Malignancy Risk for Fine-Needle Aspiration of Thyroid Lesions According to The Bethesda System for Reporting **Thyroid Cytopathology**

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Upon completion of this activity you will be able to:

- · list the 6 diagnostic categories of The Bethesda System for Reporting Thyroid Cytopathology
- cite the individual implied risks of malignancy and recommended management of the diagnostic categories of The Bethesda System for Reporting Thyroid Cytopathology. apply The Bethesda System for Reporting Thyroid Cytopathology
- nomenclature in the everyday practice for thyroid fine-needle aspirates.

Abstract

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Fine-needle aspiration (FNA) is an important test for triaging patients with thyroid nodules. The 2007 National Cancer Institute Thyroid Fine-Needle Aspiration State-of-the-Science Conference helped instigate the recent publication of The Bethesda System for Reporting Thyroid Cytopathology. We reviewed 3,080 thyroid FNA samples and recorded interpretations according to the proposed standardized 6-tier nomenclature, and pursued follow-up cytology and histology. Of the 3,080 FNAs, 18.6% were nondiagnostic, 59.0% were benign, 3.4% were atypical follicular lesion of undetermined significance (AFLUS), 9.7% were "suspicious" for follicular neoplasm (SFN), 2.3% were suspicious for malignancy (SM), and 7.0% were malignant. Of 574 cases originally interpreted as nondiagnostic, 47.9% remained nondiagnostic. In 892 cases, there was follow-up histology. Rates of malignancy were as follows: nondiagnostic, 8.9%; benign, 1.1%; AFLUS, 17% (9/53); SFN, 25.4%; SM, 70% (39/56), and malignant, 98.1%. Thus, classification of thyroid FNA samples at the University of Virginia Health System, Charlottesville, according to The Bethesda System yields similar results for risk of malignancy as reported by others. Universal application of the new standardized nomenclature may improve interlaboratory agreement and lead to more consistent management approaches.

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Fine-needle aspiration (FNA) of the thyroid gland has proven to be an important and widely accepted, cost-effective, simple, safe, and accurate method for triaging patients with thyroid nodules.¹ It is estimated that up to 30 million patients in the United States have thyroid nodules larger than 1 cm. In comparison with the high prevalence of thyroid nodules, 30,000 patients are diagnosed with thyroid malignances each year.^{2,3} FNAs provide information that guides the management of patients with thyroid nodules by identifying patients who require surgical resection and patients who require no further interventions.

Thyroid cytopathology practice requires communication and collaboration among pathologists and primary clinicians, endocrinologists, radiologists, and surgeons, as well as correlation with surgical pathology interpretations.⁴ Therefore, consistent diagnostic terminology is imperative. While there are minimal difficulties in diagnosing most benign and overtly malignant lesions, diagnostic challenges arise when aspirate samples are quantitatively or qualitatively suboptimal to reliably exclude a neoplastic process. The management of these types of lesions has been further complicated by the historic lack of universal terminology.⁵ Multiple organizations have proposed diagnostic guidelines for reporting thyroid FNA cytology results, including the Papanicolaou Society of Cytopathology Task Force⁶ and the American Thyroid Association,⁷ although none have been necessarily universally accepted.

Throughout 2007, the National Cancer Institute (NCI) organized The NCI Thyroid Fine Needle Aspiration State-ofthe-Science Conference. The current status of various aspects of thyroid FNA was discussed, including the following: (1) indications and pre-FNA requirements, (2) training and credentialing for FNA, (3) technique, (4) reporting terminology and morphologic criteria, (5) ancillary studies, and (6) post-FNA testing and treatment.⁸ Since the conference, there has been an initiative to publish an atlas and guidelines using a standardized nomenclature for the interpretation of thyroid FNAs, known as The Bethesda System for Reporting Thyroid Cytopathology.⁹⁻¹¹ The atlas describes 6 diagnostic categories of lesions: nondiagnostic or unsatisfactory, benign, atypia of undetermined signifi-

cance/follicular lesion of undetermined significance, follicular neoplasm/"suspicious" for follicular neoplasm, suspicious for malignancy, and malignant **Table 11**.

