HARVARD MEDICAL SCHOOL

Laboratory Quality Assurance

(Through the Lens of the Bethesda System for Reporting Thyroid Cytopathology)

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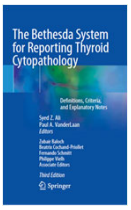

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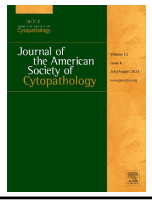
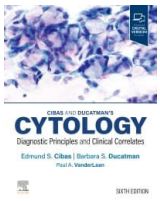
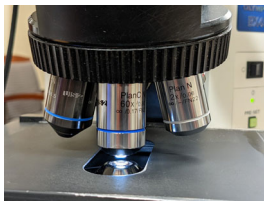
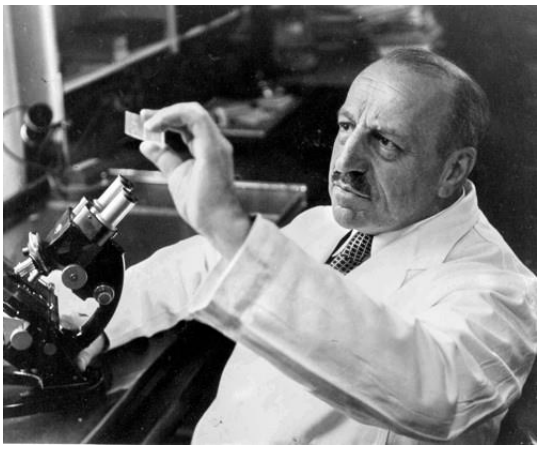
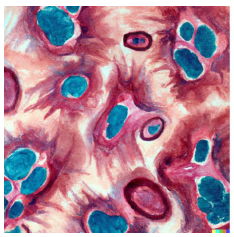


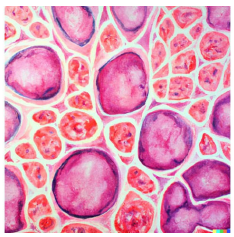
ARE YOU A GOOD CYTOPATHOLOGIST?

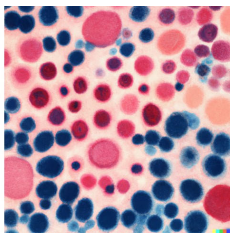






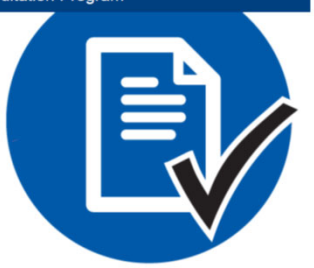






Cytopathology Checklist

CAP Accreditation Program



CYP.00125 **PT Participation - Gynecologic Cytopathology** **Phase II**

For laboratories subject to US regulations that perform gynecologic cytopathology, the laboratory and all individuals who examine gynecologic preparations participate in the CAP Gynecologic Cytology PT Program (PAP PT) or another proficiency testing program in gynecologic cytopathology approved by the Centers for Medicare and Medicaid Services (CMS).

CYP.06850 **Correlation of Results - Non-gynecologic Cytopathology** **Phase II**

The cytologic diagnoses for non-gynecologic cytopathology cases are correlated with the results of specialized studies (eg, molecular studies, immunocytochemistry).

CYP.07675 **Correlation of Results - Non-Gynecologic Cytopathology** **Phase II**

Non-gynecologic cytopathology findings are correlated with histological and clinical findings, when appropriate.

Clinical Laboratory Improvement Amendments (CLIA)

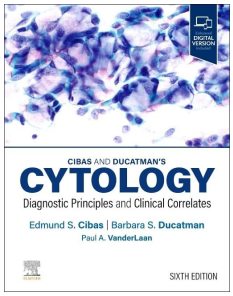
EXPLORE TOPICS

SEARCH

CLIA '88

ANNUAL STATISTICS MUST DOCUMENT:

- The number of cytology cases examined
- The number of specimens by specimen type (e.g., urine, sputum, etc.)
- The volume of cases by diagnosis (e.g., negative, atypical, suspicious, positive)
- The number of unsatisfactory cases
- The number of Pap tests with discrepant histologic results
- The number of negative Pap tests that were reclassified as abnormal
- The number of Paps reported as HSIL, adenocarcinoma, or other malignant neoplasm with no histologic follow-up



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Laboratory Management
PAUL A. VANDERLAAN AND EDMUND S. CIBAS

Can laboratory statistics be used to ensure practice patterns are in line with accepted norms?

REVIEW

Quality Metrics to Assess Cytopathology Practice Patterns: Focus on Thyroid Fine-Needle Aspiration Cytology

Paul A. Vander Laan, MD, PhD

For a cytology laboratory, performance metrics should be chosen based on 3 key features. The measures should:

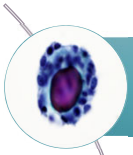
(1) be based on data that are relatively easily obtained,

(2) monitor aspects of practice that can impact patient care,

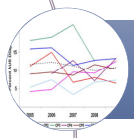
(3) provide information to help explain cytologist practice patterns, hopefully with insights as how to correct any values that might fall outside standard practice norms.

AJSP: Reviews & Reports 2022;27: 154–157

Key Cytopathology Quality Measures

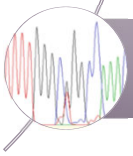


Adhere to established diagnostic criteria

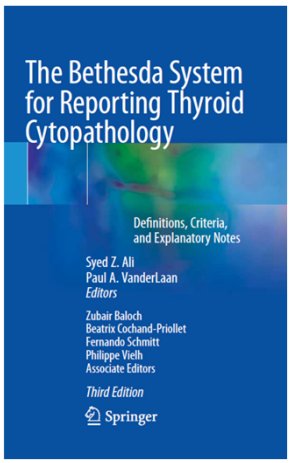


Monitoring diagnostic category utilization rates

Surgical follow up → local ROM



Incorporate molecular testing results



Criteria

Specimens are moderately to markedly cellular.
The sample consists exclusively (or almost exclusively) of **oncocytes**:

- Abundant finely granular cytoplasm (blue or gray-pink with Romanowsky stains, green with Papanicolaou, pink with hematoxylin and eosin).
- Enlarged, central or eccentrically located, round nucleus.
- Prominent nucleolus.
- Small oncocytes with high nuclear/cytoplasmic (N/C) ratio.
- Large oncocytes with at least 2× variability in nuclear size.
- Oncocytes can be dispersed as isolated cells, arranged in sheets, or crowded groups.
- Binucleation is fairly common.
- There is usually little or no colloid.
- There are virtually no lymphocytes (excluding blood elements) or plasma cells.
- Transgressing vessels are present in some cases as well as intracytoplasmic "colloid" inclusions (lumens) [22].

Explanatory Notes

The FN-OFN aspirate is at least moderately cellular (Fig. 6.1), and excluding blood elements, is composed almost exclusively of oncocytes (Fig. 6.2) [8, 23–26]. Sparsely cellular samples do not qualify for this interpretation, and a diagnosis of AUS should be considered in this scenario instead. A small number of benign follicular cells may be present, but this is uncommon and usually represents sampling of the adjacent thyroid tissue. Similarly, lymphocytes are usually absent or rare. The oncocytes are often dispersed as isolated cells (Fig. 6.3) or as irregular three-dimensional groups (Fig. 6.2) [25, 26]. Oncocytic cells often show atypia, of which there are two dominant types. The atypia can be in the form of very large cells with

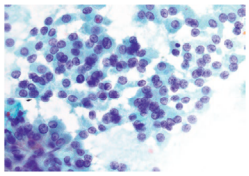


Fig. 6.1 Follicular neoplasm (oncocytic follicular neoplasm). The aspirate is hypercellular and consists of oncocytes of variable size arranged as isolated cells and in crowded groups; colloid is absent (smear, Papanicolaou stain)

