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Update on the WHO Reporting Systems in Cytopathology

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No disclosures

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- ✓ MOU
  - IAC-IARC-WHO
  - 2020
- ✓ Organization
  - Standing Committee
  - Expert Editorial Board
    - Bibliometric/geographic
    - RA, Editors
  - Additional co-authors
- ✓ Follows tumor classification of WHO Blue Books
  - Hyperlinks between the books

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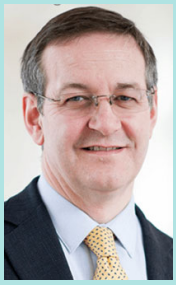
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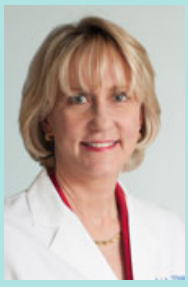
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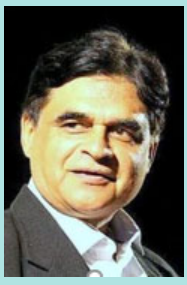
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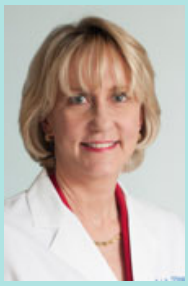

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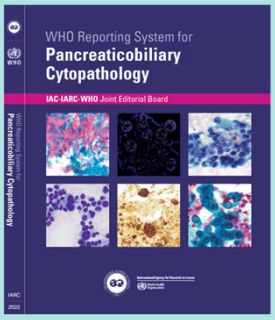

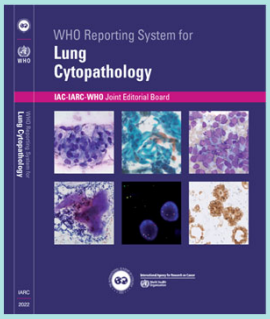

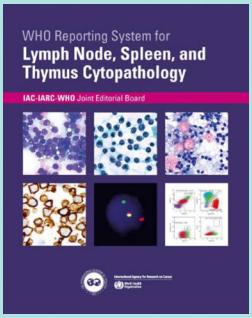

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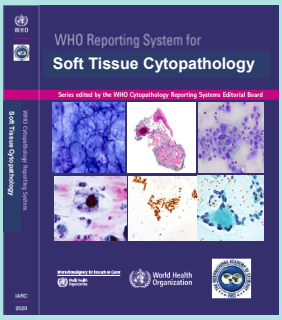

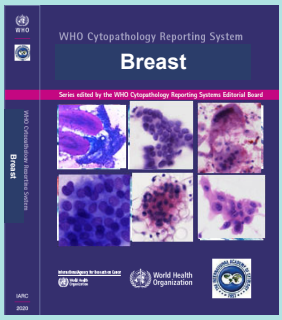

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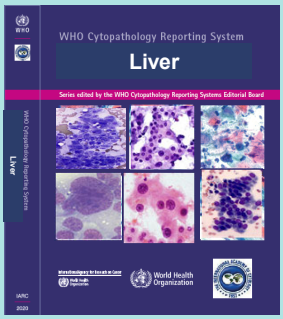
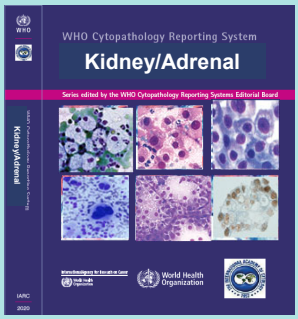
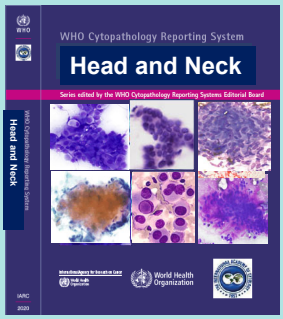






Mock-up of covers

WHO Reporting Systems in Cytopathology Contents

- Introductory chapter on the role of cytopathology
- Techniques in acquiring and preparation of the specimens.
- Sections on ROSE and the use of imaging modalities.
- Role and best practice of ancillary testing.
- Chapters covering each category with an introduction, definitions, discussion and background, and ROM as well as management recommendations.

WHO Reporting Systems in Cytopathology Contents

- Each category chapter has sections on the lesions/tumors that commonly are found in that category.
- Each lesion/tumor has subheadings for brief clinical presentation, imaging and histopathology (linked to the corresponding WHO tumor classification books) and then “key diagnostic cytopathological criteria” followed by a discussion, differential diagnosis and ancillary testing.
- Each category chapter includes “sample reports”

WHO Reporting Systems in Cytopathology

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

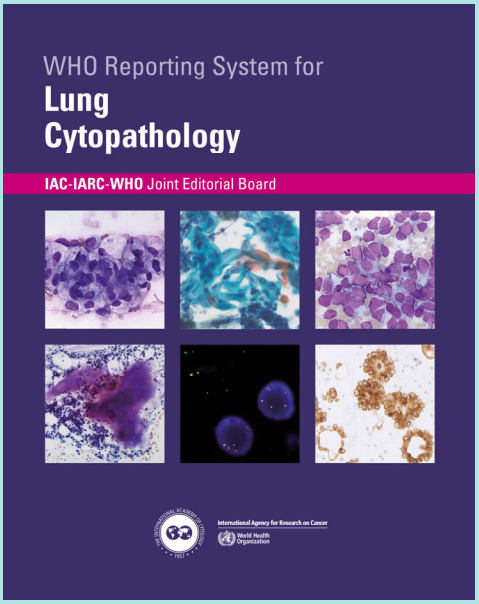
- **Type of Specimen:**
- -sputum, bronchial wash, bronchial lavage, bronchial brush, FNAB (EBUS, transthoracic), BDB, pancreas FNA, pancreas mass or cyst, lymph node (location), soft tissue mass (location)

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

- **Diagnostic Category:** (example: Malignant)
  - *-using terminology not a number*

- **Diagnosis:** *-specific diagnosis or differential diagnosis*

- *Comment, microscopic description optional (preferred if diagnosis is indeterminate)*



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Diagnostic Categories

1. Insufficient/inadequate/nondiagnostic
2. Benign
3. Atypical
4. Suspicious for Malignancy
5. Malignant

Diagnostic Categories with ROM and Management for Lung FNAB

Diagnostic category	Estimated ROM[a]	Clinical management options[b]
"Insufficient/Inadequate/Non-diagnostic"	43–53%	Correlate with CLIN-IMG-MICRO, ideally discuss at an MDT meeting, and perform repeat FNAB with or without CNB
"Benign"	19–64%	Correlate with CLIN-IMG-MICRO; if these confirm a benign diagnosis, then routine follow-up at 3–6 months; if no correlation, perform repeat FNAB with or without CNB
"Atypical"	46–55%	Correlate with CLIN-IMG-MICRO, and ideally discuss at an MDT meeting; if all show a benign diagnosis, then routine follow-up at 3–6 months; if no correlation, perform repeat FNAB with ROSE with or without CNB
"Suspicious for malignancy"	75–88%	Correlate with CLIN-IMG-MICRO, and ideally discuss at an MDT meeting; if all four support a diagnosis of malignancy, consider definitive treatment; if no correlation that lesion is malignant, perform repeat FNAB with ROSE with or without CNB
"Malignant"	87–100%	Correlate with CLIN-IMG-MICRO, and ideally discuss at an MDT meeting; if all four support a diagnosis of malignancy, provide definitive treatment; if no correlation that lesion is malignant, consider repeat FNAB with ROSE with or without CNB

Diagnostic Categories with ROM and Management for Sputum, Bronchial Washing and Bronchial Brushing

Diagnostic category	Estimated ROM[a]	Clinical management options[b]
"Insufficient/Inadequate/Non-diagnostic"	Sputum sample: 0–100% BW: 38–81% BB: 0–75%	Consider repeating the sampling or use BB/BW (in case of sputum sample) and/or FNAB, depending on CLIN-IMG-MICRO
"Benign"	Sputum sample: 0–42% BW: 38–42% BB: 32–38%	Correlate with CLIN-IMG-MICRO; if these confirm a benign diagnosis, then routine follow-up at 3–6 months; if no correlation, consider new sampling
"Atypical"	Sputum sample: 86–100% BW: 62–86% BB: 79–100%	Correlate with CLIN-IMG-MICRO; if these are "Benign", repeat; if "Atypical" or "Suspicious for malignancy", perform BB/BW or FNAB with or without CNB
"Suspicious for malignancy"	Sputum sample: 100% BW: 83–100% BB: 75–100%	Correlate with CLIN-IMG-MICRO, and perform BB/BW or FNAB with or without CNB; these cases need to be discussed at MDT meetings
"Malignant"	Sputum sample: 100% BW: 98–100% BB: 94–100%	Correlate with CLIN-IMG-MICRO, and perform BB/BW or FNAB with or without CNB to confirm diagnosis before definitive treatment

WHO Reporting System for Lung Cytopathology

World Health Organization

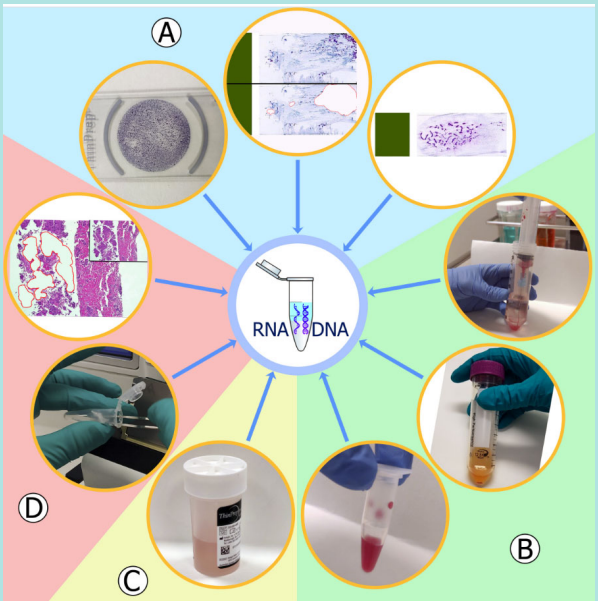
Different types of FNAB techniques and indications

Source:

Type of FNAB	Indications	Advantages	Limitations
Percutaneous transthoracic FNAB	New or enlarging solitary lung nodules on CXR or CT that are not amenable to diagnosis by bronchoscopy	High diagnostic yield Avoids open lung biopsy	Risk of pneumothorax
Ultrasound-guided	Sonographically visible subpleural or superficial lesions that are in contact with the chest wall	Quick and easy to perform	Only for superficial lesions
CT-guided	For deep parenchymal lesions	Deep lesions can be sampled	Time-consuming
	Endobronchial lesions		
	Peribronchial parenchymal lesions		
	Bronchial submucosal lesions		
Transbronchial/endobronchial FNAB without imaging guidance (blind/conventional TBFNAB)	Mediastinal, hilar, and subcarinal lymph nodes or hilar mass lesions for staging lung cancer, diagnosis of granulomatous diseases, lymphoma, extrapulmonary metastasis, or workup of nonspecific mediastinal lymphadenopathy	High sensitivity	Limited accessibility of mediastinum
EBUS-TBFNAB (lung)	Same as conventional TBFNAB	Can also access peripheral pulmonary lesions with the help of radial probe (radial EBUS) Can access nodal stations 10 (hilar), 11 (interlobar), and partial 12 (lobar)	Cannot access posteroinferior mediastinum and upper lobe lesions Costly; limited availability
EBUS-TBFNAB (lymph nodes)	Mediastinal lymphadenopathy of stations 8 (para-oesophageal, below carina) and 9 (pulmonary ligament)	Can be done safely alongside EBUS in a single session	n/a

EBUS, endobronchial ultrasound; EBUS-TBFNAB, endobronchial ultrasound–guided transbronchial FNAB; n/a, not applicable; TBFNAB, transbronchial FNAB.

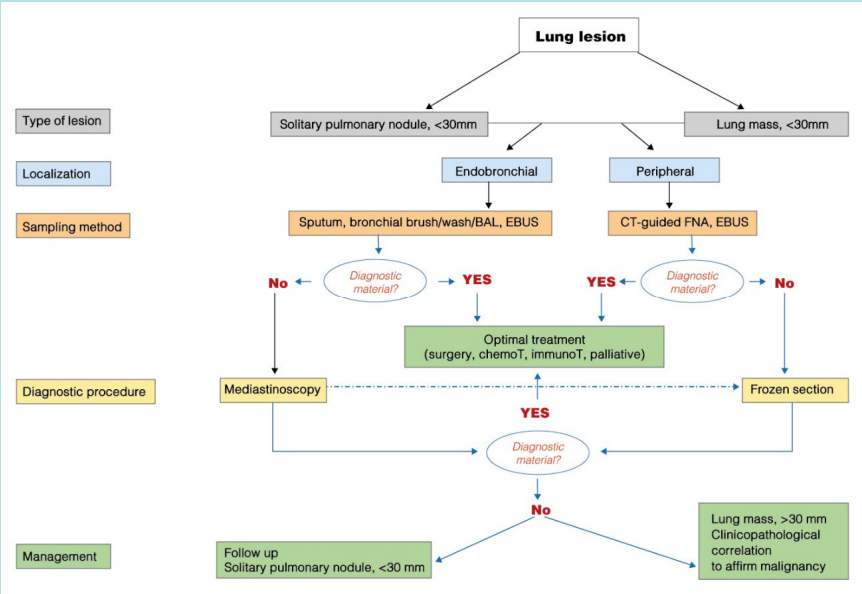
(from WHO Reporting System for Lung Cytopathology, Chapter 2)



Legend: Different types of cytological samples. **A** Direct smears (with/without microdissection/macrodissection). Pap-stained and Giemsa-stained and/or unstained slides. Cell scraping preferred. **B** Needle-rinse, supernatant, and fresh samples. **A** and **B** give high-quality DNA/RNA. **C** Optimal quality for extraction of DNA/RNA. **D** Cell blocks; long formalin fixation can lead to C>T or G>A artefacts.