The 6 diagnostic categories of the forthcoming Bethesda System have individual implied risks of malignancy that influence management paradigms **Table 21**, reflecting literature reviews and institutional studies.^{9,12-14} Herein, we review the experience at the University of Virginia Health

■Table 1■ The Bethesda System for Reporting Cytopathology: Recommended Diagnostic Categories¹¹

Ι.	Nondiagnostic or unsatisfactory Cyst fluid only Virtually acellular specimen Other (obscuring blood, clotting artifact, etc)
11.	Benign
	Consistent with a benign follicular nodule (includes adenomatoid nodule, colloid nodule, etc) Consistent with lymphocytic (Hashimoto) thyroiditis in
	the proper clinical context
	Consistent with granulomatous (subacute) thyroiditis
.	Atypia of undetermined significance/follicular lesion of undetermined significance
IV.	Follicular neoplasm/"suspicious" for follicular neoplasm Specify if Hürthle cell type
V.	Suspicious for malignancy
	Suspicious for papillary carcinoma
	Suspicious for medullary carcinoma
	Suspicious for metastatic carcinoma
	Suspicious for lymphoma
VI.	Malignant
	Papillary thyroid carcinoma Poorly differentiated carcinoma
	Medullary thyroid carcinoma
	Undifferentiated (anaplastic) carcinoma
	Squamous cell carcinoma
	Carcinoma with mixed features Metastatic

System, Charlottesville, with thyroid FNA modified to reflect this new reporting system and compare it with previous large-scale studies.

Materials and Methods

The cytology database at the University of Virginia Health System was searched for all FNAs of the thyroid between 1992 and 2009. Interpretations were recorded by 3 pathologists as per the current recommended nomenclature. Cases using descriptive diagnoses were placed into the best overall categories. Most thyroid FNAs performed at the University of Virginia Health System use rapid Romanowsky– and Papanicolaoustained smears, and only occasionally ThinPrep slides (Hologic, Bedford, MA) are generated (usually with cysts).

Diagnostic Criteria and Examples

Nondiagnostic or Unsatisfactory

We applied the term *nondiagnostic* to include cases diagnosed as predominantly blood or characterized by the absence of colloid or an insufficient number or fixation quality of follicular cells. Aspirates diagnosed as "cyst fluid only" were recorded as such but categorized as nondiagnostic.

Benign

Cases were recorded as benign if they were diagnosed or described as colloid nodule or thyroiditis, eg, *thyroid, right lobe, FNA:* Abundant hemosiderin-laden macrophages, scant benign follicular cells, some colloid, and rare Hürthle cells consistent with hemorrhagic colloid nodule.

Atypia of Undetermined Significance/Follicular Lesion of Undetermined Significance

Aspirates grouped in the atypia of undetermined significance/follicular lesion of undetermined significance (AFLUS) category were considered adequate and had indefinite diagnoses and/or notes suggesting that the best course of action was reaspiration. Examples include the following: (1) *Thyroid*,

Table 2

The Bethesda System for Reporting Thyroid Cytopathology: Implied Risk of Malignancy and Recommended Clinical
Management ¹¹

Diagnostic Category	Risk of Malignancy (%)	Usual Management
Nondiagnostic	_	Repeat FNA with ultrasound
Benign	0-3	Clinical follow-up
Atypical follicular lesion of undetermined significance	5-15	Repeat FNA
"Suspicious" for follicular neoplasm	15-30	Surgical lobectomy
Suspicious for malignancy	60-75	Near-total thyroidectomy or surgical lobectomy
Malignant	97-99	Near-total thyroidectomy

FNA, fine-needle aspiration.

right lobe, FNA: Scattered clusters of atypical follicular cells and scant colloid. Cannot exclude a neoplasm (see note). Note: Cellular material is insufficient for a definitive interpretation. (2) *Thyroid, right lobe, FNA*: Few benign-appearing follicular cells and very scant colloid (see note). Note: The differential diagnosis within this aspirate that contains benign-appearing follicular cells and very scant colloid includes a hypercellular colloid nodule and a cellular follicular lesion. Resampling of this lesion should be clinically considered.

Follicular Neoplasm/Suspicious for Follicular Neoplasm

We classified cases as suspicious for follicular neoplasm (SFN) when the aspirate was diagnosed or described to have moderate to high cellularity, scant or absent colloid, and predominantly microfollicular or trabecular configuration of follicular cells. We did not include cases with features suspicious for papillary carcinoma. Cases suspicious for Hürthle cell neoplasm were included. Reaspiration was not believed to be helpful for these cases, eg, *thyroid, right lobe, FNA*: Cellular follicular lesion.

