

Welcoming the new, revisiting the old: a brief glance at cytopathology reporting systems for lung, pancreas, and thyroid

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This review addresses new reporting systems for lung and pancreatobiliary cytopathology as well as the most recent edition of The Bethesda Reporting System for Thyroid Cytopathology. The review spans past, present, and future aspects within the context of the intricate interplay between traditional morphological assessments and cutting-edge molecular diagnostics. For lung and pancreas, the authors discuss the evolution of reporting systems, emphasizing the bridge between past directives and more recent collaborative efforts of the International Academy of Cytology and the World Health Organization in shaping universal reporting systems. The review offers a brief overview of the structure of these novel systems, highlighting their strengths and pinpointing areas that require further refinement. For thyroid, the authors primarily focus on the third edition of The Bethesda System for Reporting Thyroid Cytopathology, also considering the two preceding editions. This review serves as an invaluable resource for cytopathologists, offering a panoramic view of the evolving landscape of cytopathology reporting and pointing out the integrative role of the cytopathologist in an era of rapid diagnostic and therapeutic advancements.

Key Words: Thyroid gland; Lung; Pancreas; Cytology; Review literature as topic

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Cytopathology has entered an exciting phase highly influenced by rapid advancements in molecular technologies. These developments have elevated the role of cytology in molecular diagnostics, enabling targeted therapies and personalized medicine. With these innovations comes the imperative for global standardization of organ-based reporting systems to ensure seamless integration of fast-paced developments into a cohesive framework that supports evolution of the field. These systems draw from insights and data documentation of previous reporting systems such as the Papanicolaou Society of Cytopathology (PSC) System [1] and the Japan Lung Cancer Society/Japanese Society of Clinical Cytology system [2], which are unified under the

foundational World Health Organization (WHO) pathology guidelines, tailored for worldwide application. This integration streamlines the practice of cytopathology, ensuring consistency and clarity across the discipline.

The International Academy of Cytology, in collaboration with the International Agency for Research on Cancer (IARC) and the WHO, has released in 2022 the inaugural editions of the WHO reporting systems for lung and pancreaticobiliary cytopathology. These pioneering resources are accessible at the WHO website and in print [3,4].

The introductory sections of the WHO lung and pancreaticobiliary reporting systems outline the essential elements of a cy-

topathology report and the role of cytopathology in a diagnostic workup. These sections also define the reporting categories, indicate the risk of malignancy (ROM) associated with each category based on available literature, and provide recommendations for additional diagnostic procedures.

Following the introduction, there is a detailed chapter in each guidance document on optimal sampling techniques for lung, pancreatic, and biliary tissue. Protocols to obtain lung samples include sputum collection, bronchial washings and brushes, bronchoalveolar lavage, and fine-needle aspiration (FNA) as guided by imaging, while those to obtain pancreatic and biliary samples include percutaneous or endoscopic ultrasound-guided FNA and biliary brushings. This section also discusses specimen triage and preparation, as well as the utility of ancillary tests.

Subsequent sections delve into individual diagnostic categories, providing definitions, context, suggested ROMs, and management recommendations, which are key elements of a solid reporting system. These sections also provide sample reports to promote standardized documentation, along with guidance to align with local practices and system constraints.

The WHO Cytopathology Blue Books also discuss differential diagnoses for a given pattern of cytopathological features and current best practices for ancillary testing to help ensure the systems are applicable globally, including in low- and middle-income countries where access to additional testing may be limited.

To increase consistency across the field of cytopathology, the third edition of The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) has been released in 2023. This recent update builds upon the 2007 and 2017 editions and upon a robust compendium of research and experience garnered through clinical application. While operating independently from the World Health Organization's reporting systems, the 2023 edition of the TBSRTC shared a similar objective to refine and harmonize cytopathological practices on an international scale.