(from WHO Reporting System for Lung Cytopathology, Chapter 2; source Maria Lozano)

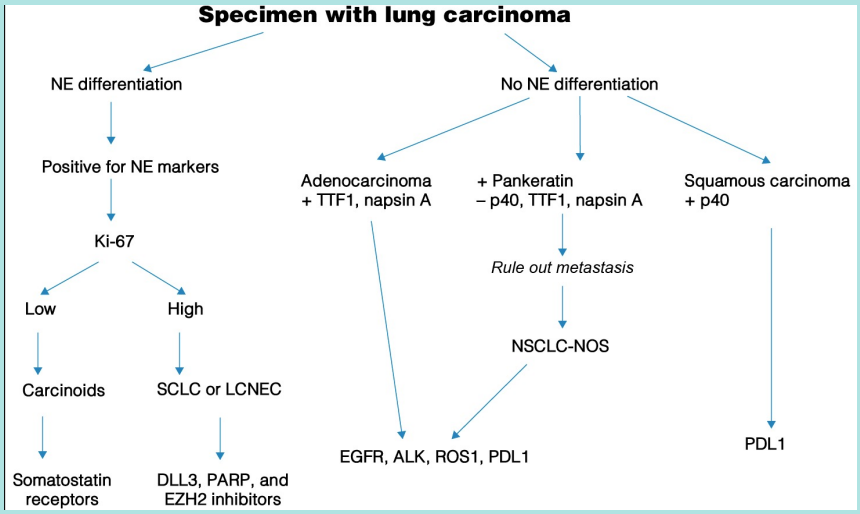
Management Algorithm for Insufficient/Inadequate/Nondiagnostic Specimen



(from WHO Reporting System for Lung Cytopathology, Chapter 8; Source Sule Canberk Schmitt)

Algorithm or Evaluating Lung FNAB

(from WHO Reporting System for Lung Cytopathology, Chapter 2; source Claire Michael)



Legend: Immunocytochemistry (ICC) algorithm for subtyping lung cancer. LCNEC, large cell neuroendocrine carcinoma; NE, neuroendocrine; NSCLC, non-small cell lung carcinoma; PARP, poly (ADP-ribose) polymerase; SCLC, small cell lung carcinoma; TTF1, thyroid transcription factor 1.

Differential Diagnosis of Mesothelioma

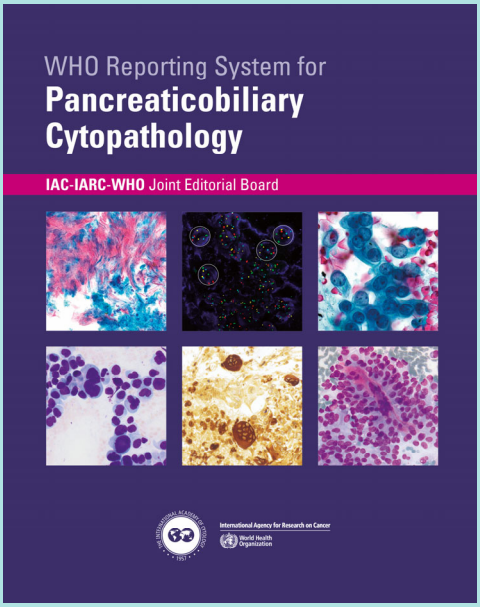
(from WHO Reporting System for Lung Cytopathology, Chapter 7; Source Claire Michael)

Feature	Mesothelioma	Reactive mesothelium	Carcinoma
Gross examination of pleural fluid:			
Consistency	Thick, tar-like	Thin	Generally thin
Appearance	Serosanguineous or bloody	Serosanguineous	Serosanguineous or bloody
Background:			
Clear	Some cases	Most cases	Some cases
Bloody	Frequently	Rare cases[a]	Most cases
Obscuring matrix	Frequent (hyaluronan)	Absent	In cases with mucin
Inflammation	May be present	Frequent	May be present
Low magnification:			
Cellularity	Strikingly high[b]	Moderate to high	Usually high
Tissue fragments	Plentiful, vary in size	Few, small	May be numerous, little variation in size
Single cells	Alone or combined with tissue fragments	Most cases	Alone or combined with tissue fragments
Populations	Monotonous population of mesothelial cells with wide variation in size	Monotonous population of mesothelial cells with minimal variation in size	Alien population in background of mesothelial cells
Tissue fragments:			
Shape	Predominantly 3D, berry-like morules with scalloped borders or spheres	Predominantly 2D tissue fragments with scalloped borders	3D tissue fragments with common cell borders
Architecture	Variable size and complexity, sometimes very complex branching papillae	Mostly simple and small	Variable complexity depending on primary
Collagenous core	Occasionally present and may be conspicuous	Rare	Uncommon, fibrovascular cores in papillary tumours
Hollow tissue fragments	May be present	Absent	Not characteristic

Immunostains for Work-up of Pulmonary Metastases

(from WHO Reporting System for Lung Cytopathology, Chapter 7; Source Zubair Baloch)

Site of origin	Immunocytochemistry profile[a]
Gastrointestinal tract	
Oesophagus (adenocarcinoma)	CK7+, CK20−, TTF1−, CDX2+/−, CEA+, EMA (MUC1)−/+, MUC5AC−/+, SATB2−
Stomach	CK7+, CK20+, TTF1−, CEA+, CDX2−/+, EMA (MUC1)−/+, MUC5AC−/+
Colon and rectum	CK7−, CK20+, CDX2+, SATB2+, MOC31+
Breast	CK7+, CK20−, GATA3+, mammaglobin+/−, GCDFP-15−/+, ER+, PR+, TTF1
Melanoma	SOX10+, melan-A+, MART1+, S100+, HMB45+, CK7−, CK20−
Pancreas (adenocarcinoma)	CK7+, CK20+, SMAD4 (DPC4)−/+, CK17+/−, VHL protein−, maspin+, S100+, MOC31+, MUC5AC+
Liver (hepatocellular)	CK7−, CK20−, HepPar1+, AFP+, GPC3+, ARG1+, CD10+, polyclonal CEA+, monoclonal CEA−
Genitourinary tract	
Urinary bladder (urothelial)	CK7+, CK20+/−, GATA3+, p63+, p40+, CK5/6+, S100+, 34βE12 (CK903)+, uroplakin+, thrombomodulin+
Prostate (adenocarcinoma)	CK7−, CK20−, PSA+, NKX3-1+, PAP+, AMACR (P504S)+
Ovary (serous)	CK7+, CK20−, PAX8+, ER+, WT1+, TTF1−, TFF3−, GATA3−
Ovary (clear cell)	CK7+, CK20−, VHL protein+, napsin A+, WT1−, ER−, AFP−
Ovary (mucinous)	CK7+, CK20−, SMAD4 (DPC4)+, CA125+, CDX2+/−
Endometrium	CK7+, CK20−, ER+, PR+, PAX8+, CEA+ (foci of squamous metaplasia)
Uterine cervix (adenocarcinoma)	CK7+, CK20−, p16+, CEA+, PR−, PAX8+/−
Kidney	
Clear cell	CK7−, PAX8+, PAX2+, CAIX+, CD10+, RCCm+, AE1/AE3+, CAM5.2+, EMA+, AMACR+/−, GATA3−, TTF1−
Clear cell papillary	CK7+, PAX8+, CAIX+, CD10−, RCCm+/−, AMACR−, GATA3−/+ (rare cases)



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2022

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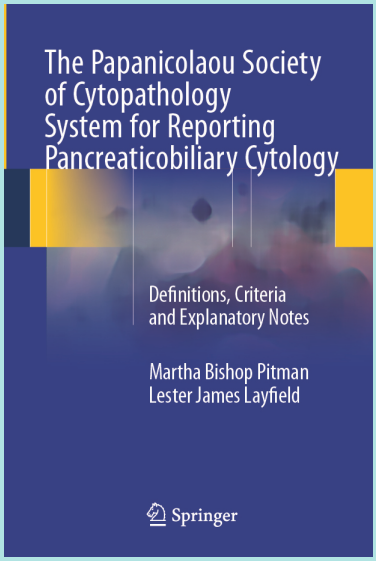

2015

Standardized Terminology and Nomenclature for Pancreaticobiliary Cytology: The Papanicolaou Society of Cytopathology Guidelines

Diagn Cytopathol. 2014 Apr;42(4):338-50.

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Table 1 Diagnostic categories of PSC system.

Diagnostic category	Examples of diagnostic entities
I. Nondiagnostic	Acellular aspirate with no evidence of a mucinous etiology
	Gastrointestinal contamination
	Benign pancreatic parenchyma, if a well-defined mass is identified on imaging
II. Negative for malignancy	Benign pancreatic parenchyma, if a well-defined mass is not identified on imaging
	Acute pancreatitis
	Chronic pancreatitis
	Autoimmune pancreatitis
	Pseudocyst
	Lymphoepithelial cyst
	Ectopic splenic tissue
III. Atypical	Atypical ductal cells, obscured by artifact
IV. Neoplastic: benign	Serous cystadenoma
	Lymphangioma
IV. Neoplastic: other	Neuroendocrine tumor, well-differentiated
	Intraductal papillary mucinous neoplasm (including all grades of dysplasia)
	Mucinous cystic neoplasm (including all grades of dysplasia)
	Solid pseudopapillary neoplasm
V. Suspicious for malignancy	Rare markedly atypical epithelial cells, insufficient in quality or quantity for positive or malignant diagnosis
VI. Positive or malignant	Pancreatic ductal adenocarcinoma
	Cholangiocarcinoma
	Acinar cell carcinoma
	Neuroendocrine carcinoma, poorly differentiated
	Pancreatoblastoma
	Lymphoma
	Metastatic malignancy

Abbreviation: PCS, Papanicolaou Society of Cytopathology.
Data from Pitman et al.[5]

Table 3 Absolute risk and relative risk of malignancy of the diagnostic categories in the PCS system.

Diagnostic category	Absolute risk of malignancy (%)	Relative risk	*P* value (relative to benign category)
I. Nondiagnostic	7.7	7.7	0.07
II. Negative for malignancy	1.0	1.0	NA
III. Atypical	28.0	28.0	0.001[a]
IV. Neoplastic: benign	0.0	0.0	1.00
IV. Neoplastic: other, all grades of atypia	30.3	30.3	<0.001[a]
With low-grade atypia	4.3	4.3	0.23
With high-grade atypia	90.0	90.0	<0.001[a]
V. Suspicious for malignancy	100.0	100.0	<0.001[a]
VI. Positive or malignant	100.0	100.0	<0.001[a]

Abbreviations: NA, not applicable; PCS, Papanicolaou Society of Cytopathology.
[a]Statistically significant ($P < 0.05$).

Journal of the American Society of Cytopathology (2019) 8, 120–127

	PSC System		WHO System		
1	Nondiagnostic			Inadequate/insufficient/ nondiagnostic	1
2	Negative (for Malignancy)	Non-neoplastic only	Non-neoplastic and neoplastic (SCA)	Benign/Negative (for Malignancy)	2
3	Atypical			Atypical	3
4	Neoplastic				
4a	Neoplastic:Benign	SCA	low-grade MCN Low-grade IPMN Also, low-grade PanIN, BilIN	Pancreaticobiliary Neoplasm- low risk/low-grade (Pan-Low)	4
4b	Neoplastic:Other	IPMN,MCN, PanNET, SPN	High-grade MCN High-grade IPMN IOPN ITPN Also, high-grade PanIN, BilIN	Pancreaticobiliary Neoplasm- high risk/high-grade (Pan-High)	5
5	Suspicious (for malignancy)			Suspicious (for malignancy)	6
6	Positive (for malignancy)		PDAC, Acinar Cell ca., PanNET, PanNEC,	Malignant	7

Table 1. The World Health Organization System for Reporting Pancreatic Cytopathology: implied risk of malignancy and clinical management options by diagnostic category for Pancreatic FNAB.

Diagnostic category	Estimated risk of malignancy (%)[a]	Clinical Management Options[b]
Insufficient/inadequate/nondiagnostic	5 – 25	Repeat FNAB
Benign/Negative for Malignancy	0 – 15	Correlate clinically
Atypical	30 – 40	Repeat FNAB
Pancreatic Neoplasm: low risk/low-grade (PaN-Low)	5 – 20	Correlate clinically
Pancreatic Neoplasm: high risk/high-grade (PaN-High)	60 – 95	Surgical Resection in surgically fit patients Conservative management optional
Suspicious for Malignancy	80 – 100	If patient to be surgically managed, treat as positive If patient requires pre-operative therapy, repeat FNAB
Malignant	99 – 100	Per clinical stage

Abbreviation: FNAB, fine-needle aspiration biopsy.
[a] Estimated risks of malignancy are based on retrospective and prospective studies with risk analysis based on pancreatic neoplasia with low-grade and high-grade cytopathological atypia.
[b] Management options for patients with pancreatic lesions may depend on a variety of factors, including clinical and imaging characteristics and the overall functional status of the patient. Some clinical management suggestions are outlined as above.

Hoda RS, Arpin RN 3rd, Rosenbaum MW, Pitman MB. Risk of malignancy associated with diagnostic categories of the proposed World Health Organization International System for Reporting Pancreaticobiliary Cytopathology. Cancer Cytopathol. 2021 Oct 8. doi: 10.1002/cncy.22514. Epub ahead of print. PMID: 34623767.

Table 2. The World Health Organization International System for Reporting Pancreaticobiliary Cytopathology: implied risk of malignancy and clinical management options by diagnostic category for Bile Duct Brushing Specimens.

Diagnostic category	Estimated risk of malignancy (%)[a]	Clinical management options[b]
Insufficient/inadequate/nondiagnostic	28 – 69	Repeat ERCP with cholangioscopy, brushing, and biopsies
Benign/Negative for Malignancy	26 – 55	Correlate clinically
Atypical	25 – 77	Repeat ERCP with cholangioscopy, brushing, and biopsies; consider ancillary testing with FISH and/or NGS
Pancreatic Neoplasm-low-grade (PaN-low)	NA[c]	NA
Pancreatic Neoplasm-high-grade (PaN-high)	NA[c]	NA
Suspicious (for malignancy)	74 – 100	Repeat sampling with ancillary testing (FISH and/or NGS) or, if other factors support malignancy, surgical intervention; for neoadjuvant therapy, repeat ERCP with cholangioscopy/brushings/biopsies/ancillary studies
Malignant	96 – 100	Per clinical stage

Abbreviation: ERCP, endoscopic retrograde cholangiopancreatography; FNAB, fine-needle aspiration biopsy; FISH, fluorescence in-situ hybridization; NA, not available/not applicable; NGS, next-generation sequencing.

[a] Estimated risks of malignancy are based on retrospective and prospective studies with risk analysis based on pancreatic neoplasia with low-grade and high-grade cytologic atypia {10049415,24167030,26596524,28411396,32649050,34800330,35163571}.

[b] Management options for patients with bile duct strictures may depend on a variety of factors, including clinical and imaging characteristics and overall functional status of the patient. Some clinical management suggestions are outlined as above.

[c] Cytological criteria for premalignant neoplasms of the bile duct are lacking and, thus, there are no data on bile duct categorization in the PaN-low and PaN-high categories.

