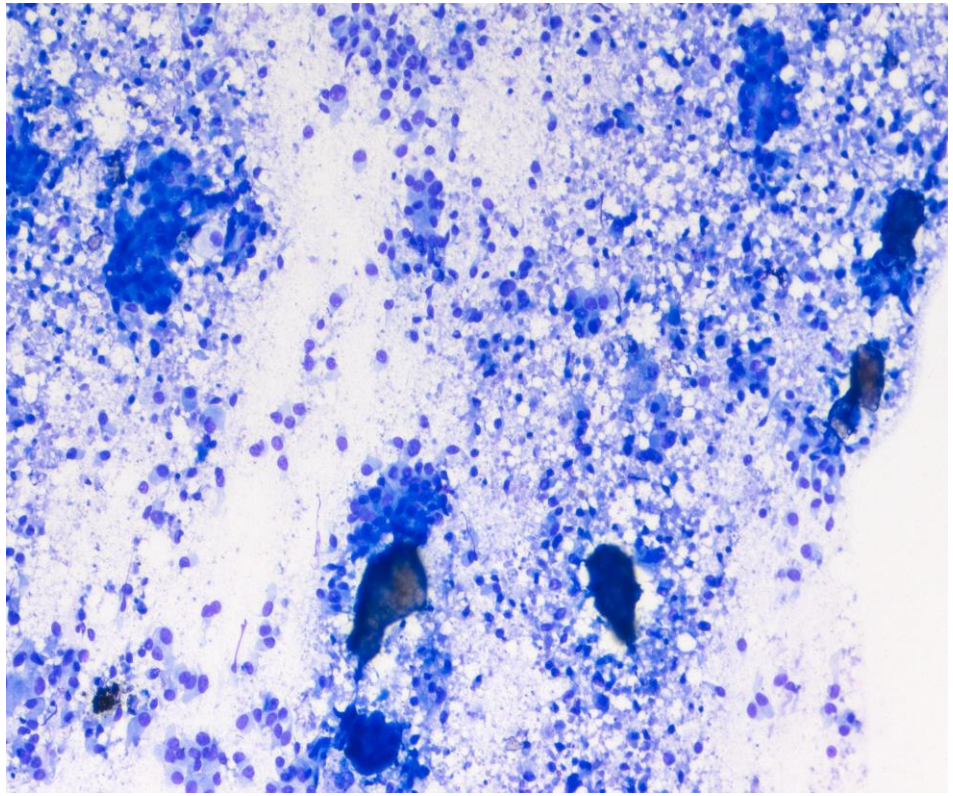


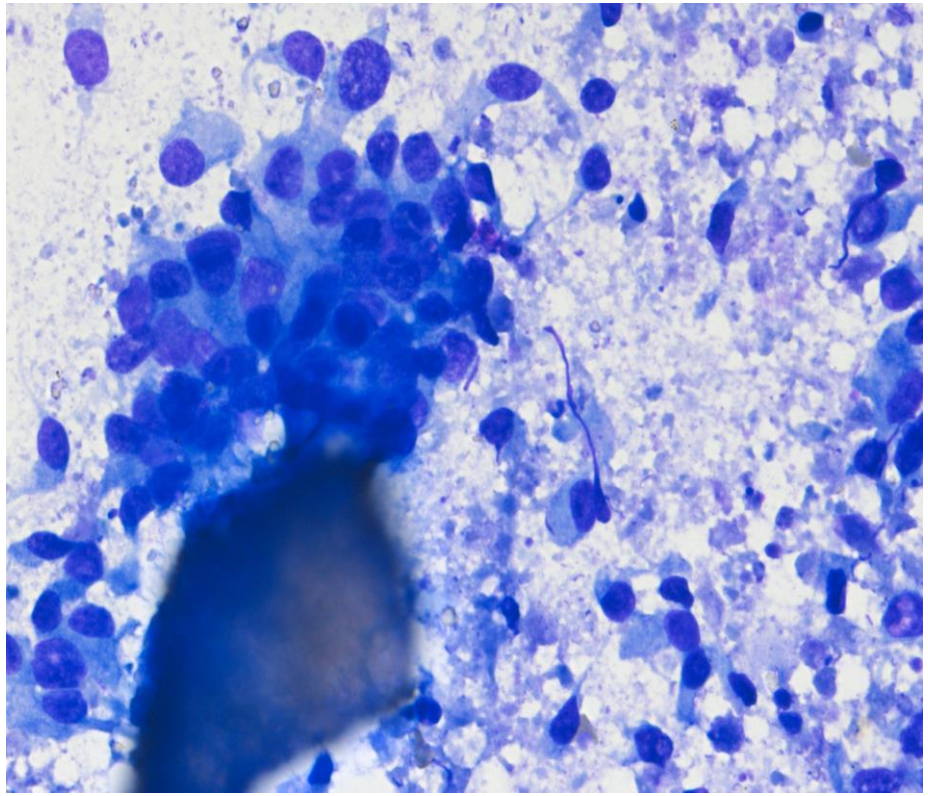


High Grade Ductal Carcinoma in Situ

- **Extensive necrosis with calcifications** and low cellularity consisting of single **highly atypical epithelial cells and tissue fragments** of crowded similar atypical cells are seen in HGDCIS
- But **necrosis can be seen in some high grade invasive carcinomas no special type and in metaplastic or 'basal-like' carcinomas**
- **If HGDCIS is suspected consider the use of 'suspicious of malignancy', raise the possibility of 'carcinoma is present with features suggesting a HGDCIS component'**
- Many of these cases will be called 'Malignant', so correlate with the imaging
- CNB should be recommended
- Can we diagnosis absolutely the presence of invasion?

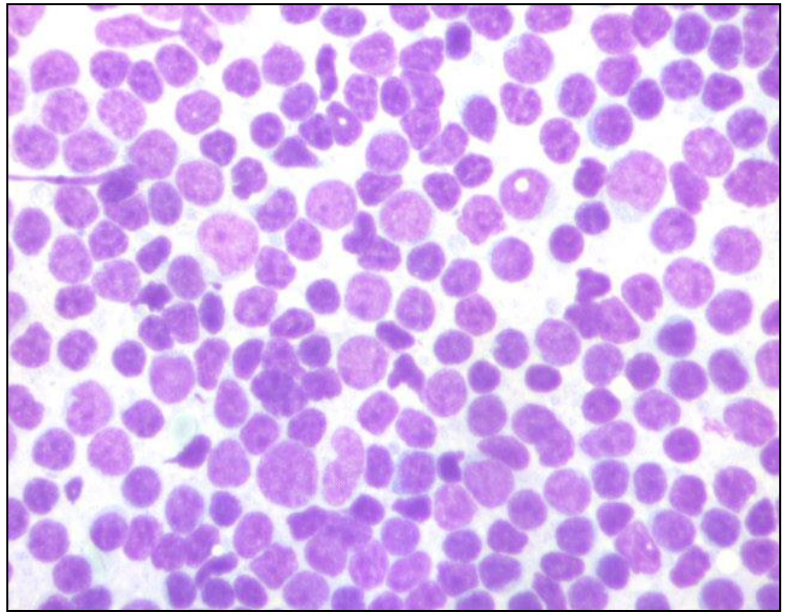
CYTOLOGICAL INTERPRETATION

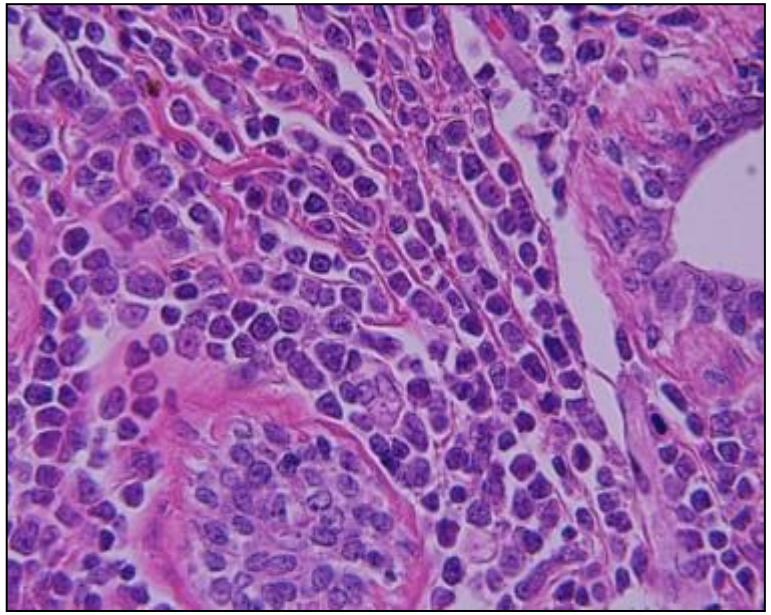




CYTOLOGICAL INTERPRETATION

Other malignancy





NON-HODGKIN LYMPHOMA

Categories For The WHO Reporting System for Breast Cytopathology

Malignant

- *A cytology specimen classified as ”Malignant" provides a definitive statement of malignancy. The diagnosis implies that the sample is of satisfactory quantity and cellular quality. The type of malignancy should be identified when possible.*
- INCIDENCE: 10-30%. Our rate: 6%
- Reported ROM: 99-100%
- MAIN CAUSES: Carcinoma NST, High-Grade DCIS, Subtypes of breast carcinoma, other malignancies, metastases.
- MANAGEMENT: In practical terms, malignant cytological diagnoses are part of the ‘triple test’ with clinical and radiographic findings in palpable as well as non-palpable breast lesions, with a PPV approaching 100%.
- Patients with triple tests that are discordant in any way, such as malignant cytology in a case with benign imaging or clinical exam, require further investigation most commonly a core needle biopsy (CNB) prior to definitive treatment.