In this review, our goal was to present a concise guide to the essential aspects of these reporting systems in practice. We highlight the most substantial modifications of categorization schemes that have been included in the recent updates to the lung, pancreaticobiliary, and thyroid cytopathology reporting systems. We also endeavored to identify and document the strengths and limitations of these reporting systems from the perspective of practicing cytopathologists to inform improvements for future editions.

LUNG

Pulmonary masses and nodules are increasingly recognized

by imaging techniques and subsequently targeted for cytologic and/or small-volume biopsy evaluation, responsible for the diagnosis of an estimated 70% of pulmonary malignancies and allowing disease staging [3]. In fact, lung cancer is mostly a time-sensitive condition, as a significant fraction of patients present with or rapidly progress to advanced stages, hampering a surgical approach and relying on cytological and histological samples to further determine potential therapies.

Rationale, historical background, and state of the art

In 1999, the PSC Task Force on Standards of Practice issued detailed guidelines for handling each type specimen obtained using lower-respiratory-exfoliative or FNA techniques and briefly outlined six recommended categories for reporting these samples (Fig. 1) [1,5,6]. The 1999 guidelines emphasized safety and efficiency and underlined that, despite the main use of diagnosis of malignancy, the guidelines could also be used to identify benign conditions [7].

The 2016 update of the guidelines proposed a new standardized terminology, recognizing that the lack of homogeneity in reporting could be hindering the clinical decision-making process [1]. The diagnostic criteria were refined, specific diagnoses/entities were listed, expected ROM rates were reported, and the categories were renamed and sequentially numbered (Fig. 1). The assessment of regional lymph nodes (mediastinal and hilar) was nested under the same classification system. Recommendations for ancillary studies were also included [1], primarily addressing the evaluation of predictive markers (such as programmed death-ligand 1 [PD-L1] and potential oncogenic genetic changes) using immunohistochemistry and molecular techniques. Institutional data [8] confirmed the overall ROM for each category and shed light on inconsistencies in overall diagnostic accuracy and ROM estimation across the various procedural approaches used to assess a given lesion.

The PSC System for Reporting Respiratory Cytology [9] was subsequently published in 2019. This atlas expanded the morphologic criteria and was supported by an extensive assortment of photographs and explanatory notes, sample reports, and updated ROM rates (stratified by primary lesion and nodal assessment). The directives for ancillary studies were included but indicated that PD-L1 testing lacked comprehensive validation and did not provide specific recommendations.

In 2022, the International Academy of Cytology and the IARC, which oversees the WHO Classification of Tumors, combined forces to develop an analogous series of WHO reporting systems for lung cytopathology. Indeed, the so-called WHO Blue Books

1999	2019	2022		
Papanicolaou Society of Cytopathology Guidelines	Papanicolaou Society of Cytopathology System for Reporting Respiratory Cytology	WHO Reporting System for Lung Cytopathology		
Categories	Categories	Categories	ROM	Management recommendations
Nondiagnostic	I. Nondiagnostic	Insufficient/inadequate/Nondiagnostic	43-53%	CLIN-IMG-MICRO correlation → MDT meeting → repeat FNA (± CNB)
Benign (specific lesions)	II. Atypical	Benign/negative for malignancy	19-64%	CLIN-IMG-MICRO correlation; if BENIGN → 3-6 months follow-up; if unclear → repeat FNA
Atypical cells present, probably benign	IIIa. Neoplasm, benign	Atypical	46-55%	CLIN-IMG-MICRO correlation → MDT meeting; if BENIGN → 3-6 months follow-up; if unclear → repeat FNA (+ ROSE ± CNB)
Atypical, suspicious for malignancy	IIIb. Neoplasm, undetermined malignant potential/ low-grade malignancy	Suspicious for malignancy	75-88%	CLIN-IMG-MICRO correlation → MDT meeting; if MALIGNANT → treatment; if unclear → repeat FNA (+ ROSE ± CNB)
Malignancy present	IV. Suspicious for malignancy	Malignant	87-100%	CLIN-IMG-MICRO correlation → MDT meeting; if MALIGNANT → treatment; if unclear → repeat FNA (+ ROSE ± CNB)
	V. Malignant			