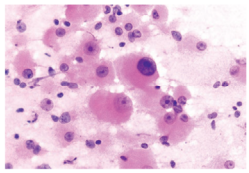


Fig. 6.2 Follicular neoplasm (oncocytic follicular neoplasm). The aspirate consists of a pure population of oncocytes with variation in cell size. The background lacks colloid and lymphocytes (smear, modified H&E stain)

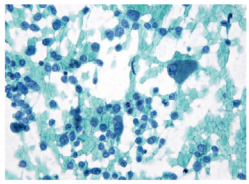


Fig. 6.3 Follicular neoplasm (oncocytic follicular neoplasm). The aspirate is cellular and consists exclusively of oncocytes in an isolated cell pattern simulating medullary thyroid carcinoma. An intranuclear pseudoinclusion is also observed (smear, Papanicolaou stain)

abundant granular cytoplasm that demonstrate at least twofold variability in nuclear size (Figs. 6.4 and 6.5) or relatively smaller oncocytes notable for less abundant granular cytoplasm and a higher nuclear to cytoplasmic ratio than the former (Figs. 6.6 and 6.7) [19, 27, 28]. Admixtures of small and large oncocytes are seen in some cases (Figs. 6.8 and 6.9). Importantly, oncocytic atypia by itself is an unreliable feature for the diagnosis, since very marked hyperchromasia, anisonucleosis, and nuclear membrane irregularity of oncocytes can be seen in MNG and LT [8]. Cellular cases lacking oncocytic atypia are suggestive of a benign nodule. Colloid is usually scant or absent, although a rare subset of oncocytic carcinomas with colloid has been described [28, 29]. Transgressing vessels are present in some cases and strongly support the diagnosis of a neoplasm over a non-neoplastic/metaplastic proliferation (Figs. 6.10 and 6.11) [22].

When an aspirate has all (or most) of the aforementioned features, the diagnosis of FN-OFN is straightforward. Problems arise with regard to: (1) the minimum necessary criteria for the diagnosis, (2) the best way to handle oncocytic proliferations in a patient with MNG or LT, and (3) the distinction from

Diagnostic Categories

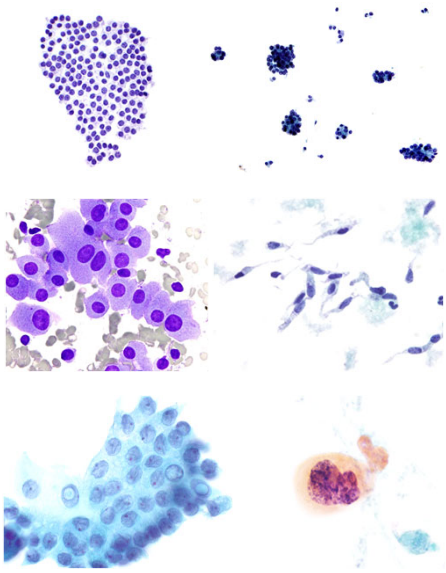
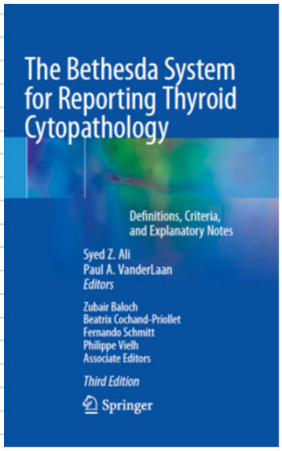
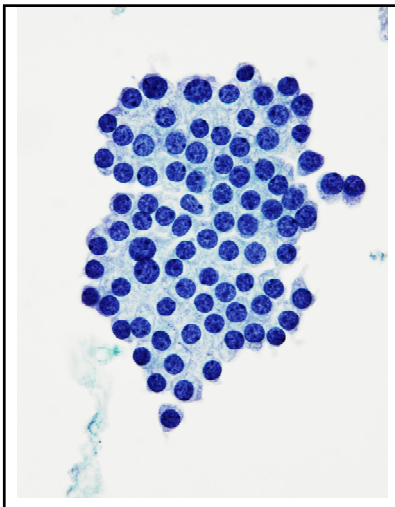
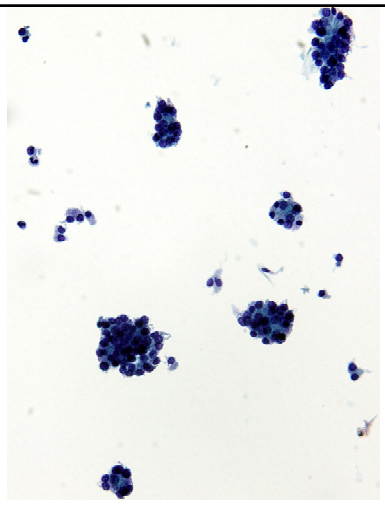


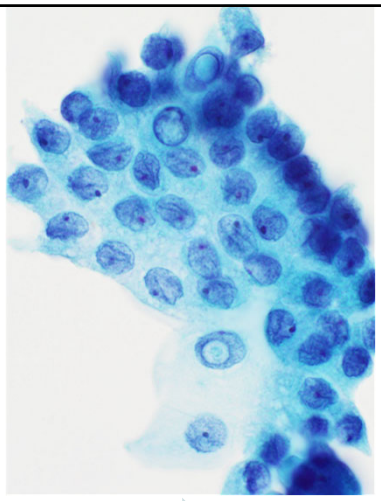
Table 1.1 The Bethesda System for Reporting Thyroid Cytopathology; diagnostic categories

I. Nondiagnostic
Cyst fluid only
Virtually acellular specimen
Other (obscuring blood, clotting artifact, drying artifact, etc.)
II. Benign
Consistent with follicular nodular disease (includes adenomatoid nodule, colloid nodule, etc.)
Consistent with chronic lymphocytic (Hashimoto) thyroiditis in the proper clinical context
Consistent with granulomatous (subacute) thyroiditis
Other
III. Atypia of Undetermined Significance
Specify if AUS-nuclear atypia or AUS-other
IV. Follicular Neoplasm
Specify if oncocytic (Hürthle cell) type
V. Suspicious for Malignancy
Suspicious for papillary thyroid carcinoma
Suspicious for medullary thyroid carcinoma
Suspicious for metastatic carcinoma
Suspicious for lymphoma
Other
VI. Malignant
Papillary thyroid carcinoma
High-grade follicular cell-derived non-anaplastic thyroid carcinoma
Medullary thyroid carcinoma
Undifferentiated (anaplastic) carcinoma
Squamous cell carcinoma
Carcinoma with mixed features (specify)
Metastatic malignancy
Non-Hodgkin lymphoma
Other









Benign → AUS → Follicular Neoplasm → Suspicious for Malignancy → Malignant

Categorical data!

REVIEW

Quality Metrics to Assess Cytopathology Practice Patterns: Focus on Thyroid Fine-Needle Aspiration Cytology

Paul A. Vander Laan, MD, PhD

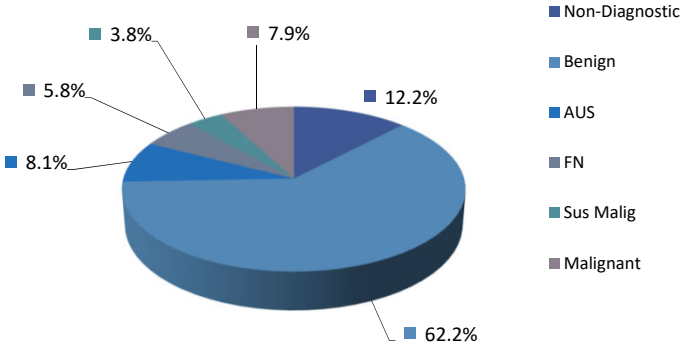
TABLE 1. Summary of Potential Cytology Laboratory Performance Metrics for Monitoring Thyroid FNA Specimens

Performance Metric	Example	Strengths	Limitations
Diagnostic category utilization rate	AUS rate, 12.2% (upper limit 10%)	+ Straightforward metric + Easy to calculate + Component of other more advanced metrics	− May not explain *why* practice deviates from norms − May be unduly impacted by low specimen volumes
Diagnostic category ratios	AUS:M ratio, 2.8 (upper limit, 3.0)	+ Straightforward metric + Easy to calculate + Corrects for local prevalence of disease	− Lacks widespread validation − Can introduce additional source of error/variance − May not explain *why* practice deviates from norms
Surgical outcome data	AUS ROM, 38% (expected range, 20%–30%)	+ Gold standard + Provides ultimate cytologic-histologic correlation + Enables local ROM calculation	− Not all nodules are resected (verification bias) − Subjectivity on resection specimen classification − Temporal gap between FNA and resection (lagging indicator) − Data collection labor intensive
Combined diagnostic category rate/ratios with molecular testing results	High AUS rate (18%) with low-molecular- testing abnormal rate	+ Includes data from larger number of cases + Usually binary result for molecular testing + May provide insights into practice patterns	− Relies on surrogate end points − Inferior to gold standard of surgical outcome data − New metric, additional validation needed

Review Article *Cancer Cytopathol* 2020;128:238-249.