Suspicious for Malignancy

Aspirates called suspicious for malignancy (SM) or described to have cytology suggestive of papillary carcinoma, medullary carcinoma, metastatic carcinoma, and lymphoma were included in this category, eg, *thyroid*, *right lobe*, *FNA*: Suspicious for cystic papillary thyroid carcinoma (see note). Note: The majority of the slides show abundant hard and watery colloid with marked cystic degeneration. Many groups of follicular cells have bland nuclei in macrofollicular sheets. However, a minority of epithelial groups show nuclear enlargement, nuclear grooves, overlapping nuclei, and rare nuclear pseudoinclusions. While these features are concerning for a papillary thyroid carcinoma with cystic degeneration, we cannot entirely exclude a follicular or Hürthle cell lesion with cystic degeneration.

Malignant

These aspirates included all that were interpreted as unequivocally malignant (eg, papillary carcinoma, medullary carcinoma, metastatic carcinoma, anaplastic carcinoma, and lymphoma).

Follow-up Cytology and Histology

Follow-up cytology and histology were pursued in our pathology database. We recorded all histopathologic diagnoses on each resection (which is why the number of diagnoses totals more than the number of resections reported). Incidental papillary carcinomas (<1 cm) on resection were not considered malignant, except when prior cytologic interpretation was "suspicious for malignancy" or "malignant." For the purposes of this study, hyalinizing trabecular adenomas were considered variants of papillary carcinoma and classified as malignant. In calculating the malignancy follow-up rate for the benign category, the total number of original FNA diagnoses was used as the denominator, as similarly performed in other studies.¹² For all other diagnostic categories, malignancy follow-up rates were calculated by using the number of cases with follow-up histology results. If a patient had multiple FNA samples in the same procedure yielding 2 different diagnoses, only the diagnosis with higher malignant potential was used for calculating malignancy follow-up rates (eg, for 1 FNA with "colloid nodule" and "suspicious for papillary carcinoma" on 2 separate passes, the case was included in the calculation for the SM follow-up rate and not for the benign group).

Results

There were 3,080 thyroid FNA diagnoses representing 2,790 unique FNA procedures. The overall distribution of diagnoses was as follows: 574 nondiagnostic, including 126 cyst fluid only specimens (18.6%); 1,817 benign (59.0%); 104 AFLUS (3.4%); 298 SFN, including 98 Hürthle cell types (9.7%); 71 SM (2.3%); and 216 malignant (7.0%). **Table** 3 lists the frequency of these diagnoses. Of the cases, 304 underwent repeated FNA, and 892 cases were followed by surgical resection (partial or total thyroidectomy). There were 276 total cases of malignancy on resection, giving an overall surgical yield of malignancy of 30.9%. **Table 4** presents the total number of benign and malignant cases on resection and the overall distribution of malignancies. The rates of malignancy for each FNA diagnostic group were as follows: nondiagnostic, 8.9%; benign, 1.1%; AFLUS, 17% (9/53); SFN, 25.4%; SM, 70% (39/56); and malignant, 98.1% Table 5.

Of the FNA samples, 509 were nondiagnostic only, with no other concomitant diagnosis. There were 144 followup FNAs for these cases. On repeated aspiration, 69 cases (47.9%) remained nondiagnostic. The distribution of diagnoses on follow-up FNA was as follows: 60 benign (41.7%); 3

Table 3

Frequency of Cytologic Diagnoses Between 1992 and 2009 at the University of Virginia Health System, Charlottesville (N = 3,080)

Diagnostic Category	No. (%) of Cases
Nondiagnostic Benign Atypical follicular lesion of undetermined significance	574 (18.6) 1,817 (59.0) 104 (3.4)
"Suspicious" for follicular neoplasm Suspicious for malignancy Malignant	298 (9.7) 71 (2.3) 216 (7.0)

Table 4 Summary of Diagnoses and Distribution of Malignancies on Surgical Resection (N = 892)

Diagnosis on Resection	Total No. (%) of Cases
Benign	616 (69.1)
Malignant	276 (30.9)
Papillary carcinoma	204
Follicular carcinoma	35
Medullary carcinoma	17
Poorly differentiated carcinoma	2
Anaplastic carcinoma	6
Lymphoma	7
Other*	6

^{*} Includes parathyroid adenocarcinoma, metastatic clear cell (conventional) renal cell carcinoma, spindle cell carcinoma, synovial sarcoma, squamous cell carcinoma, and adenoid cystic carcinoma.