Categories For The WHO Reporting System for Breast Cytopathology

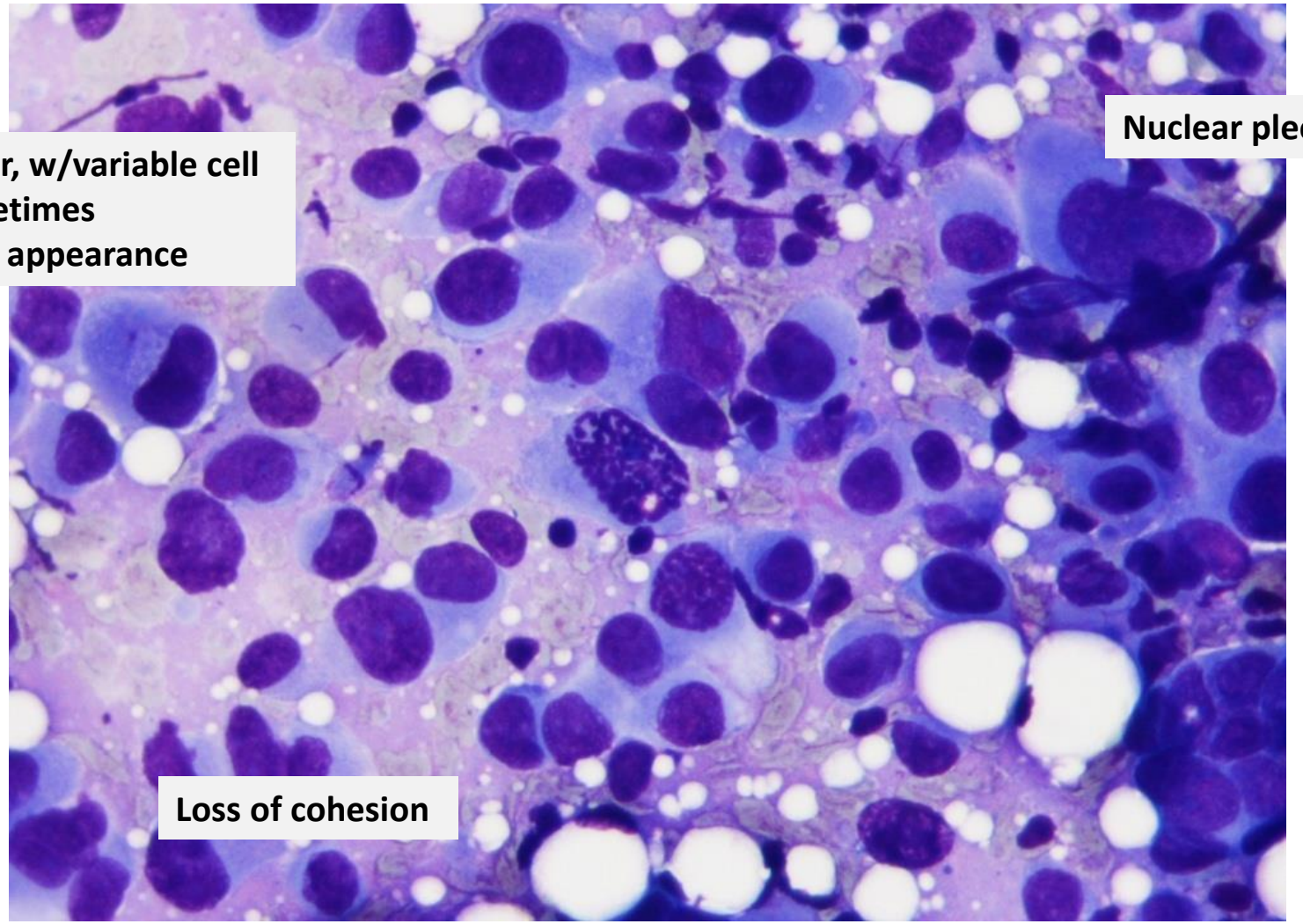
Malignant

Entities in the Malignant Category:

- 9.1.1: Malignant epithelial tumours
  - 9.1.1.1: Invasive carcinoma, no special type and high-grade DCIS
  - 9.1.1.3: Low grade DCIS, papillary ductal carcinoma in situ, encapsulated papillary carcinoma and solid papillary carcinoma (in situ and invasive)
  - 9.1.1.2: Lobular carcinoma
  - 9.1.1.4: Paget disease of nipple
  - 9.1.1.5: Tubular carcinoma
  - 9.1.1.6: Cribriform carcinoma
  - 9.1.1.7: Mucinous carcinoma
  - 9.1.1.8: Secretory carcinoma
  - 9.1.1.9: Invasive micropapillary carcinoma
  - 9.1.1.10: Carcinoma with apocrine differentiation
  - 9.1.1.11: Metaplastic carcinoma
  - 9.1.1.12: Salivary gland-type carcinomas including acinic cell, adenoid cystic, mucoepidermoid
  - 9.1.1.13: Tall cell carcinoma with reverse polarity - to be deleted
  - 9.1.1.14: Neuroendocrine tumour and carcinoma
- 9.1.2: Borderline and malignant phyllodes tumours
  - 9.1.2.1: Borderline and malignant phyllodes tumours
- 9.1.3: Malignant mesenchymal tumours
  - 9.1.3.1: Angiosarcoma of breast including primary and post-irradiation
  - 9.1.3.2: Liposarcoma
  - 9.1.3.3: Other malignant spindle cell tumours
- 9.1.4: Haematolymphoid neoplasms
  - 9.1.4.1: B-cell lymphomas of the breast
  - 9.1.4.2: Breast implant associated ALCL
- 9.1.5: Metastases
  - 9.1.5.1: Metastatic tumours
- 9.1.6: Sample reports

