Adult Patients with Thyroid Nodules
American Thyroid Association 2015 Guideline

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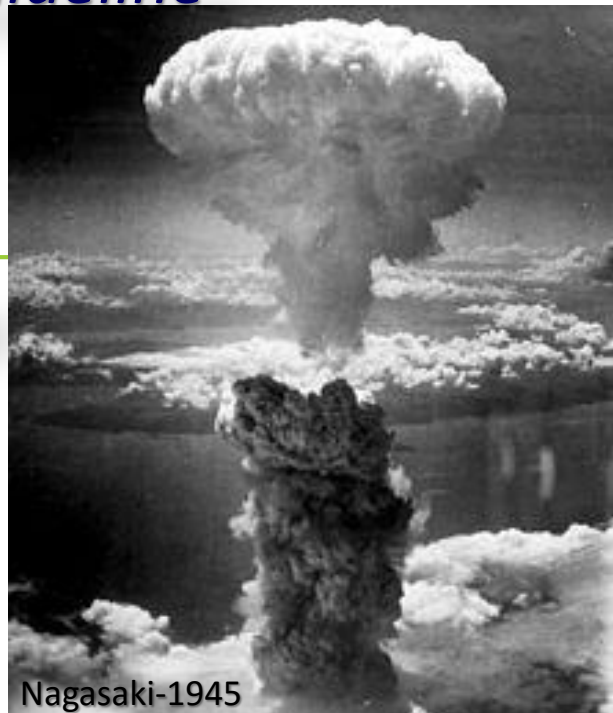
April 23, 2016


Nagasaki-1945

Disclosure:

No Conflicts of Interest to Disclose

This presentation is intended for educational purposes only and does not replace independent professional judgment.

I am expressing my own views based on my reading, analysis and interpretation of the scientific information.

I am a member of SPED and a Federal Government employee but I am **not** speaking in representation of or presenting the views of the Veterans Administration, Puerto Rican Society of Endocrinology and Diabetes, State or Federal Government Agency or Department, other Professional Societies, Public or Private Corporation, or Pharmaceutical Company.

Learning Objectives

- At the end of this lecture, participants will be able to:
  - Outline how to manage a patient with a thyroid nodule
  - Risk stratify thyroid nodules by ultrasonography characteristics
  - Recognize when to proceed with a thyroid fine needle aspiration
  - Appraise the cytology report and role of molecular markers in the evaluation and management of the patient with thyroid nodules.

Thyroid Nodules ATA 2015 Guideline

How many have read the complete guideline?

- The complete guideline has 133 pages, 92 of text, with more than 101 recommendations.
- Thyroid nodules part has ~34 recommendations
  - 25 Strong Recommendations
    - 4 High Evidence
    - 14 Moderate Evidence
    - 7 Low Evidence
  - 6 Weak Recommendations
  - 3 No Recommendations

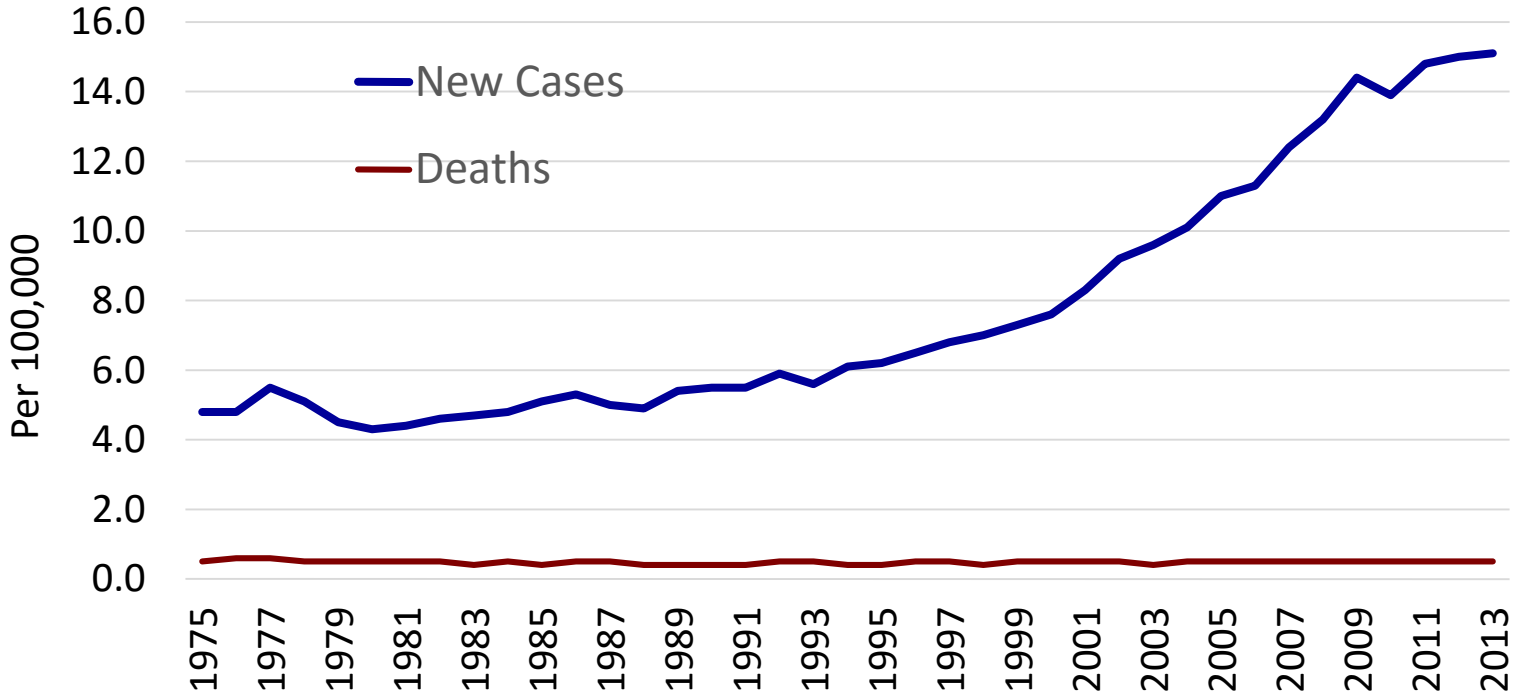
Haugen BR, et al. ***Thyroid*** 2016;26:1-132

Thyroid Cancer

64,300 Estimated New Cases in 2016

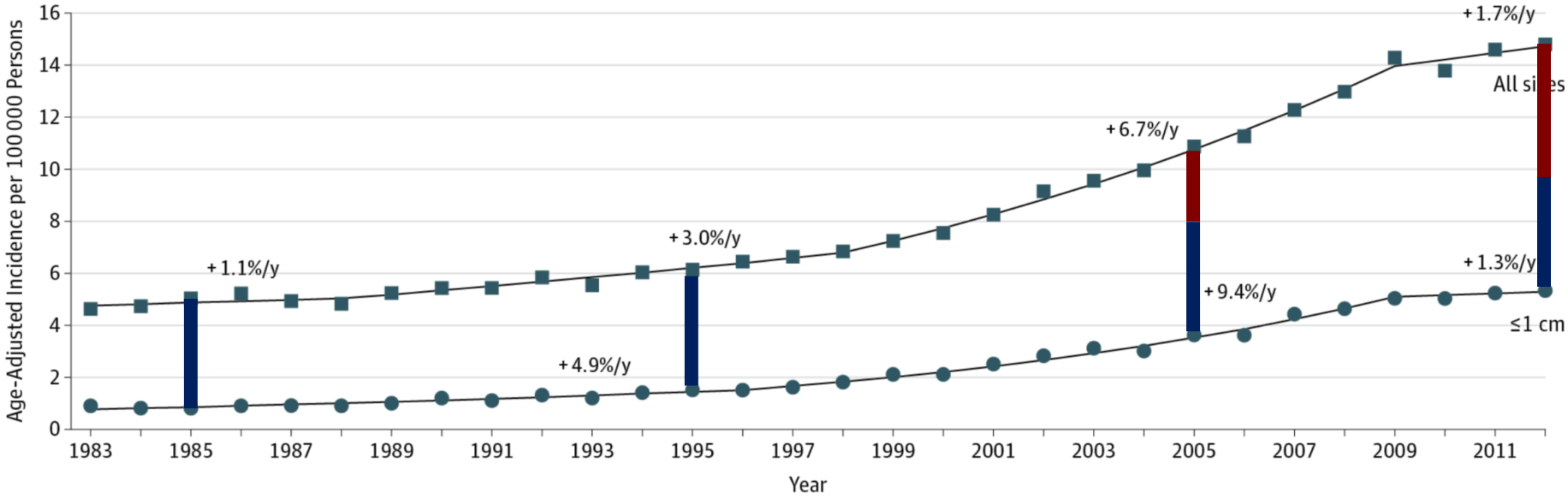
1,980 Estimated Deaths in 2016

98.1% Survival 2006-2012



http://seer.cancer.gov/statfacts/html/thyro.html

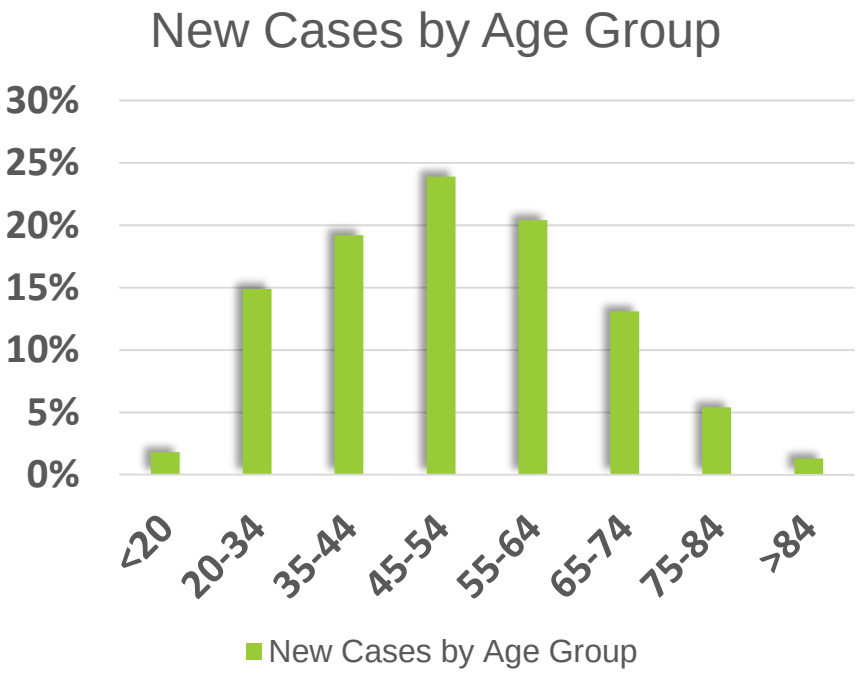
Time Trends in Incidence of Thyroid Cancer for All Sizes and Those of 1 cm or Less



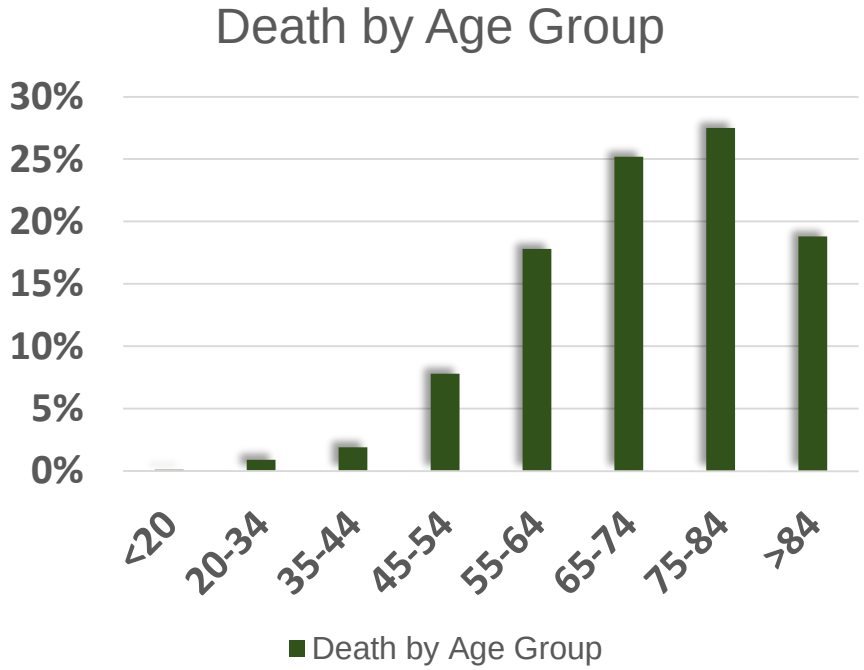
Morris LG *JAMA Otolaryngol Head Neck Surg*. Online April 14, 2016. doi:10.1001/jamaoto.2016.0230

Thyroid Cancer

Median Age at Diagnosis if 51 years



Median Age at Death is 73 years



http://seer.cancer.gov/statfacts/html/thyro.html

Thyroid Nodules

No Recommendation
Neither For or Against

- Screening in people with familial DTC
  - Syndromes associated with DTC warrant screening as per syndrome
- Routine serum calcitonin
- Nodules >1cm with very low suspicion sonographic pattern or pure cyst surveillance.