Differences in Surgical Resection Rate and Risk of Malignancy in Thyroid Cytopathology Practice Between Western and Asian Countries: A Systematic Review and Meta-Analysis

Huy Gia Vuong, MD, PhD[1]; Hanh Thi Tuyet Ngo, MD, PhD[2]; Andrey Bychkov, MD, PhD[3,4]; Chan Kwon Jung, MD, PhD[5]; Trang Huyen Vu, MD[6]; Kim Bach Lu, MD[6]; Kennichi Kakudo, MD, PhD[7]; and Tetsuo Kondo, MD, PhD[1]

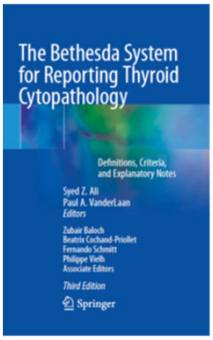


n=145,066 FNAs (38 studies; 22 west,16 east)

TABLE 3. Resection Rate and Risk of Malignancy for 6 Categories of The Bethesda System for Reporting Thyroid Cytopathology in Western and Asian Series

FNA Category	Pooled Proportion (95% CI), % Western Series (n = 22)	Asian Series (n = 16)	P[a]
Nondiagnostic			
Frequency	11.9 (9.1-14.7)	12.6 (6.7-18.5)	.827
RR	14.9 (11.4-18.5)	11.5 (7.8-15.2)	.896
ROM	13.2 (9.6-16.7)	26.5 (16.4-36.6)	.151
Benign			
Frequency	64.2 (60.0-68.4)	59.8 (51.6-67.9)	.353
RR	11.0 (8.4-13.5)	16.0 (8.3-23.6)	.235
ROM	4.1 (2.8-5.4)	13.8 (9.0-18.6)	**.001**
AUS/FLUS			
Frequency	7.7 (5.1-10.2)	8.4 (5.5-11.4)	.647
RR	40.5 (32.2-48.8)	29.5 (21.0-38.0)	.354
ROM	21.5 (17.0-26.0)	45.0 (33.4-56.5)	**.001**
FN/SFN			
Frequency	7.9 (5.7-10.1)	3.5 (1.9-5.1)	**.008**
RR	63.4 (55.6-71.1)	55.5 (46.2-64.8)	.078
ROM	27.3 (24.4-30.2)	32.8 (27.5-38.1)	.335
Suspicious for malignancy			
Frequency	3.3 (2.6-4.1)	4.3 (2.6-6.1)	.291
RR	72.6 (65.4-79.9)	65.4 (56.4-74.4)	.310
ROM	75.1 (69.8-80.4)	88.1 (82.8-93.4)	**.033**
Malignant			
Frequency	4.9 (3.8-6.0)	10.9 (7.1-14.7)	**.007**
RR	74.8 (68.2-81.5)	68.6 (58.3-78.9)	.314
ROM	99.2 (98.8-99.5)	98.6 (97.6-99.5)	.633

Abbreviations: AUS/FLUS, atypia of undetermined significance/follicular lesion of undetermined significance; FNA, fine needle aspiration; FN/SFN, follicular neoplasm/suspicious for follicular neoplasm; ROM, risk of malignancy; RR, resection rate.



Explanatory Notes

AUS usage varies widely; this interpretation has been reported to account for as little as 1% to over 20% of thyroid FNAs [3]. Many initial studies of AUS were retrospective, with pre-TBSRTC terminology retrofitted to TBSRTC categories. Despite efforts to define this category and provide specific criteria, AUS has, at best, only fair reproducibility [22, 23]. A provisional goal of limiting AUS interpretations to approximately 7% of all thyroid FNAB interpretations was proposed in the first edition of TBSRTC atlas [1]. Since many laboratories struggled to achieve this figure, an upper limit of 10% was adopted as a more achievable target in the second edition and remains a reasonable figure [27]. Additionally, it has also been proposed that the AUS:Malignant ratio may be a useful laboratory quality measure that should not exceed 3.0 [43]. Other quality measures involving the AUS rate of the overall laboratory or individual practitioners have been proposed as well, including correlation of AUS rates with molecular testing outcomes [44].

TBSRTC recommends subclassification of AUS to improve risk stratification of malignancy and enable guidance for the next step in patient management: repeat

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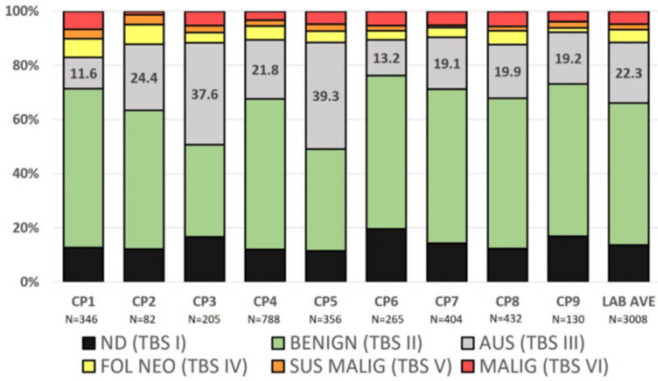
journal homepage: www.jascyto.org/

Molecular testing results as a quality metric for evaluating cytopathologists' utilization of the atypia of undetermined significance category for thyroid nodule fine-needle aspirations

Paul A. VanderLaan, MD, PhD*, Michiya Nishino, MD, PhD



The Atypia of Undetermined Significance/Follicular Lesion of Undetermined Significance:Malignant Ratio

A Proposed Performance Measure for Reporting in The Bethesda System for Thyroid Cytopathology

Jeffrey F. Krane, MD, PhD[1]; Paul A. VanderLaan, MD, PhD[1]; William C. Faquin, MD, PhD[2]; and Andrew A. Renshaw, MD[3]