CYTOLOGICAL CRITERIA OF INVASIVE CARCINOMA NST

Cellular smear, w/variable cell pattern, sometimes plasmacytoid appearance

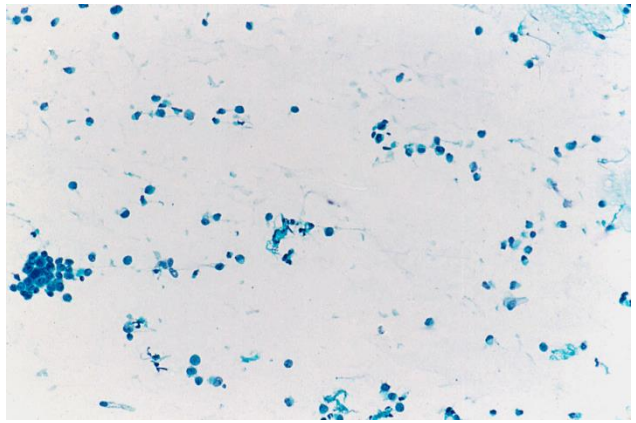


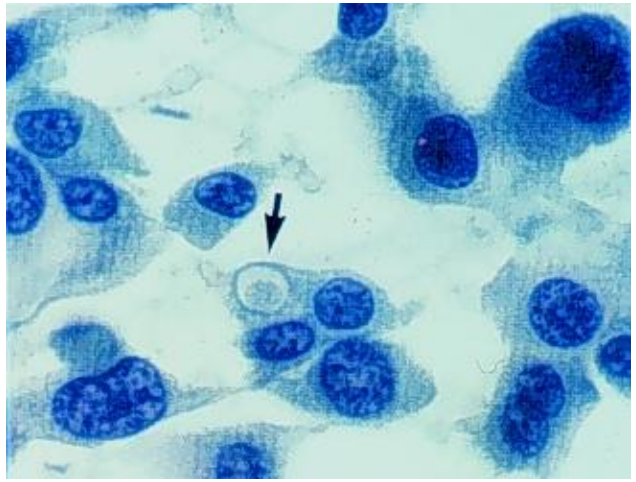
Nuclear pleomorphism

Loss of cohesion

CYTOLOGICAL INTERPRETATION

Invasive lobular carcinoma

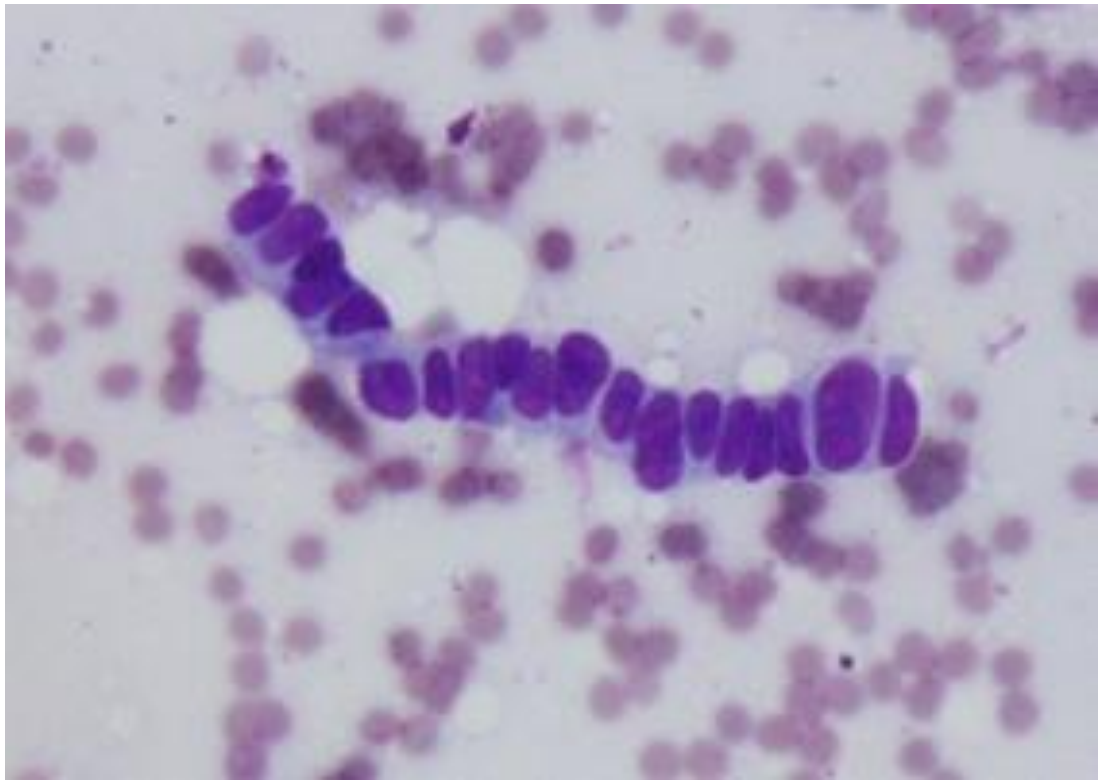




- Variable cellularity. In some cases very poor cell yield.
- Cells single and in small clusters, short single files common.
- Epithelial cells have small dark nuclei with scanty cytoplasm. The lack of pleomorphism can be cause of a false-negative diagnosis.
- Intracytoplasmic lumina/vacuoles.

CYTOLOGICAL INTERPRETATION

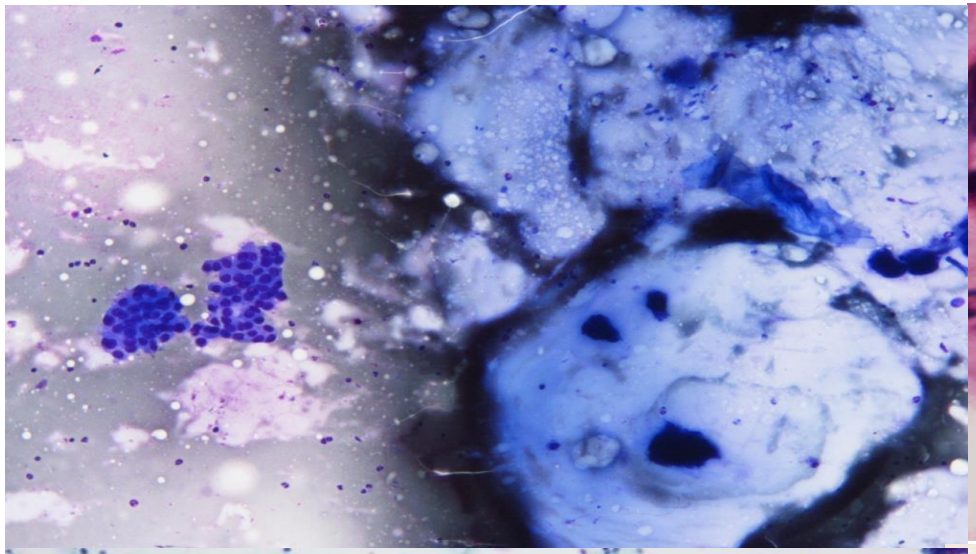
Invasive lobular carcinoma

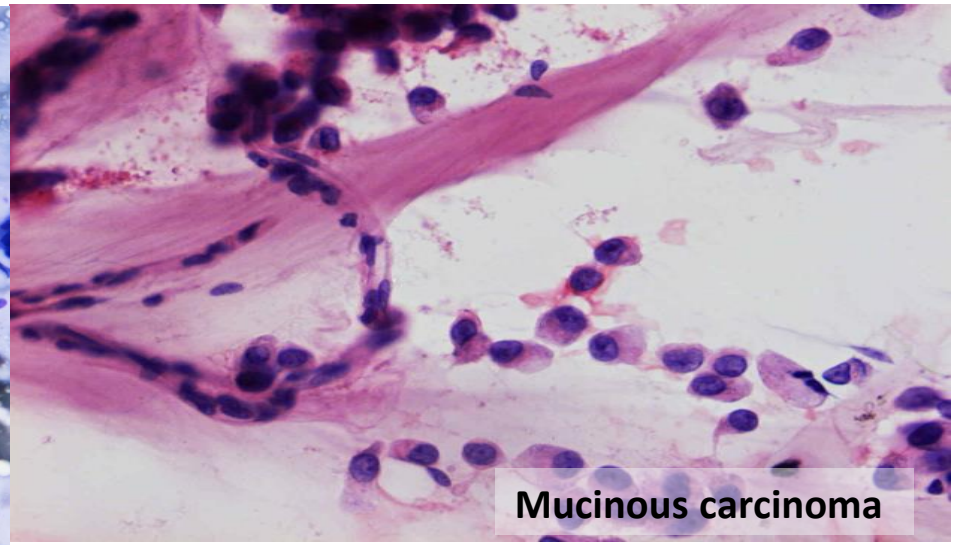


A most valuable clue on ILC is the tendency to form small chains of cells in the aspirates