Haugen BR, et al. ***Thyroid*** 2016;26:1-132

Not Recommended

- Thyroid scan if the TSH if normal or elevated
- Serum thyroglobulin for initial thyroid nodule evaluation
- Routine TSH suppression therapy for benign thyroid nodules in iodine sufficient populations.
  - Potential harm outweighs benefit for most patients

Haugen BR, et al. ***Thyroid*** 2016;26:1-132

We Are Going To Be Talking About Common Garden Variety and Not Special Situations

- Special situations:
  - Associated hoarseness or dysphagia
  - History of rapid growing mass
  - Personal history of head and neck or total body xRT
  - Exposure to ionizing radiation
  - Family history of thyroid cancer or syndrome associated to thyroid cancer
  - Fixation to surrounding tissue
  - Associated cervical lymphadenopathy

Haugen BR, et al. ***Thyroid*** 2016;26:1-132

Thyroid Nodule

- Radiological diagnosis
  - "…discrete lesion within the thyroid gland that is radiologically distinct from the surrounding thyroid parenchyma."
    - Non-Palpable nodules: incidentaloma

Haugen BR, et al. ***Thyroid*** 2016;26:1-132

Most Thyroid Nodules are Low Risk

Primum Non Nocere or Non-Maleficence Principle

- "…given the unfavorable cost/benefit considerations, attempts to diagnose and treat all such small thyroid cancers in an effort to prevent exceedingly rare outcomes is deemed to cause more harm than good."

Haugen BR, et al. ***Thyroid*** 2016;26:1-132

Initial Evaluation

You suspect or palpate a lump in the thyroid. How do you proceed?

Serum TSH

- Normal or High TSH
  - Thyroid sonography with survey of cervical lymph nodes
- Low TSH
  - Radionuclide thyroid scan
  - Thyroid ultrasound
    - Hot nodule (s)
      - Concordant with ultrasound do not require FNA
    - Warm or Cold areas should be evaluated as having normal or high TSH

Haugen BR, et al. ***Thyroid*** 2016;26:1-132

If a nodule is identified in the ultrasound
and
the TSH is NOT low,
then comes the determination if aspiration biopsy should be done or not.

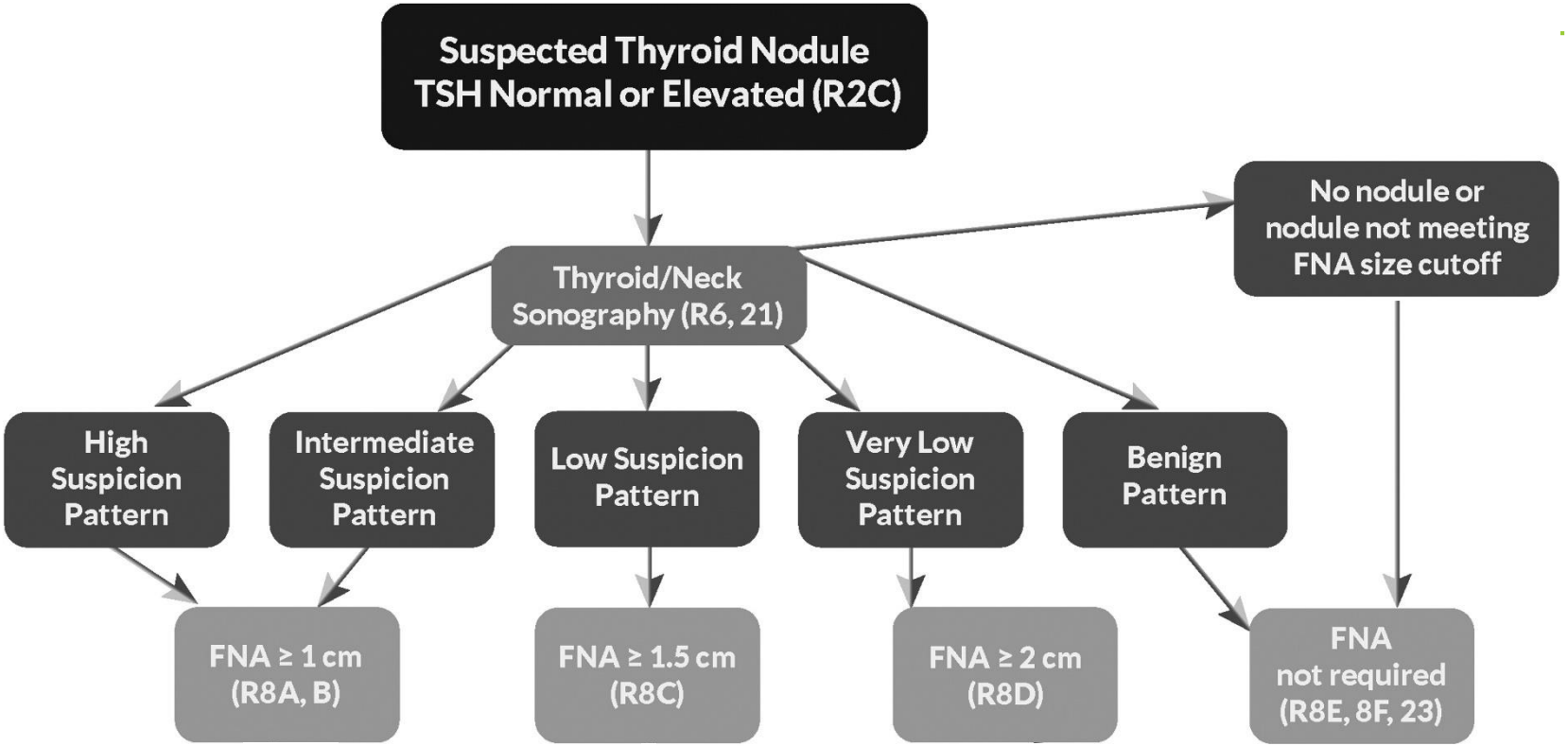
Thyroid Sonography

- Information looked:
  - Is there truly a nodule?
  - Specify size of the nodule
  - US imaging characteristics
  - Cystic component*
  - Location of the nodule*
  - Suspicious cervical lymphadenopathy
- Report should describe:
  - Thyroid parenchyma & gland Size
  - Nodule size (3 dimensions), location, composition, echogenicity, margins, presence and type of calcifications, shape and vascularity.
  - Presence or absence of cervical lymph nodes in the central or lateral compartments

*Decrease the accuracy of FNA by palpation.

Haugen BR, et al. ***Thyroid*** 2016;26:1-132

Ultrasonographic Risk Stratification

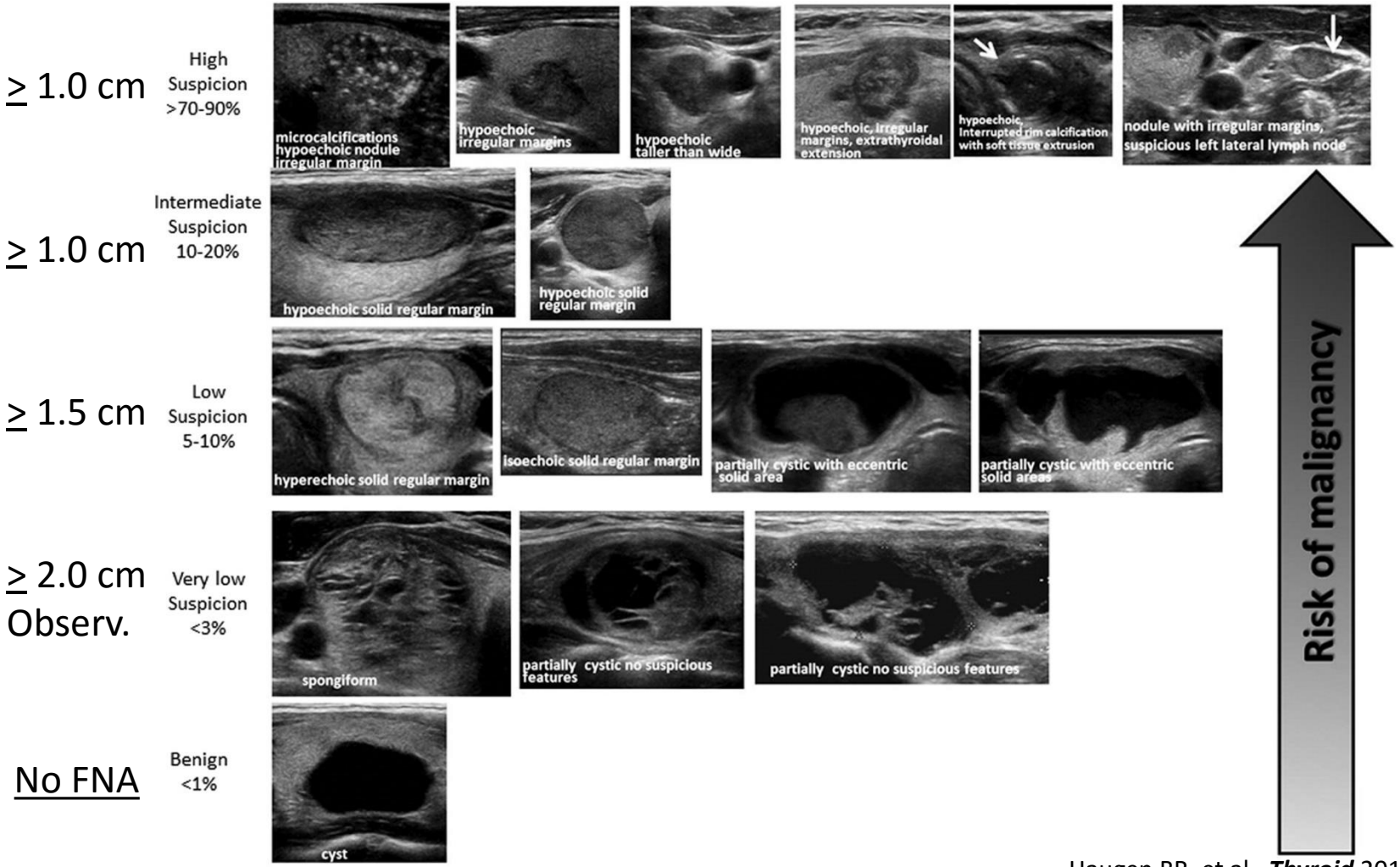


Haugen BR, et al. *Thyroid* 2016;26:1-132

Malignancy Stratification	US Features	Malignancy Risk	Cutoff For FNA
High Risk	Irregular margins (≠Poorly defined margins) Microcalcifications (Bright Reflectors) Taller than wide in transverse view Rim Ca with extrusive soft tissue component Extrathyroidal extension	>70-90%	≥ 1.0 cm
Intermediate	Hypoechoic without High Risk Features	10-20%	≥ 1.0 cm
Low	Isoechoic, hyperechoic, or partially cystic with eccentric solid areas without High Risk Features	5-10%	≥ 1.5 cm
Very Low	Spongiform or partially cystic without High Risk Features	<3%	≥ 2.0 cm Or Observ.
Benign	Purely cystic	<1%	No Bx

