



## Thyroid FNA: Molecular analysis Becomes reality

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## Bethesda FNA Groups

- I: Benign
- II: non-diagnostic
- III: FLUS/AUS (follicular lesion of undetermined significance/atypia of undetermined significance)
- IV: Follicular neoplasm/suspicious for follicular neoplasm
- V: Suspicious for malignancy
- VI: Malignant





## Follicular lesions

- III: FLUS/AUS
- IV: Follicular neoplasm





*Diagnostic surgery recommended  
(or repeat FNA for FLUS/AUS)*

## Affirma assay

- Company founded in 2009 by a former lab technician
- 167 genes probed (gene expression classifier)
- Aspirate is shipped to the company in So. SF; cytopathology performed by independent group; GEC on indeterminate
- Validation obtained by 49-center study (published in August 2012); 3789 pts


*Alexander E, et al. N Eng J Med, 2012*

## Affirma assay

### *Purported advantages*

- Avoid unnecessary surgery in up to 50% of patients (93 of 180) with NPV of 94%
- Not as robust for “rule in” cancer (52% PPV)





## Affirma assay

### *Disadvantages*

- Cost - \$3500 (limited patient liability)
- Technical challenges – either abdicate cytopathology or 2<sup>nd</sup> FNA
- Evolving corporate policy regarding reading of the cytology



Asuragen assay

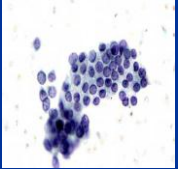
- Developed by Yuri Nikiforov (University of Pittsburgh pathologist)
- Mutational analysis based on the 4 genes known to be associated with >75% of differentiated thyroid cancers
- BRAF, RAS, PAX8/PPAR $\gamma$ , RET/PTC

*Nikiforov Y, et al. J Clin End Metab, 2011*

Asuragen assay

*Purported advantages*

- Increase certainty of diagnosis of malignancy
- Help make recommendation for total thyroidectomy
- Avoid the need for second surgery



Asuragen assay

*Disadvantages*

- Cost - \$300
- Technical challenges – either second FNA or dual FNAs (store sample)
- Cytology not required

Asuragen assay

*Summary*

*2 molecular analysis options*

- If FNA is benign, suspicious for malignancy, malignant or non-diagnostic – **no role for molecular cytology**
- If FNA is indeterminate (FLUS/AUS/FN/SFN) *and*:
  1. Pt. will have surgery regardless of FNA result (size, pt preference, etc) – **no role for gene classifier**
  2. Pt. will have total thyroidectomy regardless of FNA result (contralateral nodules, pt preference, etc) – **no role for mutational analysis**

Asuragen assay

*Patient scenario 1*



- 32 year old female; 1.8 cm follicular neoplasm
- **Affirma negative**
- Observation




Asuragen assay

*Patient scenario 2*

- 32 year old
- Other lobe normal, pt losing sleep over nodule and wants removal of one lobe only
- **Molecular analysis not indicated**

### Patient scenario 3

- 52 year old female with follicular neoplasm
- **Asuragen positive**
- Total thyroidectomy – pathology FVPTC



### Patient scenario 4

- 52 year old
- Contralateral nodules and follicular neoplasm – slight compressive symptoms
- **Molecular analysis not indicated**