Fig. 1. Lung cytopathology reporting: historical perspective and state of the art. CLIN-IMG-MICRO, clinical, imaging, and microbiological findings; CNB, core needle biopsy, including endobronchial biopsy; FNA, fine-needle aspiration biology; MDT, multidisciplinary team; ROSE, rapid onsite evaluation [1,5,6].

and the WHO cytopathology system are directly linked and are both offered in print and online forms. The main goal was to define a universal lexicon and specify criteria by which robust cytopathological diagnoses could be achieved worldwide, even by laboratories with limited resources. Five categories applicable to all types of specimens were established (Fig. 1; see also below). Under the banners of “Benign” and “Malignant,” the authors explained specific lesions or entities through subsections that echo the WHO Blue Books structure. Additional sections described best practices for specimen collection and handling, provided recommendations for ancillary testing (formally including PD-L1 determinations) and for management of each diagnostic category, emphasizing the role of multidisciplinary study and rapid onsite evaluation (ROSE) [3]. The five primary diagnostic categories are presented as follows.

Insufficient/inadequate/nondiagnostic

This category applies to specimens that cannot be reliably diagnosed due to inadequate cellularity, poor preparation, or obscuring factors. Each institution should resort to a single term to label this category and document the reasons for specimen insufficiency. The presence of any atypical cells upgrades the specimen to a higher category. The overall ROM for this category ranges from 40% to 60%; repeated sampling increases the sensitivity, especially of exfoliative specimens.

Benign

Specimens in this category show clear cytopathologic signs of

benign processes or neoplasms. It is essential to thoroughly compare these findings with imaging results; any disparities should be noted, with recommendations for further diagnostic steps, including a conservative approach, prompt reassessment of the morphological lesion, or (in such cases as an infection secondary to bronchial obstruction), surgical treatment. The ROM was projected to be 20% to 40%, and further assessment is necessary to refine this estimate.

Atypical

This category includes specimens displaying predominantly benign characteristics but featuring worrisome findings that raise the suspicion for malignancy, without sufficient evidence for conclusive diagnosis. These cases require correlation with clinical and imaging data and carry an ROM of 50% to 60%.

Suspicious for malignancy

Specimens that show features indicative of malignancy but lack conclusive evidence for a definitive diagnosis fall into this category. This category implies a degree of uncertainty while maintaining a high positive predictive value, with an ROM around 82%. Further investigation is typically warranted, and ancillary techniques can help refine the diagnosis.

Malignant

This definitive category is used when the specimen exhibits clear-cut features of malignancy without ambiguity; subclassification based on cytopathologic features and immunocytochem-

istry markers may also be undertaken. The ROM in this category exceeds 90%, and the diagnosis should be supported by clinical and imaging data to guide appropriate treatment.

Cytopathological practice

The *WHO Reporting System for Lung Cytopathology* reflects a convergence of principles from previous classifications and ongoing initiatives to address the challenges in lung cancer diagnosis. The framework is structured to document and interpret small-volume biopsies, standardize procedures, and stratify the ROM, the latter of which is particularly important given early detection can significantly impact treatment outcomes.

Faced with continuing instrument development, pathologists in the field must make deliberate efforts to adhere to the directives to reduce subjectivity and variability. The ROM should be considered with a critical outlook, and professionals should assume responsibility for institutional cytohistological correlation series, on whose account the ROM will be periodically revisited.

Future perspectives

Like so many other fields in pathology, the scientific knowledge of lung cancer is constantly evolving, not only with respect to basic science, but also with respect to clinical trial data that may quickly alter the standard of care; the WHO Reporting System must remain adaptable to this dynamic landscape. In particular, the emergence of liquid biopsies has the potential to provide deeper insights into the molecular profile of each tumor, while likely relying on morphological correlation for validation.