World Health Organization

Pancreatic Tumor Classification:
WHO Digestive System Tumours, 5th Edition

10: Tumours of the pancreas

10.0: Tumours of the pancreas: Introduction

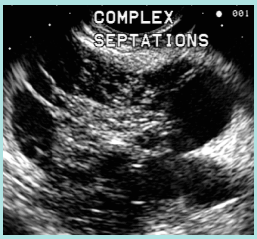
10.3.6: Epithelial tumours

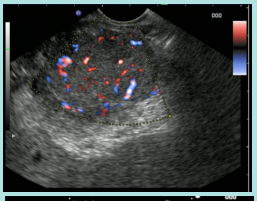
- 10.1: Benign epithelial tumours and precursors
  - 10.1.1: Acinar cystic transformation of the pancreas
  - 10.1.2: Serous neoplasms of the pancreas
  - 10.2.1: Pancreatic intraepithelial neoplasia
  - 10.2.2: Pancreatic intraductal papillary mucinous neoplasm
  - 10.2.3: Pancreatic intraductal oncocytic papillary neoplasm
  - 10.2.4: Pancreatic intraductal tubulopapillary neoplasm
  - 10.2.5: Pancreatic mucinous cystic neoplasm
- 10.3: Malignant epithelial tumours
  - 10.3.1: Pancreatic ductal adenocarcinoma
  - 10.3.3: Pancreatic acinar cell carcinoma
  - 10.3.4: Pancreatoblastoma
  - 10.3.5: Solid pseudopapillary neoplasm of the pancreas
- 11.6: Pancreatic neuroendocrine neoplasms
  - 11.6b: Pancreatic neuroendocrine neoplasms: Introduction
  - 11.6.1.1: Non-functioning pancreatic neuroendocrine tumours
  - 11.6.1: Functioning pancreatic neuroendocrine tumours
    - 11.6.1.2: Insulinoma
    - 11.6.1.5: Gastrinoma
    - 11.6.1.6: VIPoma
    - 11.6.1.3: Glucagonoma
    - 11.6.1.4: Somatostatinoma
    - 11.6.1.8: ACTH-producing neuroendocrine tumour
    - 11.6.1.7: Serotonin-producing neuroendocrine tumour
  - 11.6.2: Pancreatic neuroendocrine carcinoma
  - 11.6.3: Pancreatic MiNENs

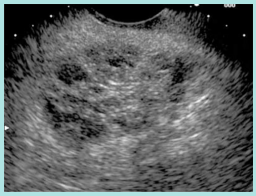
WHO Reporting System for PB Cytopathology

World Health Organization

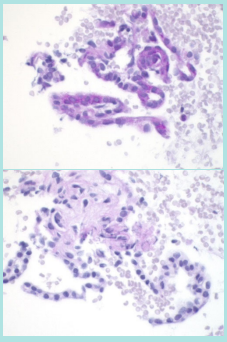
Clinical and Imaging Features



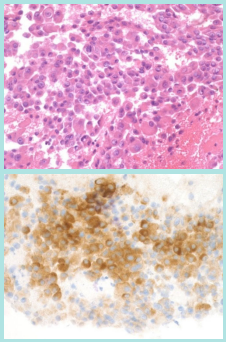




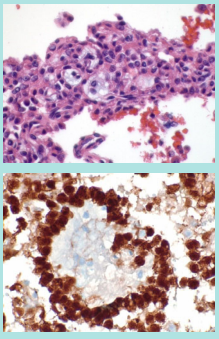
Cytomorphology, Special Stains and Immunohistochemistry



PAS and PASD



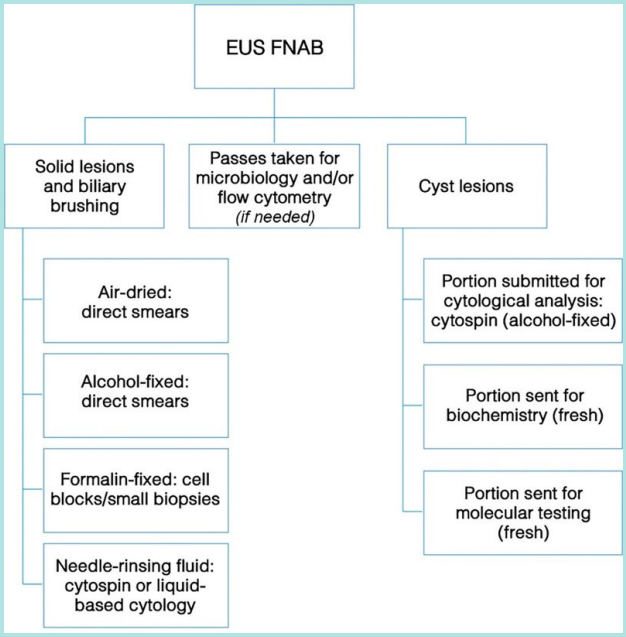
Synaptophysin



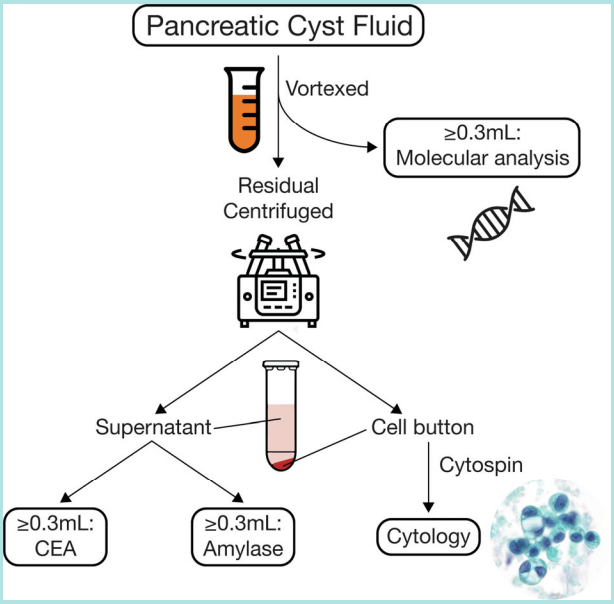
Beta catenin

Biochemical and Molecular analysis of Cyst Fluid

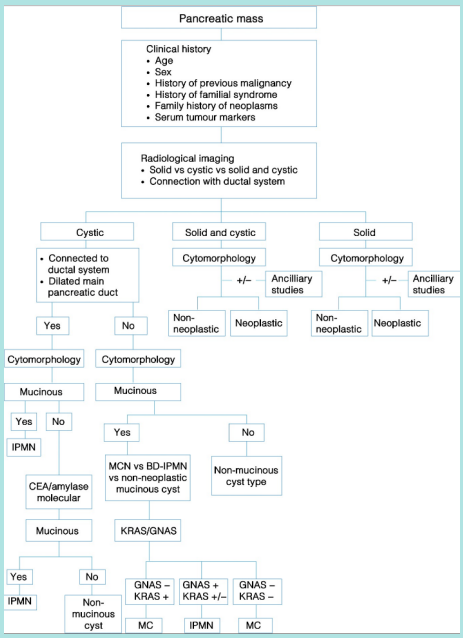
Cyst	Biochemical tests		Molecular Tests					
	CEA	Amy	KRAS	GNAS	3p25 (VHL)	P53	P16 (CDKN2A/INK4A)	SMAD4
PCT	↓	↑↑	-	-	-	-	-	-
SCA	↓↓	↓↓	-	-	+	-	-	-
IPMN	↑↓	↑↑	+	+	-	+[a]	+[a]	+[a]
MCN	↑↓	↓↑	+	-	-	+[a]	+[a]	+[a]



(from WHO Reporting System for PB Cytopathology, Chapter 2; Source Carlos de Andrea)



(from WHO Reporting System for PB Cytopathology, Chapter 2; Source Lisa Zhang)



(from WHO Reporting System for PB Cytopathology, Chapter 1; Source Barbara Centeno)

ICC stain	Target	Diagnostic utility	Limitations
SMAD4	Loss of nuclear staining	Adenocarcinoma	Strong staining in non-tumour disorders and other tumours; lost in ~50% of adenocarcinomas
p53	Positive nuclear staining	Adenocarcinoma	Also mutated in high-grade intraepithelial neoplasia
Mesothelin	Positive cytoplasmic staining	Adenocarcinoma	Focal staining in pancreatitis
IMP3	Strong cytoplasmic staining	Adenocarcinoma	Focal staining in pancreatitis
S100P	Strong cytoplasmic and nuclear staining	Adenocarcinoma	Strong staining of gastric epithelium
Monoclonal CEA	Strong cytoplasmic staining	Adenocarcinoma	
CA125 (MUC16)	Strong cytoplasmic staining	Adenocarcinoma	
VHL protein	Loss of membranous and cytoplasmic staining	Adenocarcinoma	Membranous and cytoplasmic expression in normal biliary and pancreatic ductal cells; loss in AIP
Synaptophysin	Strong, diffuse cytoplasmic staining	Neuroendocrine neoplasms	Focal staining in other tumours and normal islet cells
Chromogranin A	Strong to patchy cytoplasmic staining	Neuroendocrine neoplasms	Patchy staining, sometimes weak
INSM1	Strong, diffuse nuclear staining	Neuroendocrine neoplasms	Focal staining in other tumours
Trypsin	Strong cytoplasmic granular staining	Acinar cell carcinoma and other acinar proliferations	High background staining; focal staining in other tumours
Chymotrypsin	Strong cytoplasmic granular staining	Acinar cell carcinoma and other acinar proliferations	High background staining; focal staining in other tumours
BCL10	Cytoplasmic staining	Acinar cell carcinoma and other acinar proliferations	
CD99	Perinuclear dot-like pattern	Solid pseudopapillary neoplasm	Specific
β-Catenin	Strong nuclear staining	Solid pseudopapillary neoplasm	Nuclear staining in other tumours, but usually much more high-grade (acinar cell carcinoma)

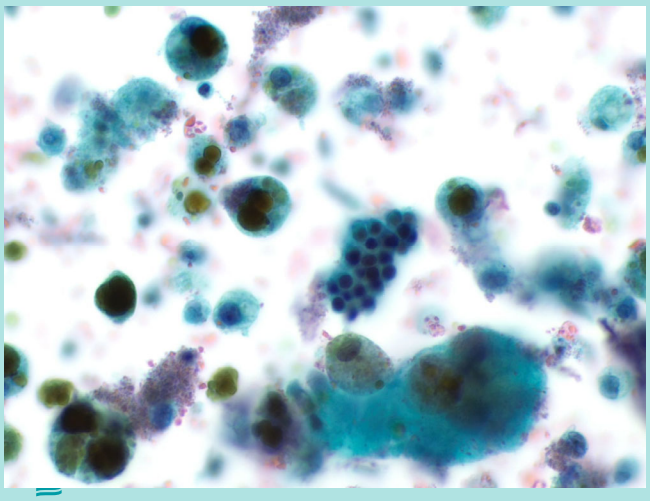
(from WHO Reporting System for PB Cytopathology, Chapter 2; Source Barbara Centeno)

2. Benign/Negative (for malignancy)

- 4.0.1: Benign non-neoplastic processes
  - 4.0.1.1: Normal pancreatic and biliary parenchyma and contaminants
  - 4.0.1.2: Acute pancreatitis
  - 4.0.1.3: Cholangitis
  - 4.0.1.4: Chronic Pancreatitis
  - 4.0.1.5: Groove/para-duodenal pancreatitis
  - 4.0.1.6: Autoimmune and IgG4-related Pancreatitis
  - 4.0.1.7: Lymphoepithelial Cyst
  - 4.0.1.8: Pseudocyst
  - 4.0.1.9: Splenule (accessory spleen)
- 4.0.2: Benign neoplastic processes
  - 4.0.2.1: Serous Cystadenoma
  - 4.0.2.2: Schwannoma
  - 4.0.2.3: Lymphangioma
  - 4.0.2.4: Other Rare Benign Neoplasms (leiomyoma, granular cell tumors, hemangioma, etc)

2. Benign/Negative (for Malignancy)

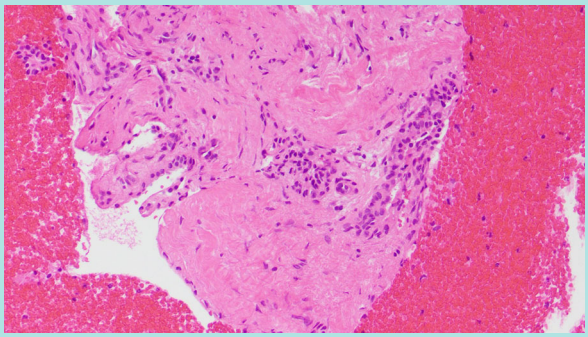
Serous Cystadenoma

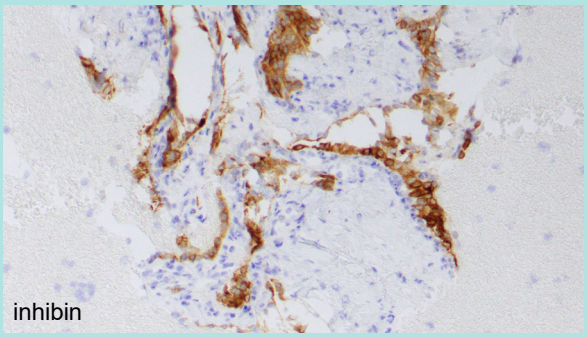


- Multilobulated, multicystic mass
- Cuboidal , glycogen-rich, non-mucinous epithelium
- +/- hemosiderin-laden macrophages
- Low CEA, low amylase (<250 U/L)
- 3p (VHL) gene mutation (+/-)

2. Benign/Negative (for Malignancy)

Serous Cystadenoma – fork tipped needle





4. Pancreatic neoplasm: low risk/ low-grade (Pan-low)

- ✓ A specimen categorized as 'Pancreaticobiliary neoplasm: low risk/low-grade' has features of an intraductal and/or cystic neoplasm with low-grade epithelial atypia.
- ✓ Extracted from the 'Neoplastic: Other' category of the Papanicolaou System for Reporting Pancreaticobiliary Cytology
- ✓ Low-grade epithelial atypia encompasses low-grade and intermediate-grade dysplasia and has a low risk of disease progression.

