



Memorial Sloan Kettering  
Cancer Center

# Negative ThyroSeq® Genomic Testing for Indeterminate Thyroid Nodules:

## The Memorial Sloan Kettering Cancer Center Experience

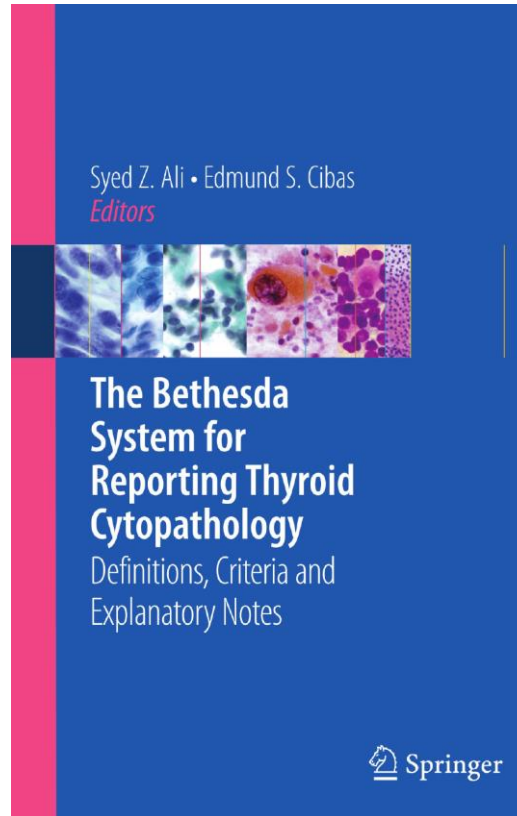
September 8, 2019  
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[www.MSKCC.org](http://www.MSKCC.org)

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Dr. Darren Buonocore declares he has no conflict(s) of interest to disclose.

# Cytologic Evaluation of Thyroid Nodules



# Bethesda Classification

Diagnostic category	Risk of malignancy(%)	Usual management <sup>a</sup>
Nondiagnostic or Unsatisfactory	<sup>b</sup>	Repeat FNA with ultrasound guidance
Benign	0–3	Clinical follow-up
Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance	~5–15 <sup>c</sup>	Repeat FNA
Follicular Neoplasm or Suspicious for a Follicular Neoplasm	15–30	Surgical lobectomy
Suspicious for Malignancy	60–75	Near-total thyroidectomy or surgical lobectomy <sup>d</sup>
Malignant	97–99	Near-total thyroidectomy <sup>d</sup>