First, determination of PD-L1 in ethanol-fixed non-cellblock specimens should be validated through large-scale studies. Second, a more structured role could be carefully outlined for ROSE, potentially involving a dedicated and abbreviated classification, with consideration of the use of teletytopathology platforms, an invaluable resource for a growing number of institutions.

Digital pathology, artificial intelligence, and machine learning could streamline workflows by pre-selecting samples warranting examination and possibly identifying viral cytopathic effects or microorganisms. These measures may reduce the need for supplementary investigations that can consume both the often limited sample material and economic resources. In addition, subtle morphological changes that could otherwise be overlooked may be detected, enhancing accuracy and promoting consistency across categories.

PANCREAS

The *WHO Reporting System for Pancreaticobiliary Cytopathology* is part of a new series aligned with the fifth edition of the Classification of Digestive System Tumors [10,11]. This system standardizes reporting based on modifications of the 2015 PSC System [12]. The new system introduces seven categories, including “Pancreaticobiliary neoplasm: low-risk/grade” and “High-risk/grade,” based on a two-tiered stratification of cytological atypia. Notably, neuroendocrine tumors and solid pseudopapillary neoplasms are now in the “Malignant” category, while benign tumors like serous cystadenoma are classified as “Benign/Negative for malignancy.” The following sections offer a concise overview of these changes, providing insights into diagnostic categories, rationale for updates, and management implications.

Rationale, historical background, and state of the art

The *WHO Reporting System for Pancreaticobiliary Cytopathology* updates the 2015 PSC system for reporting Pancreaticobiliary Cytopathology [12]. Many entities have been reclassified in other categories in alignment with the *WHO Classification of Digestive System Tumors*. Ancillary studies like fluid biochemical assays, immunocytochemistry, fluorescent in situ hybridization (FISH), and next-generation sequencing (NGS) are essential in the diagnosis of pancreatic cysts and cases with suspicious morphology. Pancreatic FNA specimens and bile duct cytology have different ROMs owing to the inherent nature of the lesion and sampling techniques.

In the new system, there are seven categories compared to six in the PSC system. Tumors that were placed in the “Neoplastic: other” category like pancreatic mucinous neoplasm, ductal lesions, biliary and pancreatic intraepithelial neoplasia (PanIN) are placed in “Pancreaticobiliary neoplasm: low-risk/grade or high-risk/grade” based on the cytological atypia.

The seven diagnostic categories are as follows.

Insufficient/inadequate/nondiagnostic

This category has three options depending on the context and institutional practice. The categorization of tissue requires clinical and radiological correlation. If native tissue is sampled, it is prudent to categorize it as “Inadequate” rather than “Benign.” In contrast, even when extracellular mucin is devoid of epithelial cells, if the cyst fluid shows increased carcinoembryonic antigen (CEA) and corroborating radiological findings, it can be diagnostic. The ROM range for this category is 5%–25% [13]. Bile-duct stricture brushings have a higher ROM of 28%–69% due

to sampling bias.

Benign/negative for malignancy

This category combines the nomenclature of the PSC system and the *WHO Classification of Digestive System Tumors*. Either terminology can be used. These terms include both non-neoplastic entities such as pancreatitis, pseudocyst, and lymphoepithelial cyst and benign neoplasms such as serous cystadenoma and, rarely, schwannoma, or lymphangioma. The ROM is 0%–15% [13,14]. For bile-duct brushings, the ROM is 55%. This increased risk is due to the high threshold for malignancy leading to false negative cases.