Cancer Cytopathology April 25, 2012

Utility of using *internally derived statistics*

~ ASCUS:SIL ratio Pap Smears

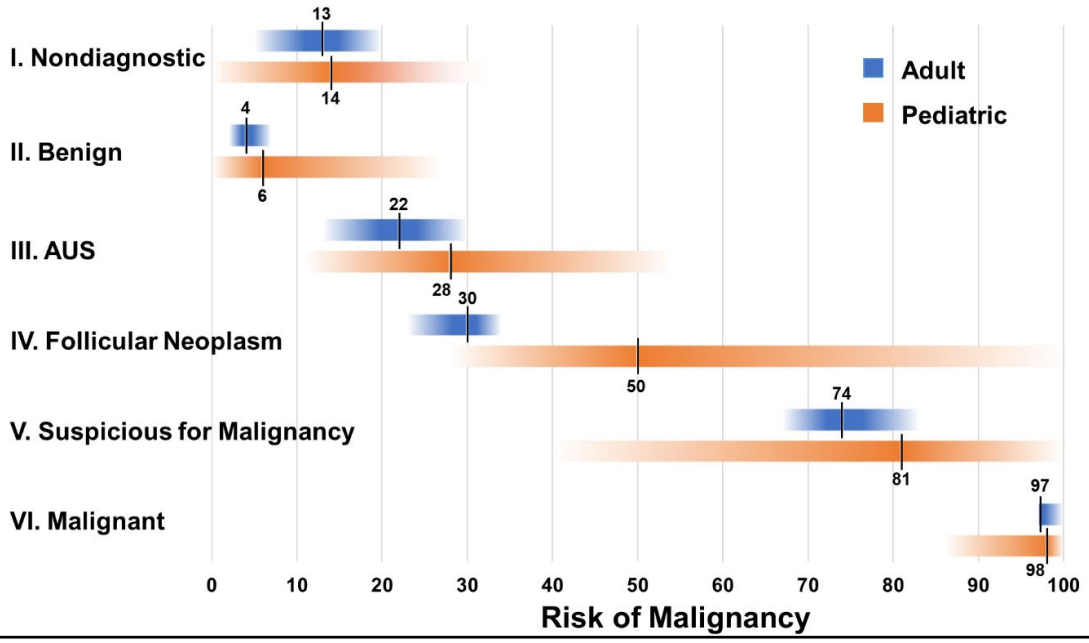
AUS:M ≤ 3.0

Table 4. Potential Performance Measures and Laboratory Data

	Ratios		Category			
Study	AUS:M	(AUS+SusF+SUS):M	AUS, %	SusF, %	SUS, %	Malignant, %
Jo 2010[5]	0.5	2.2	3.4	9.7	2.3	7.0
Theoharis 2009[13]	0.6	1.9	3.0	5.5	1.3	5.2
Kim 2011[6]	1.0	1.5	16.3	1.2	6.2	16.2
Renshaw 2010[12]	1.8	4.3	7.7	8.6	1.8	4.2
VanderLaan 2011[14]	2.1	3.8	10.9	4.2	4.5	5.2
Faquin (unpublished data)	2.6	3.9	10.0	2.0	3.2	3.9
Nayar & Ivanovic 2009[9]	3.6	5.2	17.8	5.9	1.9	4.9
Marchevsky 2010[8]	4.9	6.8	9.8	1.5	2.3	2.0

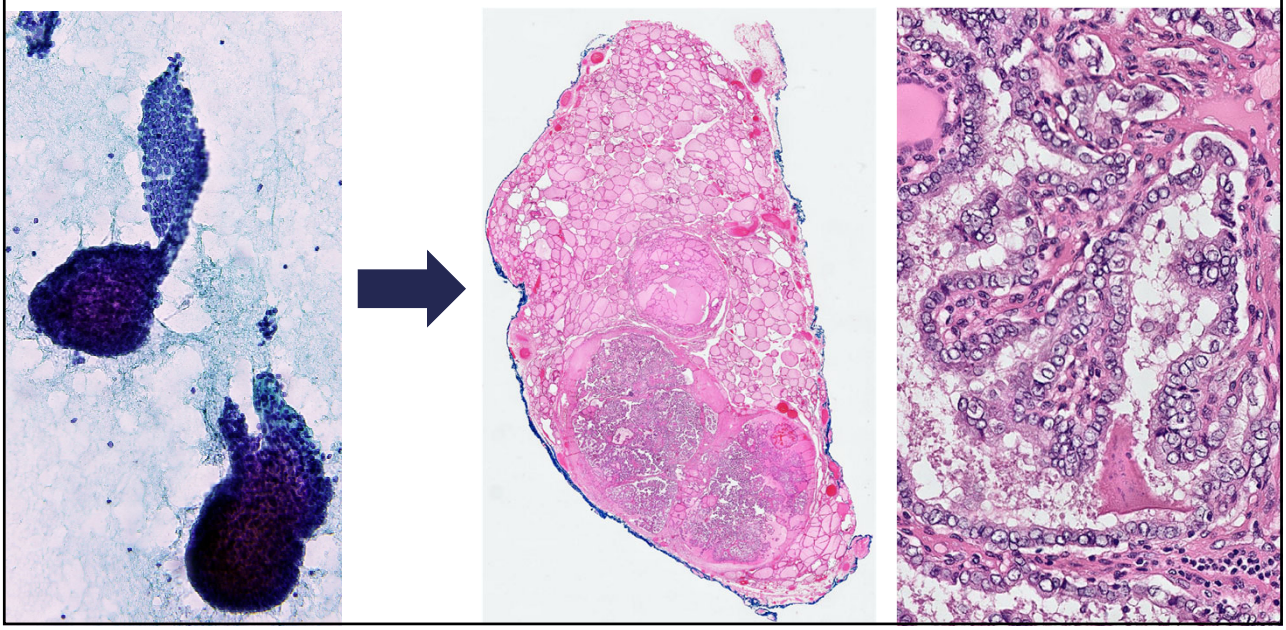
Abbreviations: AUS, atypia of undetermined significance/follicular lesion of undetermined significance; M, malignant; SUS, suspicious for malignancy; SusF, suspicious for a follicular or Hurthle cell neoplasm.

TBSRTC 3rd ed Risk of Malignancy: both means and expected ranges



VanderLaan and Ali. *Diagn Histopathol.* 2023;29(11):499-502

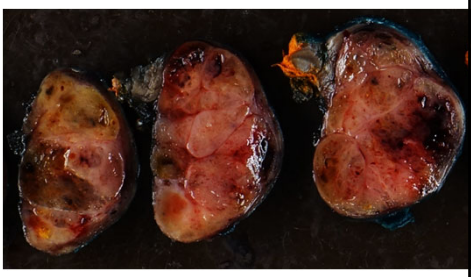
ROM Gold standard: surgical resection correlation

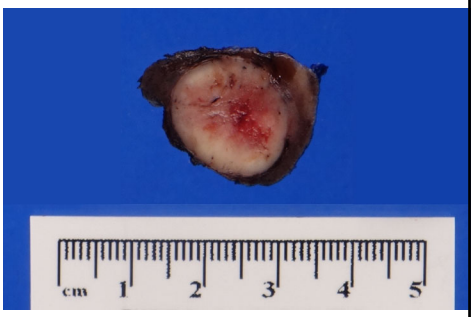


Issues with surgical end points

- Not all nodules are resected (especially Thyroid - AUS)
  - ✓ Verification bias
- Additional layer of diagnostic subjectivity by the surgical pathologist
  - ✓ Multiple degrees of freedom to control
- Temporal gap between FNA and resection
  - ✓ Lagging outcome indicator
- Surgical outcome data is a labor-intensive manual process
  - ✓ Worth the effort?

Are there viable alternatives?





Molecular testing in cytopathology: a suitable surrogate endpoint?

U.S. FOOD & DRUG ADMINISTRATION

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Home / About FDA / FDA Facts: Biomarkers and Surrogate Endpoints

FDA Facts: Biomarkers and Surrogate Endpoints

Surrogate endpoints vs. clinical outcomes in clinical trials:

- ✓ when the clinical outcomes might take a very long time to study
- ✓ where the clinical benefit of the surrogate endpoint is well established in disease
  - ➢ Must predict or correlate with clinical outcome

→Between 2010 and 2012, the FDA approved 45 percent of new drugs on the basis of a surrogate endpoint.

www.fda.gov/about-fda/innovation-fda/fda-facts-biomarkers-and-surrogate-endpoints

Molecular testing – suitable surrogate endpoint?

Advantages:

TAT: Molecular testing done concurrently (or reflexively) with cytology.

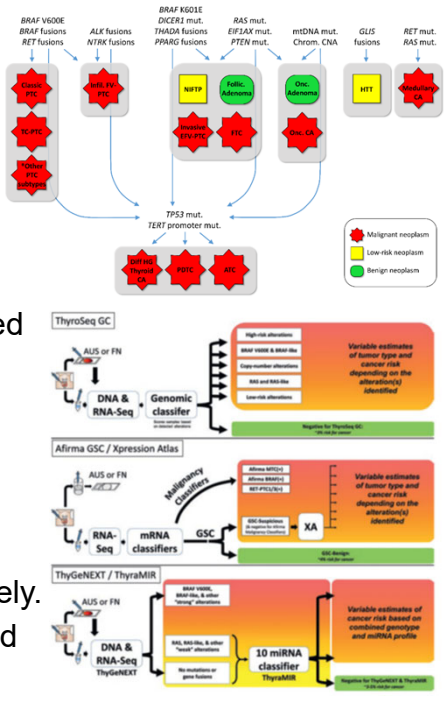
Accuracy: Many genomic alterations are highly correlated with malignancy/neoplasia.