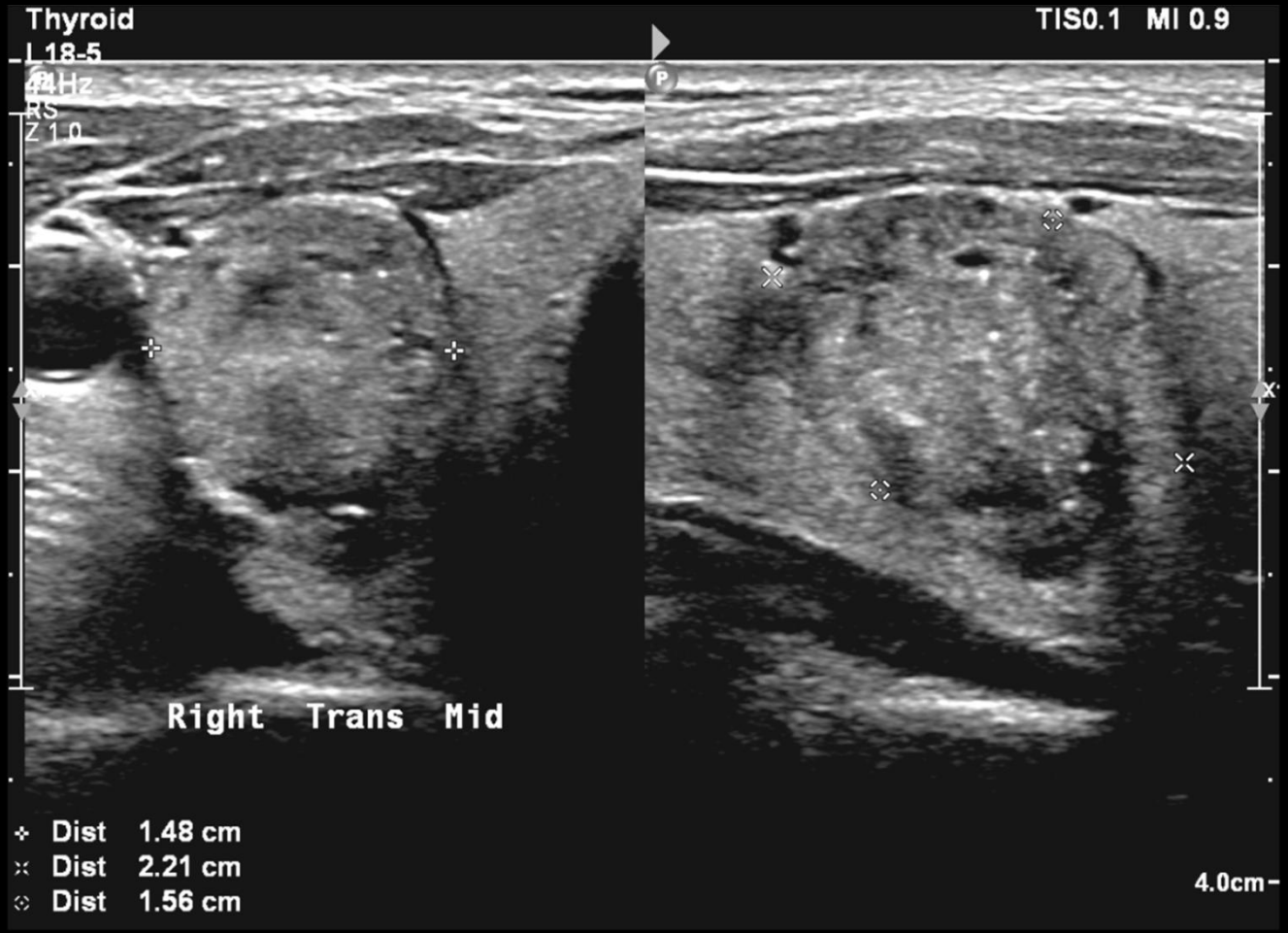
Vascularity is NOT used to stratify the nodules.

Haugen BR, et al. ***Thyroid*** 2016;26:1-132

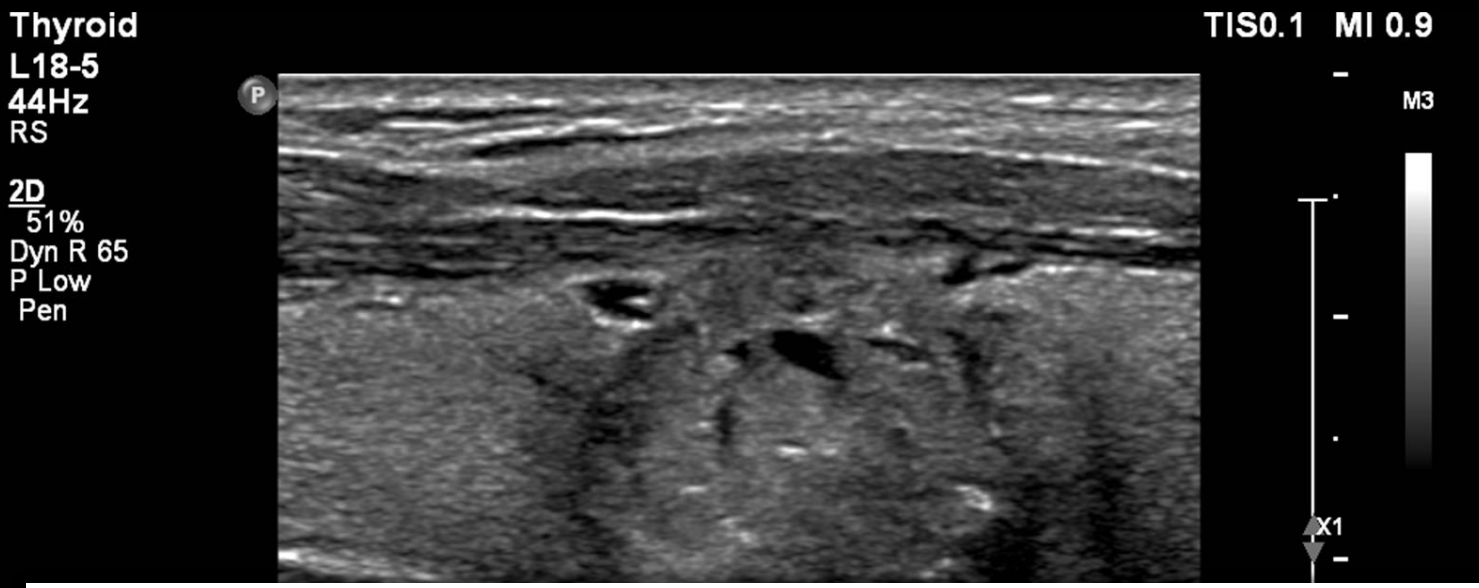


Haugen BR, et al. ***Thyroid*** 2016;26:1-132

Pte A


Thyroid
L 18-5
RS
Z 1.0
TIS0.1 MI 0.9
Right Trans Mid
Dist 1.48 cm
Dist 2.21 cm
Dist 1.56 cm
4.0cm
146/60
Image #:10/27

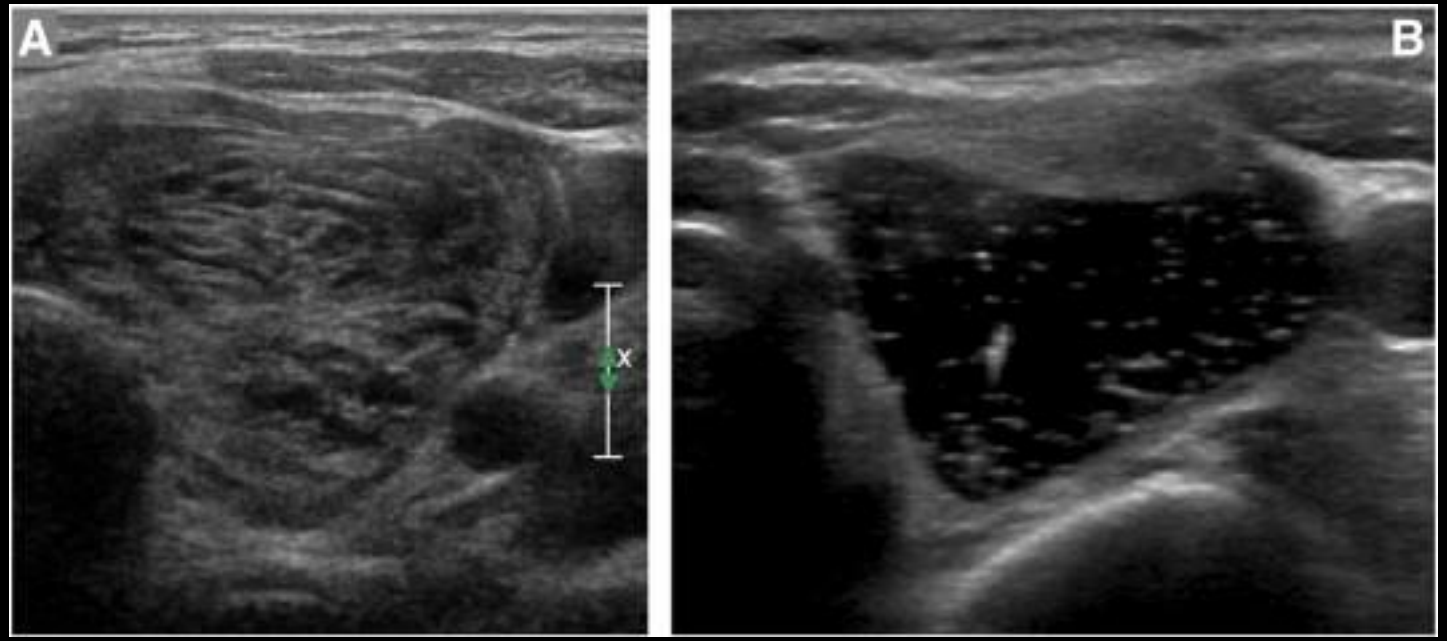
Pte A



Presence of abundant follicular cells with focal architectural and cytologic atypia, giant multinucleated histiocytes, hemosiderin laden macrophages, Hurthle cells, mixed inflammatory cells, colloid and blood.