# The Solution to Our Problems?

Afirma®

GENOMIC SEQUENCING CLASSIFIER



ThyroSeq®

Thyroid Genomic Classifier

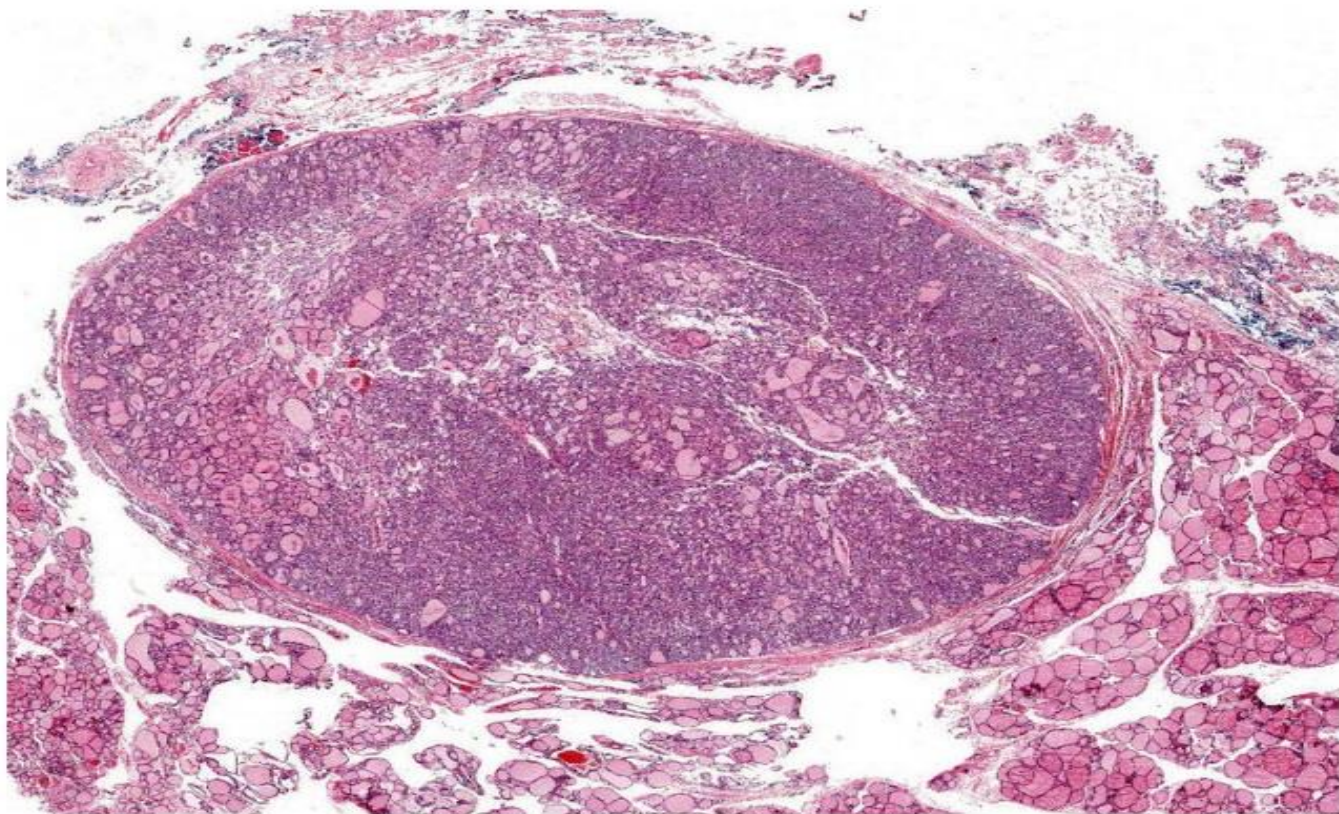
Precision  
Assurance  
Guidance



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# *It's Not Cancer: Doctors Reclassify a Thyroid Tumor*

By GINA KOLATA APRIL 14, 2016



A noninvasive follicular thyroid neoplasm with papillary-like nuclear features, or Niftp, a type of tumor that was previously considered a kind of cancer, but has been downgraded by a panel of doctors. Yuri Nikiforov

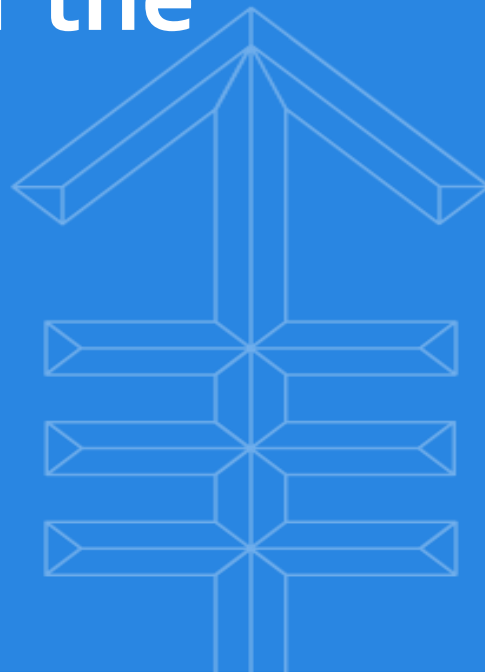


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# What does this mean for the Bethesda System?





# The 2017 Bethesda System for Reporting Thyroid Cytopathology

Edmund S. Cibas<sup>1</sup> and Syed Z. Ali<sup>2</sup>

THYROID  
Volume 27, Number 11, 2017  
© Mary Ann Liebert, Inc.  
DOI: 10.1089/thy.2017.0500

<i>Diagnostic category</i>	<i>Risk of malignancy if NIFTP ≠ CA (%)</i>	<i>Risk of malignancy if NIFTP = CA (%)</i>	<i>Usual management<sup>a</sup></i>
Nondiagnostic or unsatisfactory	5–10	5–10	Repeat FNA with ultrasound guidance
Benign	0–3	0–3	Clinical and sonographic follow-up
Atypia of undetermined significance or follicular lesion of undetermined significance	6–18	~ 10–30	Repeat FNA, molecular testing, or lobectomy
Follicular neoplasm or suspicious for a follicular neoplasm	10–40	25–40	Molecular testing, lobectomy
Suspicious for malignancy	45–60	50–75	Near-total thyroidectomy or lobectomy <sup>b,c</sup>
Malignant	94–96	97–99	Near-total thyroidectomy or lobectomy <sup>c</sup>



# American Thyroid Association guidelines

- Suggest the use of molecular studies in the management of patients with an indeterminate cytology diagnosis





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# ThyroSeq®



# ThyroSeq® Performance in Bethesda III/IV

**94%**  
Sensitivity

**82%**  
Specificity

**97%**  
NPV

**66%**  
PPV



# The Memorial Sloan Kettering Experience

- We propose to evaluate the NPV of ThyroSeq® at MSKCC, a major cancer center in the U.S. in which the prevalence of malignancy is high.



# Methods

- Cytology material from 252 thyroid nodules diagnosed as indeterminate which were submitted for ThyroSeq<sup>®</sup> analysis
- The results were reported as negative in 151 cases.
- Twenty-one of these 151 cases were surgically resected.