Disadvantages:

Cost: Molecular tests can be expensive, and their widespread use may increase healthcare costs.

Technical Expertise: Adequate technical expertise is required to perform and interpret molecular tests accurately.

Standardization: Standardization of testing protocols and reporting guidelines is essential for consistent results.



Nishino M et al. Ch 14. The Bethesda System for Reporting Thyroid Cytopathology 3rd ed.

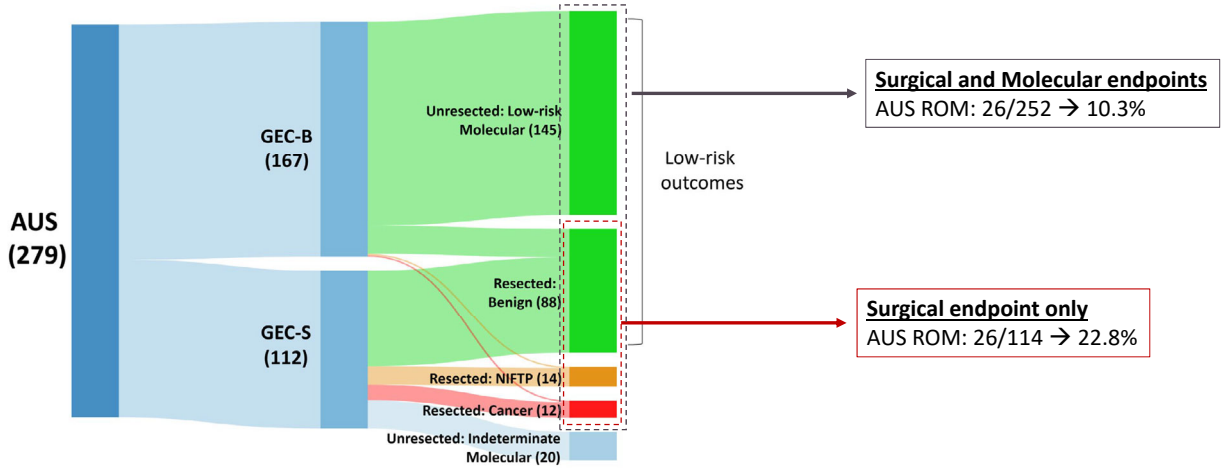
Original Article

Cancer Cytopathol 2021;129:947-955.

Thyroid molecular testing provides more accurate ROMs

Combined Molecular and Histologic End Points Inform Cancer Risk Estimates for Thyroid Nodules Classified as Atypia of Undetermined Significance

Allison M. Onken, MD [1]; Paul A. VanderLaan, MD, PhD [1]; James V. Hennessey, MD[2]; Pamela Hartzband, MD[2]; and Michiya Nishino, MD, PhD [1]



Journal of the American Society of Cytopathology (2024) 13, 23–32

Available online at www.sciencedirect.com

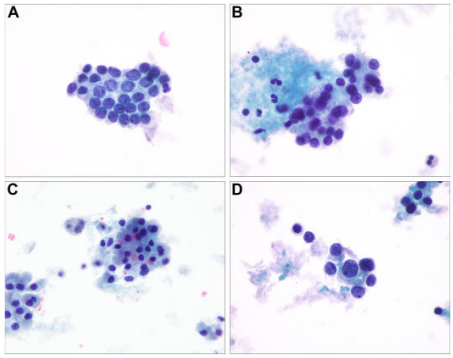
ScienceDirect

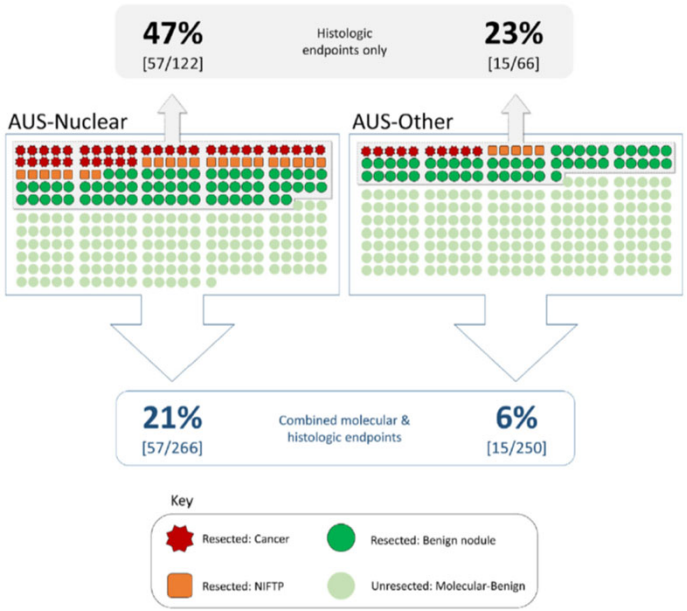
journal homepage: www.jascyto.org/

ELSEVIER

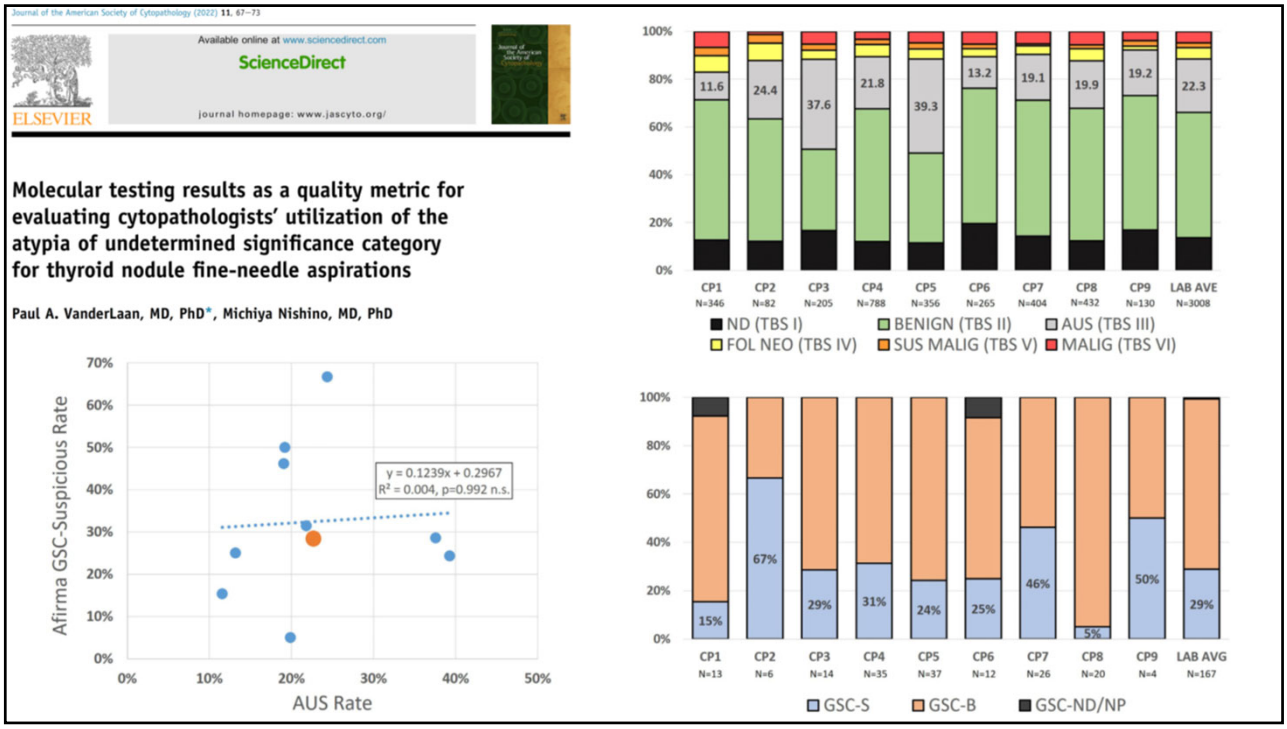
Binary subclassification scheme (AUS-Nuclear versus AUS-Other) adequately risk-stratifies thyroid fine needle aspiration specimens classified as Atypia of Undetermined Significance