Diagnosis:

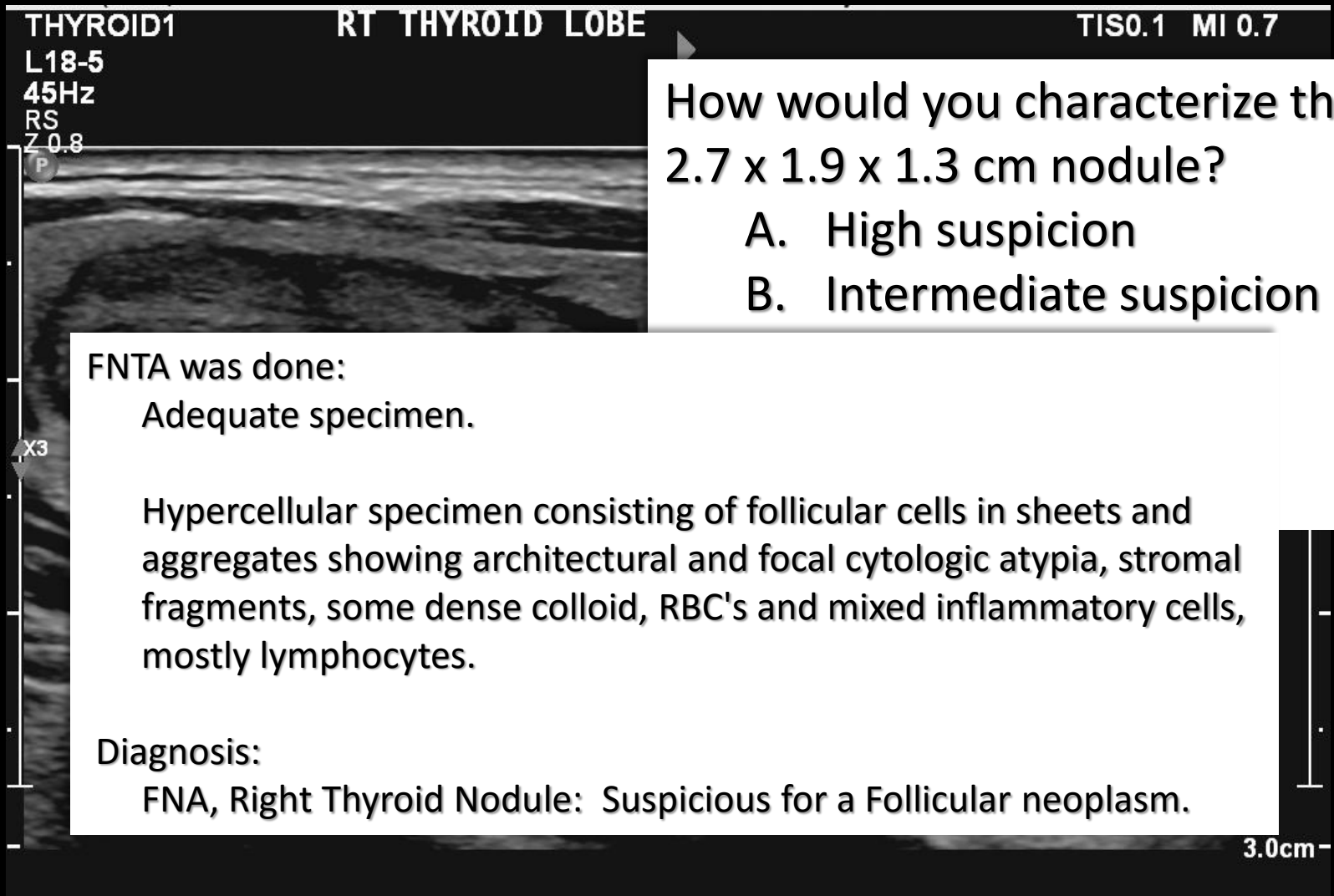
FNA, Right Thyorid Nodule: Follicular Neoplasm/Suspicious for a Follicular neoplasm.



Transverse grayscale images of histology-proven benign thyroid nodules from a 73-year-old woman with multinodular goiter. (A) This nodule has spongiform appearance and a hypoechoic halo. (B) This typical colloid nodule in the same patient is predominantly cystic with internal colloid (tiny echogenic foci with posterior comet tail artifacts).

Junwei Zhang, Zhaojin Chen, Gopinathan Anil
Ultrasound-guided thyroid nodule biopsy: outcomes and correlation with imaging features
Clinical Imaging, Volume 39, Issue 2, 2015, 200–206
http://dx.doi.org/10.1016/j.clinimag.2014.10.019

Kim JY *Ultrasonography* 2015;34:304



How would you characterize this 2.7 x 1.9 x 1.3 cm nodule?

A. High suspicion
B. Intermediate suspicion

FNTA was done:

Adequate specimen.

Hypercellular specimen consisting of follicular cells in sheets and aggregates showing architectural and focal cytologic atypia, stromal fragments, some dense colloid, RBC's and mixed inflammatory cells, mostly lymphocytes.

Diagnosis:

FNA, Right Thyroid Nodule: Suspicious for a Follicular neoplasm.

Report from a Well Respected Hospital PR

April 2015

STUDY: US THYROID

STUDY:

THYROID ULTRASOUND:

THE ISTHMUS MEASURES 0.3 CM. THE RIGHT THYROID GLAND MEASURES 3.9 X 1.8 X 1.5 CM. THE LEFT THYROID GLAND MEASURES 3.3 X 1.7 X 0.9 CM. THERE IS A LARGE SOLID NODULE IN THE RIGHT THYROID GLAND MEASURING 1.9 X 2.0 X 1.4 CM.

IMPRESSION:

LARGE SOLID NODULE IN THE RIGHT THYROID GLAND.

DATE: MARCH 11, 2016

STUDY:

Thyroid ultrasound

The thyroid gland is enlarged. The thyroid gland has inhomogeneous echotexture.

The right thyroid gland measures 4.5 cm long x 1.1 cm AP x 1.5 cm transverse. The left thyroid gland measures 4.3 cm x 0.9 cm AP x 1.4 cm transverse. The isthmus measures 0.2 cm.

There are solid nodules in the right thyroid gland measuring 1.1 x 0.7 x 1.1 cm lower pole, 0.6 x 0.3 x 0.5 cm in the mid pole, 0.3 x 0.2 x 0.3 cm in the upper pole. There are also solid nodules in the left thyroid gland measuring 0.9 x 0.6 x 0.9 cm in the upper pole, 0.4 x 0.5 x 0.6 cm in the lower pole. There is a solid nodule in the isthmus measuring 1.2 x 0.7 x 1 cm.

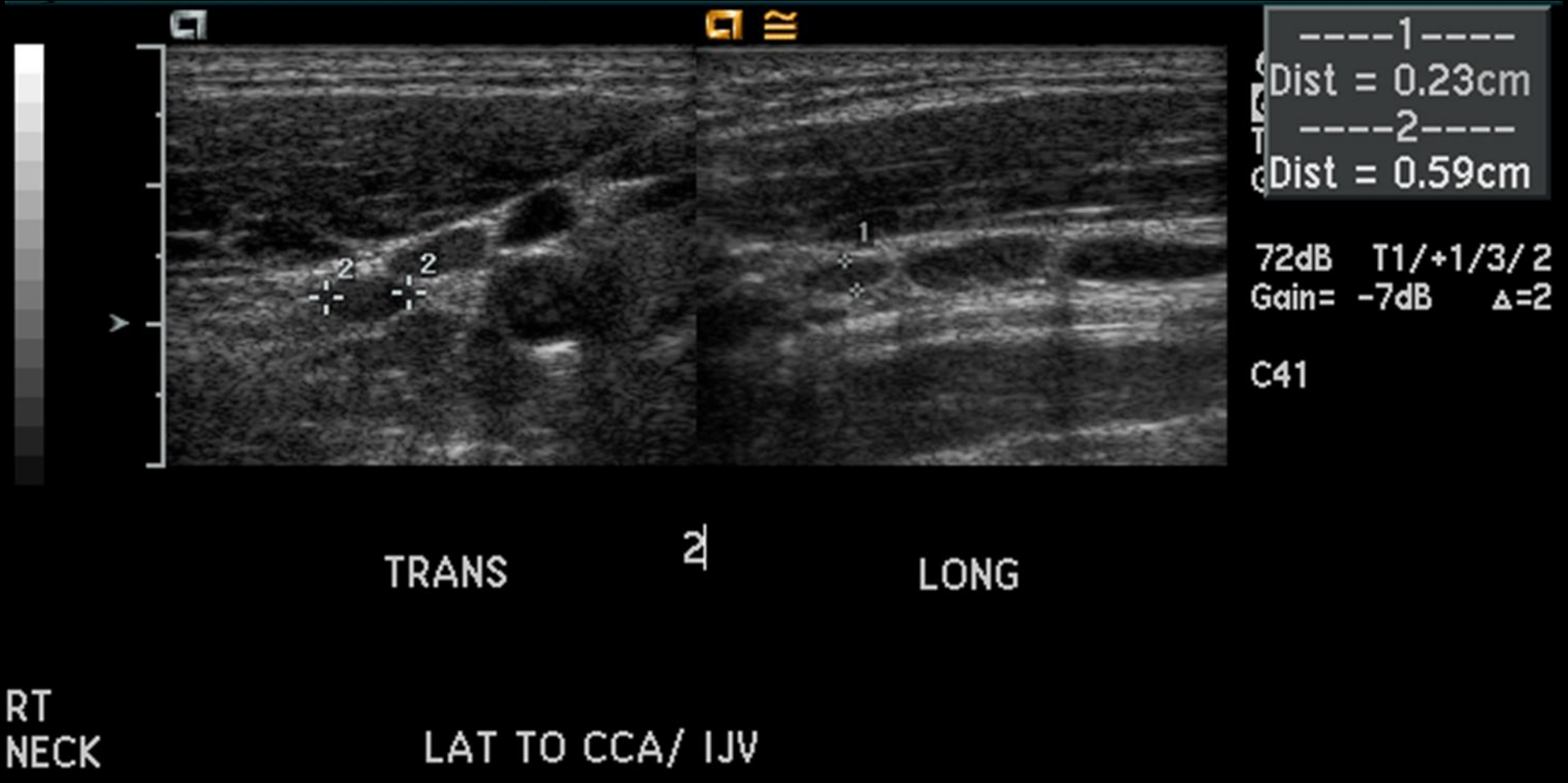
Impression:

Solid nodules in the thyroid gland as described above.

Cervical Lymphadenopathies

- Sonographic evaluation of the anterior cervical lymph node compartments (central and lateral) should be performed whenever thyroid nodules are detected.
- If cervical lymph nodes are sonographically suspicious, FNA should be performed for cytology and washout for Tg measurement if indicated.
  - In this scenario nodules less than 1cm should be considered for FNA if likely to represent the primary tumor based in sonographic features.

Haugen BR, et al. ***Thyroid*** 2016;26:1-132


----1----
Dist = 0.23cm
----2----
Dist = 0.59cm
72dB T1/+1/3/2
Gain= -7dB Δ=2
C41
TRANS
LONG
RT
NECK
LAT TO CCA/ IJV

