

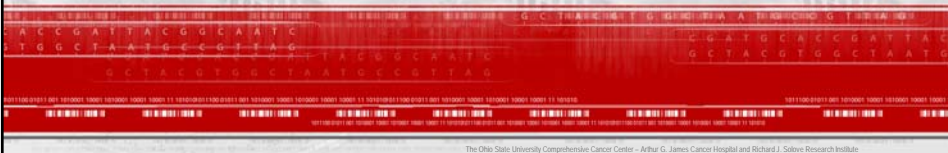
# Thyroid Cancer Guidelines 2015: Evolving Approaches to Thyroid Nodules and Cancer

Matthew D. Ringel, MD  
Ralph W. Kurtz Chair and Professor of Medicine  
Director, Division of Endocrinology  
The Ohio State University  
Co-Leader, Molecular Biology and Cancer  
Genetics Program  
Arthur G. James Comprehensive Cancer Center

OSU Clinical Endocrinology Update  
2016

The James

 THE OHIO STATE UNIVERSITY  
COMPREHENSIVE CANCER CENTER



## Disclosures

- Funding from NIH
- Member NCCN Thyroid Cancer Guidelines Panel
- Not member of ATA Guidelines Panel

The James

 THE OHIO STATE UNIVERSITY  
COMPREHENSIVE CANCER CENTER

## 2015 Guidelines: Focus on Individualization

- **Staging and Risk Stratification Expanded to Include three distinct time points**
  - Better matches clinical management
  - Based on Residual/Recurrence Data as well as Survival
- **Pattern Recognition of Individual Nodules**
- **AJCC/UICC Staging to Predict Mortality**
- **Initial Risk Stratification:** New in 2009 and Modified in 2015 to modify therapy based on residual/recurrence risk
- **Response to Therapy** Used to Reassess Risk: New 2015. Recognizes Outcomes Depend on Response to Treatment.

The James



## Clinical Case

- 23 year old woman who noted a lump in the neck in 5/2015. She saw her physician who thought it was likely a node. She had no other symptoms. TSH was normal in 1/2015 at an annual physical.
- It did not resolve and in 9/2015 she had a neck CT with contrast.
  - CT with right lobe nodules and nodes in the neck felt to be normal size but perhaps more on right than left.
  - Ultrasound revealed two right lobe nodules;
  - 2.4x2.5x2.1 cm, palpable, spongiform
  - 1.4x1.8x0.7 cm with calcifications, irregular border, posterior invasion, hypervascularity
  - Nodes not reported or visualized
- Referred for Evaluation

The James



4

## 2015 Guidelines approach to this patient

- **Laboratory Evaluation?** TSH is recommended. Calcitonin can be considered.
- **Adequate Ultrasound?** Guidelines recommend lymph node evaluation as part of a thyroid ultrasound
- **Fine Needle Aspiration?** Yes. Based on report, choice of nodule based on pattern recognition.
- **Molecular Testing:** In selected indeterminate cases depending on FNA result and if it will alter or drive clinical decision making based on ultrasound and individual patient clinical characteristics
  - Negative Predictive Testing: Identify Benign Nodules
  - Positive Predictive Testing: Identify Malignant Nodules

Haugen, et al Thyroid 2015

The James



5

## 2015 Guidelines Nodule FNA Selection

Pattern	Features	Estimated Risk of Cancer	FNA Size Cut-off
<b>High Suspicion</b>	Solid hypoechoic or solid/cystic with one or more of 1) irreg margins, 2) taller>wide, 3) partial rim calcification, 4)extrathyroidal extension	70-90%	>1cm
<b>Intermediate Suspicion</b>	Hypoechoic solid with smooth margins with none of the high susp features	10-20%	> 1 cm
<b>Low Suspicion</b>	Isoechoic or Hyperechoic or partial cystic with eccentric solid and no high suspicious features	5-10%	>1.5 cm
<b>Very Low Suspicion</b>	Spongiform or partially cystic nodules, no susp. features	<3%	>2 cm or observation
<b>Benign</b>	Pure cystic nodules	<1%	No FNA