Atypical

This category applies to cases that have architectural and cytological features that suggest more than a reactive process but for which there is insufficient evidence for placement in definite categories such as “Pancreaticobiliary neoplasm, low-risk/grade (PaN-low),” “Pancreaticobiliary neoplasm, high-risk/grade (PaN-high),” or “Malignant” [15]. Such limitations could be due to low cellularity, artifacts, or the inherent nature of the lesion. In cases of mass lesion in pancreas, the atypia can be due to reactive atypia in pancreatitis or poor sampling of malignant lesions. In cystic lesions, only a minority of the cases may judiciously be placed in this category, after utilization of integrated approach to place them in the specific “PaN-low” category. The ROM is 30%–40% for pancreatic FNA samples and 25%–61% for bile-duct brushings [13,16].

Pancreaticobiliary neoplasm, low risk/grade

Pancreaticobiliary neoplasm (low risk/grade) is a new category incorporating the remaining entities of PSC “Neoplastic: other” after exclusion of solid pseudopapillary neoplasm and neuroendocrine tumors. This category includes cystic neoplasms and intraductal neoplasms with low-grade epithelial atypia. The two-tiered stratification (i.e., low-grade and high-grade atypia) is similar to the histological classifications provided in the fifth edition of the *WHO Classification of Digestive System Tumors* [17]. The included entities are intraductal papillary mucinous neoplasm (IPMN) low-grade, mucinous cystic neoplasm low-grade, biliary intraepithelial neoplasia low-grade, PanIN low-grade, intraductal papillary neoplasm of bile duct low-grade, and low-grade spindle cell neoplasm.

In cystic neoplasms with mucin, the cellularity may be sparse with low- to intermediate-grade atypia [18]. The cells can be arranged in sheets and papillae. The background may show thick

colloid-like mucin. Testing the cyst fluid for elevated CEA (above 192 ng/mL) is useful to identify neoplastic mucinous cysts [19]. In addition, testing for *KRAS*, *GNAS*, and *RNF43* mutations in suspected cases of IPMN is advisable [20,21]. The estimated ROM for this category is 5%–20% [13]. The ROM for bile-duct brushings is not available.

Pancreaticobiliary neoplasm, high risk/grade

This category includes cystic neoplasms and intraductal neoplasms, as described above, that also display high-grade epithelial atypia (HGEA), as well as intraductal oncocytic papillary neoplasm and intraductal tubulopapillary neoplasm. High-grade dysplasia and invasive carcinoma can be difficult to distinguish based on cytology alone. An HGEA is defined as a cell smaller than a duodenal enterocyte (12 μ m) with high nucleus/cytoplasm ratio and chromatin abnormalities with or without necrosis [22]. Intermediate-grade dysplasia is placed in the histological “low-grade” group, creating a diagnostic dilemma. Mutation testing for *TP53*, *CDKN2A* (p16), and *SMAD4* deletion may indicate progression to malignancy [23,24]; p53 immunostaining (overexpression or null type) and loss of *SMAD4* may also aid in diagnosis. The estimated ROM for this category is 60%–95% [13].

Suspicious for malignancy

This category is used when the features are suspicious but not diagnostic of malignancy. This uncertainty could be due to low cellularity, difficulty in interpretation due to inflammation/stenting, or inadequate tissue for ancillary testing. This category may be used to reduce false-positive cases and when diagnostic features are seen in only a small number of fragments [25]. Consensus review and ancillary testing can help guide further management [26]. The ROM is 80%–100% for pancreatic FNAs and 74%–100% for bile-duct brushings [13].

Malignant

Pancreatic ductal adenocarcinoma is the most common pancreatic malignancy. Other tumors that may share overlapping morphology are acinar cell carcinoma, neuroendocrine carcinoma, and metastatic carcinoma, which must be distinguished by ancillary studies [27]. Neuroendocrine tumors and solid pseudopapillary neoplasms are included in this category in accordance with the fifth edition of the *WHO Classification of Digestive System Tumors*. False-positive results may occur due to florid reactive atypia in autoimmune pancreatitis and primary sclerosing cholangitis. Integrating ancillary studies such as FISH and NGS

will help guide further management [28]. The ROM is 99%–100% for positive pancreatic FNA and is 96%–100% for biliary tract cytology [13,16].

