Overview of Diagnostic Terminology and Reporting

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With its inception, the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) established a uniform, tiered reporting system for thyroid FNA specimens. Using TBSRTC, the cytopathologist can communicate thyroid FNA interpretations to the referring physician in terms that are succinct, unambiguous, and clinically useful [1, 2].

Since the widespread acceptance of TBSRTC in clinical practice, questions have arisen over the proper use of the diagnostic categories, the recommended management (e.g., repeat FNA vs. surgery), and the implied risks of malignancy. With regard to any revisions to the risks of malignancy of the categories, the following factors were taken into consideration with the second edition: patient demographics, nodule selection criteria, variation in cytopathologist experience and application of cytomorphologic diagnostic criteria, the overestimation of the risk of malignancy for some diagnostic categories if based only on cases that have undergone thyroid surgery [3], publication bias [3], and the newly described entity of noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) [4], formerly known as "encapsulated follicular variant of papillary thyroid carcinoma."

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Format of the Report

For clarity of communication, each thyroid FNA report should begin with a general diagnostic category. TBSRTC diagnostic categories are shown in Table 1.1. For three of the six categories, TBSRTC offers a choice of two different names. A laboratory should choose the one it prefers and use it exclusively for that category. Synonymous terms (e.g., AUS and FLUS) should not be used to denote two distinct interpretations.

Each category has an implied cancer risk, which ranges from 0 to 3% for the "benign" category to virtually 100% for the "malignant" category. As a function of these risk associations, each category is linked to evidence-based clinical management guidelines [5], as shown in Table 1.2, and discussed in more detail in the chapters that follow.

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

I.	Nondiagnostic or Unsatisfactory[a]
	Cyst fluid only
	Virtually acellular specimen
	Other (obscuring blood, clotting artifact, drying artifact, etc.)
II.	Benign
	Consistent with a benign follicular nodule (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 or Follicular Lesion of Undetermined Significance[a]
IV.	Follicular Neoplasm or Suspicious for a Follicular Neoplasm[a]
	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
	Poorly differentiated carcinoma
	Medullary thyroid carcinoma
	Undifferentiated (anaplastic) carcinoma
	Squamous cell carcinoma
	Carcinoma with mixed features (specify)
	Metastatic malignancy
	Non-Hodgkin lymphoma
	Other

[a]The two terms for these categories are synonymous. A laboratory should use only one of these for reporting results.

Table 1.2 The Bethesda System for Reporting Thyroid Cytopathology: implied risk of malignancy and recommended clinical management

Diagnostic category	Risk of malignancy (%)	Usual management[a]
Nondiagnostic or Unsatisfactory	5–10[b]	Repeat FNA with ultrasound guidance
Benign	0–3[c]	Clinical and sonographic follow-up
Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance	~10–30[d]	Repeat FNA, molecular testing, or lobectomy
Follicular Neoplasm or Suspicious for a Follicular Neoplasm[e]	25–40[f]	Molecular testing, lobectomy
Suspicious for Malignancy	50–75	Near-total thyroidectomy or lobectomy[g,h]
Malignant	97–99	Near-total thyroidectomy or lobectomy[h]

[a]Actual management may depend on other factors (e.g., clinical, sonographic) besides the FNA interpretation.
[b]The risk of malignancy varies with the type/structure of the nodule, i.e., solid vs. complex vs. ≥50% cystic. Nondiagnostic aspirates from solid nodules are associated with a higher risk of malignancy as compared to those showing ≥50% cystic change and low-risk ultrasonographic features. See Chap. 2 for discussion [6, 7, 14]
[c]Estimate extrapolated from studies showing correlation between biopsied nodule and surgical pathology follow-up [8–11]
[d]Estimates extrapolated from histopathologic data from large case cohorts (including repeat atypical FNAs) and meta-analysis of the post 2007 literature [8, 12–15]
[e]Includes cases of follicular neoplasm with oncocytic features (aka Hürthle cell neoplasm)
[f]Estimates extrapolated from histopathologic data from large case cohorts and meta-analysis of the post 2007 literature (cited above and Ref. [16, 17])
[g]Some studies have recommended molecular analysis to assess the type of surgical procedure (lobectomy vs. total thyroidectomy)
[h]In the case of "suspicious for metastatic tumor" or a "malignant" interpretation indicating metastatic tumor rather than a primary thyroid malignancy, surgery may not be indicated

In the first edition of TBSRTC, the implied risk of malignancy for each diagnostic category was calculated and provided as a range based on a review of the literature at that time: 0–3% for benign, ~5–15% for atypia of undetermined significance (AUS) or follicular lesion of undetermined significance (FLUS), 15–30% for follicular neoplasm or suspicious for follicular neoplasm, 60–75% for suspicious for malignancy, and 97–99% for the malignant category [1]. In the second edition, these ranges have been revised, especially for the so-called "indeterminate" categories, representing estimates calculated primarily from studies of large case cohorts and meta-analyses of ultrasound-guided thyroid FNA published after 2007 [6–15]. It is important to note that the traditional method of estimating the risk of malignancy (ROM), which is based on histologic follow-up, i.e., dividing the number of patients with cancer by the total number of patients with surgical follow-up, overestimates the risk of malignancy, particularly for the nondiagnostic, benign, and AUS/FLUS categories, where there is selection bias given the relatively small proportion of nodules that undergo excision. On the other hand, when calculated using the total number of FNA specimens (with and without surgical follow-up) as the denominator, assuming that unresected nodules are benign, the ROM is most certainly

Table 1.3 Anticipated changes in the implied risk of malignancy of TBSRTC diagnostic categories and recommendations for comments due to the surgical pathology diagnosis of "noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP)"

Diagnostic category	Risk of malignancy with NIFTP (%)[a]	Optional note[b]
Nondiagnostic or Unsatisfactory	No significant change	None
Benign	No significant change	None
Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance	6–18	None
Follicular Neoplasm or Suspicious for a Follicular Neoplasm	10–40	The histopathologic follow-up of cases diagnosed as such includes follicular adenoma, follicular carcinoma, and follicular variant of papillary thyroid carcinoma, including its recently described indolent counterpart NIFTP.
Suspicious for Malignancy	45–60	The cytomorphologic features are suspicious for a follicular variant of papillary thyroid carcinoma and its recently described indolent counterpart NIFTP.
Malignant	94–96	A small proportion of cases (~3–4%) diagnosed as malignant – compatible with papillary thyroid carcinoma – may prove to be NIFTP on histopathologic examination.

[a]Change in the risk of malignancy in TBSRTC due to NIFTP is based on a limited number of retrospective studies [18–21]
[b]Ref. [22, 23]

underestimated. The actual ROM is expected to be in the midrange of the values obtained using these calculations and requires some extrapolation; the best current estimates are depicted in Table 1.2.

The reclassification of some thyroid neoplasms as NIFTP has implications for the ROM [16–20], and this is accounted for in Table 1.3. Comments as shown in Table 1.3 can be included in the report, especially if the cytopathologic features raise the possibility of NIFTP [21]. These features are discussed in more detail in the chapters that follow.

For some of the general diagnostic categories, subcategorization can be informative and is often appropriate; recommended terminology is shown in Table 1.1. Additional descriptive comments (beyond such subcategorization) are optional and left to the discretion of the cytopathologist. Notes and recommendations can be useful, especially due to the introduction of NIFTP terminology (Table 1.3). Some laboratories, for example, may wish to state the risk of malignancy associated with the general category, based on their own cytologic–histologic correlation or that found in the literature (Table 1.2). Sample reports, which we hope will be a useful guide, are provided in the remaining chapters.

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