AFLUS (2.1%); 7 SFN (4.9%); 1 SM (0.7%); and 4 malignant (2.8%). Of the 144 cases, 135 had subsequent surgical resection specimens yielding the following diagnoses: colloid nodule/nodular hyperplasia, 73; lymphocytic thyroiditis, 20; follicular adenoma, 24; follicular carcinoma, 1; Hürthle cell carcinoma, 1; papillary carcinoma, including 2 follicular variants, 7; medullary carcinoma, 1; lymphoma, 1; parathyroid adenocarcinoma, 1; and other (6, all benign). Overall, 12 malignant diagnoses were made on resection, yielding a malignancy risk of 8.9%.

Of the thyroid FNA samples, 1,792 were categorized as solely benign (1,652 colloid nodule/nodular hyperplasia and 140 lymphocytic thyroiditis). Follow-up histology was available for 307 cases, yielding the following diagnoses: colloid nodule/nodular hyperplasia, 230; lymphocytic thyroiditis, 69; follicular adenoma, 34; follicular carcinoma, 5; Hürthle cell adenoma, 8; hyalinizing trabecular adenoma, 1; papillary carcinoma, including 2 follicular variants, 10; anaplastic carcinoma, 1; medullary carcinoma, 2; metastatic conventional renal cell carcinoma, 1; and other, 4, all benign. Overall, there were 20 cases of malignancy on resection of 1,792 total benign FNA diagnoses, leading to an overall malignancy risk of 1.1%.

We categorized 101 cases as AFLUS. In 8 cases, there was repeated FNA, and the following diagnoses were found:

nondiagnostic, 5; benign, 4; SFN, 1; and malignant, 1, anaplastic. Of the 101 cases, 53 were followed by surgical resection, with the following diagnoses: colloid nodule/nodular hyperplasia, 29; lymphocytic thyroiditis, 18; follicular adenoma, 14; follicular carcinoma, 2; Hürthle cell adenoma, 1; papillary carcinoma, including 3 follicular variants, 4; anaplastic carcinoma, 1; medullary carcinoma, 1; and lymphoma, 1. Thus, there were 9 overall malignancies (17%).

Of the cases, 298 were classified as SFN, including 98 Hürthle cell types. Of these cases, 177 had follow-up histology. The following diagnoses were made: colloid nodule/ nodular hyperplasia, 84; lymphocytic thyroiditis, 39; follicular adenoma, 53; follicular carcinoma, 11; Hürthle cell adenoma, 19; Hürthle cell carcinoma, 10; hyalinizing trabecular adenoma, 1; papillary carcinoma, including 9 follicular variants, 18; poorly differentiated thyroid carcinoma, 1; and medullary carcinoma, 4. Thus, there were 45 malignancies (25.4%) on follow-up histology.

Of the 71 SM cases, 56 were followed by thyroidectomy. Of these 56 cases, 39 (70%) were malignant, with the following diagnoses: follicular carcinoma, 3; papillary carcinoma, including 8 follicular variants, 33; medullary carcinoma, 1; lymphoma, 1; and spindle cell carcinoma, 1. Two of the papillary carcinomas were less than 1 cm in greatest dimension, and both were associated with biopsy site changes. Three SM cases had repeated FNA. One case was found to be lymphoma with no follow-up FNA or thyroidectomy. The second was AFLUS on repeated cytology, with follicular carcinoma on resection. The third was nondiagnostic on repeated FNA and showed papillary thyroid carcinoma on thyroidectomy.

We classified 216 thyroid FNA samples as malignant. Cytologic interpretations were as follows: papillary carcinoma, 170; poorly differentiated carcinoma, 7; anaplastic carcinoma, 10; medullary carcinoma, 9; lymphoma, 7; metastases, 4; and others, 9. Of these cases, 154 had follow-up histology, and 151 (98.1%) were confirmed as malignant. The diagnoses of malignancy on resection were as follows: hyalinizing trabecular adenoma, 1; papillary carcinoma, 1; Hürthle cell carcinoma, 1; poorly differentiated carcinoma, 1; medullary

Table 5

Rates of Malignancy on Surgical Resection for Fine-Needle Aspiration Diagnostic Categories at the University of Virginia Health System, Charlottesville