THYROID

FNA cytology plays a pivotal role in the management of thyroid nodules, reducing the need for unnecessary surgery. In 2010, TBSRTC introduced a six-tiered system to categorize thyroid FNA findings and their associated ROM [29], based on the proceedings of the October 2007 National Cancer Institute Thyroid FNA State of the Science Conference in Bethesda, Maryland [30].

The third edition of the TBSRTC, released in 2023, further refines these categories, emphasizing clarity in reporting using explicit category names. The 2023 TBSRTC updates the ROM based on recent large-scale studies and responds to the ambiguous ROM associated with indeterminate diagnoses, not distinguished despite molecular testing.

Rationale, historical background, and state of the art

In 1996, the PSC Task Force on Standards of Practice first released guidelines [30] pertaining to the evaluation of thyroid nodules by FNA. The document summarized technical matters, addressed interdisciplinary approaches, and proposed four ten-

tative diagnostic groups (Fig. 2) [29,31-33].

In 2010, the proposed TBSRTC (six-tiered system) (Fig. 2) was comprehensively explained and, regardless of being a first edition of the classification, attempted to establish the ROM of each category. The reporting system was globally acclaimed across medical specialties and readily adapted to the various national settings [34].

In 2018, a second edition of TBSRTC was published [32], in which the nomenclature (Fig. 2) and general criteria remained largely unchanged while embracing a role for molecular pathology. The tiered ROMs were recalculated based on pooled data from multiple cyto-histological correlation series published after 2010, with an effort to forecast the ROM for the newly distinguished noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP). Additionally, characterization of the type of atypia observed in Atypia of Undetermined Significance/Follicular Lesion of Undetermined Significance (AUS/FLUS) was encouraged, loosely into classifiers of “cytologic,” “architectural,” “cytologic and architectural,” “Hürthle cell aspirates,” “not other specified,” and “atypical lymphoid cells.”

In 2023, the third edition of the TBSRTC was released [33,35], reflecting the continuous effort to integrate clinical perspectives and data from imaging and genetic studies. The 2023 TBSRTC simplified the diagnostic criteria and terminology (Fig. 2) and

	1996	2010	2017	2023
	Papanicolaou Society of Cytopathology Guidelines	The Bethesda System for Reporting Thyroid Cytopathology		
		1st edition	2nd edition	3rd edition
Diagnostic groups		Categories ROM	Categories ROM	Categories ROM (adults) ROM (pediatric) Management recommendations (underlined for pediatric population)
Benign non-neoplastic lesions		ND / U -	ND / U 5-10%	ND 5-20% 0-33% <u>Repeat FNA (+ US)</u>
Cellular follicular lesions		B 0-3%	B 0-3%	B 2-7% 0-27% <u>Follow-up (CLIN + US)</u>
Hürthle cell neoplasm		AUS / FLUS ~5-15%	AUS / FLUS ~10-30%	AUS 13-30% 11-54% <u>Repeat FNA or molecular testing or surgery (lobectomy) or surveillance</u>
Malignant		FN / SFN 15-30%	FN / SFN 25-40%	FN 23-34% 28-100% Molecular testing or <u>surgery (lobectomy)</u>
		SM 60-75%	SM 50-75%	SM 67-83% 40-100% Molecular testing or <u>surgery (lobectomy vs. thyroidectomy)</u>
		M 97-99%	M 97-99%	M 97-100% 86-100% <u>Surgery (lobectomy vs. thyroidectomy)</u>

Fig. 2. Thyroid cytopathology reporting: historical perspective and state of the art [29,31-33]. ND, nondiagnostic; U, unsatisfactory; B, benign; AUS, atypia of undetermined significance; FLUS, follicular lesion of undetermined significance; FN, follicular neoplasm; SFN, suspicious for follicular neoplasm; SM, suspicious for malignancy; M, malignant; FNA, fine-needle aspiration; US, ultrasound; CLIN, clinical.