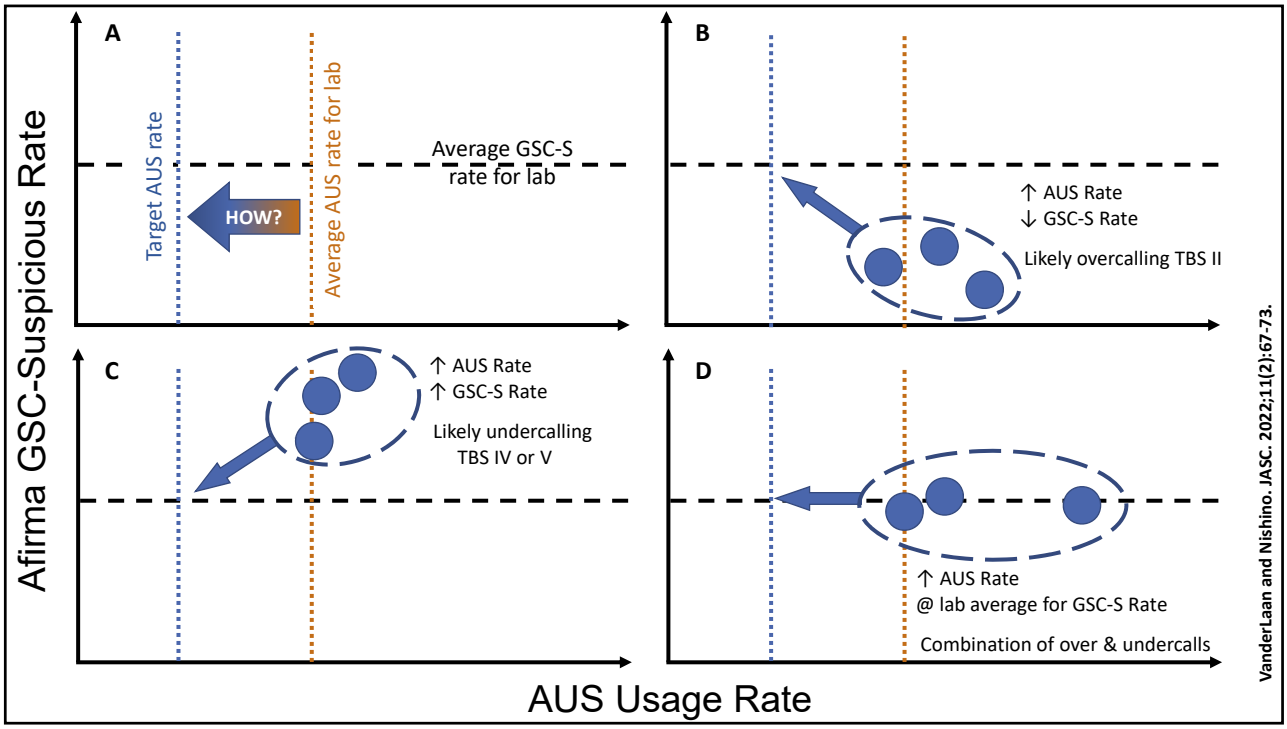
Yaileen D. Guzmán-Arocho, MD, Paul A. VanderLaan, MD, PhD, Michiya Nishino, MD, PhD*





Can you use metrics to help explain *WHY* practice patterns may deviate from targets?



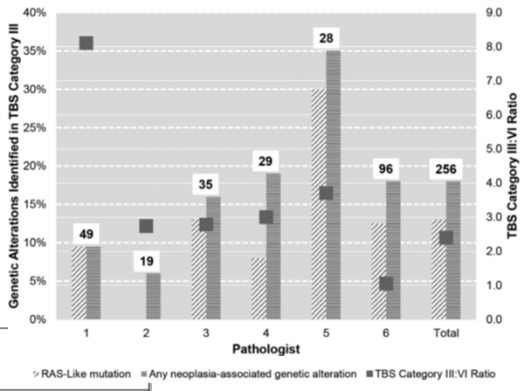


Original Article

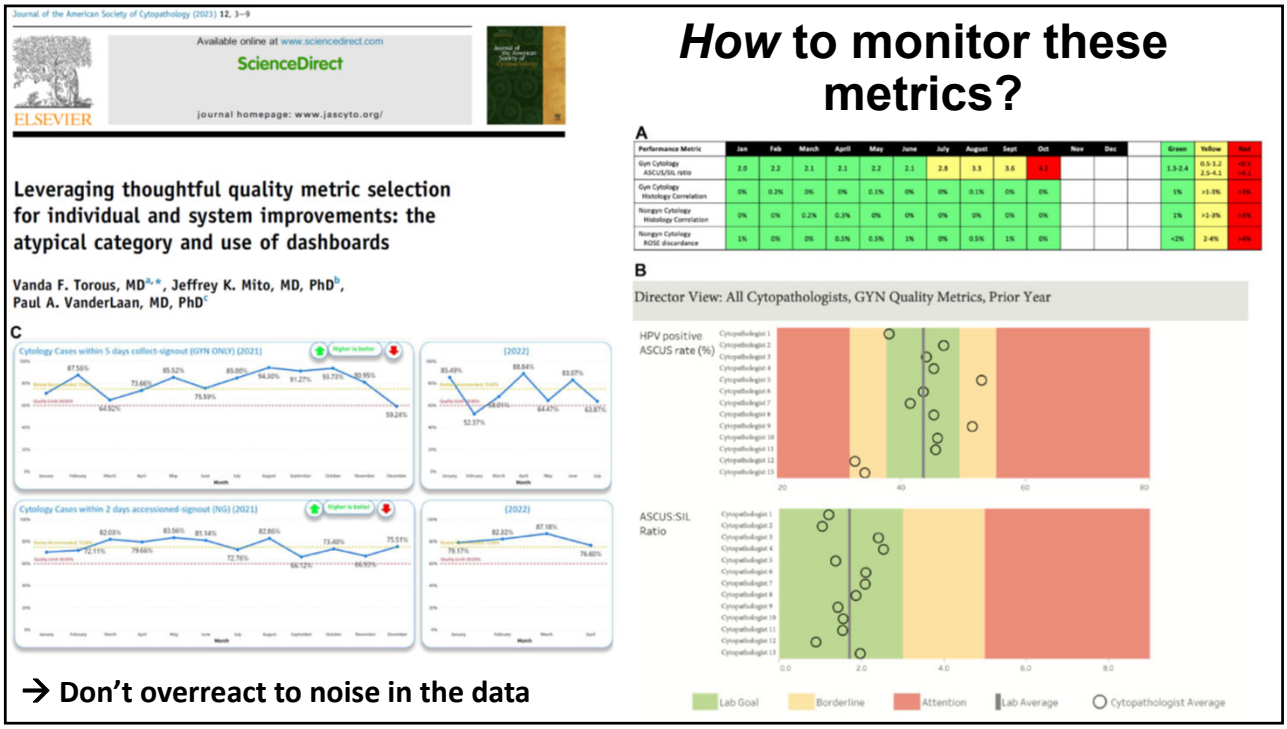
Cancer Cytopathol 2022;130:259-274.