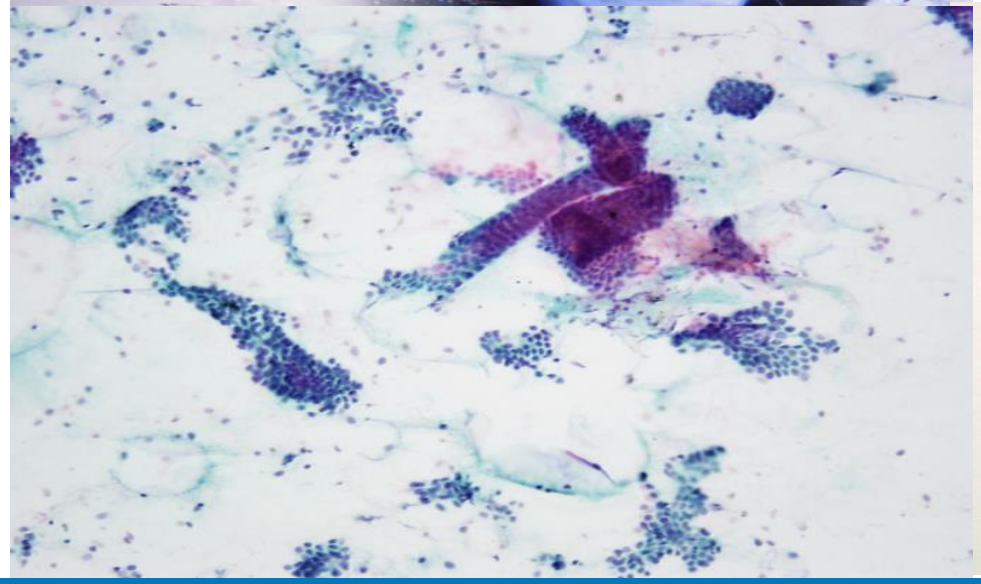
CYTOLOGICAL INTERPRETATION

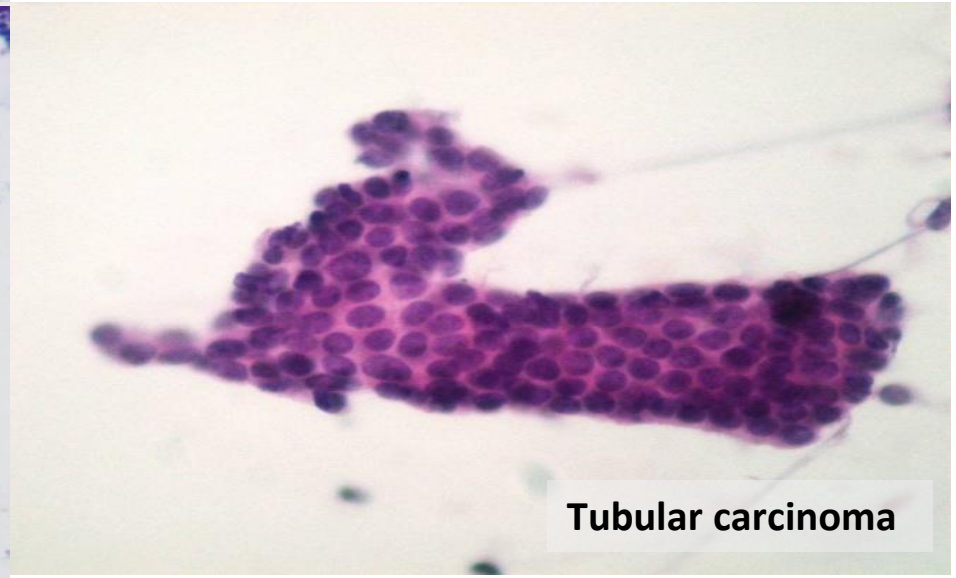
Breast carcinoma special types





Mucinous carcinoma

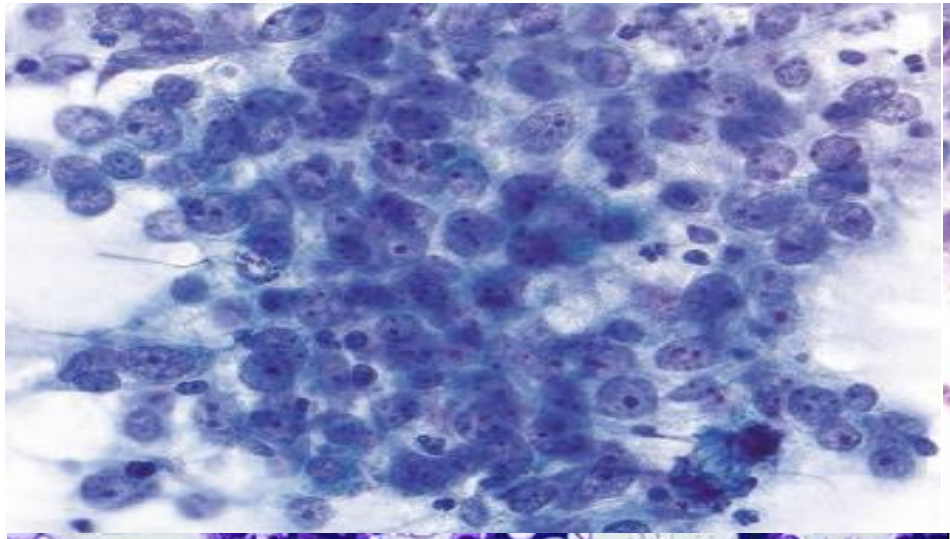


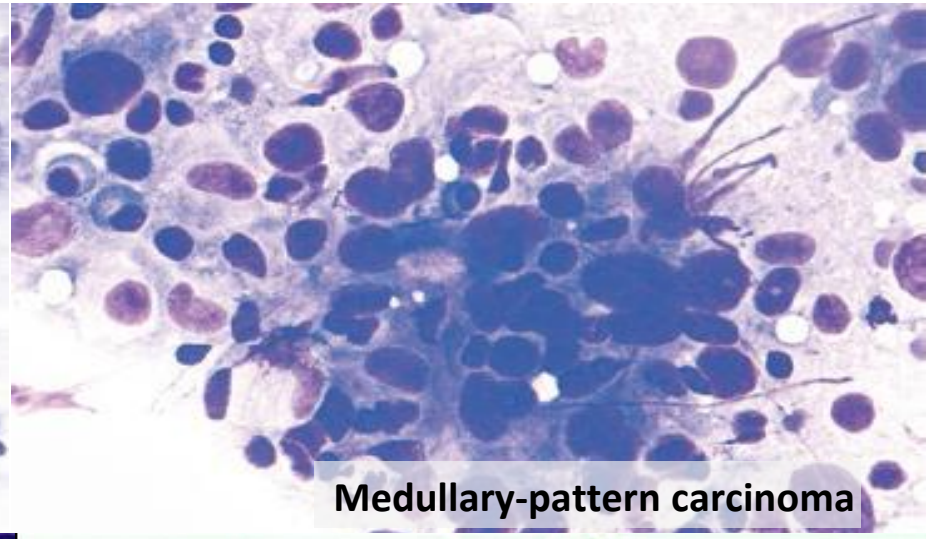


Tubular carcinoma

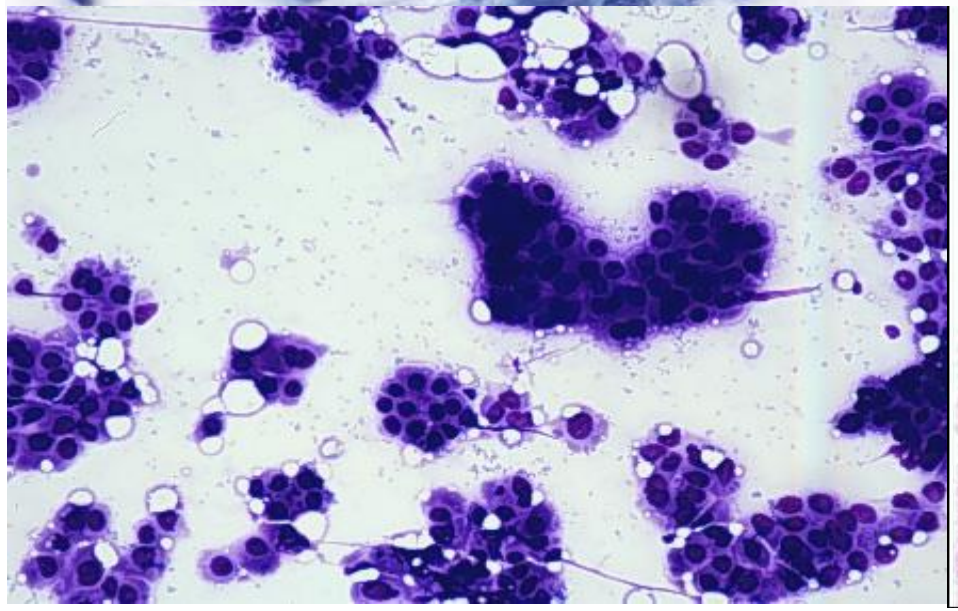
CYTOLOGICAL INTERPRETATION

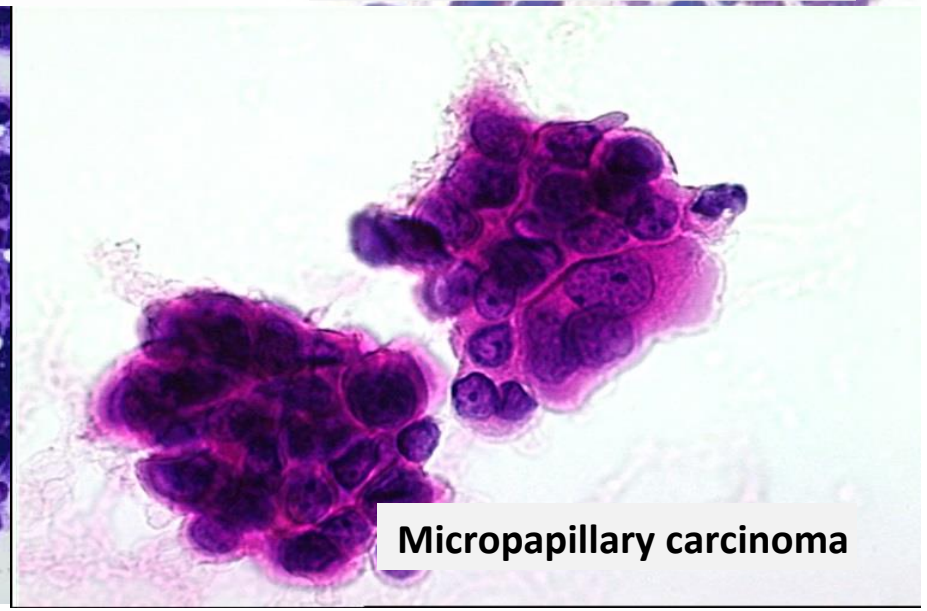
Breast carcinoma special types





Medullary-pattern carcinoma