4. Pancreatic neoplasm: low risk/ low-grade (Pan-low)

- ✓ Category is not likely to be used for BDB
  - More likely to use “atypical’ category
- ✓ Incorporates ancillary studies
  - CEA, amylase, NGS (if available)
- ✓ ROM pancreatic FNA = 5-20%
- ✓ ROM in BDB is not established
- ✓ Clinical management is usually conservative

4. Pancreatic neoplasm: low risk/ low-grade (Pan-low)

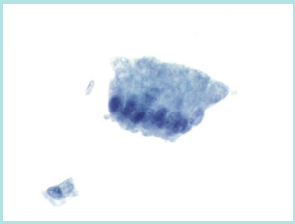
6.0.1: Specific lesions:

- 6.0.1.1: Pancreatic intraepithelial neoplasia: low-grade
- 6.0.1.2: Biliary intraepithelial neoplasia: low-grade
- 6.0.1.3: Intraductal papillary mucinous neoplasm - low-grade
- 6.0.1.4: Intraductal papillary mucinous neoplasm of the bile duct - low-grade
- 6.0.1.5: Mucinous Cystic Neoplasm-low-grade
- 6.0.1.6: Others (inc spindle cell tumours)

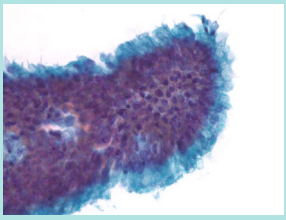
4. Pancreatic neoplasm: low risk/ low-grade (Pan-low)

- Thick, colloid-like ECM **or**
- LGA **or**
- Elevated CEA >192 ng/mL **and**
- Absent HGA and necrosis

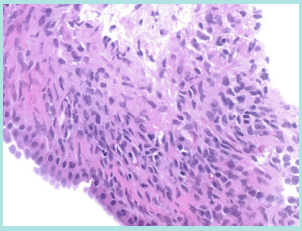
Neoplastic mucinous cyst, NOS



IPMN-LG



MCN-LG



5. Pancreatic neoplasm: high risk/ high-grade (Pan-high)

- ✓ The category is not likely to be used in BDB
  - Use “suspicious for malignancy” instead
- ✓ ROM in pancreatic FNA is 60-95%
- ✓ ROM in BDB is not established
- ✓ Clinical management is surgical resection for pancreatic lesions

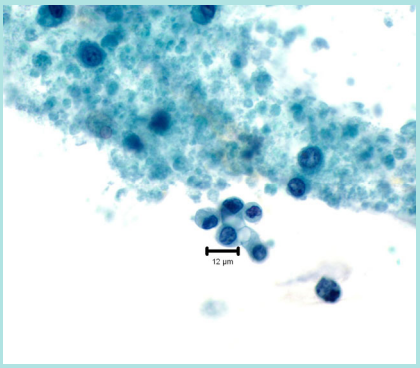
5. Pancreatic neoplasm: high risk/ high-grade (Pan-high)

7.0.1: Specific lesions:
- 7.0.1.1: Pancreatic intraepithelial neoplasia - high-grade
- 7.0.1.2: Biliary intraepithelial neoplasia - high-grade
- 7.0.1.3: Intraductal papillary mucinous neoplasm of the pancreas - high-gra
- 7.0.1.4: Intraductal papillary neoplasm of the bile duct - high-grade
- 7.0.1.5: Mucinous cystic neoplasm - high-grade
- 7.0.1.6: Intraductal oncocytic papillary neoplasm
- 7.0.1.7: Intraductal tubulopapillary neoplasm

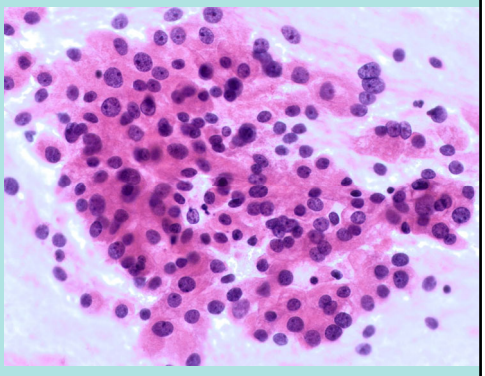
5. Pancreatic neoplasm: high risk/ high-grade (Pan-high)

High-grade Epithelial Atypia
- < 12μ duodenal enterocyte
- Increased N/C ratio
- Nuclear membrane abnormalities
- Abnormal chromatin pattern
- Prominent nucleoli +/-
- Variable residual cytoplasmic mucin
- Background necrosis in most cases
- Background inflammation variable

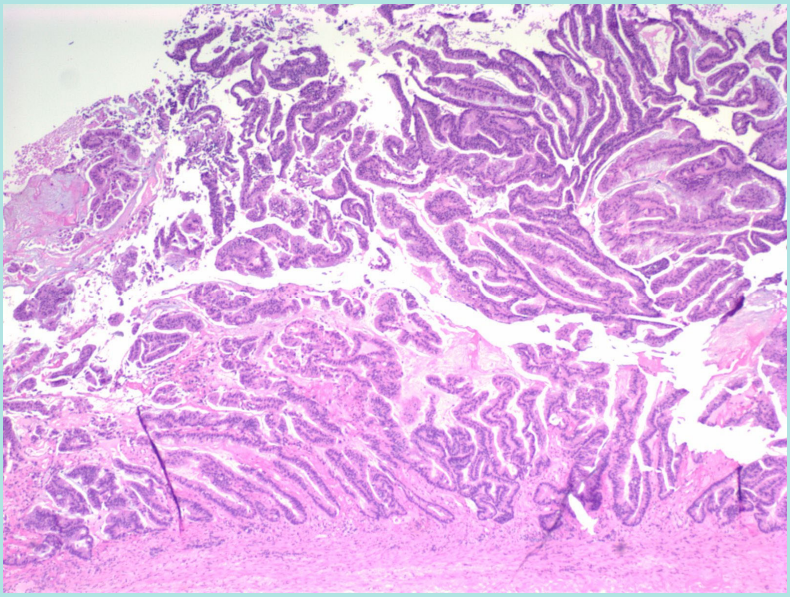
IPMN-HG



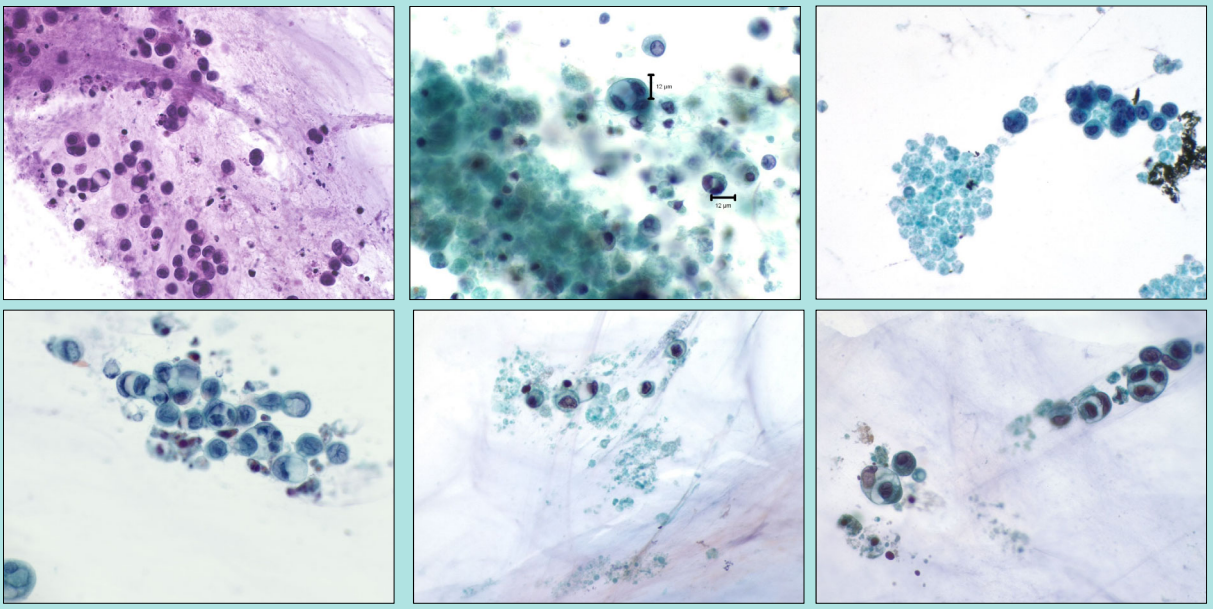
IOPN



IPMN with HGD



HGA in Mucinous Cysts

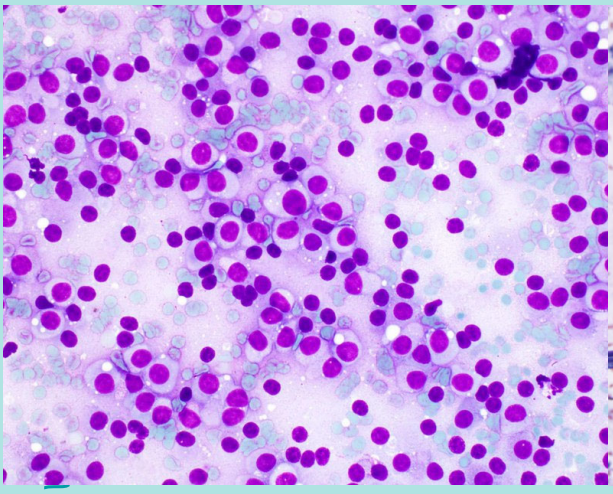


7. Malignant

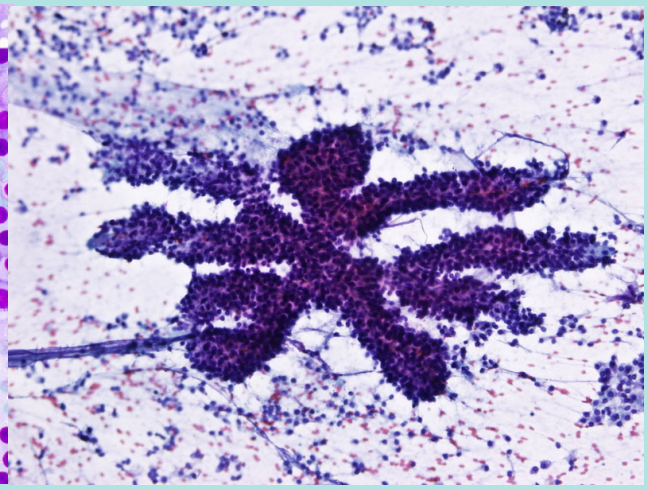
9.0.1: Specific Lesions
- 9.0.1.1: Cholangiocarcinoma
- 9.0.1.2: Pancreatic ductal adenocarcinoma
- 9.0.1.3: Pancreatic acinar cell carcinoma
- 9.0.1.4: Neuroendocrine tumour
- 9.0.1.5: Neuroendocrine carcinoma (small and large cell types)
- 9.0.1.6: Pancreatoblastoma
- 9.0.1.7: Solid-pseudopapillary neoplasm
- 9.0.1.8: Primary non-Hodgkin lymphoma (general overview; small versus large cell types)
- 9.0.1.9: Metastasis to the pancreas
- 9.0.1.10: Others (inc spindle cell tumours)

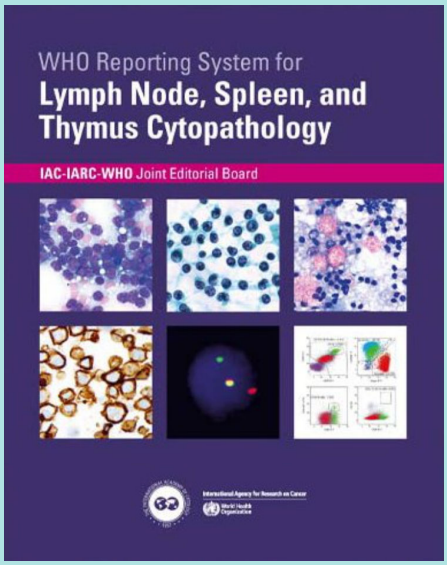
7. Malignant

PanNET



SPN





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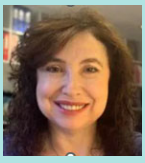
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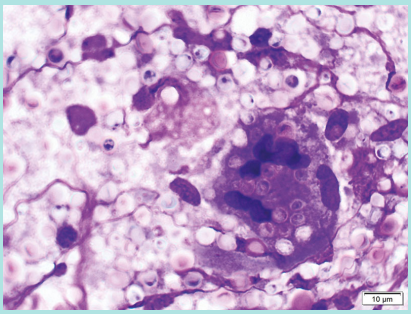
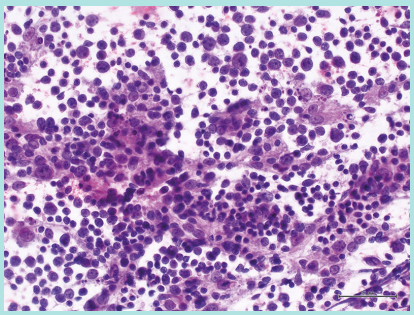
Diagnostic Categories, ROM and Management

Diagnostic category	Estimated ROM[a]	Diagnostic management options[b,c]
Inadequate/ Insufficient	17–67% (34%)	CORRELATE[d]. Repeat FNAB, ideally with ROSE and ancillary tests, and consider performing CNB.
Benign	2–16% (5%)	CORRELATE[d]. If the findings correlate with the FNAB, review clinically as required. If the findings are discrepant with the FNAB, consider repeating the FNAB, ideally with ROSE and ancillary testing, and/or perform CNB.
Atypical	29–77% (65%)	CORRELATE[d]. Consider repeating the FNAB, ideally with ROSE and ancillary testing, and/or perform CNB or excision biopsy.
Suspicious for malignancy	88–100% (93%)	CORRELATE[d]. Repeat the FNAB, ideally with ROSE and ancillary testing, and/or perform CNB or excision biopsy[e,f].
Malignant	98–100% (100%)	CORRELATE[d]. If the findings are discrepant with the FNAB or more material is required for ancillary testing, repeat the FNAB, ideally with ROSE and ancillary testing, and/or perform CNB or excision biopsy[e,f].