Haugen, et al Thyroid 2015

The James



6

## Case:

- **Neck Ultrasound Confirms the presence of the two nodules but also Neck Nodes**
  - Right jugular nodes; level 3 and 2A with malignant characteristics; largest is posterior to the jugular vein measuring 0.8x0.9x1.5 cm
  - Right posterior triangle node that is solid with hypervascularity measuring 2.3x2.1x2.2 cm.
  - Left Lobe normal
  - No concerning nodes in the left central or lateral neck
- TSH is 0.68 mU/L
- **Review of CT images also demonstrated concerning nodes in the right lateral neck; none in mediastinum; no clear tracheal invasion**

The James



## 2015 Guidelines Node FNA Selection

- **Table 8: Ultrasound features of lymph nodes predictive of malignant involvement.** (adapted with permission from the European Thyroid Association guidelines for cervical ultrasound)

<u>Sign</u>	<u>Reported sensitivity %</u>	<u>Reported specificity %</u>
▪ Microcalcifications	5-69	93-100
▪ Cystic aspect	10-34	91-100
▪ Peripheral vascularity	40-86	57-93
▪ Hyperechogenicity	30-87	43-95
▪ Round shape	37	70

Haugen, et al Thyroid 2015

The James



## Case:

- **Ultrasound-guided FNA of the right posterior node**
  - Three Passes: Smears from all three; hub washout from two passes for Tg measurement; one hub washout for liquid preparation
  - FNA Tg: 11,740 ng/ml; serum Tg is 75 ng/ml
  - Cytology: Consistent with Papillary Thyroid Cancer
- The Nodule was not aspirated in this circumstance

The James



## Next Steps per the ATA 2015 Guidelines

- **Surgery Recommendation:**
  - For intrathyroidal nodules (1-4 cm) without nodes hemithyroidectomy or total thyroidectomy are acceptable options.
  - For more extensive disease, total thyroidectomy and compartmental node dissection in selected cases with involved nodes is recommended.
- **Surgery Performed:**
  - Total thyroidectomy, central neck dissection, lateral neck dissection to include the involved compartments of the neck

Haugen, et al Thyroid 2015, In Press

## Surgical Pathology

- 2.1x.1.7 PTC with local invasion into muscle and 5 sites of vascular invasion
- 3/14 nodes positive in the central neck, all < 5 mm
- 4/14 nodes in the jugular chain positive: largest 1.2 cm with extranodal invasion
- 2/46 nodes in the lateral neck; the largest is 2.4 cm with no local invasion

### Radiology:

CT of the chest without contrast with no evidence of lung metastases

## AJCC 7<sup>th</sup> Edition/ TNM System

- Identify High-Risk Patients in whom mortality may be increased
- Allow Accurate Communication
- Maintain Common Cancer Registries
  
- Does not Predict Residual/Recurrent Disease
- Firm Age Cut-off that may not match clinical severity of disease
- Does not account well for extent of surgery

## Revised ATA Initial Risk Stratification

- **Low Risk for Recurrence**
  - Intrathyroidal differentiated 1-4 cm
  - No Local or Vascular Invasion
  - $\leq 5$  LN micromets ( $\leq 2$ mm)
  - Minimally Invasive FTC (Capsular Invasion or minor Vascular Invasion) ~15%
- **Intermediate Risk for Recurrence**
  - Everything not in Low or High Risk
  - High Risk Variants of DTC ~40%
  - Intrathyroidal 1-4 cm or multifocal micro PTC with local invasion if BRAF V600E ; Nodes 2 mm up to 3 cm
- **High Risk for Recurrence**
  - Gross Extrathyroidal Extension ~80%
  - Incomplete Resection; Large Nodes (>3 cm)
  - Distant Metastases; Extensive Vascular Inv. FTC

Modified from Erik Alexander

The James  
THE OHIO STATE UNIVERSITY  
COMPREHENSIVE CANCER CENTER

## What is the Staging and Risk Category for This Patient?

- **TNM:**
  - Stage 1 or Stage 2
    - T4a N1b Mx (M0 based on the CT scan)
    - Excellent Anticipated Long Term Survival
- **ATA Risk Category**
  - High Risk for Residual disease or Recurrence
- **Molecular Testing of Tumor**
  - Not Performed, No Impact on Therapeutic Decisions at This Time