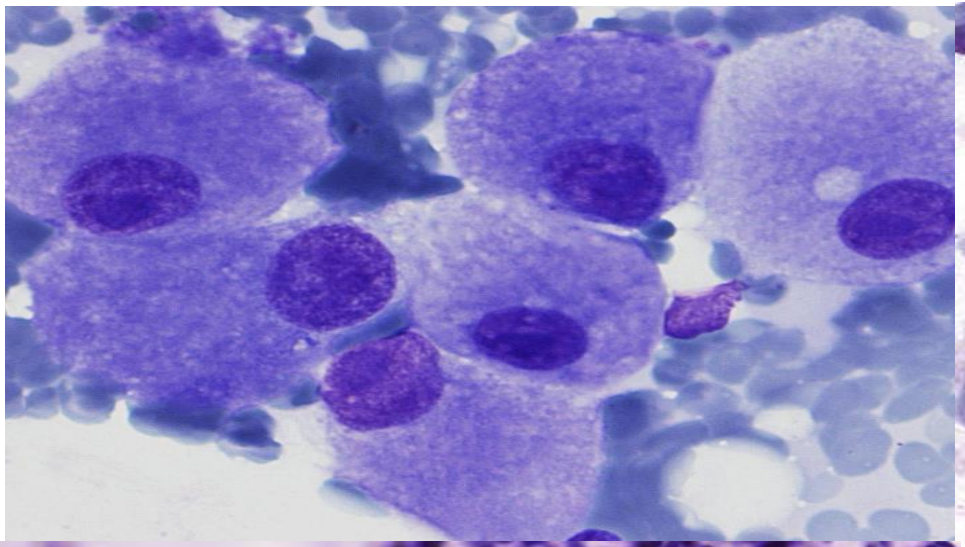


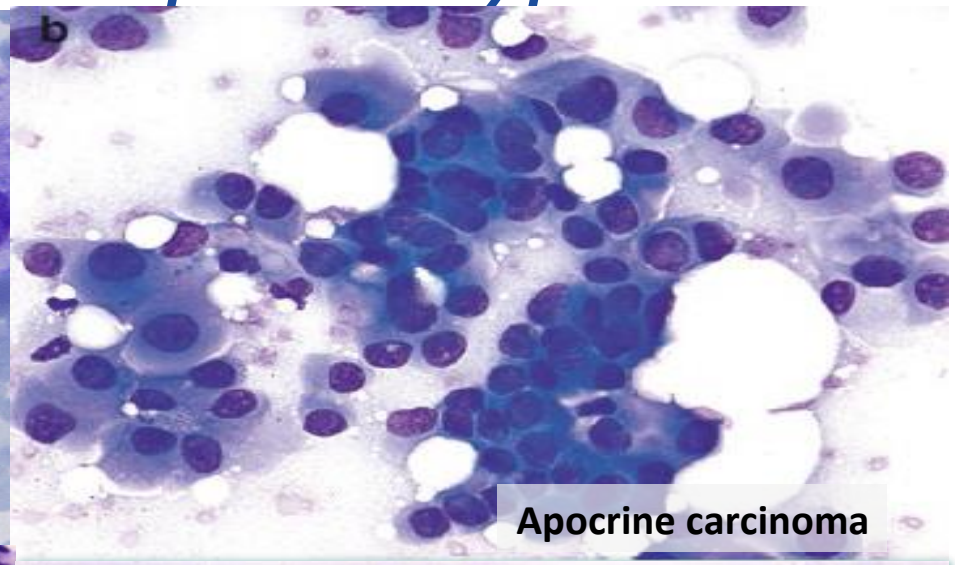


Micropapillary carcinoma

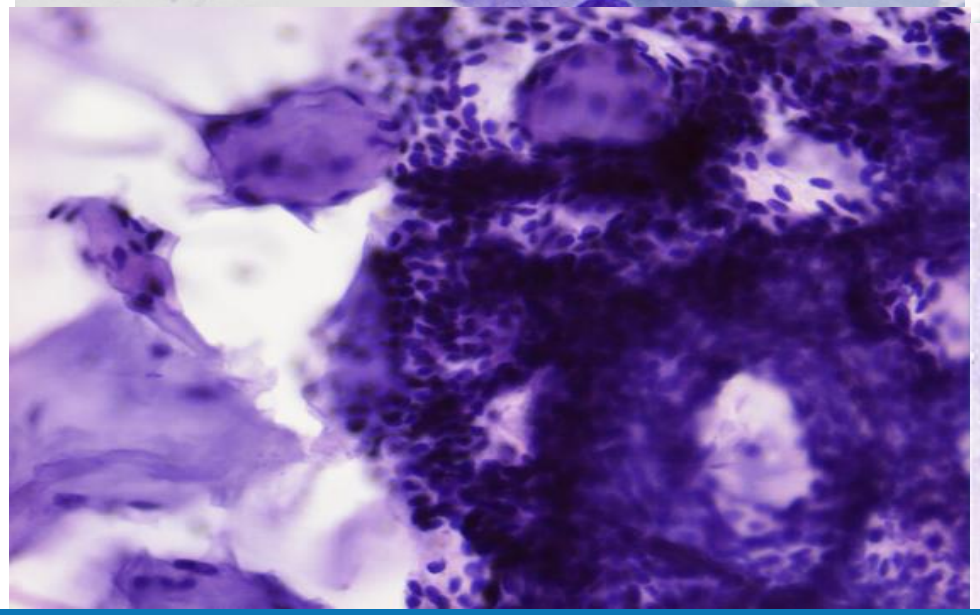
CYTOLOGICAL INTERPRETATION

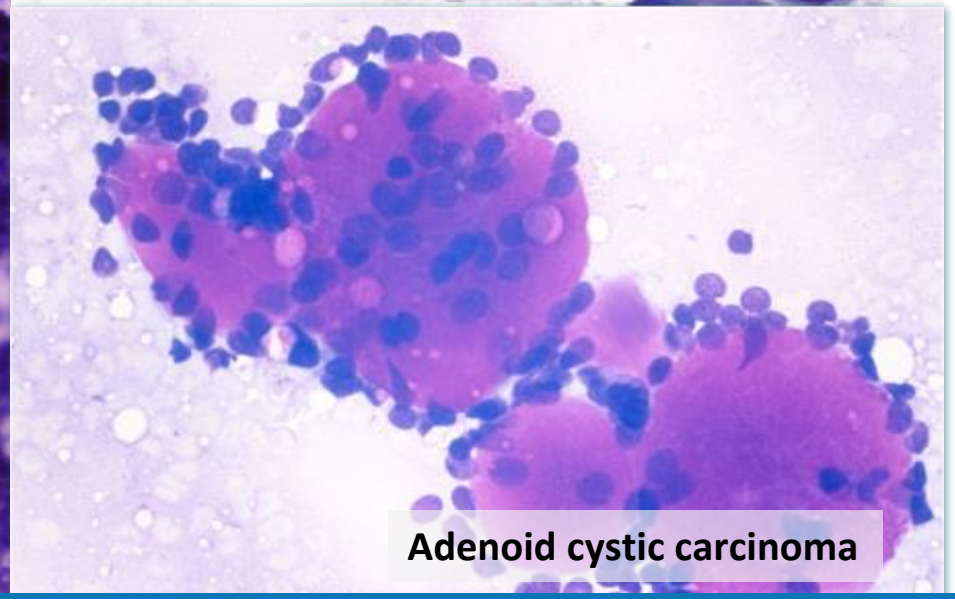
Breast carcinoma special types





Apocrine carcinoma

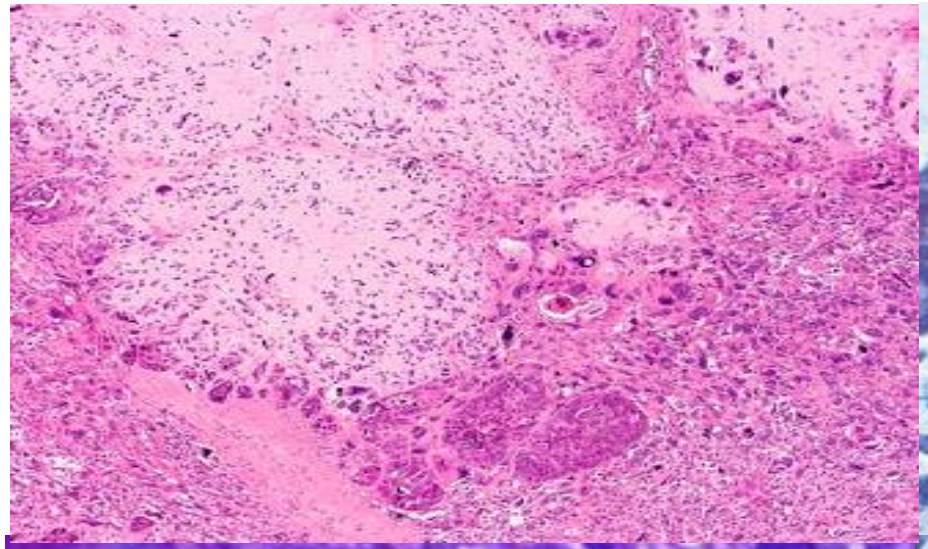


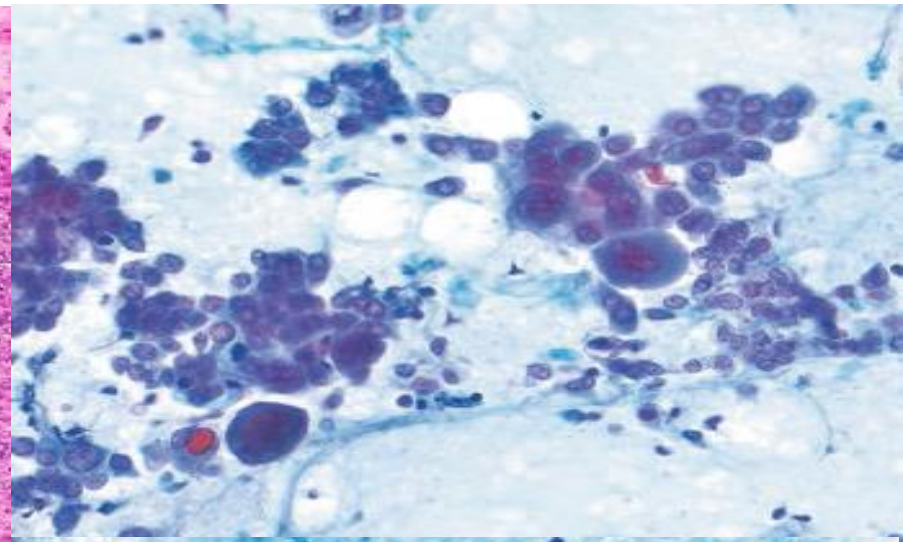


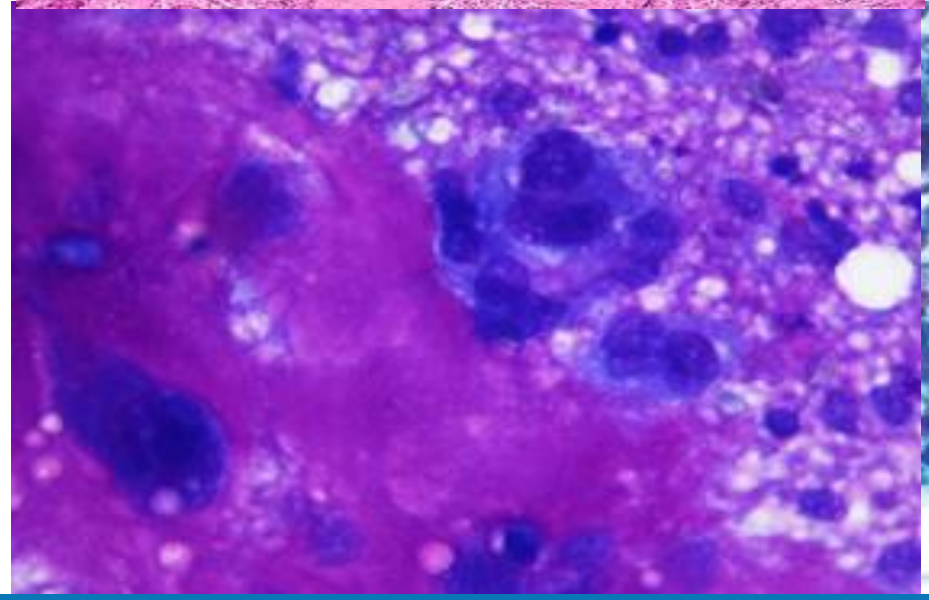
Adenoid cystic carcinoma

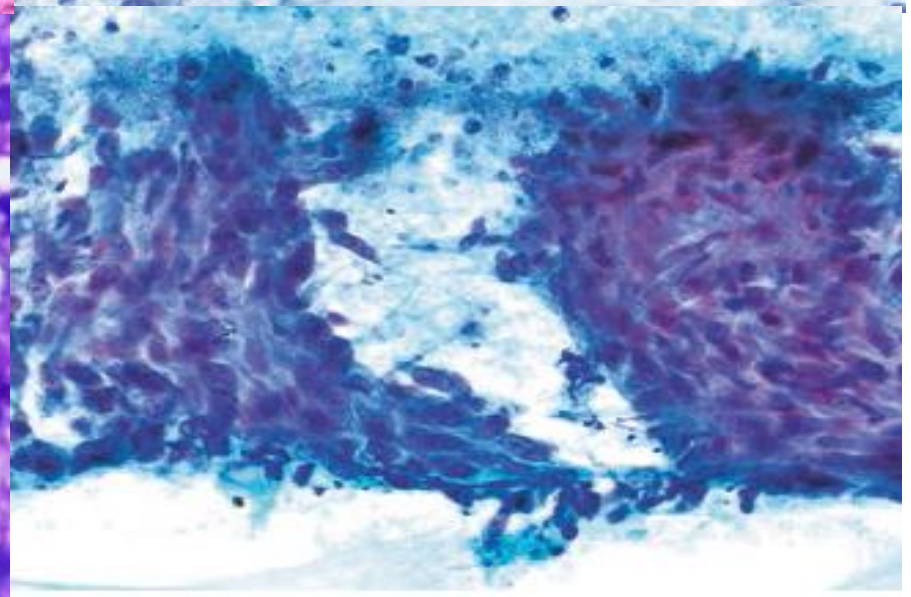