Diagnostic Category	Malignancy Rate, % (No. of Cases)	Reported Rate (%) ¹¹
Nondiagnostic (n = 135)	8.9 (12)	_
Benign $(n = 1,792)$	1.1 (20)	0-3
Atypical follicular lesion of undetermined significance $(n = 53)$	17 (9)	5-15
"Suspicious" for follicular neoplasm (n = 177)	25.4 (45)	15-30
Suspicious for malignancy $(n = 56)$	70 (39)	60-75
Malignant (n = 154)	98.1 (151)	97-99

carcinoma, 8; anaplastic carcinoma, 4; lymphoma, 4; synovial sarcoma, 1; squamous cell carcinoma, 1; and adenoid cystic carcinoma by local extension from the trachea, 1. Of the papillary carcinomas, 18 were smaller than 1.0 cm in greatest dimension (range, 5-9 mm; average, 6.9 mm). Of these incidental papillary carcinomas, 4 were multifocal, 1 case had documented biopsy site changes, and 5 cases had associated lymph node metastases. The 3 nonmalignant resection cases had the following diagnoses: colloid nodule/nodular hyperplasia (2 cases) and lymphocytic thyroiditis with an area of necrosis and psammoma bodies but no neoplastic follicular epithelium (1 case).

Discussion

We present data reflecting the experience of the University of Virginia Health System with thyroid FNAs after retrospectively applying the newly proposed Bethesda System for reporting thyroid cytopathology. While it has been established that thyroid FNA has high sensitivity and specificity for benign and malignant lesions, there has been wide variation and subjectivity in the interpretation and reporting of uncertain categories, including SFN and aspirates with atypical features. The nonuse of standardized terminology and the varying diagnostic schema used by different institutions (2 to >6 diagnostic categories) has led to inconsistent practices among pathologists, clinicians, and surgeons.

We found that classification of thyroid lesions according to the proposed standardized nomenclature yields similar results for risk of malignancy reported by others using the proposed Bethesda or comparable systems. Yassa et al¹² reported their institutional experience using 1997 guidelines by the Papanicolaou Society of Cytopathology. Their yields for malignancy, using the same calculations, were as follows: nondiagnostic, 10%; benign, 0.3%; atypical follicular lesion, 24%; suspicious for follicular neoplasm, 28%; suspicious for malignancy, 60%; and malignant, 97%. Yang et al¹³ reported the following malignancy rates: nondiagnostic, 10.7%; benign, 0.7%; atypical follicular lesion, 19.2%; suspicious for follicular neoplasm, 32.2%; suspicious for malignancy, 64.8%; and malignant, 98.4%. Nayar and Ivanovic¹⁴ performed a similar retrospective study of their institution's history with application of the 6 proposed Bethesda diagnostic categories, with calculated malignancy risks as follows: nondiagnostic, 9%; benign, 2%; indeterminate for neoplasm, 6%; follicular neoplasm, 14%; suspicious for malignancy, 53%; and malignant, 97%. Distribution of the FNA diagnoses reported by us and cited in studies is shown in **Table 61**, and comparison of reported malignancy rates is given in **Table 71**.

The diagnostic category of AFLUS is heterogeneous, which is acknowledged by committee members of the NCI State-of-the-Science meeting.⁹ It is interesting that the frequency of diagnosis and reported rate of malignancy on surgical follow-up reported by Nayar and Ivanovic¹⁴ differ significantly from our findings and the aforementioned studies for AFLUS lesions. Nayar and Ivanovic¹⁴ had 18% of total FNA samples categorized as AFLUS, with a malignancy rate of 6%. The diagnostic frequency of AFLUS was 3.4% in our study. The associated malignancy risk in our study was 17%, similar to the rates found by Yassa et al (24%)¹² and Yang et al (19%).¹³ Nayar and Ivanovic¹⁴

Table 6

Comparison of Percentages of Distribution of Fine-Needle Aspiration Diagnoses Among Published Studies¹²⁻¹⁴

Diagnostic Category	Present Study	Yassa et al ¹²	Yang et al ¹³	Nayar and Ivanovic ¹⁴
Nondiagnostic	18.6	7	10.4	5
Benign	59.0	66	64.6	64
Atypical follicular lesion of undetermined significance	3.4	4	3.2	18
"Suspicious" for follicular neoplasm	9.7	9	11.6	6
Suspicious for malignancy	2.3	9	2.6	2
Malignant	7.0	5	7.6	5