The James  
THE OHIO STATE UNIVERSITY  
COMPREHENSIVE CANCER CENTER

## Should I-131 be Administered?

- **Recommendations**
  - Based on Risk Stratification of High Risk: **YES**
- **Preparation and Dosing**
  - RhTSH vs Thyroxine Withdrawal
    - Pt and Physician Preference
  - Dosing based on goals of therapy
    - Adjuvant Therapy for Probably Residual Disease

15

The James

 THE OHIO STATE UNIVERSITY  
COMPREHENSIVE CANCER CENTER

## Continued Postoperative Restaging

- Pt on L-T4. **TSH 0.35; Tg 3.2** six weeks after surgery
- **TSH: 0.12; Tg: 0.4** three months after surgery
- **Neck Ultrasound** with postoperative change and no identifiable residual thyroid cancer.
- Should I-131 be administered?
- If so, what preparation and dose?

The James

 THE OHIO STATE UNIVERSITY  
COMPREHENSIVE CANCER CENTER



## Guidelines 2015 Recommendation

- **Recommendation 56:**
- When RAI is intended for initial adjuvant therapy to treat suspected microscopic residual disease, administered activities above those used for remnant ablation **up to 150 mCi** are generally recommended (in absence of known distant metastases).
- **Weak recommendation, Low-quality evidence**

The James



## Treatment Decision

- Based on pathology and clinical features, I-131 was recommended
- Dose was determined based on:
  - Post-operative Staging
  - Pre-therapy scan
  - Patient wishes
- Pre therapy scan: Thyroid bed uptake only
- Dosed with 100 mCi I-131
- Stimulated Tg: 28 ng/ml
- Post-therapy scan with thyroid bed and lung metastases

The James



## Post-treatment Course

- 6 months later: Tg <0.1 ng/ml with TSH 0.06 mU/L and normal Free T4
- Two episodes of significant sialoadenitis
- Otherwise doing well

19

The James

 THE OHIO STATE UNIVERSITY  
COMPREHENSIVE CANCER CENTER

## RESPONSE TO THERAPY STAGING

### Response to Therapy

### Recommendations:

#### Excellent Response:

Suppressed Tg <0.2 or Stim Tg <1.0  
Negative Ultrasound

Decrease Intensity and  
Frequency of Follow-up  
and TSH Suppression

#### Incomplete Biochemical Response

Suppressed Tg >1.0 or Stim Tg <10  
Negative Ultrasound

Stable/Lower Tg - Observe  
Rising Tg – Additional  
Investigations

#### Incomplete Structural Response

Structural Evidence of Disease

Consider Additional  
Investigations & Therapies

#### Indeterminate Response

TgAb+ Stable or declining  
Suppressed Tg 0.2-1.0 or Stim Tg 1.0-10  
Indeterminate Imaging

Continued Observation  
and Testing

The James

 THE OHIO STATE UNIVERSITY  
COMPREHENSIVE CANCER CENTER

## Response Status of the Patient

- Excellent Response Based on Tg
- With Distant Mets Plan for the following
  - TSH-stimulated Tg
  - Chest CT without Contrast
  - Neck Ultrasound
- Once completed will have a more complete assessment of response to therapy.

21

The James



## ATA Guidelines

- **Continue to Evolve over Time**
- **2005-2009:** Proposed Risk Stratification for Residual/Recurrent Disease
  - Defined Uses of I-131
  - Added Molecular Testing
  - Ultrasound FNA Choices focused on features of the nodules
- **2015:** Ultrasound Pattern recognition for FNA
  - Expanded discussions on molecular testing in FNA and tumor samples
  - Strengthened Post-Diagnosis Risk Stratification
  - Expanded Role of less aggressive surgery
  - Tightened use of I-131 for clinical benefit
  - Added Response to Therapy Definitions to Tailor Monitoring and Treatments over time

22

The James

