NIFTP
Cytologic Aspects

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So, what is the story about FVPTC and NIFTP in cytology???
FNA of the Follicular Variant of Papillary Thyroid Carcinoma

Easily recognized as PTC

More difficult to recognize as PTC
FNA of the Follicular Variant of Papillary Thyroid Carcinoma

- **Problematic Variant for FNA:**
  - 30-40% have subtle nuclear features
  - Microarchitecture mimics a follicular neoplasm or adenomatous nodule

- **FNA shows variable accuracy:**
  - 30-40% diagnosed as “MALIGNANT”
  - 25-30% diagnosed as “SUSPICIOUS FOR MALIGNANCY”
  - 25-30% diagnosed as “SUSPICIOUS FOR FOLLICULAR NEOPLASM”
  - 10-20% diagnosed as “AUS/FLUS”
Follicular Variant of PTC: Common Cause of False Negative FNA Diagnosis

With NIFTP, this could become a cause of a **False Positive** FNA diagnosis of cancer
FVPTC vs NIFTP:
Cannot be accurately distinguished by FNA

Invasive FVPTC  NIFTP
FNA of NIFTP: Cytologic Features

- Follicular-patterned
- Nuclear:
  - Enlargement
  - Pallor
  - Grooves
  - Overlap
- Rare:
  - Pseudoinclusions
- Absent:
  - Papillae
  - Psammoma bodies
NIFTP:
Solves a major problem but creates others
Regardless of the thyroid FNA reporting system that you use, NIFTP will create some issues for cytology!
Non-Invasive Follicular Thyroid Neoplasm with Papillary-Like Nuclear Features (NIFTP)

- The prospects of NIFTP for thyroid cytology:
  - The ROM for indeterminate diagnostic categories of TBSRTC will change
  - The PPV/NPV for molecular testing panels will change
  - Management issues for FVPTC
  - Medicolegal issues for FP diagnosis of PTC
- Future modifications in our approach to the indeterminate thyroid FNA will be needed
Impact of Reclassifying Noninvasive Follicular Variant of Papillary Thyroid Carcinoma on the Risk of Malignancy in The Bethesda System for Reporting Thyroid Cytopathology

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BACKGROUND: Recent discussions have focused on redefining noninvasive follicular variant of papillary thyroid carcinoma (NIFVPTC) as a neoplasm rather than a carcinoma. This study assesses the potential impact of such a reclassification on the implied risk of malignancy (ROM) for the diagnostic categories of The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC). METHODS: The study consisted of consecutive fine-needle aspiration biopsy (FNAB) cases collected between January 1, 2013 and June 30, 2014 from 5 academic institutions. Demographic information, cytology diagnoses, and surgical pathology follow-up were recorded. The ROM was calculated with and without NIFVPTC and was presented as a range: all cases (ie, overall risk of malignancy [OROM]) versus those with surgical follow-up only. RESULTS: The FNAB cohort consisted of 6943 thyroid nodules representing 5179 women and 1409 men with an average age of 54 years (range, 9-94 years). The combined average ROM and OROM for the diagnostic categories of TBSRTC were as follows: nondiagnostic, 4.4% to 23.3%; benign, 0.9% to 9.3%; atypia of undetermined significance/ follicular lesion of undetermined significance (AUS/FLUS), 12.1% to 31.2%; follicular neoplasm (FN), 21.3% to 33.2%; suspicious for malignancy (SM), 62.1% to 86.8%; and malignant, 75.9% to 99.1%. The impact of reclassifying NIFVPTC on the ROM and OROM was most pronounced and statistically significant in the 3 indeterminate categories: the AUS/FLUS category had a decrease of 5.2% to 13.6%, the FN category had a decrease of 9.9% to 15.1%, and the SM category had a decrease of 17.6% to 23.4% (P < .05), whereas the benign and malignant categories had decreases of 0.3% to 3.5% and 2.5% to 3.3%, respectfully. The trend of the effect on the ROM and OROM was similar for all 5 institutions. CONCLUSIONS: The results from this multi-institutional cohort indicate that the reclassification of NIFVPTC will have a significant impact on the ROM for the 3 indeterminate categories of TBSRTC. Cancer (Cancer Cytopathol) 2015;000:000-000. © 2015 American Cancer Society.
Non-Invasive Follicular Thyroid Neoplasm with Papillary-Like Nuclear Features (NIFTP)