Combining molecular testing and the Bethesda category III:VI ratio for thyroid fine-needle aspirates: A quality-assurance metric for evaluating diagnostic performance in a cytopathology laboratory

Hamza N. Gokozan, MD[1,2]; Thomas L. Dilcher, BS[1]; Susan A. Alperstein, CT (ASCP)[1]; Yuqing Qiu, MS[3]; Maria Mostyka, DO[2]; Theresa Scognamiglio, MD[2]; James P. Solomon, MD, PhD[4]; Wei Song, MD, PhD[4]; Hanna Rennert, PhD[3]; Shaham Beg, MD[1]; Evan Stern, DO[1]; Abha Goyal, MD[1]; Momin T. Siddiqui, MD[1]; and Jonas J. Heymann, MD[1]



III:VI Ratio	NGA Rate: Low	Intermediate*	High
High	"Overcalling benign aspirates" ***Increase diagnostic threshold for AUS***	"High uncertainty" ***Decrease the number of AUS diagnoses***	"Undercalling neoplastic aspirates" ***Decrease diagnostic threshold for SFN and SUS***
Normal (≤3.0)	"Overcalling across categories" ***Broadly increase diagnostic threshold***	TARGET	"Undercalling across categories" ***Broadly decrease diagnostic threshold***



Closing the loop: Cytopathologist Feedback

Frequency of monitoring

Overreacting to *noise* in the data

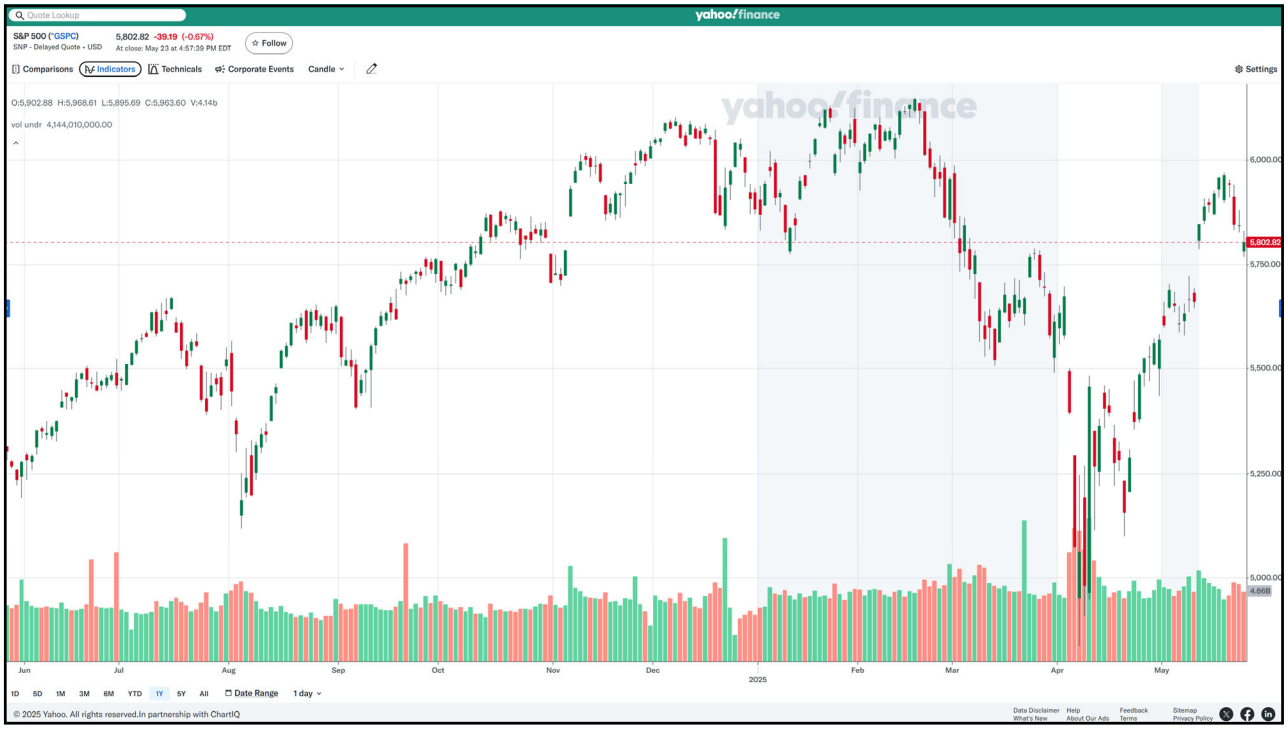
Monthly dashboard
(Reviewed quarterly)
- ✓ Unsat rates
- ✓ Specimen ID errors
- ✓ Log in TAT
- ✓ Sign-out TAT

Cytopathologist reports
(Q 6 months, confidential)
- ➢ Individual and lab averages

Non-GYN diagnostic categories
- Overall and specimen type

GYN diagnostic categories
- ASCUS/SIL ratio
- % hrHPV+ for each category

Weiss V et al. *J Am Soc Cytopathol.* 2022;11(2):87-93.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SNP - Delayed Quote • USD
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At close: May 23 at 4:57:39 PM EDT
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Technicals
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Candle
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5,802.82 -39.19 (-0.67%)
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O:5,854.15 H:5,906.64 L:5,845.02 C:5,886.55 V:5.52b
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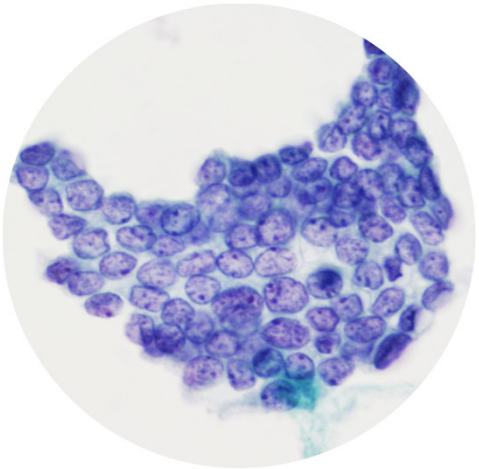
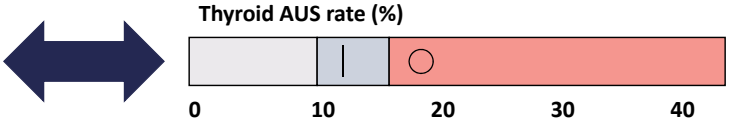
Statistics mean nothing to the individual

Inherent tension

→ Diagnosing what you see on each slide, while being mindful of individual tendencies to overcall/undercall findings





Summary

Cytology laboratory as model for quality assurance monitoring

Standardized reporting systems (categorical reporting)

-combined with-

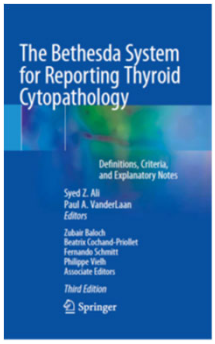
Histologic (molecular testing) outcomes

Thoughtful evaluation of metrics can:

✓Facilitate monitoring of cytopathologist performance

✓Explain WHY practice patterns may deviate from the accepted norms

✓Provide feedback to improve/modify practice



HARVARD MEDICAL SCHOOL

Laboratory Quality Assurance

(Through the Lens of the Bethesda System for Reporting Thyroid Cytopathology)

Paul VanderLaan MD, PhD

Director of Cytopathology, Surgical Pathology, and Thoracic Pathology
Beth Israel Deaconess Medical Center
Associate Professor of Pathology
Harvard Medical School
PVANDERL@BIDMC.HARVARD.EDU

Extras…

Application of molecular testing QA metrics to other specimens?