6: Chapter 5: Diagnostic category: Atypical
- 6.1.1.1: Introduction
- 6.1.1.2: Definition
- 6.1.1.3: Discussion and background
- 6.1.1.4: Risk of malignancy and diagnostic management recommendations

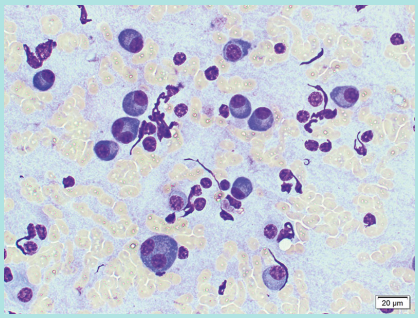
6.3.1: Sample reports: Atypical

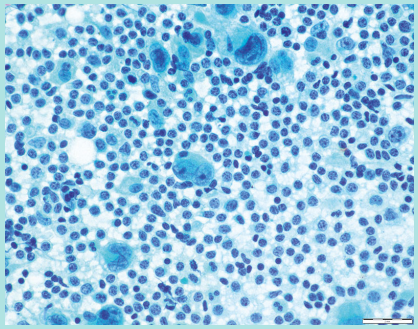
7: Chapter 6: Diagnostic category: Suspicious for malignancy
- 7.1.1.1: Introduction
- 7.1.1.2: Definition
- 7.1.1.3: Discussion and background
- 7.1.1.4: Risk of malignancy and diagnostic management recommendations

7.3.1: Sample reports: Suspicious for malignancy

8: Chapter 7: Diagnostic category: Malignant
- 8.1.1.1: Introduction
- 8.1.1.2: Definition
- 8.1.1.3: Discussion and background
- 8.1.1.4: Risk of malignancy and diagnostic management recommendations

8.6: Entities in the Malignant category
- 8.6.1: Mixed lymphoid cell pattern
  - 8.6.4.9: Follicular lymphoma
  - 8.6.4.8: Marginal zone lymphoma
  - 8.6.5.10: Nodal T follicular helper cell lymphoma, angioimmunoblastic type
- 8.6.2: Predominantly small/intermediate cell pattern
  - 8.6.4.1: Chronic lymphocytic leukaemia / small lymphocytic lymphoma
  - 8.6.4.10: Mantle cell lymphoma
  - 8.6.4.5: Lymphoplasmacytic lymphoma
  - 8.6.4.6: Plasma cell neoplasms
  - 8.6.2.8: Mastocytosis
- 8.6.3: Predominantly intermediate/large/pleomorphic/blastic cell pattern
  - 8.6.3.1: Lymphoblastic lymphoma
  - 8.6.4.11: Large B-cell lymphomas
  - 8.6.4.19: Burkitt lymphoma
  - 8.6.5.11: Anaplastic large cell lymphoma
  - 8.6.5.12: Breast implant-associated anaplastic large cell lymphoma
  - 8.6.4.18: Primary effusion lymphoma
  - 8.6.5.9: Peripheral T-cell lymphoma NOS
  - 8.6.2.7: Myeloid sarcoma
- 8.6.4: Single very large atypical cell pattern
  - 8.6.8.2A: Classic Hodgkin lymphoma
  - 8.6.6.1: Nodular lymphocyte-predominant Hodgkin lymphoma
  - 8.6.6.3A: Lymphomatoid granulomatosis
  - 8.6.4.12: T-cell/histiocyte-rich large B-cell lymphoma
- 8.6.8A: Histiocytic/dendritic cell neoplasms
  - 8.6.8.2: Langerhans cell histiocytosis
  - 8.6.8.3: Interdigitating dendritic cell sarcoma
  - 8.6.8.1: Histiocytic sarcoma
- 8.6.9: Stroma-derived neoplasms of lymphoid tissues
  - 8.6.8.4: Follicular dendritic cell sarcoma





8.6.21: Metastases
- 8.6.6.2B: Metastases from carcinomas
- 8.6.6.3B: Metastases from melanoma
- 8.6.6.4: Metastases from sarcomas

8.6.8B: Splenic neoplasms
- 8.6.4.7: Splenic neoplasms: Introduction
- 8.6.4.4: Splenic B-cell lymphoma
- 8.6.5.4: Hepatosplenic T-cell lymphoma
- 8.6.5.3: Angiosarcoma

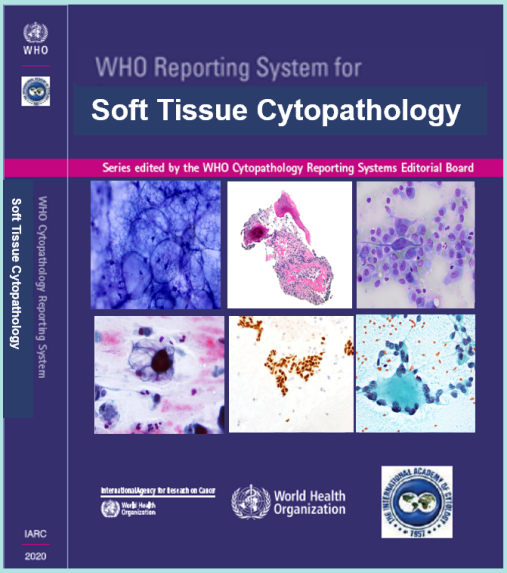
8.6.5: Thymic neoplasms
- 8.6.4.15: Thymic neoplasms: Introduction
- 8.6.4.13: Thymomas
- 8.6.4.20: Thymic B-cell lymphomas
- 8.6.4.14: Thymic carcinomas

8.7.1: Sample reports: Malignant

9: Chapter 8: Diagnostic management recommendations for each diagnostic category
- 9.2.1: Category: Insufficient/Inadequate/Non-diagnostic
- 9.2.2: Category: Benign
- 9.2.3: Category: Atypical
- 9.2.4: Category: Suspicious for malignancy
- 9.2.5: Category: Malignant

Tumour type	Useful cytoplasmic and/or membranous markers
Adrenal cortical neoplasm	MART1, inhibin, calretinin
Breast carcinoma	GCDFP-15, mammaglobin
Colorectal carcinoma	CK20, villin, CEA
Hepatocellular carcinoma	HepPar1, arginase-1, glypican-3, AFP
Lung adenocarcinoma	Napsin A
Mesothelioma	Calretinin, D2-40, mesothelin, CK5/6
Neuroendocrine neoplasm	Chromogranin, synaptophysin, CD56
Prostate carcinoma	PSA, PSAP
Renal cell carcinoma, clear cell type	RCC, carbonic anhydrase IX, CD10
Thyroid papillary and follicular carcinoma	Thyroglobulin
Thyroid medullary carcinoma	Calcitonin
Squamous cell carcinoma	p40, p63, CK5/6, p16 (HPV-related carcinoma)

Marker	Normal tissue	Likely primary site of origin or tumour type
CDX2	Small and large intestines, pancreatic ducts	Colorectal carcinomas; some pancreatobiliary carcinomas; some gastric adenocarcinomas
GATA 3	Breasts, urothelium, salivary glands, and T lymphocytes	Breast carcinomas (70% ER+); urothelial carcinomas; paragangliomas; some salivary gland tumours
NKX3-1	Prostate	Prostatic adenocarcinoma
PAX8	Renal epithelial cells, thyroid follicular cells, epithelial cells of Müllerian origin, thymus	Renal cell carcinomas; thyroid carcinomas, including medullary carcinomas; epithelial non-mucinous gynaecological tumours; some epithelial mucinous gynaecological tumours; thymomas and thymic carcinomas
SOX10	Melanocytes, myoepithelial cells, breasts	Melanoma, including melanoma of soft parts; salivary gland tumours, including pleomorphic adenomas, adenoid cystic carcinomas, basal cell adenomas and adenocarcinomas, acinic cell carcinomas, secretory carcinomas, epithelial-myoepithelial carcinomas, and rare mucoepidermoid carcinomas; triple-negative breast carcinomas
TTF1	Thyroid follicular and parafollicular cells, lung (type II and bronchial cells)	Lung adenocarcinomas (including some mucinous adenocarcinomas); small cell neuroendocrine carcinomas; some large cell neuroendocrine carcinomas; some neuroendocrine tumours; thyroid follicular and papillary carcinomas; thyroid medullary carcinomas



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Diagnostic Categories

1. Insufficient/Inadequate/Non-diagnostic
2. Benign
3. Atypical
4. Soft Tissue neoplasm of uncertain malignant potential (STNUMP)
5. Suspicious for Malignancy
6. Malignant

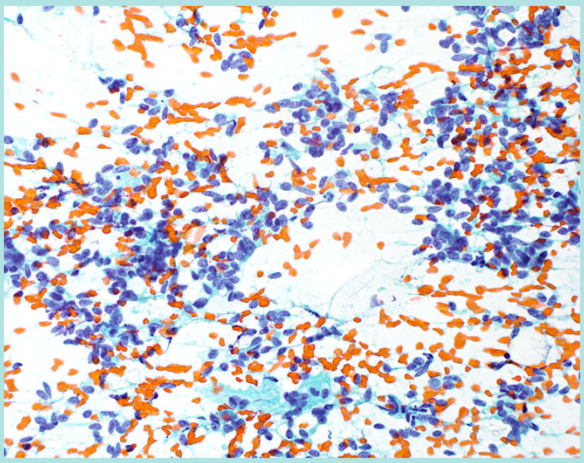
WHO System for Reporting Soft Tissue Cytopathology: Risk of Malignancy and Management

Diagnostic category	Estimated ROM	Clinical management options
Insufficient/Inadequate/Non-diagnostic	29.9% (9-42)	CORRELATE. Repeat FNAB preferably with ROSE
Benign	2.5% (0- 4)	CORRELATE, If disrepancy, repeat FNAB and/or CNB. If correlation, review when appropriate
Atypical	39.6% (46)	CORRELATE. Discuss at MDT. Repeat FNAB and/or CNB and/or surgical biopsy
STNUMP	51.4% (20-27)	CORRELATE. Discuss at MDT. Repeat FNAB and/or CNB and/or surgical biopsy
Suspicious for malignancy	68.2% (71-80)	CORRELATE. Discuss at MDT. Consider repeat FNAB to gain material for ancillary testing, but usually will require CNB and/or surgical biopsy
Malignant	97.7% (91-100)	CORRELATE. Discuss at MDT. Usually will require CNB and/or surgical biopsy

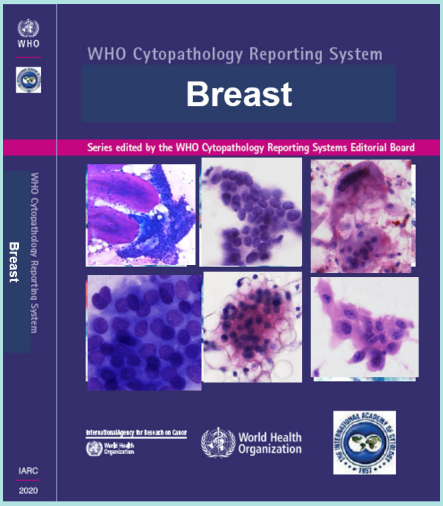
Soft Tissue Neoplasm Of Uncertain Malignant Potential (STNUMP)

Specific Entities with uncertain malignant potential:

- Dermatofibrosarcoma protuberans
- Solitary fibrous tumor
- Inflammatory myofibroblastic tumor
- Angiomatoid fibrous histiocytoma
- Gastrointestinal stromal tumor
- Myoepithelial neoplasms
- PEComa



Solitary Fibrous Tumor



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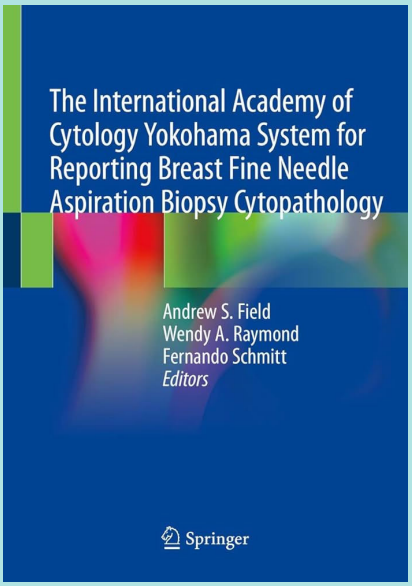

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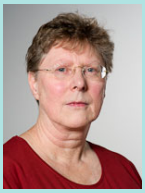

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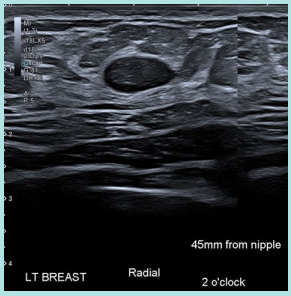
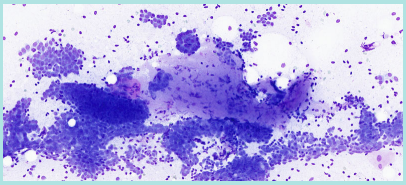
Table 1. The WHO Reporting System for Breast Cytopathology on breast FNAB: implied risk of malignancy (ROM) and clinical management options by diagnostic category.

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.





6.0: Benign

6.0.0.1: Introduction
6.0.0.2: Definition
6.0.0.3: Discussion and background
6.0.0.4: Risk of malignancy and management recommendations

6.1: Entities in the Benign Category

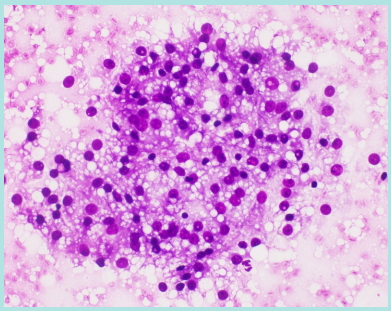
6.1.0.1: Introduction
6.1.1: Inflammatory processes
6.1.1.1: Acute inflammation and suppuration
6.1.1.2: Granulomatous inflammation
6.1.1.3: Lymphoid hyperplasia and related disorders
6.1.1.4: Fat necrosis
6.1.2: Benign epithelial proliferations and neoplasms
6.1.2.1: Hamartoma (Note: include discussion 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

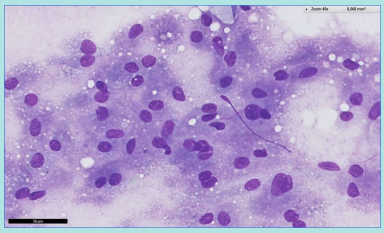
7.0: Atypical

7.0.0.1: Introduction
7.0.0.2: Definition
7.0.0.3: Discussion and background
7.0.0.4: Risk of malignancy and management recommendations
7.0.1: Sample Reports

8.0: Suspicious for malignancy

8.0.0.1: Introduction
8.0.0.2: Definition
8.0.0.3: Discussion and background
8.0.0.4: Risk of malignancy and management recommendations
8.0.1: Sample Reports



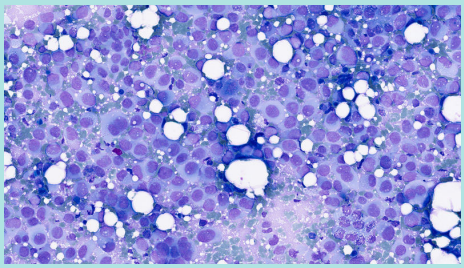


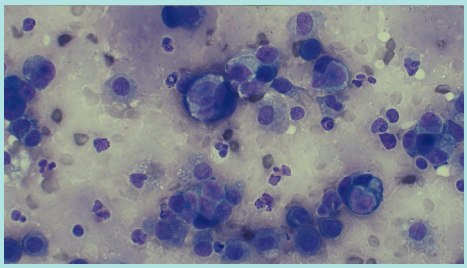
9.0: Malignant

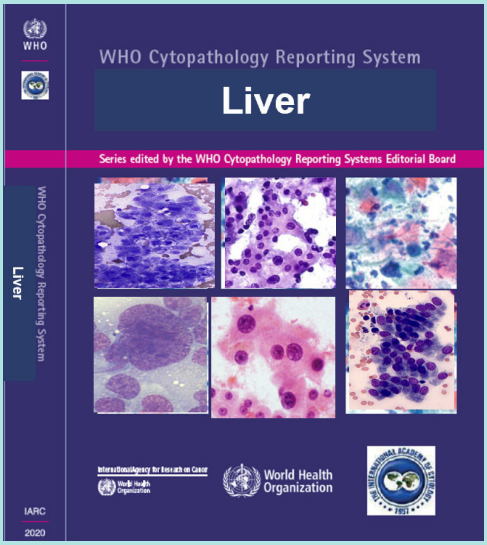
9.0.0.1: Introduction
9.0.0.2: Definition
9.0.0.3: Discussion and background
9.0.0.4: Risk of malignancy and management recommendations

9.1: 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







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WHO Reporting System for Liver Cytopathology Diagnostic Categories

1. Insufficient/inadequate/nondiagnostic
2. Benign
3. Atypical
4. Suspicious for Malignancy
5. Malignant

Liver: ROM and Management

Diagnosis	Estimated Risk of Malignancy (ROM)*	Clinical Management Options and Recommendations^
Insufficient/Inadequate/Non-Diagnostic	15-67%	A repeat sampling is recommended
Benign	3-16%	A follow up imaging study and, if necessary, tissue sampling is encouraged as necessary.
Atypical	21-100%	A repeat sampling in conjunction with imaging study is recommended
Suspicious	77-100%	Additional sampling with ancillary studies may be necessary to determine further therapy
Malignant	100%	Definitive therapy is based on the type of malignancy and stage of disease.