# Methods

- Gross description of the surgical resection specimen was compared to the radiologic findings at the time of biopsy to ensure the diagnosis correlated with the biopsied nodule
  - i.e. excluded any other carcinomas detected elsewhere in the specimen
- The ThyroSeq® results were correlated with the surgical diagnosis



# Results

- Surgical resection was performed with intent to remove the tested nodule was performed in 18 of the 21 nodules. They were commonly removed due large size, growth or patient's preference.
- Three nodules were resected due to the presence of a concurrent suspicious nodule.

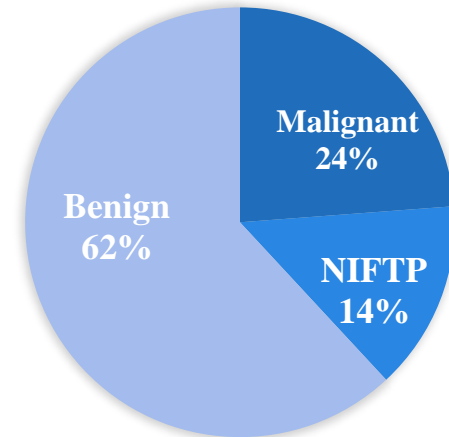




# Results

- 16 of 21 cases were confirmed to be benign or diagnosed as noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NFTIP)
  - Malignant potential of this lesion is unclear
- 5 were malignant
  - 2 classical papillary carcinoma
  - 3 follicular carcinoma

## THYROSEQ NEGATIVE NODULES



# Results

- Negative Predictive Value based on surgically resected nodules

61.9 (if NIFTP = CA)

76.2 (if NIFTP  $\neq$  CA)

## THYROSEQ POSITIVE NODULES



97%  
NPV



# Results

- Negative Predictive Value assuming unresected nodules are benign

89.4 (if NIFTP = CA)

91.3 (if NIFTP  $\neq$  CA)

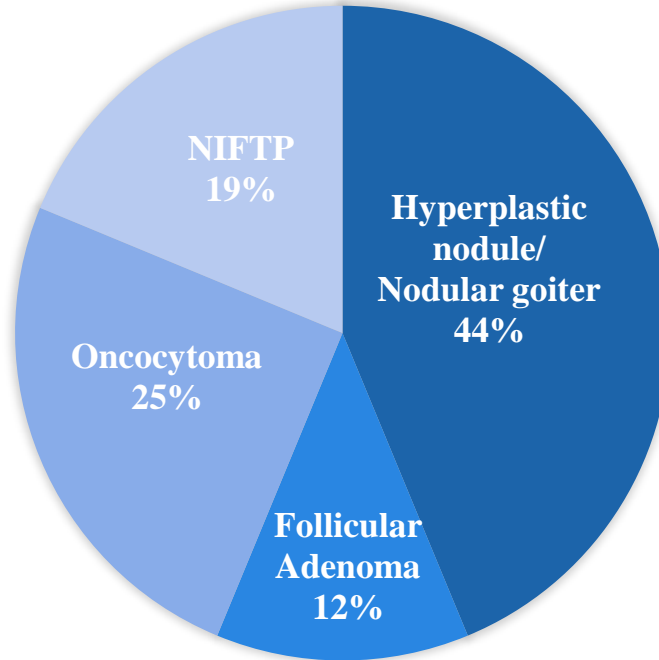
## THYROSEQ POSITIVE NODULES



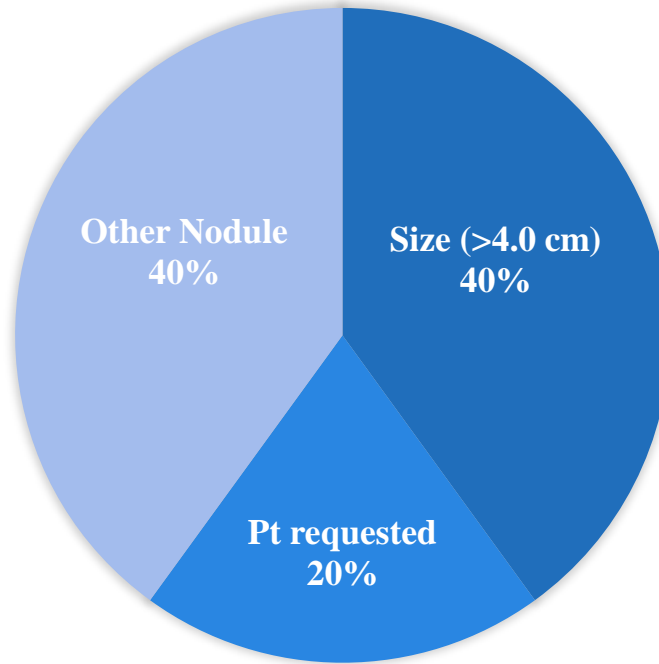
97%  
NPV



# Breakdown of Benign lesions & NIFTP



# Reasons for Surgery on Malignant



# Conclusion

- The NPV of ThyroSeq® is lower than reported and a negative result should be correlated with other clinico-radiological findings, particularly, in institutions with a high cancer prevalence.



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