Table 7

Comparison of Percentages of Follow-up Malignancy Among Published Studies¹²⁻¹⁴

Diagnostic Category	Present Study	Yassa et al ¹²	Yang et al ¹³	Nayar and Ivanovic ¹⁴
Nondiagnostic	8.9	10	10.7	9
Benign	1.1	0.3	0.7	2
Atypical follicular lesion of undetermined significance	17	24	19.2	6
"Suspicious" for follicular neoplasm	25.4	28	32.2	14
Suspicious for malignancy	70	60	64.8	53
Malignant	98.1	97	98.4	97

Our data are generated from retrospective classification, which is a limitation to our study. We did not review FNA cases, but rather used a "best-fit" philosophy. This relied on the original interpretation (given by >6 cytopathologists at the University of Virginia Health System in the period studied) and the observer's review of the original diagnosis. As most cytopathologists are aware, there can be wide variation in diagnostic thresholds and varied terminologies used by pathologists within the same department.^{16,17} As all other published studies are likewise retrospective observational reviews, these may account for some of the differences when comparing diagnostic category frequencies and malignancy risks. Prospective studies using the new Bethesda System will lend further insight into the usefulness of the proposed nomenclature. Last, the University of Virginia Health System is a tertiary center for thyroid lesions, and, thus, our data may not accurately reflect the general population. It is likely that thyroid malignancies are overly represented in our cohort.

At the University of Virginia Health System, classification of FNAs of thyroid lesions according to the proposed standardized nomenclature yields similar results for risk of malignancy reported by others.

The associated risks found for AFLUS (17%), SFN (25.4%), and SM (70%) confirm the importance of these categories in a 6-tier diagnostic system. Universal application of the new standardized diagnostic categories for reporting thyroid FNA results can improve interlaboratory agreement in the diagnosis of thyroid lesions and may lead to more consistent management approaches.

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AFLUS rate to a tendency to include adequacy-related cases in this diagnostic category, which may have otherwise been classified as inadequate by other groups. They report that the percentage of AFLUS cases would decrease to 14% if they removed adequacy-related cases. Their rate of SFN diagnosis was also lower in comparison with the other studies and, as discussed by the authors, may also be due in part to allocation of certain lesions as morphology-related AFLUS that may have been interpreted as SFN by other observers. This suggests some tendency to retain a 2-tiered system for the diagnosis of SFN, separating cases into groups more or less suspicious for neoplasm (eg, follicular lesion and follicular neoplasm).

Our findings support that classifying thyroid lesions into the AFLUS category will have an important role in triaging patients with thyroid nodules because patients with AFLUS are found to have a lower malignancy risk on surgical follow-up than patients with an initial diagnosis of SFN on cytology. However, because the category is heterogeneous and somewhat subjective, there exist and will likely remain differences between observers in using this diagnosis.¹⁵ Contributing authors to The Bethesda System recommend a limited use of this diagnostic category and classifying approximately 7% or fewer of total diagnoses as AFLUS. The typical course of management of patients with an AFLUS diagnosis is repeated FNA or observation but is primarily based on clinical correlation. In contrast, the diagnosis of SFN serves to recognize patients who need at least surgical lobectomy because definitive diagnosis relies on histologic examination of nodule architecture. It is interesting that in our retrospective application of AFLUS, only 8 cases had follow-up FNA, while 53 underwent thyroidectomy. Thus, the malignancy rate in our study (17%) may approximate the true malignancy risk for AFLUS lesions. Considering the low number of follow-up FNAs for AFLUS cases, this likely reflects treatment decisions by the clinicians at the University of Virginia Health System.

There are inherent diagnostic limitations of thyroid FNAs, which underscores the importance of clinical correlation in the management of patients with thyroid nodules. Cytopathologists are cognizant of the prevalence of sampling errors, particularly for lesions with cystic features or thyroid glands with multiple nodules. Limitations in the ability to further characterize follicular lesions on thyroid FNA alone have led to debates on management approaches. There is also an overlap of cytomorphologic features among reactive follicular cells, Hürthle cell lesions, and malignancies because the presence of nuclear grooves and even pseudoinclusions is not pathognomonic of papillary carcinomas. Practice differences between institutions may account for the variation in distribution of diagnostic categories and malignancy rates. Some of these differences can be attributed to technical reasons,

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