CYTOLOGICAL INTERPRETATION

Metaplastic breast carcinoma









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Stromal Cellular Fragments in Breast Fine Needle Aspirates: Think Outside of the Box

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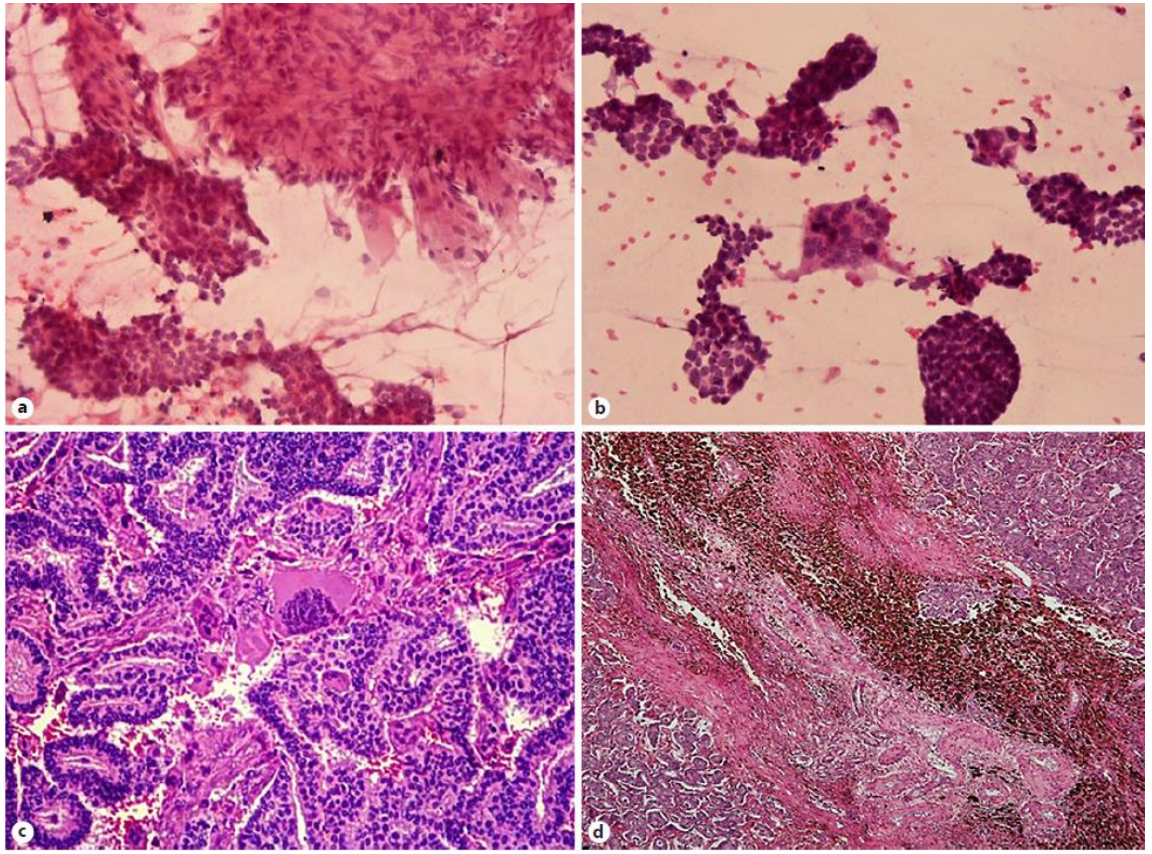
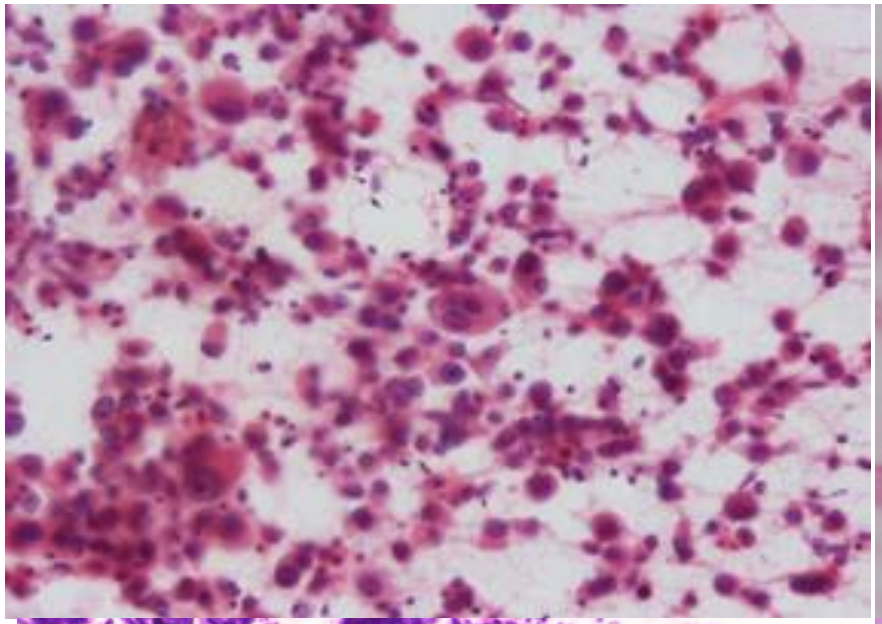
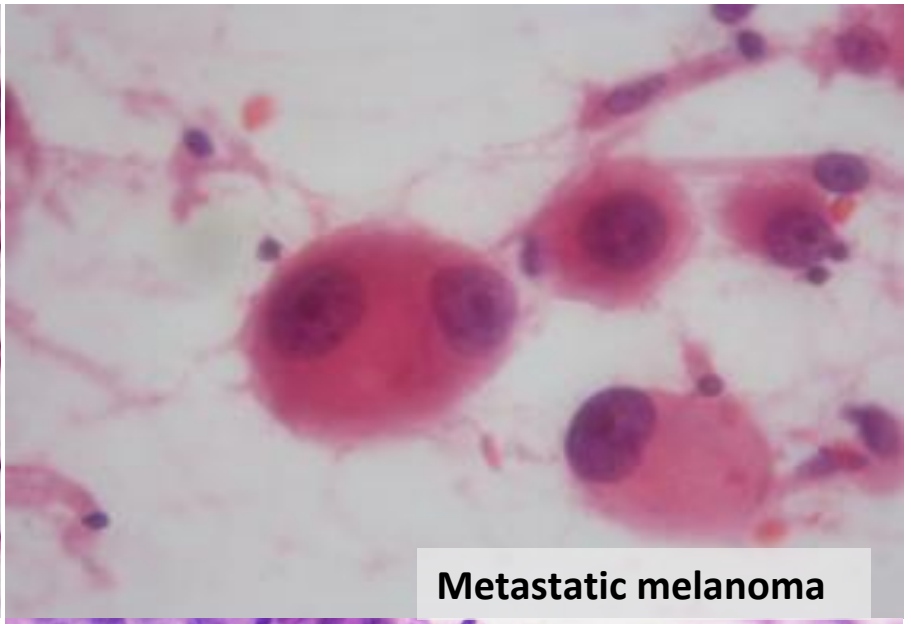
Breast carcinoma with osteoclast-like giant cells