Controversies in Devolvement of the WHO Reporting System for Liver Cytopathology

1. Techniques: FNAB and/or CNB
2. Insufficient/inadequate/nondiagnostic category and benign tissue on FNAB
3. Where to place and how to discuss premalignant lesions: MCN, IPBN, LGDN, HGDN?
4. NET/NEC as primary or metastatic malignancy?

Techniques: FNAB and/or CNB

FNAB
- Fresh tissue for culture, flow cytometry
- High tumor yield/fraction
  - Molecular testing
- ROSE
- Greater access
  - Small masses
  - Masses next to large vessels
- Lower risk
- Lower cost
- Low resource settings

CNB
- Architecture
- Ancillary testing

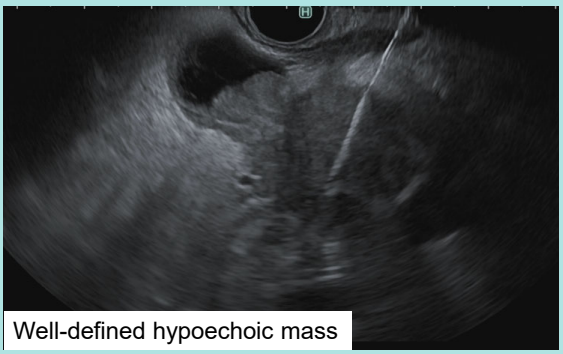
Techniques: FNAB and/or CNB

- Combined liver FNAB/CNB has a high diagnostic efficacy for malignancy and a lower false negative rate than either procedure alone, especially in metastatic tumors, HCC, and hematopoietic neoplasms.
- The combination of material also allows for better specimen triage when flow cytometry or other ancillary tests might be needed.
- If cases are split and handled by both cytopathologists and surgical pathologists, good communication and specimen comparison is essential.
  - One Procedure-One Report is optimal (J Am Soc Cytopathol. 2023 Nov-Dec;12(6):395-406)

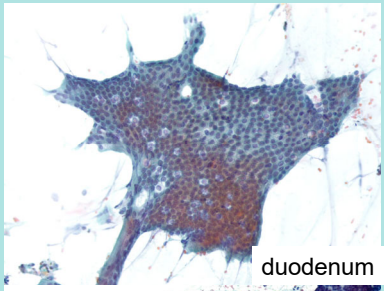
Insufficient/inadequate/non-diagnostic

- Is a specimen that for qualitative and/or quantitative reasons does not permit a diagnosis of the targeted lesion
- Precise terminology is user-dependent
  - Pick one and use consistently
- Classification of benign tissue in this category is organ specific:
  - Lung FNAB, normal tissue is typically reported as benign since normal tissue can explain a targeted mass lesion, e.g. infection, organizing pneumonia, consolidation
    - Option to classify as nondiagnostic depending on imaging
  - Pancreas FNAB, normal pancreatic epithelium does not explain a well-defined mass or cyst, so recommendation is to call nondiagnostic
    - optional to use benign + caveat

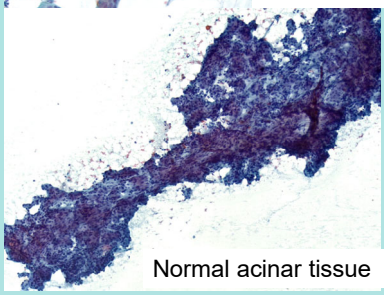
IS insufficient/inadequate/non-diagnostic in Pancreatic FNA



Well-defined hypoechoic mass



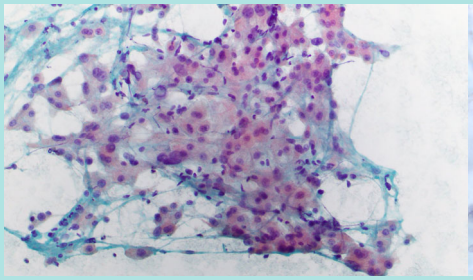
duodenum



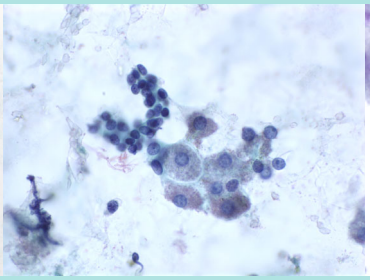
Normal acinar tissue

WHO Reporting System for Liver Cytopathology inadequate/insufficient/nondiagnostic

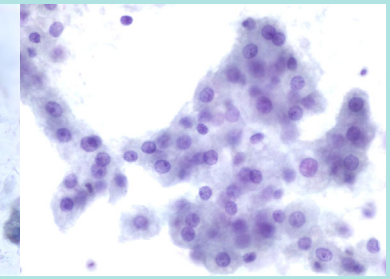
Benign hepatic tissue may explain the mass so classify benign liver tissue as BENIGN
With a note/caveat to correlate with imaging to ensure representative biopsy



Cirrhosis



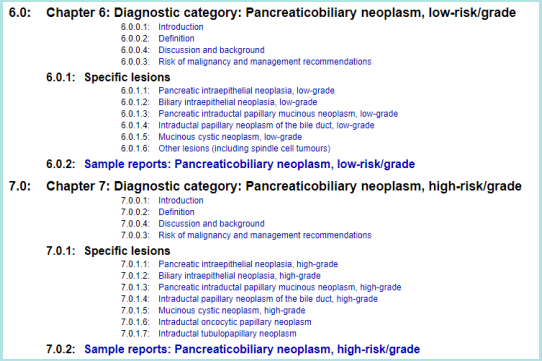
FNH



LCA

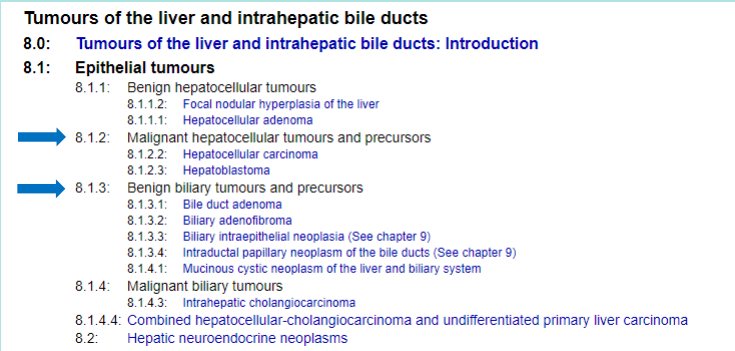
Where to place and how to discuss MCN, IPBN, LGDN, HGDN?

- All of these lesions are neoplastic, pre-malignant lesions, but are RARE
- In the WHO PB Book, there were two new categories for low risk/grade and high risk/grade neoplasms, because premalignant lesions are not rare in the pancreas



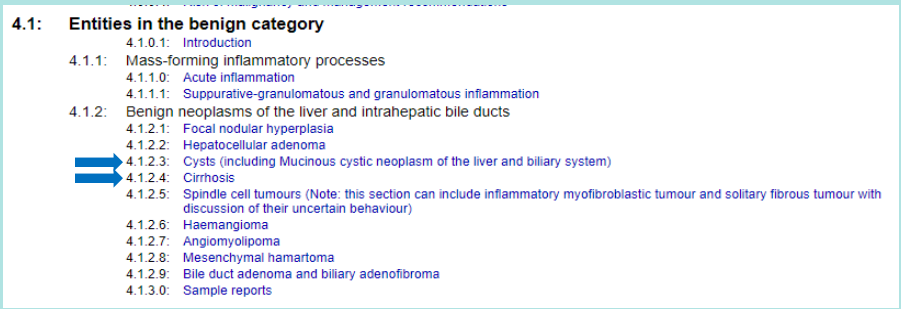
Where to place and how to discuss MCN, IPBN, LGDN, HGDN?

In WHO 5th Edition GI Bluebook of Tumour Classification, Dysplastic nodules are covered under HCC and precursors and mucinous cystic neoplasm (MCN) and intraductal papillary neoplasm of bile ducts (IPNB) are covered under benign biliary tumors and precursors



Where to place and how to discuss MCN, IPBN, LGDN, HGDN?

- Currently in the WHO Reporting System for Liver Cytopathology, DNs are introduced under cirrhosis in the BENIGN chapter and further discussed under the ATYPIA and SUSPICIOUS FOR MALIGNANCY chapters. They are not listed by name in the CONTENTS.
- Mucinous cystic neoplasm (MCN) and intraductal papillary neoplasm of bile ducts (IPNB) are classified as BENIGN under a section called CYSTS



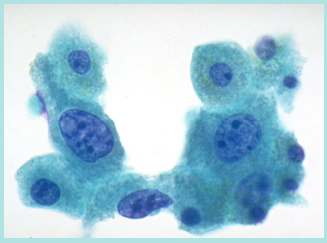
Where to place and how to discuss MCN, IPBN, LGDN, HGDN?

- Rationale
  - These lesions are very rare without well-defined diagnostic cytological criteria
  - Most of these lesions when encountered will not be specifically diagnosed on cytology
  - Atypical and suspicious categories for any of these lesions will suffice

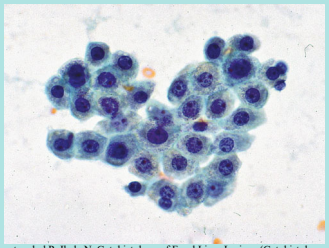
Dysplastic Nodules

- Dysplastic nodules (DNs) are usually 5–15 mm in diameter and are detected macroscopically or by imaging in cirrhotic livers, as single or multiple lesions. Their prevalence in cirrhotic livers ranges from 11% to 40%
- These dysplastic lesions are BENIGN lesions composed of atypical (LCC) to suspicious (SCC) hepatocytes

- Low-grade DN exhibits large cell change with “atypical” cells sporadically placed within otherwise benign and reactive hepatocytes.



- High-grade DN exhibits small cell change with a uniform small hepatocyte population raising the “suspicion” for HCC



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Wee A, Sampatanukul P, Jhala N. Cytohistology of Focal Liver Lesions (Cytohistology of Small Tissue Samples), 1st ed. Eds: Kim R. Geisinger & Martha B. Pitman. Cambridge University Press, 2014

Mucinous Cystic Neoplasm

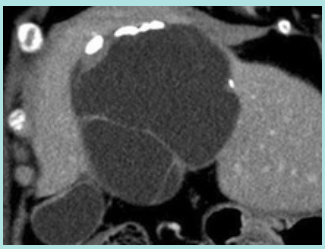
- MCN of the liver and biliary system is a cyst-forming epithelial neoplasm, composed of cuboidal to columnar, variably mucin-producing epithelium, associated with ovarian-type subepithelial stroma.
- MCNs are classified as either low-grade or high-grade, or with invasive carcinoma

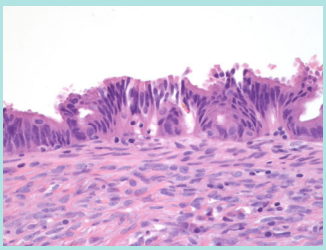
Part A. Cyst aspirate

Diagnostic Category: **Benign**
Diagnosis: Mucinous cyst contents

Part B. Cyst wall biopsy

Diagnosis: Mucinous Cystic Neoplasm, low-grade





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Intraductal Papillary Neoplasm of The Bile Ducts

- Very rare premalignant neoplasms are benign unless invasive carcinoma
- Cytological criteria are not well-defined
- Cytomorphology will direct categorization into benign, atypical, suspicious or malignant
  - Holds true in the WHO PB book even though described in Pan-Lo and Pan-high diagnostic categories

Neuroendocrine Neoplasms (NET/NEC): primary or metastatic malignancy?

- Primary hepatic NET (PHNET) is extremely rare
- Most NET/NEC identified in the liver are metastatic from other organs.
- First case of PHNET was reported by Edmondson in 1958.
- Literature review (Li *et al.*) shows only about 150 case reports of PHNET.

8240/3 Neuroendocrine tumour NOS
- 8240/3 Neuroendocrine tumour, grade 1
- 8249/3 Neuroendocrine tumour, grade 2
- 8249/3 Neuroendocrine tumour, grade 3

8246/3 Neuroendocrine carcinoma NOS
- 8013/3 Large cell neuroendocrine carcinoma
- 8041/3 Small cell neuroendocrine carcinoma

8154/3 Mixed neuroendocrine–non-neuroendocrine neoplasm (MiNEN)

Neuroendocrine Neoplasms (NET/NEC): primary or metastatic malignancy?

Pathogenesis

• Primary hepatic neuroendocrine tumors (PHNET) can arise anywhere within the liver.

Clinical implications

• PHNETs are characterized by non-specific clinical and imaging results, which can be easily confused with other liver lesions, including HCC and CCA.

• NETs account for 0.4% of resected hepatic primaries, and NECs or MiNENs make up 0.5% .

• Due to its rarity, rigorous exclusion of metastasis is mandatory before the tumor can be accepted as a hepatic primary.

• For this practical reason, NET/NEC entities are discussed under “Metastases” in this reporting system.

Neuroendocrine Neoplasms (NET/NEC): primary or metastatic malignancy?