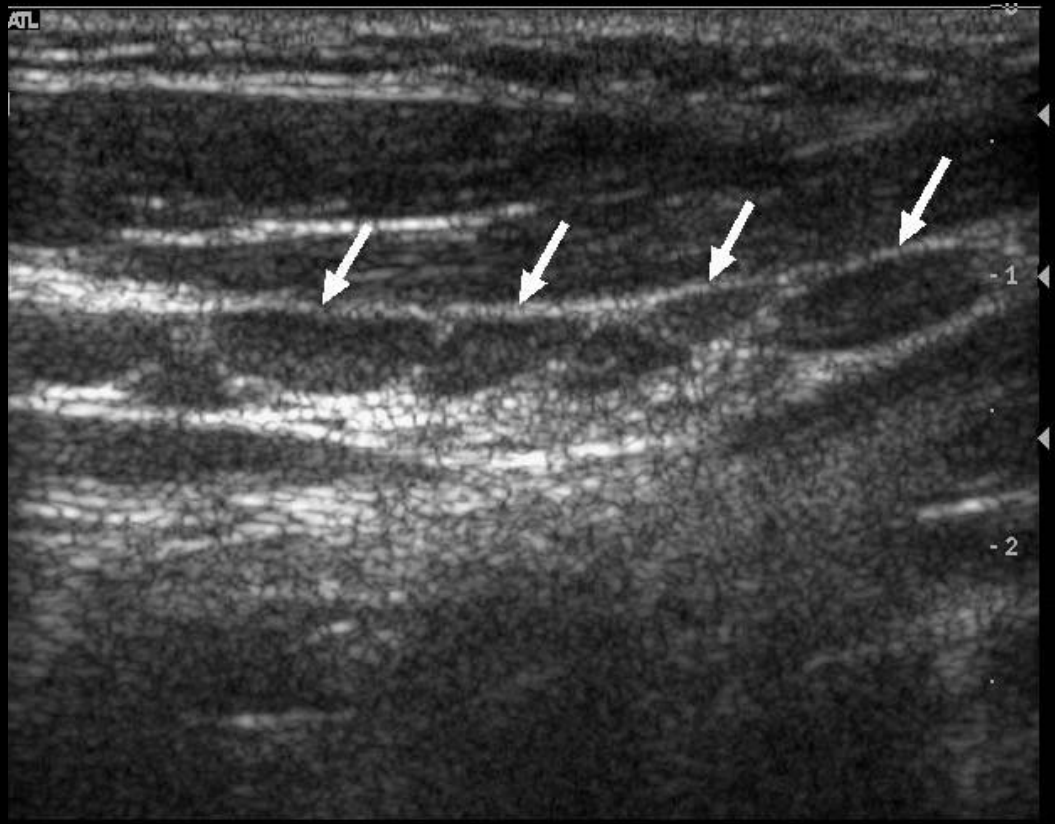
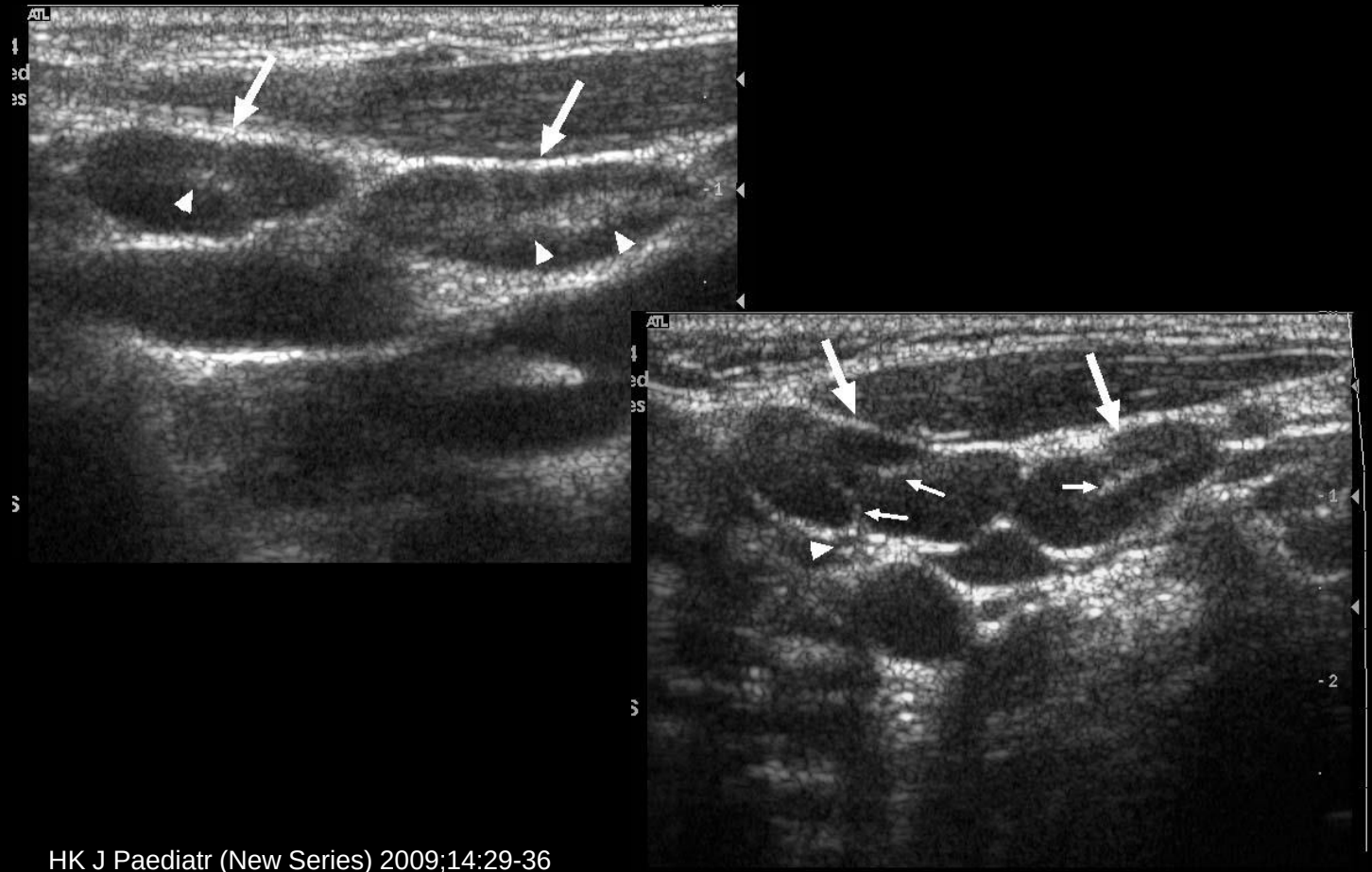


Figure 2 Longitudinal sonogram showing multiple normal lymph nodes (arrows) in the posterior triangle of a 9-year-old child. Note the lymph nodes are well-defined, hypoechoic and oval-shaped.

HK J Paediatr (New Series) 2009;14:29-36



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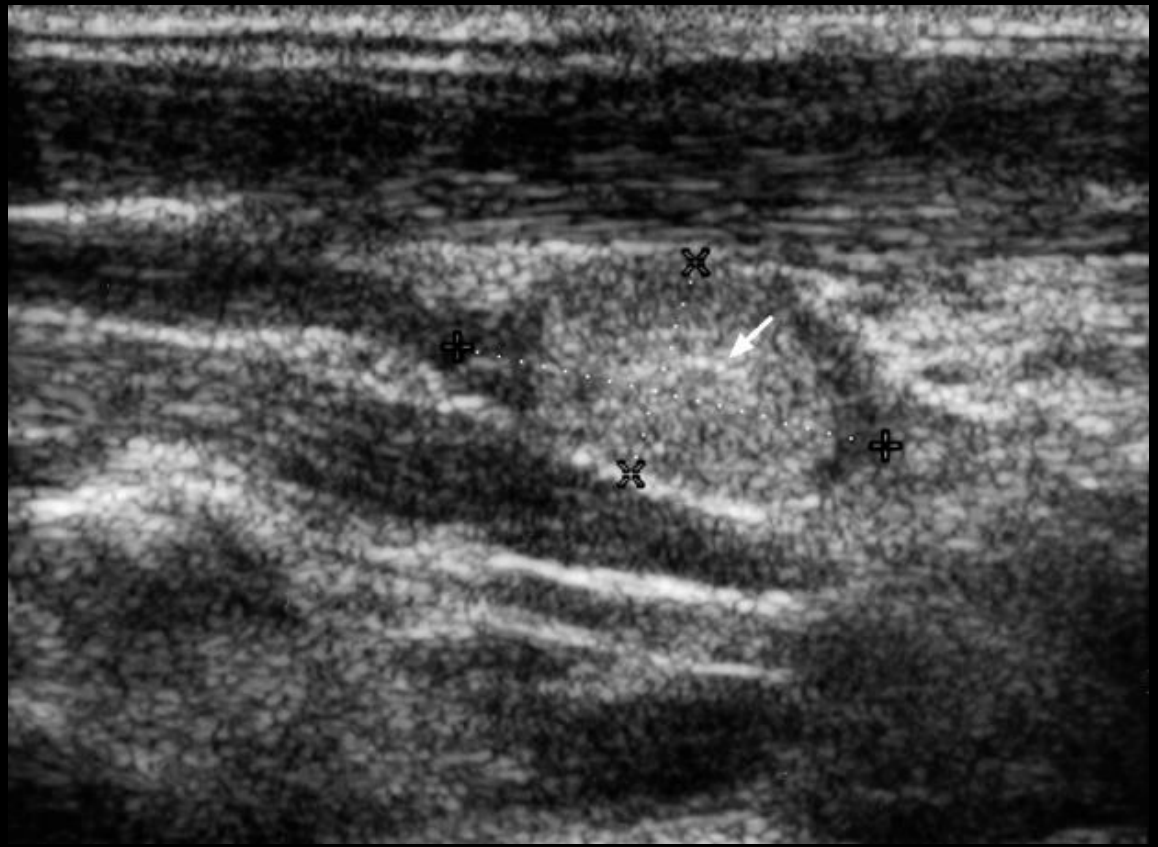
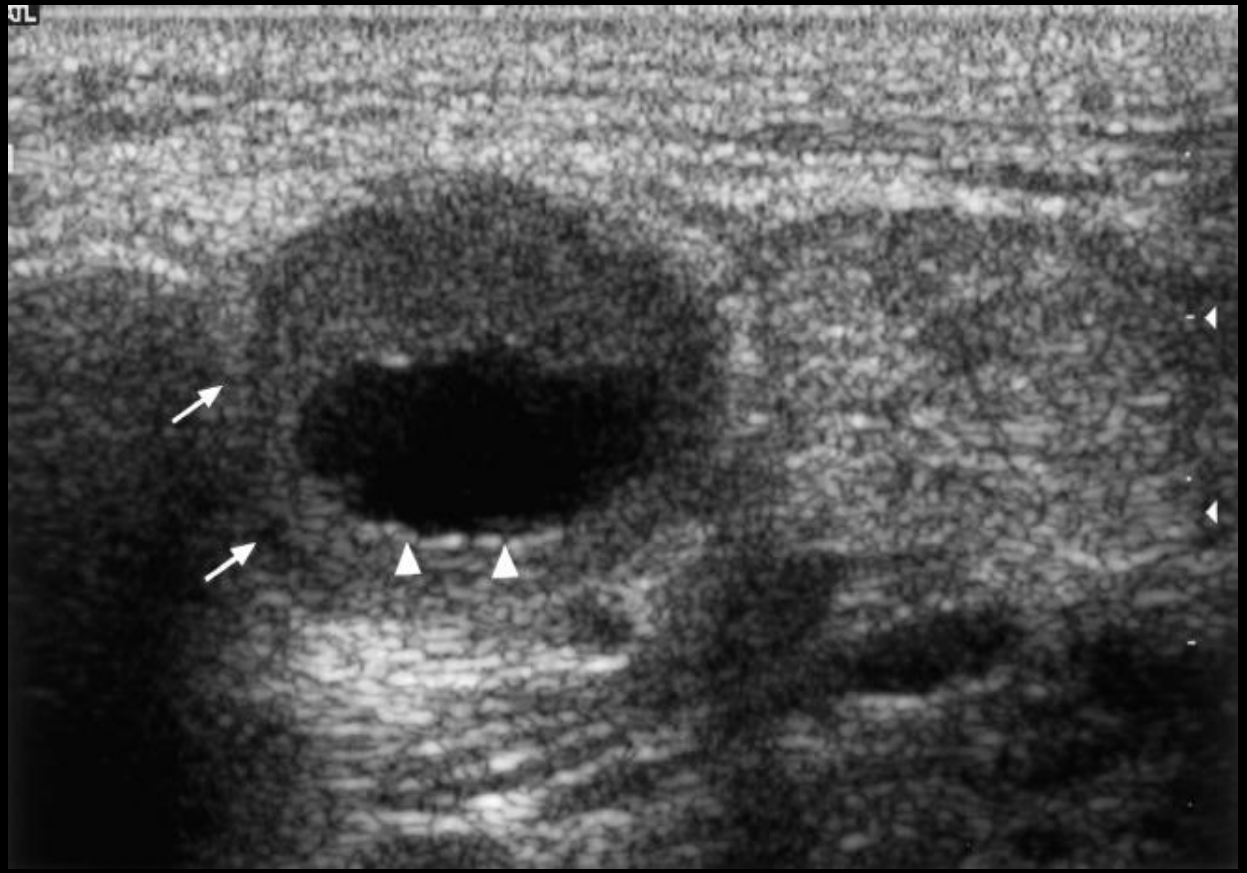