- Malignant Surgical Follow-Up (877)
  - 756 were PTC
  - 173 PTC cases were NIFTP (23% of PTC)
- Distribution of NIFTP Cases:
  - Non-Diagnostic 0.6%
  - Benign 8.7%
  - AUS/FLUS 31.2%
  - Foll Neoplasm 26.6%
  - Susp Mal 24.3%
  - Malignant 8.7%
Effect of NIFTP reclassification on ROM for different Bethesda categories
The Impact of Non-Invasive Follicular Variant of Papillary Thyroid Carcinoma on Rates of Malignancy for Fine Needle Aspiration Diagnostic Categories

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Thyroid, 2015

- Brigham and Women’s Hospital, Boston, MA USA
- Consecutive Thyroid FNAs with corresponding resection over 22 months
- 655 thyroid FNAs
- Assess the ROM +/- NIFTP for each Bethesda diagnostic category
## NIFTP Study: ROM +/- NIFTP

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<thead>
<tr>
<th>Category</th>
<th>MGH</th>
<th>BWH</th>
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<tbody>
<tr>
<td><strong>Non-Diagnostic</strong></td>
<td>4.4-25.3%</td>
<td>18.9%</td>
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<tr>
<td></td>
<td>4.1-23.9%</td>
<td>17.0%</td>
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<tr>
<td><strong>Benign</strong></td>
<td>0.9-9.3%</td>
<td>13.2%</td>
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<td></td>
<td>0.5-5.8%</td>
<td>5.4%</td>
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<tr>
<td><strong>AUS/FLUS</strong></td>
<td>12-31.2%</td>
<td>39.2%</td>
</tr>
<tr>
<td></td>
<td>6.8-17.6%</td>
<td>21.6%</td>
</tr>
<tr>
<td><strong>Foll Neoplasm</strong></td>
<td>21.8-33.2%</td>
<td>45.5%</td>
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<tr>
<td></td>
<td>11.8-18%</td>
<td>37.5%</td>
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<tr>
<td><strong>Susp Mal</strong></td>
<td>62.1-82.6%</td>
<td>87.2%</td>
</tr>
<tr>
<td></td>
<td>44.5-59.2%</td>
<td>45.7%</td>
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<tr>
<td><strong>Malignant</strong></td>
<td>75.9-99.1%</td>
<td>98.7%</td>
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<tr>
<td></td>
<td>73.4-95.7%</td>
<td>93.6%</td>
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Non-Invasive Follicular Thyroid Neoplasm with Papillary-Like Nuclear Features (NIFTP)

Cytological features of “non-invasive follicular thyroid neoplasm with papillary-like nuclear features” and their correlation with tumor histology

Francesca Maletta MD, Federica Massa MD, Liborio Torregrossa MD, PhD, Eleonora Duregon MD, PhD, Gian Piero Casadei MD, Fulvio Basolo MD, Giovanni Tallini MD, Marco Volante MD, PhD, Yuri E. Nikiforov MD, PhD, Mauro Papotti MD

- NIFTP classified as AUS/FLUS (15%), FN (56%), SM (27%), Malignant (2%)
- Nuclear features are indistinguishable from invasive EFVPTC
  - Nuclear enlargement, pallor, grooves
  - Lack papillary architecture and infrequent intranuclear inclusions
- Cannot be reproducibly diagnosed preoperatively
How should FNA classification & clinical management change based upon expected impacts on the ROM for thyroid FNA reporting categories?

- Modify the cytologic criteria for classifying follicular patterned FNAs:
  - FN with atypia vs Susp Malignancy
  - Avoid diagnosing follicular patterned PTC as malignant
- Put a disclaimer statement about possible NIFTP on Susp for PTC cases
- Rely more on pre-op molecular testing (BRAF vs RAS)
- Use frozen section to guide the surgery
- Increase clinical threshold for performing TT
An option is to add a NIFTP disclaimer note on the cytology report for SM and Malignant categories

SUSPICIOUS MAL NOTE (BWH): “The overall cytomorphologic features are suggestive of a follicular variant of papillary carcinoma or its recently described indolent counterpart, noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP). Definitive distinction among these entities is not possible on cytologic material.”
A Final GOOD Word about FNA of NIFTP...

- Most NIFTP are detected by FNA +/- molecular testing
- Most NIFTP are triaged for surgery
- NIFTP is considered a potential precursor to carcinoma...
- Lobectomy is an appropriate treatment for NIFTP
- Most FP diagnoses of NIFTP can be avoided
Thank You!