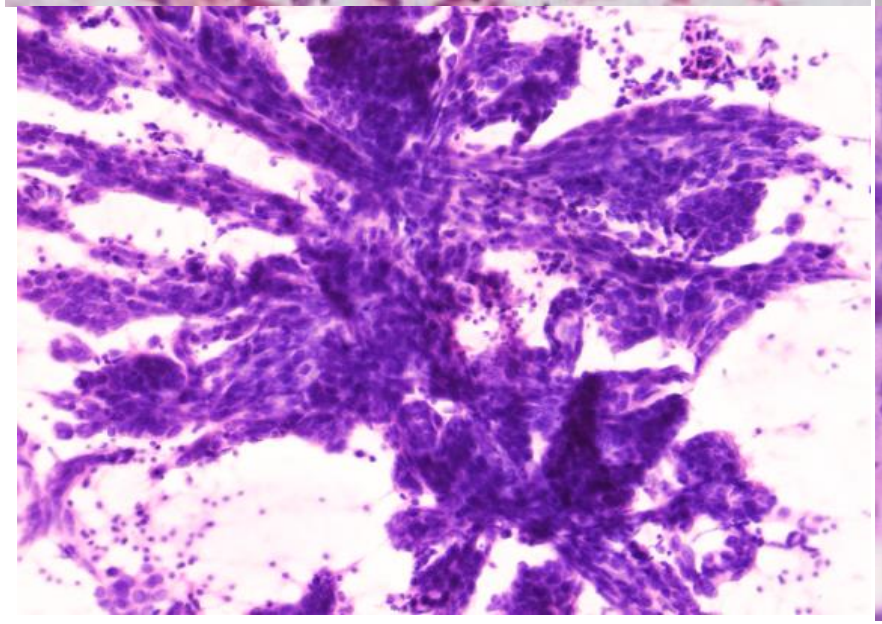


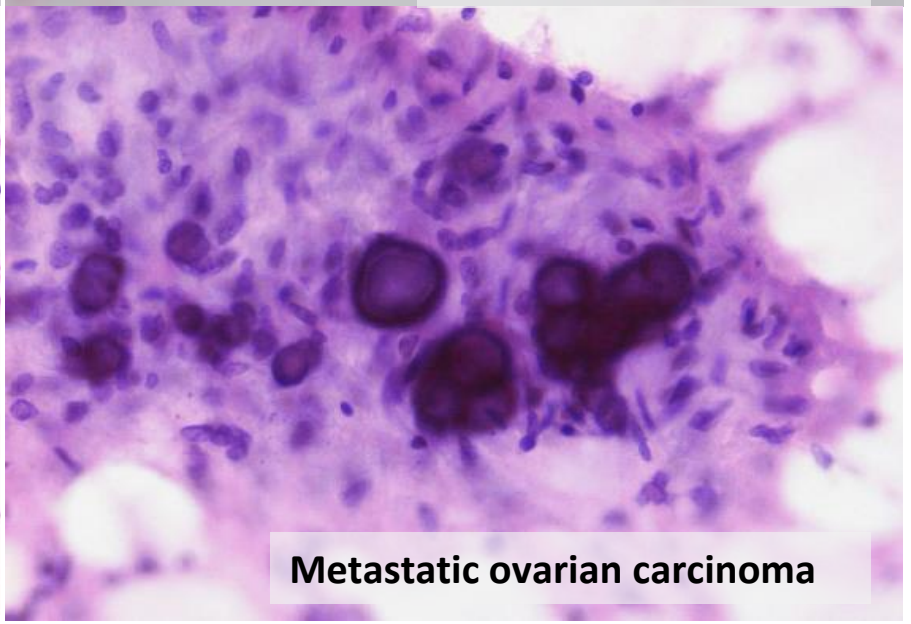
Metastatic malignancy





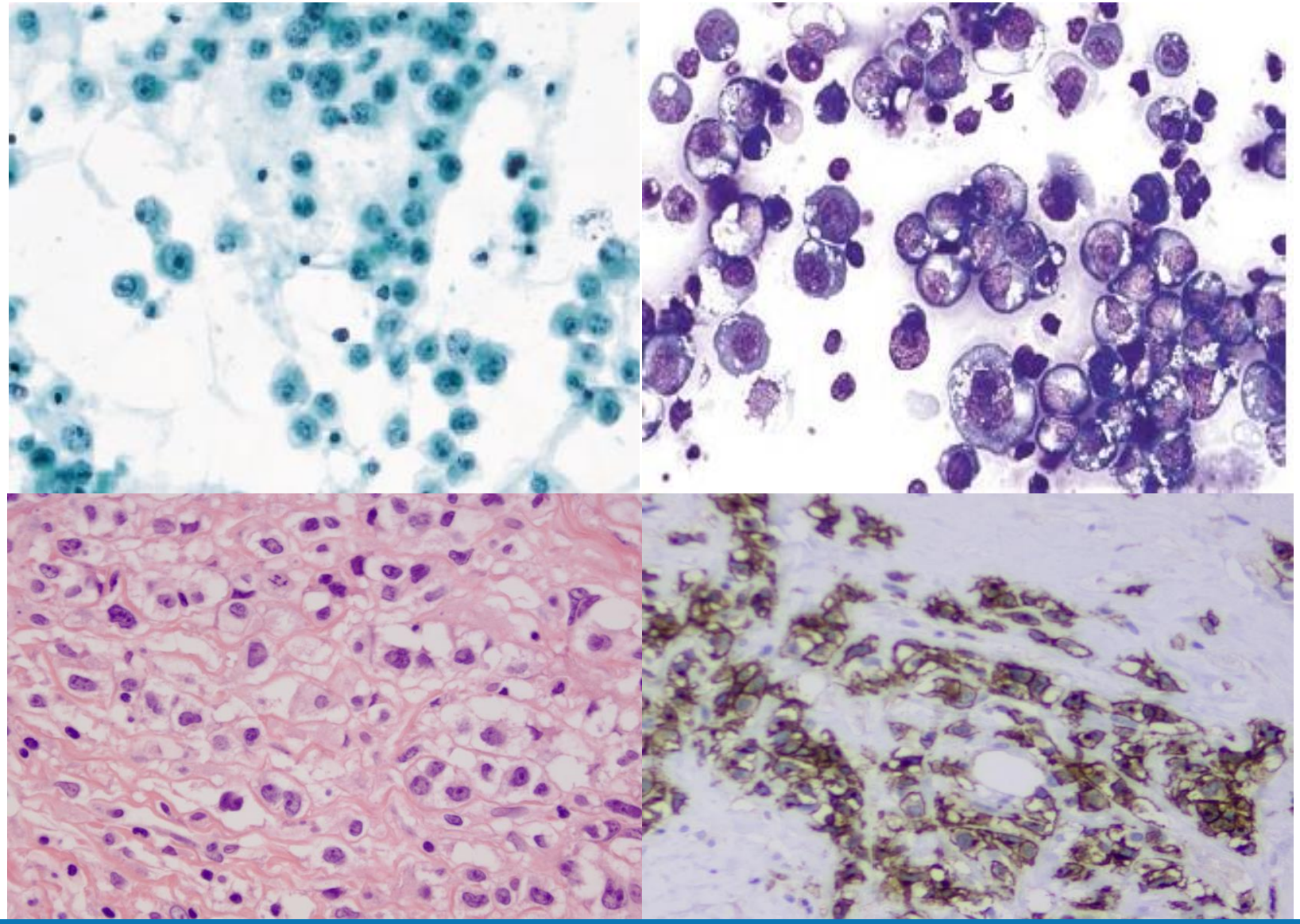
Metastatic melanoma





Metastatic ovarian carcinoma

Breast Implant-Associated Anaplastic Large Cell Lymphoma



The Standardized Cytopathology Report

- **Demographic information:**
  -patient's name, date of birth, address, patient identifiers, date of request and laboratory accession number
  -referring doctor and contact details

- **Type of Specimen:**
  - FNAB, nipple discharge

- **Clinical & Imaging information:**
  -site, size (mm), imaging (ultrasound, mammography, MRI) features
  -previous cytopathology procedures and results and previous other biopsy results when available

- **Category:** (example: Malignant)

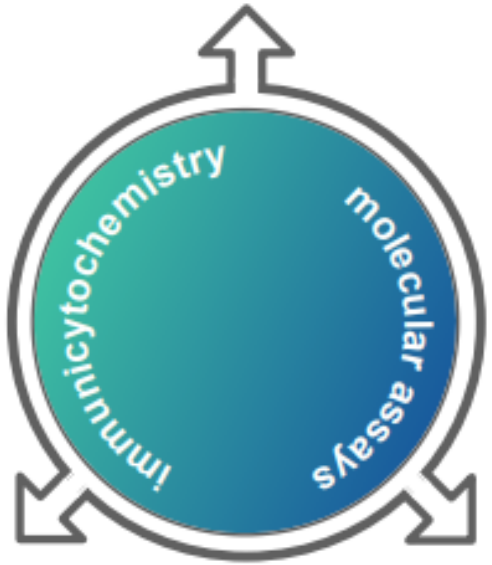
- **Diagnosis:** (example: cytological findings of invasive carcinoma)

-reporting system Category: using terminology not a number
-specific diagnosis or differential diagnosis

ANCILLARY TESTS in BREAST CARCINOMA

Prognostic/Predictive Markers

- ER, PR and Her-2 evaluation in selected settings



Primary Diagnosis

- Differential diagnosis in epithelial proliferative lesions
- Subtyping of breast carcinomas
- Differential diagnosis of spindle cell lesions
- Lymphoproliferative neoplasms in the breast
- Confirmation of organ of origin in metastasis to the breast

Metastasis

- Confirmation of breast as the site of origin
- Tracking of tumor evolution
- Tracking the development of drug resistance

Beca F, Schmitt F. Acta Cytol 2019

Biomarkers in Cell-Blocks

Table S4 – Analysis of concordance for estrogen receptor, progesterone receptor, HER2 and Ki67 status in the 15 cell blocks submitted to re-staining and re-evaluation in Portugal by a third pathologist (quality control).