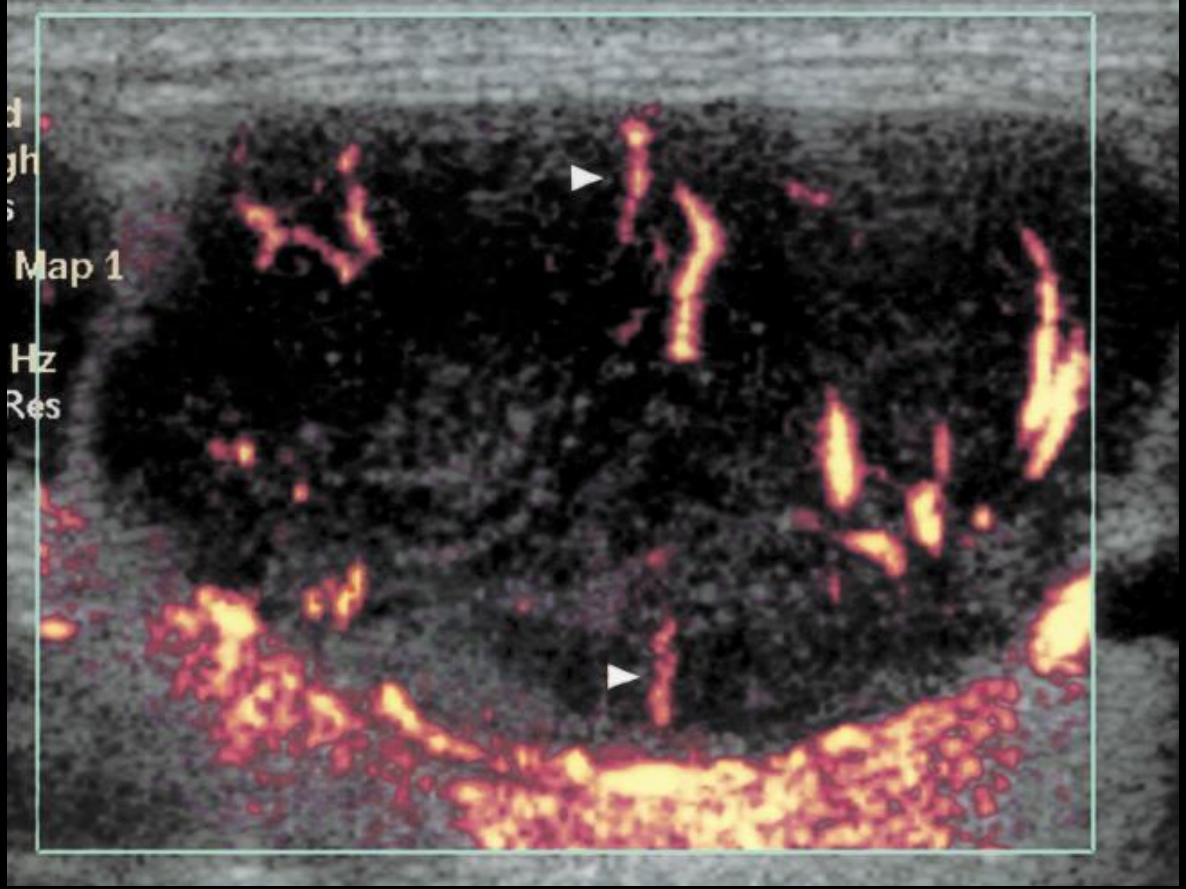
Longitudinal scan of a hyperechoic metastatic node from papillary carcinoma of the thyroid (calipers). Note the punctate calcification within the lymph node which is common in metastases from papillary carcinoma of the thyroid

Clinical Radiology (2003) 58: 359–366



Sonogram of a metastatic node (arrows) with intranodal cystic necrosis (arrowheads).

Clinical Radiology (2003) 58: 359–366



Power Doppler sonogram of a malignant node with peripheral vascularity (arrowheads).

Clinical Radiology (2003) 58: 359–366

Nodules During Pregnancy

- FNA of clinically relevant thyroid nodules should be performed in euthyroid and hypothyroid pregnant women.
- If TSH is suppressed beyond 16 weeks gestation, FNA may be deferred until after pregnancy and cessation of lactation.
- Thyroid nodules will enlarge slightly throughout gestation, though this does NOT imply malignant transformation.

Haugen BR, et al. ***Thyroid*** 2016;26:1-132

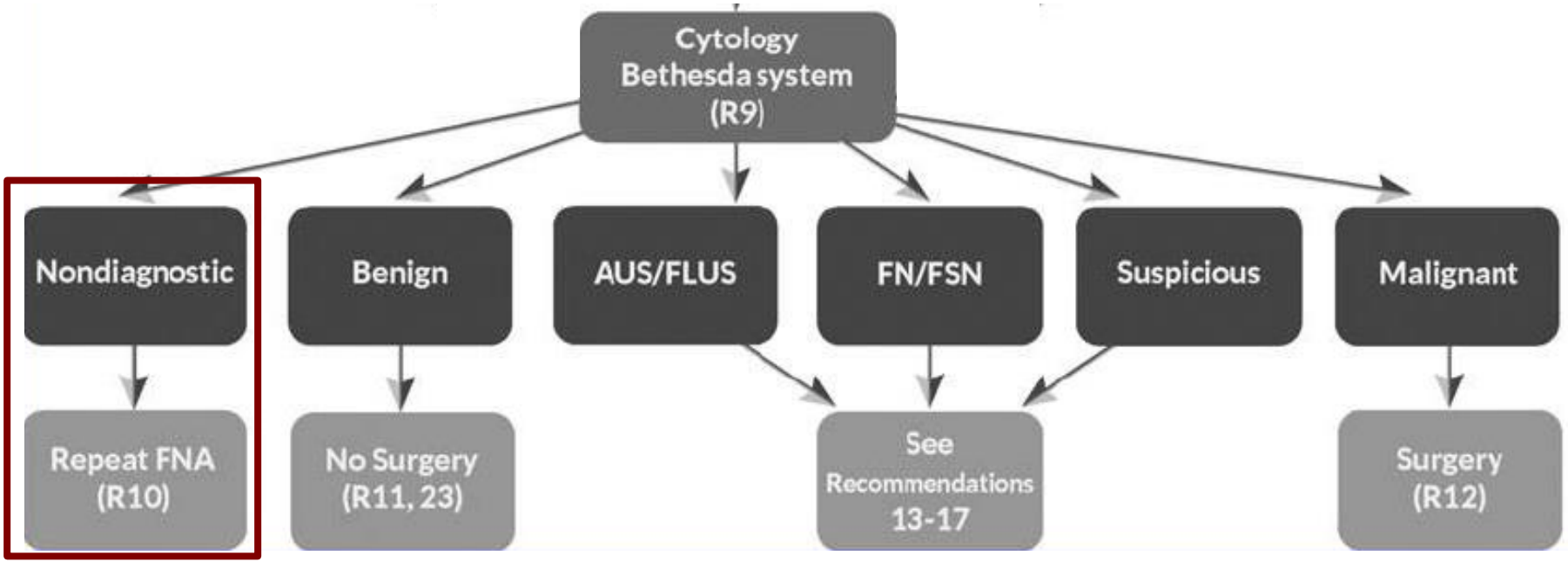
After the aspiration…

Reporting Thyroid Cytopathology Bethesda System Should be Used

Diagnostic Category	Predicted Risk Of Malignancy
Nondiagnostic	1-4%
Benign	0-3%
Atypia of Undetermined Significance (AUS) Follicular lesion of Undetermined Significance (FLUS)	5-15%
Follicular neoplasm (FN) Suspicious for Follicular Neoplasm (SFN) Hürthle Cell neoplasm/suspicious	15-30%
Suspicious of Malignancy (SUSP)	60-75%
Malignant	97-99%

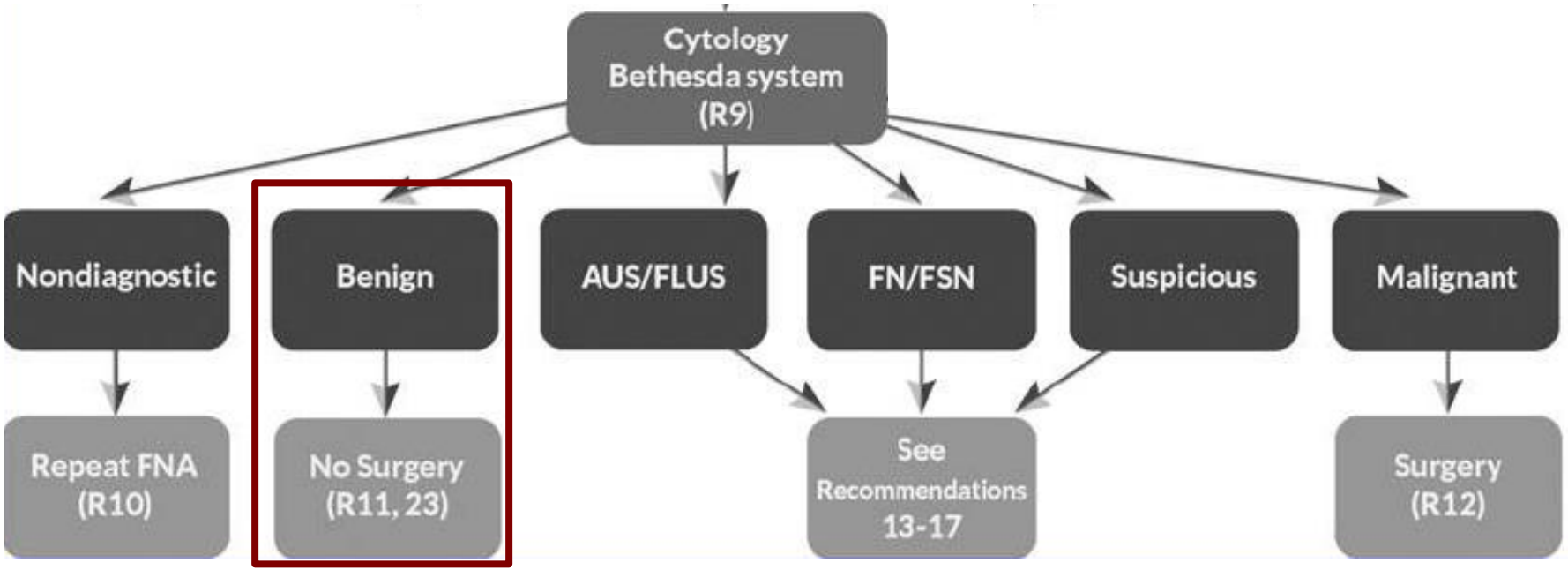
Haugen BR, et al. ***Thyroid*** 2016;26:1-132