Neuroendocrine Neoplasms are discussed under “Metastases” in the WHO Reporting System for Liver Cytopathology

7: Malignant

7.0.0.1: Introduction
7.0.0.2: Definition
7.0.0.3: Discussion and background
7.0.0.4: Risk of malignancy and management recommendations

7.1: Entities in the malignant category

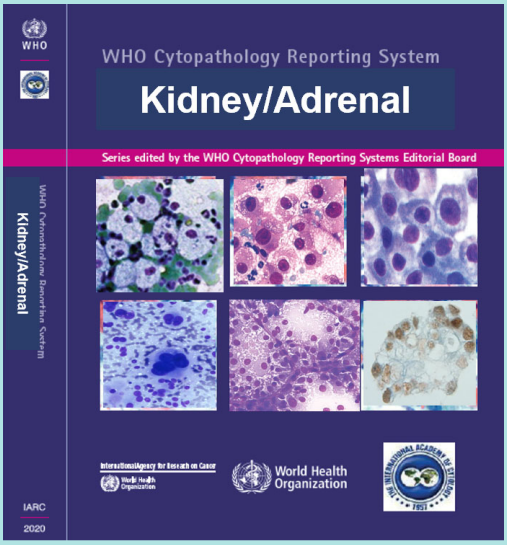
7.1.1: Malignant hepatocellular tumours
7.1.1.1: Hepatocellular carcinoma
7.1.1.2: Paediatric and fibrolamellar hepatocellular carcinoma
7.1.1.3: Hepatoblastoma

7.1.2: Malignant biliary tumours
7.1.2.1: Intrahepatic cholangiocarcinoma
7.1.2.2: Combined hepatocellular-cholangiocarcinoma and undifferentiated primary liver carcinoma

7.1.3: Haematolymphoid neoplasms
7.1.3.1: Hepatosplenic T-cell lymphoma NOS
7.1.3.2: Other lymphomas involving liver

7.1.4: Mesenchymal tumours
7.1.4.1: Epithelioid haemangioendothelioma
7.1.4.2: Angiosarcoma
7.1.4.3: Kaposi sarcoma
7.1.4.4: Embryonal sarcoma of liver
7.1.4.5: Leiomyosarcoma
7.1.4.6: EBV sarcomas

→ 7.1.5: Metastatic tumours
7.1.5.1: Metastases (inc GIST, NEN, GCTs)
7.1.6.0: Sample reports



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Modern Pathology (2021) 34:1392–1424
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USCAP

ARTICLE

New developments in existing WHO entities and evolving molecular concepts: The Genitourinary Pathology Society (GUPS) update on renal neoplasia

Modern Pathology (2021) 34:1167–1184
https://doi.org/10.1038/s41379-021-00737-6

USCAP

ARTICLE

Novel, emerging and provisional renal entities: The Genitourinary Pathology Society (GUPS) update on renal neoplasia

Clear Cell RCC
Papillary RCC

Chromophobe RCC

Oncocytoma and the spectrum of "difficult to classify" low-risk tumors

Clear cell papillary RCC

Tubulocystic RCC
MiT Family Translocation-Associated RCC

Acquired cystic disease-associated RCC
SMARCB1-deficient RCC: Renal Medullary Carcinoma, "Unclassified RCC with Medullary Phenotype" and Dedifferentiated RCC with Secondary SMARCB1 Loss
Mucinous tubular and spindle cell carcinoma
Metanephric adenoma and related tumors
Hereditary Renal Carcinoma Syndromes

Eosinophilic solid and cystic RCC
RCC with fibromyomatous stroma
Eosinophilic vacuolated tumor
Low-grade oncocytic tumor
Anaplastic lymphoma kinase rearrangement-associated RCC
Thyroid-like follicular carcinoma of kidney
Atrophic kidney-like lesion
Biphasic hyalinizing psammomatous RCC

The good news

Clear cell RCC
Papillary RCC
Chromophobe RCC
Oncocytoma

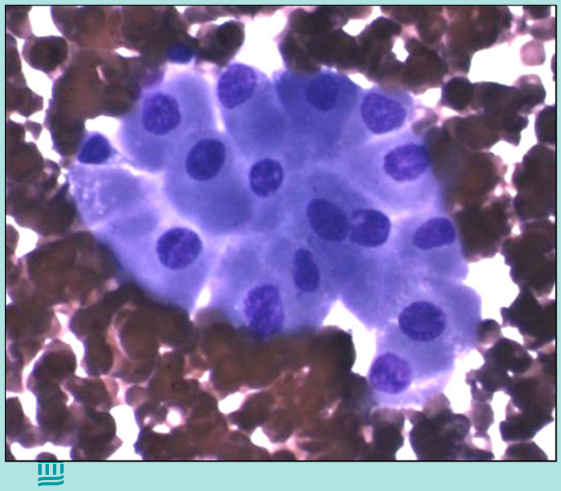
→ 90% of renal tumors in adults

The most commonly encountered renal tumors can be diagnosed with morphology and a limited IHC panel

	CK7	CD117	CAIX	AMACR	CD10	SDH	TFE3	S100A1
CCRCC	-	-	+	-	+	+	-	-
PRCC	+	-	-	+	+	+	-	-
Oncocytoma	rare	+	-	-	+/-	+	-	+
ChRCC	+	+	-	-	-	+	-	-
CCPRCT	+	-	+*	-	-	+	-	-
MTSCC	+	-	-	+	-/+	+	-	-
TFE3-rRCC	-	-	+/-	+	+/-	+	+	-
SDH-dRCC	-	-	-	-	-	-	-	-

Oncocytic tumors of the Kidney

Heterogeneous category with very different ROM (2-100%)



- Oncocytoma
- Chromophobe RCC
- Papillary RCC
- Clear Cell RCC
- Fumarate hydratase-deficient RCC
- TFE3-translocation RCC
- Tubulocystic carcinoma
- Papillary neoplasm with reverse polarity
- Low grade oncocytic tumor (LOT)(recently recognized renal oncocytic neoplasm that is CK7 +, CD117 -)
- Eosinophilic solid and cystic RCC
- Eosinophilic vacuolated Tumor
- "Hybrid" tumors in Birt-Hogg-Dubé Syndrome

Low-risk oncocytic renal neoplasm

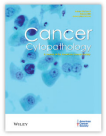
- Oncocytoma
- ChRCC
- PRCC (the old type 2)
- CCRCC
- Fumarate hydratase-dRCC
- TFE3-tRCC
- Tubulocystic carcinoma
- Papillary neoplasm with reverse polarity
- LOT
- Eosinophilic solid and cystic RCC
- EVT
- “Hybrid” tumors in BHD

- **Oncocytoma**
- **Eosinophilic variant of ChRCC**
- **Hybrid tumors of BHD syndrome**

COMMENTARY

Low-risk oncocytic renal neoplasm: A useful cytologic diagnosis

Andrew A. Renshaw MD[1] | Merce Jorda MD[2] | Eva M. Wojcik MD[3] | Martha B. Pitman MD[4]

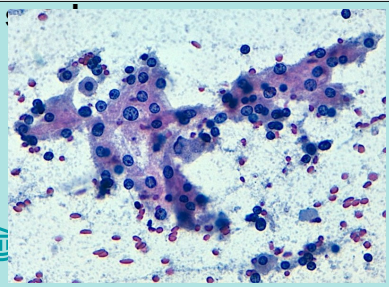


Volume 132, Issue 2
February 2024
Pages 84-86

- **Oncocytoma**
- **Eosinophilic variant of ChRCC**
- **Hybrid tumors of BHD**

=

- Oncocytic cells
- Loosely cohesive tissue fragments
- No nuclear atypia (such as the wrinkled nuclei of ChRCC)
- No macronucleoli
- Positive for CD117 immunochemistry



Renshaw AA, Pitman MB. Risk of malignancy in renal biopsy: A review. Cancer Cytopathol.

Volume 132, Issue 3
March 2024
Pages 140-143

TABLE 2 Risk of malignancy separating indeterminate diagnoses: Fine-needle aspiration and core-needle biopsies combined using immunohistochemistry.[a]

Cytologic diagnoses	Risk of malignancy
Nondiagnostic	82%
Benign	24%
Atypical	83%
Neoplastic	100%
Suspicious	100%
Positive for malignant cells	99%

[a]Yang 2017[3]; Patel et al., 2016[4]; Scanga & Maygarden, 2014[5]; Lau et al. 2018.[6]

Renshaw AA, Pitman MB. Risk of malignancy in renal biopsy: A review. Cancer Cytopathol.

Volume 132, Issue 3
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Pages 140-143

TABLE 3 Estimated risk of malignancy: Fine-needle aspiration and core-needle biopsies combined using immunohistochemistry.

Cytologic diagnoses	Risk of malignancy
Nondiagnostic	80%
Benign	2%[a]
Low-risk oncocytic renal neoplasm	21%[b]
Oncocytic tumor	2%–100%
Atypical	80%
Suspicious	90%
Positive for malignant cells	99%

[a]Based on data for oncocytoma (Zhu et al., 2020[8]).
[b]Five-year survival rate ≥95% (Renshaw et al., 2023[12]).

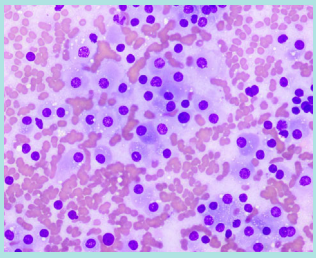
Low-risk oncocytic renal neoplasm category

- **Oncocytoma**
- **Eosinophilic variant of ChRCC (41% of ChrRCC)**
- **Hybrid tumors of BHD syndrome (very rare)**

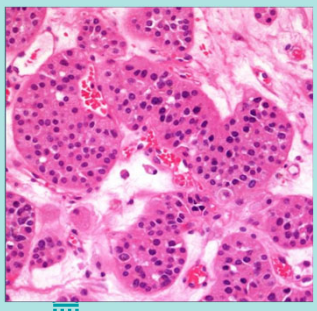
Risk of malignancy
Risk of clinical progression

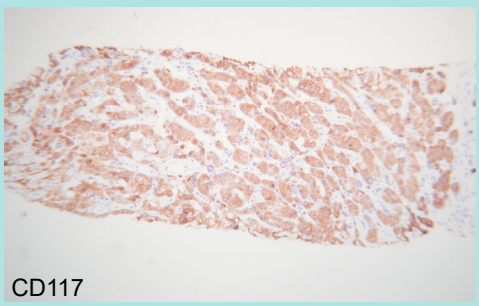
ROM: 21%
5 year SR: 95-100%

Low Risk Oncocytic Renal Neoplasm



Diagnosed using FNA+CNB+ICC
No nuclear atypia or nucleoli
A tissue sample is necessary for diagnosis (nested pattern)
CD117 positive
If Cytology only, use the Atypical category with a differential diagnosis





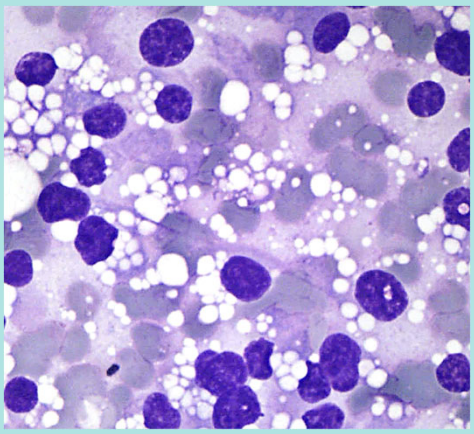
CD117

Kidney, Left, FNAB/FNB
Satisfactory for Evaluation
Low Risk Oncocytic Renal Neoplasm
Oncocytic tumor favor oncocytoma. See note.

Note: The smears show a bland oncocytic tumor without nuclear atypia or nucleoli. The CB/FNB shows tumor cells in a nested pattern that stain with CD117. The overall features favor an oncocytoma but an eosinophilic variant of ChrRCC cannot be excluded. ROM =21%; risk of progression low (5yr SR 95-100%).

Adrenal gland FNAB

- Metastases are extremely common, and the primary is usually known
- Metastases can resemble adrenal cortical carcinoma, so immunostains are a good idea
- The diagnosis of adrenal cortical adenoma versus carcinoma is not always posible on FNA/CNB. Option: adrenal cortical neoplasm



WHO Reporting System for Kidney and Adrenal Gland Cytopathology Diagnostic Categories

1. Insufficient/inadequate/nondiagnostic
2. Benign
3. Atypical
4. Low-risk oncocytic renal neoplasm
5. Suspicious
6. Malignant

Risk of Malignancy

Kidney

Diagnostic Category	Risk of malignancy
Nondiagnostic	65-80%
Benign	2-20%, 5 year survival at least 95%[a]
Low risk oncocytic renal neoplasm	2-20%, 5 year survival at least 95%[a]
Atypical	60-80%
Suspicious (for Malignancy)	70-90%
Malignant	97-99%

Adrenal

Diagnostic Category	Risk of malignancy
Nondiagnostic	30%
Benign$	0%
Atypical	48%
Suspicious (for Malignancy)	100%
Malignant	99%

DRAFT

WHO Reporting System for Kidney and Adrenal Gland Cytopathology

WHO Reporting System for Kidney and Adrenal Gland Cytopathology

4.0: Benign

- 4.0.0.1: Introduction
- 4.0.0.2: Definition
- 4.0.0.3: Discussion and background
- 4.0.0.4: Risk of malignancy and management recommendations

4.1: Entities in the Benign Category:

- 4.1.1: Non-neoplastic processes of kidney and adrenal
  - 4.1.1.1: Abscesses
  - 4.1.1.2: Suppurative-granulomatous and granulomatous inflammation
  - 4.1.1.3: Kidney cysts
  - 4.1.1.4: Adrenal cysts
- 4.2.1: Kidney neoplasms
  - 4.2.1.1: To be deleted - Introduction
  - 4.2.1.3: Oncocytoma
  - 4.2.1.4: Renal papillary tumour
  - 8.1.1.3: Clear cell papillary renal cell tumour
  - 4.2.1.5: Metanephric adenoma
  - 4.2.1.6: (Mixed epithelial and stromal tumour of the kidney - remove and discuss elsewhere?)
  - 4.2.1.7: to be deleted - (Paediatric cystic nephroma - remove and discuss in cysts?)
  - 4.2.1.8: Angiomyolipoma/PECOMA
  - 8.1.7.2: Spindle cell tumors (include SFT, inflammatory myofibroblastic tumour)
- 4.2.2: Adrenal Gland neoplasms
  - 4.2.2.2: Adrenal cortical nodules
  - 4.2.2.3: Myelolipoma
  - 4.2.2.4: (Adrenal sex cord stromal tumour)
  - 4.2.2.5: (Adenomatoid tumour)
  - 4.2.2.6: To be deleted - (Hemangiomas)
- 4.2.3: Sample reports

6.0: Low risk oncocytic renal neoplasms

- 6.0.0.1: Introduction (ensure to cover concerns discussed at EB)
- 6.0.0.2: Definition
- 6.0.0.3: Discussion and background
- 6.0.0.4: Risk of malignancy and management recommendations
- 6.0.1: Sample Reports

WHO Reporting System for Kidney and Adrenal Gland Cytopathology

7.0: Suspicious for malignancy

- 7.0.0.1: Introduction
- 7.0.0.2: Definition
- 7.0.0.3: Discussion and background
- 7.0.0.4: Risk of malignancy and management recommendations
- 7.0.1: Sample Reports

8.0: Malignant

- 8.0.0.1: Introduction
- 8.0.0.2: Definition
- 8.0.0.3: Discussion and background
- 8.0.0.4: Risk of malignancy and management recommendations

8.1: Entities in the Malignant Category:

- 8.1.1: Tumours of the kidney, morphologically defined
  - 8.1.1.1: Introduction: (NOTE any carcinomas not described or very rarely described in the FNAB literature can be cut, and where appropriate discussed in the DD of other more common carcinomas)
  - 8.1.1.2: Clear cell renal cell carcinoma
  - 8.1.1.4: Papillary renal cell carcinoma
  - 8.1.1.5: Chromophobe renal cell carcinoma
  - 8.1.1.6: Collecting duct carcinoma
  - 8.1.1.7: Mucinous tubular and spindle cell carcinoma
  - 8.1.1.8: Renal cell carcinoma NOS
- 8.1.2: Molecularly defined renal carcinomas (NOTE any carcinomas not described or very rarely described in the FNAB literature can be cut, and where appropriate discussed in the DD of other more common carcinomas; if a molecularly defined carcinoma has cytopathology similar or part of the DD of a more common or other carcinoma, then it can be also discussed in that carcinoma's section)
  - 8.1.2.1: Introduction
  - 8.1.2.2: TFE3-rearranged renal cell carcinomas
  - 8.1.2.3: To be deleted - TFEB-altered renal cell carcinomas
  - 8.1.2.4: To be deleted - ELOC-mutated renal cell carcinoma
  - 8.1.2.5: To be deleted - Fumarate hydralase-deficient renal cell carcinoma
  - 8.1.2.6: To be deleted - Succinate dehydrogenase deficient renal cell carcinoma
  - 8.1.2.7: To be deleted - ALK rearranged renal cell carcinomas
  - 8.1.2.8: SMARCB1-deficient renal medullary carcinoma

WHO Reporting System for Kidney and Adrenal Gland Cytopathology

8.1.3: Paediatric renal tumours
- 8.1.3.1: Nephroblastoma
- 8.1.3.2: Rhabdoid tumor
- 8.1.3.3: Clear cell sarcoma
- 8.1.3.4: Rare malignant paediatric tumours

8.1.4: Tumours of the urinary tract
- 8.1.4.1: Introduction
- 8.1.4.2: Urothelial carcinoma
- 8.1.4.3: Squamous cell carcinoma
- 8.1.4.4: Adenocarcinoma

8.1.5: Tumours of the adrenal gland
- 8.1.5.1: Introduction
- 8.1.5.2: Adrenal cortical carcinoma
- 8.1.5.3: Neuroblastoma
- 8.1.5.4: Ganglioneuroma
- 8.1.5.5: Phaeochromocytoma (Paraganglioma and subtypes)

8.1.6: Haematolymphoid tumours of kidney and adrenal
- 8.1.6.1: Mature B-cell lymphomas (include extranodal MZL-MALT, DLBCL, plasmacytoma)
- 8.1.6.2: Juvenile xanthogranuloma

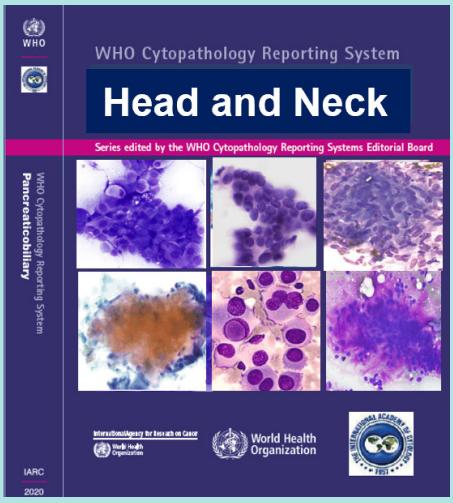
8.1.7: To be deleted - Mesenchymal tumours of the kidney and adrenal
- 8.1.7.1: To be deleted - Angiofibroma

8.1.8: Metastases from other sites
- 8.1.8.1: Metastatic tumours

8.1.9: Sample reports

9.0: Recommendations for Management Subsequent to Cytopathology Report Categories
- 9.0.0.1: Introduction

9.1: Management Options Recommended Subsequent to a Diagnostic Category Report
- 9.1.0.1: Category: Insufficient/Inadequate/Non-diagnostic
- 9.1.0.2: Category: Benign
- 9.1.0.4: Category: Low risk oncocytic renal neoplasms
- 9.1.0.3: Category: Atypical
- 9.1.0.5: Category: Suspicious of Malignancy
- 9.1.0.6: Category: Malignant



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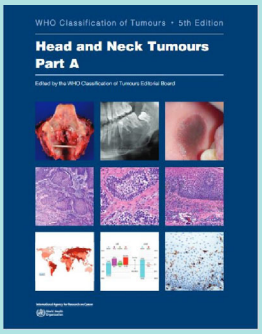
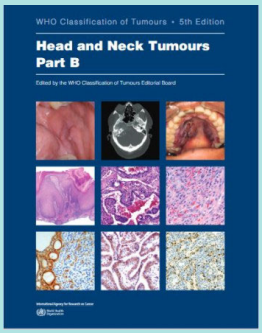


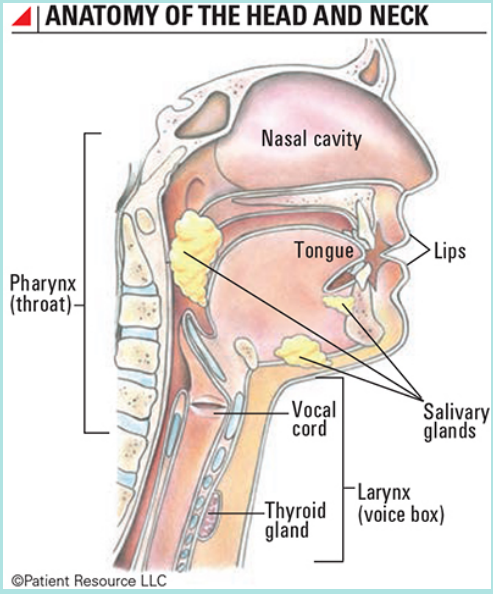


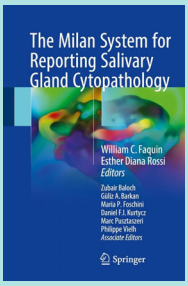
Part A

1. Nasal, paranasal, and skull base tumours
2. Nasopharyngeal tumours
3. Hypopharyngeal, laryngeal, tracheal, and parapharyngeal tumours
4. Salivary gland tumours
5. Oral cavity and mobile tongue tumours
6. Oropharyngeal tumours
7. Odontogenic and maxillofacial bone tumours

Part B

8. Ear tumours
9. Soft tissue tumours
10. Haematolymphoid proliferations and neoplasia
11. Melanocytic tumours
12. Tumours and tumour-like lesions of the neck and lymph nodes
13. Germ cell tumours
14. Metastasis
15. Neuroendocrine neoplasms and paraganglioma
16. Genetic tumour syndromes involving the head and neck



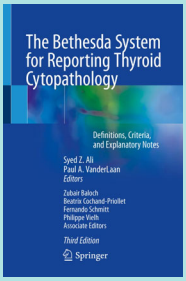


Diagnostic Category	ROM	Management
1: **Non-Diagnostic**	25% (0-67%)	Clinical and radiologic correlation or repeat FNA
2: **Non-Neoplastic**	10% (0-20%)	Clinical follow-up and radiologic correlation
3: **Atypia of Undetermined Significance (AUS)**	10-35%	Repeat FNA or surgery
4: **Neoplasm**		Surgery or clinical follow-up
i) **Benign**	<5% (0-13%)	
ii) Salivary Gland Neoplasm of Uncertain Malignant Potential (**SUMP**)	35% (0-100%)	
5: **Suspicious for Malignancy**	60% (0-100%)	Surgery
6: **Malignant**	90% (57-100%)	Surgery

/MilanSystem

Table 1. Bethesda System for Reporting Thyroid Cytopathology, third edition, 2023,[1] with the expected ranges for implied risk of malignancy, examples of diagnostic entities in each category, and clinical management options

Diagnostic category	Examples of diagnostic entities	Range of estimated ROM (%)	Clinical management options
Nondiagnostic	■ Cyst fluid only ■ Virtually acellular specimen ■ Obscuring blood, clotting artifacts, drying artifact, etc.	5–20%	Repeat FNA with ultrasound guidance
Benign	■ Consistent with FND (includes AN, CN, etc.) ■ Consistent with CLT in the proper clinical context ■ Consistent with granulomatous (subacute) thyroiditis	2–7%	Clinical and ultrasound follow-up
Atypia of undetermined significance (AUS)	AUS–nuclear type AUS–other	Overall 13–30% AUS–nuclear atypia: ROM 36–44% AUS–other: ROM 15–23%	Repeat FNA, molecular testing, diagnostic lobectomy, or surveillance
Follicular neoplasm (FN)	FN FN–oncocytic type	23–34%	Molecular testing, diagnostic lobectomy
Suspicious for malignancy (SFM)	■ Suspicious for PTC ■ Suspicious for MTC ■ Suspicious for metastatic carcinoma ■ Suspicious for lymphoma	67–83%	Molecular testing, lobectomy, or near-total thyroidectomy
Malignant	■ PTC ■ HGFCDTC ■ MTC ■ ANTC ■ SCC ■ Carcinoma with mixed features (specify) ■ Metastatic malignancy ■ NHL	97–100%	Lobectomy or near-total thyroidectomy



Diagnostic Categories for Head and Neck Cytopathology:

- Insufficient/Inadequate/Non-Diagnostic
- Benign
- Atypical
- Neoplasm of Uncertain Malignant Potential (NUMP)
- Suspicious for Malignancy
- Malignant

1.0: The WHO International System for Reporting Head and Neck Cytopathology

- 1.0.0.1: Introduction
- 1.0.0.2: The role of Head & Neck cytopathology
- 1.0.0.3: The integration of clinical, imaging and key FNAB cytopathological features with ancillary testing in a diagnostic approach
- 1.0.0.4: Paediatric cytopathology
- 1.0.0.5: Cystic lesions of the head and neck
- 1.0.0.6: Diagnostic categories and report structure
- 1.0.0.7: Risk of malignancy and diagnostic management recommendations

2.0: Sampling methods

- 2.0.0.1: FNAB techniques and specimen management
- 2.0.0.2: Ultrasound guidance of FNAB
- 2.0.0.3: Rapid on site evaluation450
- 2.0.0.4: Cell preparation methods

3.0: Ancillary Testing

- 3.0.0.1: Introduction: the role of ancillary testing
- 3.0.0.2: Flow cytometry
- 3.0.0.3: Immunocytochemistry
- 3.0.0.4: In situ hybridisation
- 3.0.0.5: Molecular testing

4.0: Insufficient/Inadequate/Non-diagnostic

- 4.0.0.1: Introduction
- 4.0.0.2: Definition
- 4.0.0.3: Discussion and background
- 4.0.0.4: Risk of malignancy and management recommendations
- 4.0.0.5: Sample Reports

5.0: Benign

5.0.0.1: Introduction
5.0.0.2: Definition
5.0.0.3: Discussion and background
5.0.0.4: Risk of malignancy and management recommendations
5.0.0.5: Sample Reports

5.1: Entities in the Benign Category:

5.1.1: HEAD &NECK
5.1.1.1: Acute and suppurative inflammation
5.1.1.2: Granulomatous inflammation
5.1.1.3: Cysts
5.1.1.3.1: Introduction
5.1.1.3.2: Ranula
5.1.1.3.3: Branchial cleft cyst
5.1.1.3.5: Thyroglossal duct cyst
5.1.1.3.6: Dermoid and teratoid cysts
5.1.1.3.7: Giant cell lesions and bone cysts
5.1.1.4: Epithelioid cell tumours
5.1.1.5: Granular cell tumour
5.1.1.6: Ectopic thyroid
5.1.1.7: Ameloblastoma

5.1.2: Skin
5.1.2.1: Pilomatricoma
5.1.2.2: Epithelial inclusion cyst
5.1.2.3: Trichilemmoma
5.1.2.4: Soft tissue
5.1.2.5: Adipocytic tumours
5.1.2.6: Spindle cell tumours
5.1.2.7: Haemangiomas and lymphangiomas
5.1.2.8: Myxoma
5.1.2.9: Rhabdomyoma
5.1.2.10: Bone and Cartilaginous tumours
5.1.2.11: Fibro-osseous dysplasias

5.1.3: Lymph nodes
5.1.3.1: Reactive lymphoid hyperplasias
5.1.3.2: Rosai Dorfman disease
5.1.3.3: Kikuchi's disease

5.1.4: Salivary Gland
5.1.4.1: Introduction
5.1.4.2: Cysts
5.1.4.3: Sialoadenitis/sialolithiasis/lymphoepitheilial sialadenitis/lymphoepithelial lesion
5.1.4.4: Canalicular adenoma
5.1.4.5: Mucocele
5.1.4.6: Pleomorphic adenoma
5.1.4.7: Warthin tumour
5.1.4.8: Oncocytoma

5.1.5: Thyroid
5.1.5.0: Introduction
5.1.5.1: Acute thyroiditis
5.1.5.2: Chronic lymphocytic thyroiditis
5.1.5.3: Granulomatous thyroiditis Reidel/IgG4-RD
5.1.5.4: Follicular nodular disease
5.1.5.5: Parathyroid neoplasms

6.0: Atypical

6.0.0.1: Introduction
6.0.0.2: Definition
6.0.0.3: Discussion and background
6.0.0.4: Risk of malignancy and diagnostic management recommendations
6.0.0.5: Sample reports

7.0: Head and Neck neoplasms of uncertain malignant potiential NUMP

7.0.0.1: Introduction
7.0.0.2: Definition
7.0.0.3: Discussion and background
7.0.0.4: Risk of malignancy and diagnostic management recommendations

7.1: Specific entities included in NUMP:

7.1.1: HEAD & NECK
7.1.1.1: Introduction
7.1.1.2: Spindle cell mesenchymal tumours:
7.1.1.2.1: Introduction
7.1.1.2.2: Solitary fibrous tumour
7.1.1.2.3: Low grade myofibroblastic sarcoma
7.1.1.2.4: Inflammatory myofibroblastic tumuor
7.1.1.3: Meningioma
7.1.1.4: Langerhans cell histiocytosis

7.1.2: SALIVARY GLAND
7.1.2.1: Introduction
7.1.2.2: Cellular oncocytic neoplasms
7.1.2.3: Clear cell neoplasms
7.1.2.4: Basaloid tumours
7.1.2.5: Myoepithelial neoplasms
7.1.2.6: Ceruminous adenoma of external auditory canal

7.1.3: THYROID
7.1.3.1: Introduction
7.1.3.2: Follicular neoplasms
7.1.3.2.1: Follicular adenoma and follicular carcinoma
7.1.3.2.2: Non-invasive follicular thyroid neoplasm with papillary-like nuclear features and invasive encapsulated follicular variant of papillary thyroid carcinoma
7.1.3.2.3: Follicular thyroid lesion of uncertain malignant potential & well differentiated tumour of uncertain malignant potential
7.1.3.3: Hyalinizing trabecular tumour
7.1.3.4: Oncocytic neoplasms
7.1.3.5: Sample Reports

8.0: Suspicous for malignancy

8.0.0.1: Introduction
8.0.0.2: Definition
8.0.0.3: Discussion and background
8.0.0.4: Risk of malignancy and management recommendations
8.0.0.5: Sample reports

WHO Reporting Systems in Cytopathology