aligned them with the 2022 WHO Thyroid Tumor Classification [36] by adopting updated histopathological nomenclature and discarding outdated terms like “Hürthle cell.” This 2023 edition continues to differentiate atypia on the basis of nuclear or architectural patterns, reflecting their heterogeneous implications for the ROM, and distinguishing the qualifiers of “atypia of undetermined significance” into “nuclear atypia” and “other.” The ROMs were revised and stratified by adult and pediatric age, and the bias introduced by NIFTP was acknowledged, with an estimated projected percent reduction of the ROM by category. New sections offer insights into radiologic correlations, molecular diagnostics, and pediatric-specific management.

Cytopathology practice

Given TBSRTC is among the most established cytopathology reporting systems, it is commonly referenced by the many disciplines encompassed by thyroidology. It provides a standardized language for communication clarity and consistency as pathologists can quickly craft a detailed report that conveys their reasoning without concern for potential interpretation bias, and intra- and interdepartmental datasets can be evaluated across institutions or even countries and continents. Use of the TBSRTC also contributes to a solid stratification and management, by serving as a blueprint to guide multidisciplinary decisions. The six tiers can serve as a helpful starting point for pathologists faced with challenging cases, allowing them to approach report drafting considering the clinical outcome first, rather than focusing solely on labeling a diagnosis.

The system is not free from criticism. As expected for any non-dichotomic classification (benign versus malignant), categories that are less determinate (grey zones) can become mired in uncertainty; some of the uncertainty can be resolved by molecular pathology, but this technique is not available at many institutions. In addition, the overlap between some categories complicates a precise ROM calculation and selection of the most appropriate management. The ROM data stem from retrospective studies with a selection bias (i.e., lesions undergoing surgery), and tissue samples are obtained from very diverse populations and frequently from tertiary institutions, with significant variability in the criteria applied by cytopathologists and surgical pathologists, and questionable histological correlation with aspirated nodules [34].

In this context, the contrast between Asian (namely Korean) and Western settings must be addressed. As reported in the literature, the former population is enriched for the conventional form of papillary thyroid carcinoma (PTC), allowing strict nu-

clear criteria assessment and targeted molecular *BRAF* V600E testing in cytology samples without loss of sensitivity. On the other hand, Western practices tend to be less conservative to not underdiagnose so-called RAS-like neoplasms and, in some instances, rely on broader molecular panels or even diagnostic lobectomy/thyroidectomy; this approach leads to surgical series filled with low-grade neoplasms that could be successfully managed through watchful monitoring, as established in Asian settings. These studies also underline the burden on healthcare systems stemming from the evaluation of minute nodules (< 1 cm in diameter) without overt clinical or radiological malignant features, which cytopathology teams should strongly advise against in multidisciplinary settings [37-41].

Future perspectives

A consistent classification scheme should be revised periodically to address new information. In particular, the ROMs merit an update, especially with regard to stratification for adult and pediatric ages and the advent of entities like NIFTP. Moreover, several authors have noted that the “Follicular Neoplasm” category could be improved by further subdivision to account for the presence of nuclear features of PTC [42].

Novel molecular data are frequently published and should be incorporated into cytology classification schemes, paving the way for tailored approaches. Special efforts should be devoted to developing inexpensive surrogate markers for actionable oncogenic variants and morphologic techniques with a high positive predictive value to identify high-risk lesions.

Finally, digital pathology, artificial intelligence, and machine learning are poised to assume a more substantial—synergistic—role in the future. Potential applications may include automating triage tasks in centers with high workloads or limited staff potential, as well as identifying subtle nuclear features and performing overall pattern analysis to aid pathologists in faster and more accurate diagnoses, which may be particularly valuable in cases with artifacts or processing issues.

Ethics Statement

Not applicable.

Availability of Data and Material

Data sharing not applicable to this article as no datasets were generated or analyzed during the study.

Code Availability

Not applicable.

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Conflicts of Interest

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