Most useful for monitoring the Indeterminate categories

Cervical cytology

Cytopathology Checklist

CAP Accreditation Program

CYP.07653 HR-HPV Records Phase I

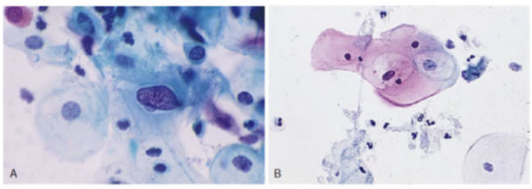
If available, records are maintained for high-risk human papillomavirus (HR-HPV) tests performed on ASC-US including:

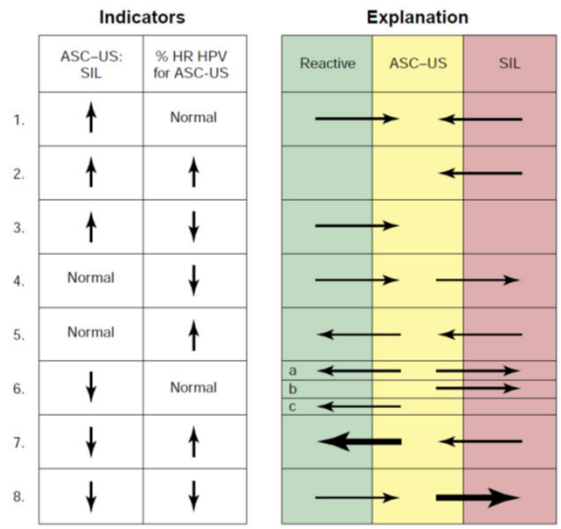
1. Total number of HR-HPV tests performed on ASC-US cases
2. Total number of positive HR-HPV ASC-US cases

NOTE: The percentage of ASC-US cases with a positive HR-HPV result may be a helpful quality metric for both overall laboratory performance and individual performance of pathologists, especially when combined with an individual's ASC-SIL ratio. Data for other HR-HPV testing results (eg, co-testing with a Pap test in women > 30 years of age) may also be helpful quality metrics but should be kept separately.

ThinPrep**
Laboratory Percentile-Reporting Rate

CATEGORY	5th	10th	25th	Median	75th	90th	95th
Unsatisfactory (%)	0.2	0.4	0.9	1.7	2.9	4.8	5.7
LSIL (%)	0.4	0.9	1.7	2.4	3.3	4.8	6.6
HSIL (%)	0.1	0.1	0.2	0.4	0.6	1.0	1.3
ASC-US (%)	1.0	1.9	3.6	5.4	7.9	11.7	15.2
ASC-H (%)	0.0	0.1	0.2	0.4	0.6	1.1	1.5
AGC (%)	0.0	0.0	0.1	0.2	0.4	0.7	1.1
ASC/SIL	0.7	1.1	1.6	2.0	2.7	3.6	4.4





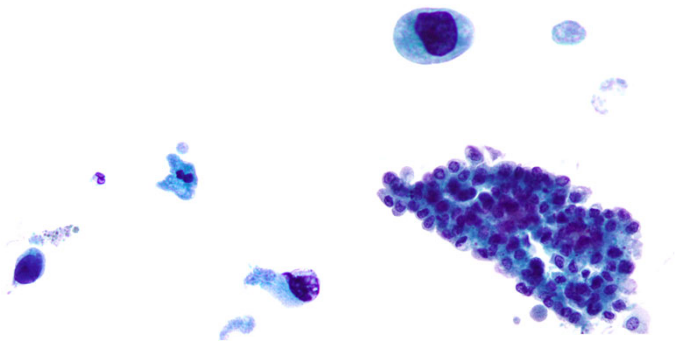
• **Fig. 19.1** Behavioral explanations for variations from the expected ASC-US:SIL ratio and high-risk (HR) HPV-positivity rate for ASC-US. Eight different anomalies with regard to these two variables are illustrated. For example, an individual with pattern 1 has an elevated ASC-US:SIL ratio but a normal HR HPV positivity rate for ASC-US. The horizontal arrows show how movement of interpretations from one diagnostic category to another can affect the ASC-US:SIL ratio and the rate of high-risk HPV-positivity for ASC-US in different ways. (From Cibas ES, Zou KH, Crum CP, Kuo F. Using the rate of positive high-risk HPV test results for ASC-US together with the ASC-US:SIL ratio in evaluating the performance of the cytopathologist. *Am J Clin Pathol*. 2008;129:97–101).

Cibas and Ducatman's Cytology 6th ed. 2026.

Application of molecular testing QA metrics to other specimens?

<u>Urine cytology</u>

- Atypical rate
- Correlation with ancillary testing



Ancillary Techniques

ANCILLARY TECHNIQUES

- DNA aneuploidy (flow cytometry, image analysis)
- Bard bladder tumor antigen test
- Nuclear matrix protein NMP22 test
- Telomerase assays
- Microsatellite instability assays
- Hyaluronidase and hyaluronic acid
- Growth factors
  - Acidic fibroblast growth factor
  - Basic fibroblast growth factor
  - Autocrine motility factor
  - Epidermal growth factor
  - Transforming growth factor-beta
- Cell adhesion molecules
- Fibrinogen degradation products
- Tumor-associated and blood group antigens
- FISH
- Cell-free microRNA
- Long noncoding RNA
- Next-generation sequencing assays
- Immunohistochemistry

Application of molecular testing QA metrics to other specimens?

Journal of Molecular Pathology

MDPI

Review

Practical Applications of Molecular Testing in the Cytologic Diagnosis of Pancreatic Cysts

Mingjuan Lisa Zhang * and Martha B. Pitman *

J Mol Pathol. 2021;2(1):11-22.

CBD brushings/EUS-FNA

Atypical – Over/under call?

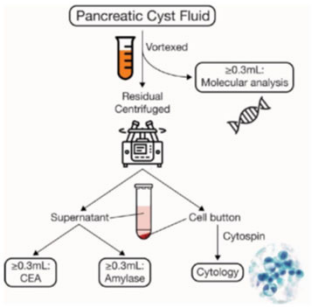
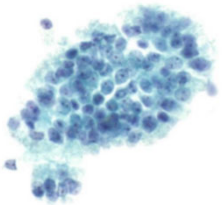
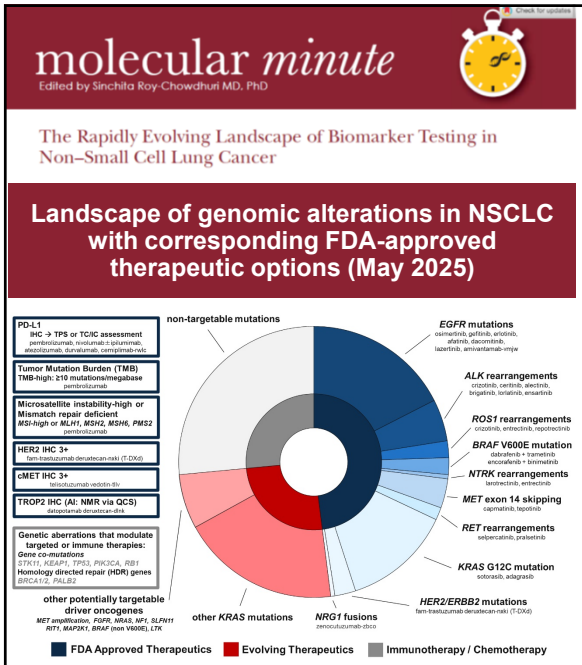


Table 1. Pancreatic cyst fluid analysis of cystic pancreatic lesions.

Cystic Entity	Biochemical Tests		Genetic Mutations					
	CEA	Amylase	*KRAS*	*GNAS*	3p25 (*VHL*)	*p53*	*p16*	*SMAD4*
Pseudocyst	↓	↑↑	–	–	–	–	–	–
SCA	↓↓	↓↓	–	–	+	–	–	–
LEC	↑↑	↓	–	–	–	–	–	–
IPMN	↑↓	↓↑	+	+	–	+(HR)	+(HR)	+(HR)
MCN	↑↓	↓↑	+	–	–	+(HR)	+(HR)	+(HR)
PanNET *	↓↓	↓↑	–	–	+/–	–	–	–
PDAC *	↑↓	↓↑	+	–/+ **	–	+	+	+ (55%)





Updated from:

VanderLaan *et al. Cancer Cytopathol.* 2021;129(3):179-181.

Journal of the American Society of Cytopathology (2022) 11, 403–414

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journal homepage: www.jascyto.org/

Molecular testing of cytology specimens: overview of assay selection with focus on lung, salivary gland, and thyroid testing

Paul A. VanderLaan, MD, PhD[a], Sinchita Roy-Chowdhuri, MD, PhD[b], Christopher C. Griffith, MD, PhD[c], Vivian L. Weiss, MD, PhD[d], Christine N. Booth, MD[c,*]