FNA Cytology



Haugen BR, et al. ***Thyroid*** 2016;26:1-132

FNA Cytology



Haugen BR, et al. ***Thyroid*** 2016;26:1-132

Benign Cytology

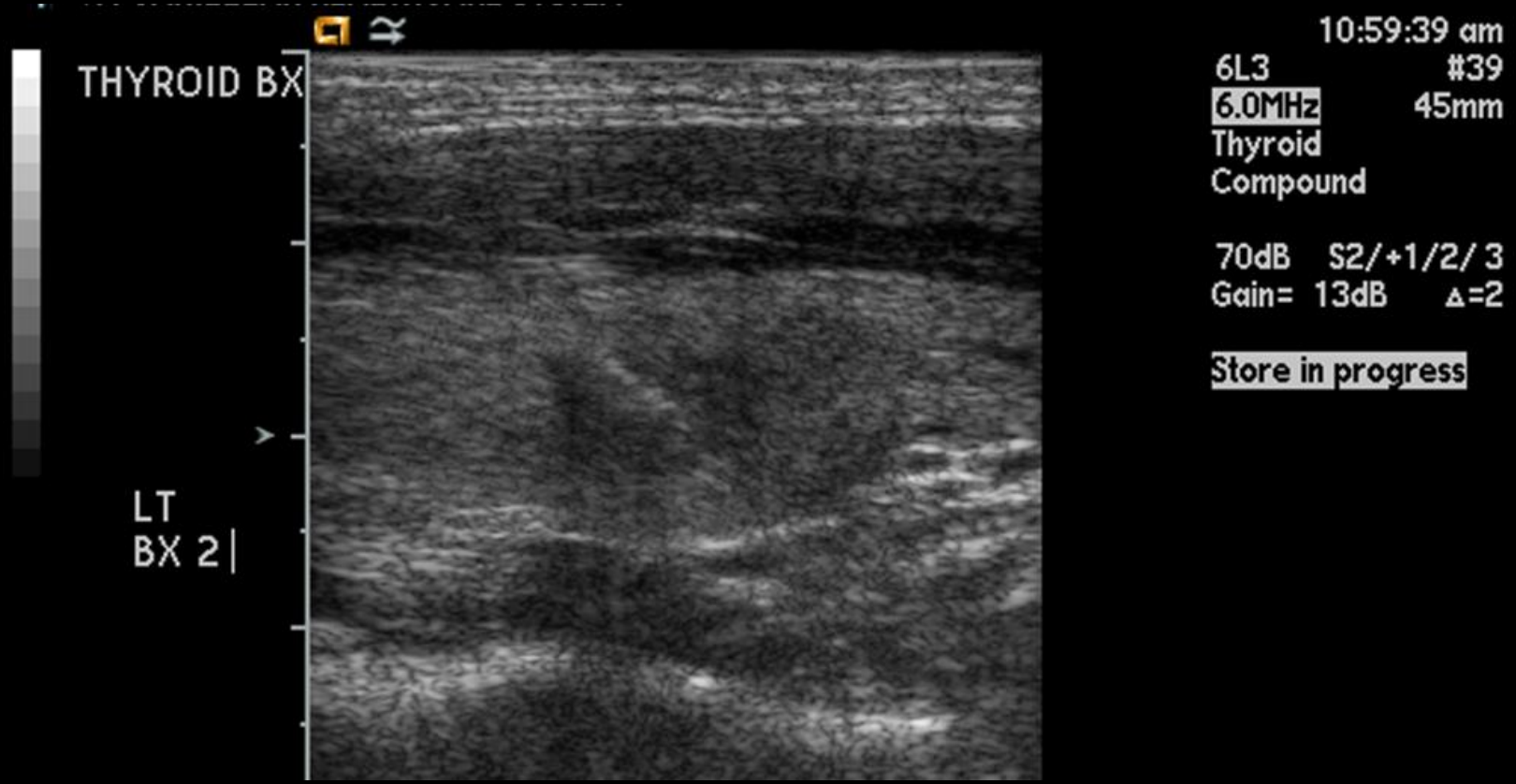
Malignancy Risk: 0-3%

- Accuracy depends of:
  - Operator skill
  - FNA technique
  - Specimen preparation
  - Cytology interpretation
  - False-Negatives to be considered in:
    - Nodules 4cm or larger
    - Suspicion sonographic pattern

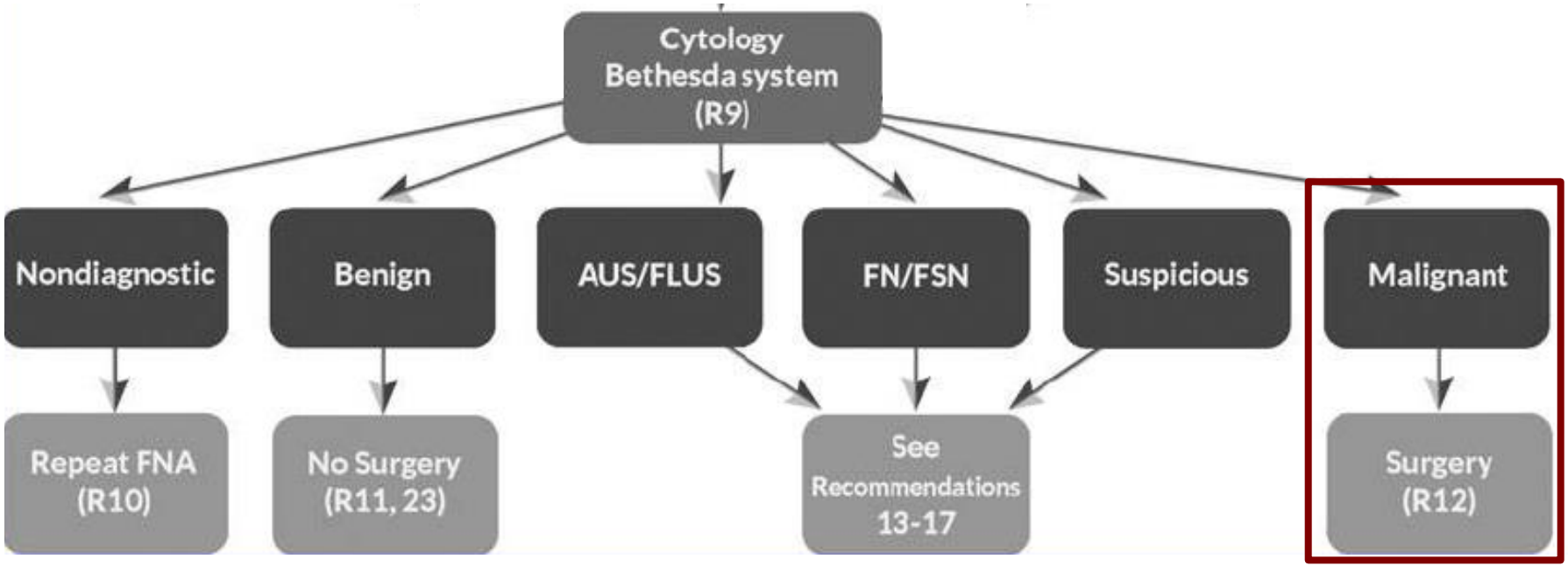
"…initially benign FNA confers negligible mortality risk during long-term follow-up despite a low but real risk of false negatives…"

Haugen BR, et al. ***Thyroid*** 2016;26:1-132

You need to sample correctly in order to have a valid test.



FNA Cytology



Haugen BR, et al. ***Thyroid*** 2016;26:1-132

Malignant

Malignancy Risk: 97-99%

- Although surgery is usually done due to lack of clinical features that can differentiate PTMC destined to progress from the larger group of indolent PTMC that will not cause significant disease, "…observation is a safe and effective alternative to immediate surgical resection."
  - ***BRAF*** in isolation has low positive predictive value
  - Molecular markers may help in the future

PTMC: Papillary Thyroid Micro Carcinoma

Haugen BR, et al. ***Thyroid*** 2016;26:1-132

If You Recommend Surgery due to Malignancy, a Preoperative Neck Ultrasonography Should be Done.

- Preoperative neck US for cervical (central and especially lateral neck compartments) lymph nodes is recommended for all patients undergoing thyroidectomy for malignant or suspicious for malignancy cytologic or molecular findings.
- US-guided FNA of sonographically suspicious lymph nodes ≥8-10 mm in the smallest diameter should be performed to confirm malignancy if this would change management.
  - Thyroglobulin washout may be difficult in patients with intact thyroid gland
  - False positive Tg washout may occur, particularly in lymph nodes in the central compartment.

Haugen BR, et al. ***Thyroid*** 2016;26:1-132

Sonographic Features Suggestive of Abnormal Metastatic Lymph Nodes Include:

- Enlargement
- Loss of the fatty hilum
  - ~29% specificity
- Rounded rather than oval shape
- Hyperechogenicity
- Cystic change
- Calcifications
- Peripheral vascularity

Sign	Sensitivity	Specificity
MicroCa^{++}	5-69%	93-100%
Cystic	10-34%	91-100%
Periph Vasc	40-86%	57-93%
HyperEchoic	30-87%	43-95%
Round	37%	70%

Haugen BR, et al. ***Thyroid*** 2016;26:1-132

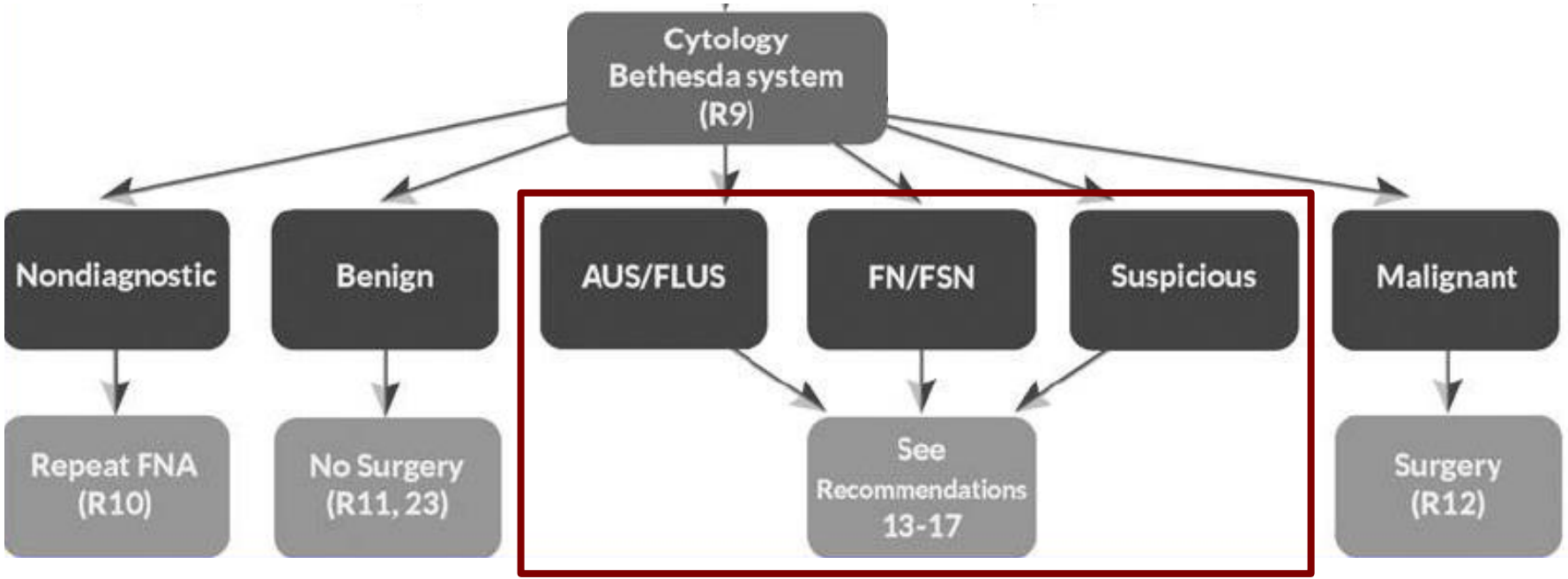
Other Pre-Operative Imaging

- Preoperative use of cross-sectional imaging studies (CT, MRI) with intravenous (IV) contrast is recommended as an adjunct to US for patients with clinical suspicion for advanced disease, including invasive primary tumor, or clinically apparent multiple or bulky lymph node involvement.
- Iodine is generally cleared within 4–8 weeks in most patients. Improved anatomic imaging outweighs delay in RAI.
- Routine preoperative ^{18}FDG-PET scanning is not recommended.

Haugen BR, et al. ***Thyroid*** 2016;26:1-132

FNA Cytology: Indeterminate Cytology

AUS/FLUS; FN/FSN; Suspicious



Haugen BR, et al. ***Thyroid*** 2016;26:1-132

Cytopathology

- ~90% concordance in benign and malignant cytologic diagnoses
- ~75% Intra- and 64% inter-observer concordance for indeterminate cytologic diagnosis
- Lower volume cytopathologists are more likely to categorize a nodule indeterminate rather than benign.

Ferris RL, et al. ***Thyroid*** 2015;25:760.

Atypia of Undetermined Significance
Follicular Lesion of Undetermined Significance

Malignancy Risk: 5-15 %

- Was intended to represent 7% of samples but has been used ~1%-27%.
- In practice malignancy risk has been 15% [6%-48%]

Alternatives

- 2nd opinnion
- Surveillance
- Repeat FNA
  - 10%-30% stay AUS/FLUS
- Molecular testing
- Diagnostic Surgery

Considerations:

- Clinical risk factors
- Sonographic pattern
  - 90-100% if stratified as High
  - 58% if stratified low or Intermediate
  - 8% if stratified as very low
- Patient preference

Haugen BR, et al. ***Thyroid*** 2016;26:1-132

Follicular Neoplasm
Suspicious of Follicular Neoplasm

Malignancy Risk:
15-30 %

- "Diagnostic surgical excision is the long-established standard of care for the management of FN/SFN cytology nodules. However, after consideration of clinical and sonographic features, molecular testing may be used to supplement malignancy risk assessment data in lieu of proceeding directly with surgery. Informed patient preference and feasibility should be considered in clinical decision-making."

