

Supplemental Table 1

| The 2017 Bethesda System for Reporting Thyroid Cytopathology: Implied Risk of Malignancy and Recommended Clinical Management | | | | |
|--|---|--------------------------------------|--------------------------------------|---|
| Bethesda category | Diagnostic category | Risk of Malignancy if NIFTP ≠ CA (%) | Risk of Malignancy if NIFTP = CA (%) | Standard of care management recommendations (a) |
| I | Nondiagnostic or unsatisfactory | 5-10 | 5-10 | Repeat FNA with ultrasound guidance |
| II | Benign | 0-3 | 0-3 | Clinical and sonographic follow-up |
| III | Atypia of undetermined significance or follicular lesion of undetermined significance | 6-18 | 10-30 | Repeat FNA, molecular testing, or lobectomy |
| IV | Follicular neoplasm or suspicious for a follicular neoplasm | 10-40 | 25-40 | Molecular testing, lobectomy |
| V | Suspicious for Malignancy | 45-60 | 50-75 | Near-total thyroidectomy or lobectomy (b, c) |
| VI | Malignant | 94-96 | 97-99 | Near-total thyroidectomy or lobectomy (c) |

Adapted from Ali and Cibas*

a Actual management may depend on other factors (e.g., clinical, sonographic) besides the FNA interpretation.

b Some studies have recommended molecular analysis to assess the type of surgical procedure (lobectomy vs. total thyroidectomy).

c 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.

NIFTP, noninvasive follicular thyroid neoplasm with papillary-like nuclear features; CA, carcinoma; FNA, fine-needle aspiration.

*Cibas ES, Ali SZ. The 2017 Bethesda System for Reporting Thyroid Cytopathology. *Thyroid*. 2017;27:1341-1346.

Supplemental Table 2

| Summary of Most Prevalent Molecular Testing Assays | | | | |
|--|--------------------------------|----------------------------------|---|--------------------------------------|
| | Afirma[®] GSC | ThyroSeq[®] v3.0 | ThyGeNEXT[®] & ThyraMIR[®] | Rosetta GX[™] Reveal |
| Method | Next Generation Sequencing RNA | Next Generation Sequencing | Next Generation Sequencing & microRNA expression | microRNA expression classifier |
| Sensitivity | 91.10% | 98.00% | 88.60% | 85.00% |
| Specificity | 68.30% | 81.80% | 85.10% | 72.00% |
| NPV | 96.10% | 97.40% | 94.00% | 91.00% |
| PPV | 47.10% | 85.70% | 73.80% | 59.00% |
| Cancer Prevalence | 23.70% | 28.0% | 32.10% | 50.00% |

Supplemental Table 3

| Summary of Non-surgical (minimally invasive) Treatment Options for Benign Thyroid Nodules | | | | | |
|---|---|---|---------------------|--------------------------|--|
| | Chemical Technique | Thermal Techniques | | | |
| | Ethanol | Radiofrequency Ablation (RFA) | Laser Ablation (LA) | Microwave Ablation (MWA) | High-Intensity Focused Ultrasound (HIFU) |
| Indications | Compressive symptoms, Cosmetic concerns, Suboptimal surgical candidates and/or Patients that refuse surgical intervention | | | | |
| Pre-procedure Requirements | Ensure thyroid nodule is benign by means of FNA cytology assessment (two separate samplings preferred), Hold anticoagulation therapy for appropriate time period, | | | | |
| Maximum Thyroid Nodule Volume Reduction | ↓ | ↓↓↓↓ | ↓↓↓ | ↓↓ | ↓↓ |
| Complications | Leakage Pain Hoarseness | Hoarseness; Brachial plexus nerve injury; Local infection; Massive colliquative necrosis and Nodule rupture with fasciitis; Potential changes in thyroid hormone levels | | | Subcutaneous edema Mild skin redness |
| Thyroid Cyst | +++ | --- | --- | --- | --- |