		Portugal			Concordance (%)	κ
		ER-negative		ER-positive		
Mozambique	ER-negative	4		1	93.3%	0.842
	ER-positive	0		10		
		PR-		PR+		
	PR-negative	5		1	93.3%	0.857
	PR-positive	0		9		
		HER2 0/1+	2+	3+		
	HER2 0/1+	10	0	0	80.0%	0.541
	HER2 2+	1	1	0		
	HER2 3+	1	1	1		
		Ki67 low		Ki67 high		
	Ki67 low	6		4	50.0%	0.248
	Ki67 high	3		1		

Positive estrogen receptor (ER) and progesterone receptor (PR) status defined with a ≥1% cut-off and high Ki67 was defined as >29%.

Regarding Ki67 evaluation, there was one sample in which Ki67 was not tested.

ESMO Open 2020;5:e000829. doi:10.1136/esmoopen-2020-000829

Pathobiology

Review Article

Pathobiology
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Immunohistochemistry Applied to Breast Cytological Material

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Table 3. Theranostic immunohistochemistry in breast cancer and different cytology sample types

Marker	Sample type		
	smears	LBC	cellblocks
ER PR	Yes – using antigen retrieval with a heat-mediated method		
HER2	Yes – using antigen retrieval with a heat-mediated method Higher number of uncertain (2+) results expected; ethanol fixation may increase false positives		Yes – use a solution of formaldehyde as a fixative; perform antigen retrieval as in tissue
Ki-67	Results vary; may have no correlation with prognosis	Not reported	

LBC, liquid-based cytology.

Precision Medicine and Imaging

Clinical Cancer Research

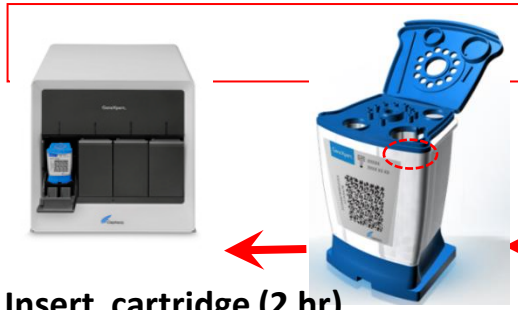
DNA Methylation Markers for Breast Cancer Detection in the Developing World

Bradley M. Downs[1], Claudia Mercado-Rodriguez[1], Ashley Cimino-Mathews[2], Chuang Chen[3], Jing-Ping Yuan[4], Eunice van den Berg[5], Leslie M. Cope[1], Fernando Schmitt[6], Gary Tse[7], Syed Z. Ali[2], Danielle Meir-Levi[1], Rupali Sood[1], Juanjuan Li[1,3], Andrea Richardson[2], Marina B. Mosunjac[8], Monica Rizzo[9], Suzana Tulac[10], Kriszten J. Kocmond[10], Timothy de Guzman[10], Edwin W. Lai[10], Brian Rhees[10], Michael Bates[10], Antonio C. Wolff[1], Edward Gabrielson[2], Susan C. Harvey[11], Christopher B. Umbricht[2,12], Kala Visvanathan[1,13], Mary Jo Fackler[1], and Saraswati Sukumar[1]

- Quantitative Multiplex Methylation-Specific PCR assay is an automated, cartridge-based system that provides quantitative measures of DNA methylation within hours of FNA
- 24 breast cancer-specific DNA methylation markers (selected through comprehensive methylome analysis) were tested to discriminate malignant from benign breast disease.

US probe
Biopsy needle

Add FNA to Lysis Reagent vial, add PK Vortex to mix



Transfer template DNA to GX Methylation cartridge

Insert cartridge (2 hr)

Convert DNA template with sodium bisulfite

Insert cartridge (2 hr)

Precision Medicine and Imaging

Clinical Cancer Research

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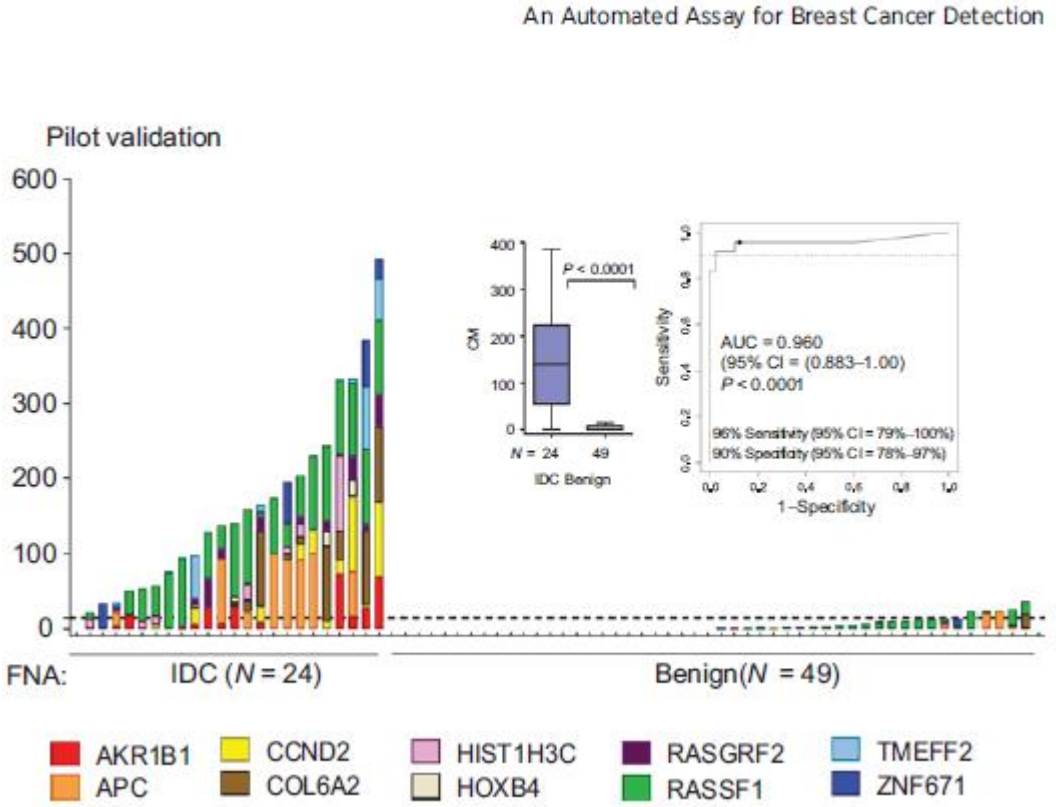

Conclusions: We developed and piloted a fast and accurate methylation marker–based automated cartridge system to detect breast cancer in FNA samples. This quick ancillary test has the potential to prioritize cancer over benign tissues for expedited pathologic evaluation in poorly resourced countries.

Breast FNAC
I am still doing…

- Aspiration should be directed to a defined target.
- FNAC is a multi-step procedure and obtaining a good material is essential for the diagnosis.
- The cytological diagnosis should be done only with the knowledge of the clinical context and preferential in a multidisciplinary environment.
- Breast FNAC and CNB are complementary methods.

BRIEF REPORT

WILEY

Value of combined use of fine-needle aspiration and core needle biopsy in palpable breast tumors performed by pathologist: Institut Curie experience

Pavla Sustova MD | Jerzy Klijanienko MD, PhD, MIAC

The strengths of our study are that we included both benign and malignant lesions, we included lesions not just surgically removed but also those with clinical follow-up/other treatment and the most important that both FNA and CNB were performed on the same lesion at the same time by one pathologist. This allows for comparison of FNA and CNB. This was done just by some studies where some of them are listed in Table 5.[4,5,8-15]

Diagnostic Cytopathology. 2020;48:71–77.

The role of breast fine needle aspiration during and post-COVID-19 pandemic: A fast and safe alternative to needle core biopsy

Cytopathology. 2020;00:1–3.

Daniel Pinto[1,2]
Fernando Schmitt[3,4]

- ✓ COVID-19 overburden health systems, deferring elective diagnostic and therapeutic procedures.
- ✓ In the case of breast, this led to a backlog of patients, which will only worsen as imaging and diagnostic activity is resumed.
- ✓ FNA is cost-effective, and quick to perform and their perceived limitations have been addressed.
- ✓ Pathologists may no longer be used to these samples, but extraordinary times require extraordinary measures. Through the use of the Yokohama system good communication with clinicians and image correlation, FNA may be a valuable diagnostic tool in the world of COVID-19.

CYTOPATHOLOGIST NEED TO BE IN THE FRONTLINE

THANK YOU
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SAVE
THE DATE
The 22nd
International
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ICC 2025
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May 11 - 15, 2025
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