Haugen BR, et al. ***Thyroid*** 2016;26:1-132

Suspicious for Papillary Carcinoma

Malignancy Risk: 60-75 %

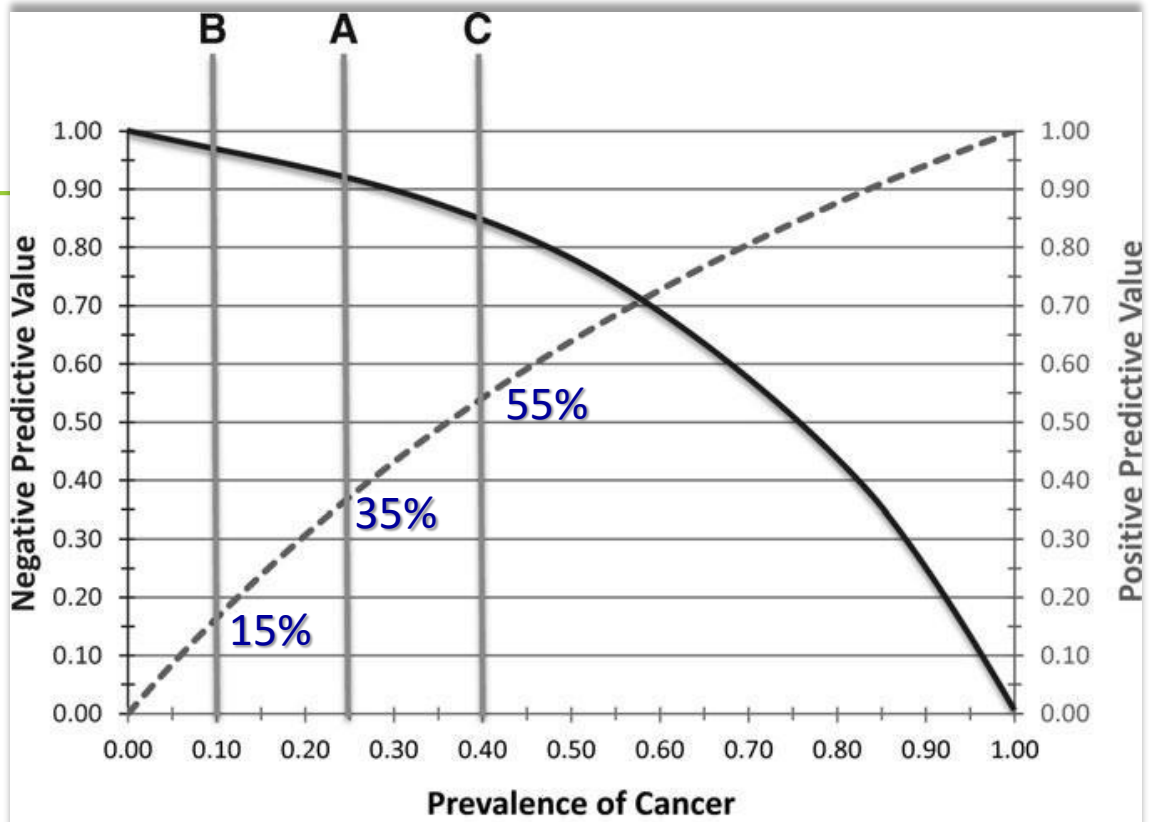
- Surgical management should be similar to that of malignant cytology.
- Molecular markers may be considered if such data would be expected to alter surgical decision making.
  - Gene expression classifier is NOT indicated in this cytology
  - Mutational Panel if anything is going to be done

Haugen BR, et al. ***Thyroid*** 2016;26:1-132

Molecular Markers

Effect of Prevalence On Test Predictive Value

- Clinician are urged to be aware of the prevalence of disease by cytologic category in their tested patients.



Test performance based on population disease prevalence:
If disease prevalence is 25%, then NPV=92%, PPV=38%
If disease prevalence decreases to 10%, then NPV=96%, PPV=17%
If disease prevalence increases to 40%, then NPV=85%, PPV=54%

Ferris RL, et al. ***Thyroid*** 2015;25:760.

Indeterminate Cytology: AUS/FLUS, FN, SUSP

- Molecular markers
  - Surgical approach stratification
    - Long term outcome data using molecular markers to guide therapeutic decision making is currently lacking.
  - "If molecular testing is being considered, patients should be counseled regarding the potential benefits and limitations…"
  - Type of molecular markers:
    - Mutations and Rearrangements
    - Gene expression classifier (mRNA)
    - Immunohistochemical stains

Haugen BR, et al. ***Thyroid*** 2016;26:1-132

Molecular Markers

Molecular Markers	Sensitivity	NPV	Specificity	PPV
Gene Expression Classifier	↑ (74%-98%)	↑ (79%-99%)	↓ (48%-53%)	↓ (33%-80%)

Haugen BR, et al. ***Thyroid*** 2016;26:1-132
Ferris RL, et al. ***Thyroid*** 2015;25:760.

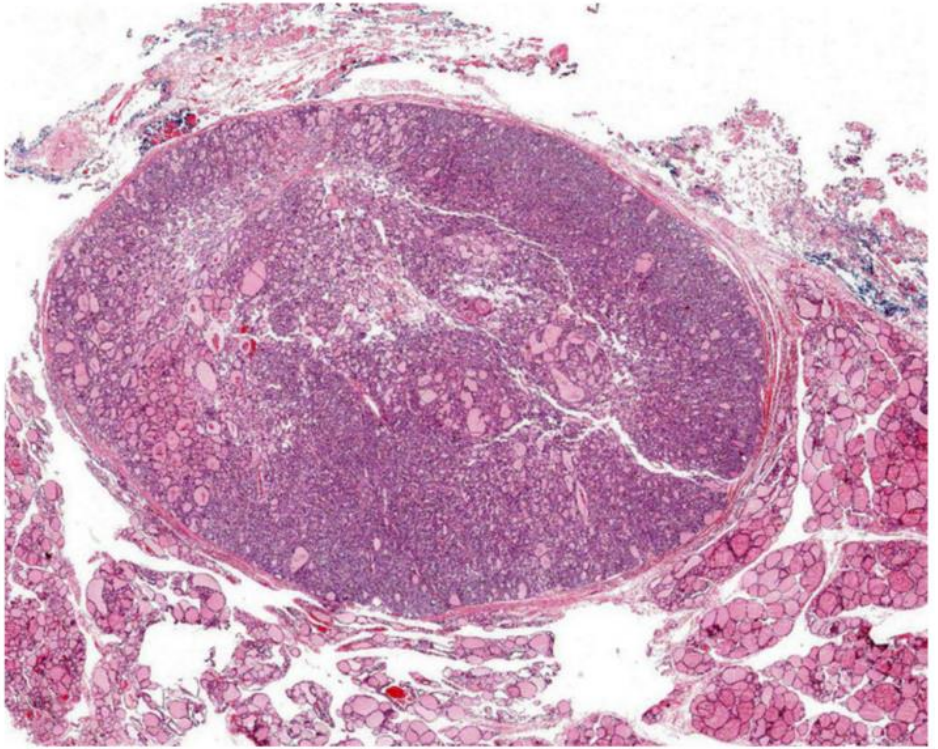
Tumor Renamed

- "Encapsulated follicular variant of papillary thyroid carcinoma," now will be called "noninvasive follicular thyroid neoplasm with papillary-like nuclear features," or NIFTP

The New York Times

It's Not Cancer: Doctors Reclassify a Thyroid Tumo

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

Nikiforov YE JAMA Oncol 2016;
Online April 14, 2016 doi:10.1001/jamaoncol.2016.0386

Hyalinizing trabecular tumors (HTT)

- **Hyalinizing trabecular tumors** (HTT) will display similar cytomorphology on thyroid FNA smears with nuclear pseudo- inclusions and grooves. However, on resection, histologic features are incompatible with papillary thyroid carcinoma (PTC). HTTs are considered benign although there are rare reports of metastatic HTTs. Since they carry a RET/PTC mutation, they are considered related to PTC. Surgical resection is curative.

Molecular Markers

- “In summary, there is currently no single optimal molecular test that can definitively rule in or rule out malignancy in all cases of indeterminate cytology, and long-term outcome data proving clinical utility are needed.”

Haugen BR, et al. ***Thyroid*** 2016;26:1-132

Surgery for Indeterminate Nodules

- If solitary, thyroid lobectomy is the recommended initial surgical approach. This approach may be modified based on clinical or sonographic characteristics, patient preference, and/or molecular testing when performed.
- If bilateral nodular disease, those with significant medical comorbidities, or those who prefer to undergo bilateral thyroidectomy to avoid the possibility of requiring a future surgery on the contralateral lobe, may undergo total or near-total thyroidectomy, assuming completion thyroidectomy would be recommended if the indeterminate nodule proved malignant following lobectomy.

Haugen BR, et al. ***Thyroid*** 2016;26:1-132

Total Thyroidectomy

- Total thyroidectomy may be preferred in patients with indeterminate nodules that are cytologically suspicious for malignancy, positive for known mutations specific for carcinoma, sonographically suspicious, or large (>4 cm), or in patients with familial thyroid carcinoma or history of radiation exposure, if completion thyroidectomy would be recommended based on the indeterminate nodule being malignant following lobectomy.
- Coexistent hyperthyroidism may be an indication for total thyroidectomy depending upon the etiology.

Haugen BR, et al. ***Thyroid*** 2016;26:1-132

FNA Cytology Consistent with PTC during Pregnancy

- Monitor sonographically. Surgery may be deferred until after delivery.
- Surgery should be considered during pregnancy if before 24-26 weeks gestation:
  - Substantial growth
  - There are cervical lymph nodes that are suspicious for metastatic disease
  - High risk sonographic features
- If the patient's serum TSH is >2 mU/L, it may be reasonable to initiate thyroid hormone therapy to maintain the TSH between 0.3 to 2.0 mU/L for the remainder of gestation.

Haugen BR, et al. ***Thyroid*** 2016;26:1-132

Follow-Up of Nodules with FNA

- Based on sonographic stratification:
  - **High Suspicion:** Repeat US and FNA within 12 months
  - **Low to Intermediate Suspicion**: Repeat US at 12-24 months
    - If new suspicious sonographic feature or growth, then repeat FNA
      - Growth:
        - 20% increase in at least 2 dimensions with a minimal increase of 2mm
        - More than 50% increase in volume
  - **Very Low Suspicion:** If US repeated, it should be ≥ 24 months
- **Two benign FNA** No US surveillance indicated

Haugen BR, et al. ***Thyroid*** 2016;26:1-132

Follow-Up of Nodules that Did NOT Meet FNA Criteria

- Based on sonographic stratification:
  - **High Suspicion:** Repeat US in 6-12 months
  - **Low to Intermediate Suspicion**: Repeat US at 12-24 months
  - **Very Low Suspicion:** If US repeated, it should be ≥ 24 months

- Nodules ≤ 1 cm with very low suspicion US pattern do NOT require routine sonographic follow-up.

Haugen BR, et al. ***Thyroid*** 2016;26:1-132

Follow-Up

- Surgery may be considered for growing nodules that are benign after FNA if they are large (>4cm), causing compressive or structural symptoms, or based upon clinical concern.
  - Most asymptomatic nodules demonstrating modest growth should be followed without intervention.

Haugen BR, et al. ***Thyroid*** 2016;26:1-132

Multinodular Goiter

- Each nodule carries an independent risk of malignancy
- When multiple nodules ≥ 1cm are present, FNA should be performed preferentially based upon nodule sonographic pattern and size.
- If non of the nodules has a high or moderate suspicion sonographic pattern, the likelihood of malignancy is low and it is reasonable to aspirate the largest nodule (≥2 cm) or continue surveillance without FNA.
- Radionuclide scanning may also be considered in patients with multiple thyroid nodules with the goal of identifying and aspirating appropriate hypofunctioning nodules.

Haugen BR, et al. ***Thyroid*** 2016;26:1-132

^{18}FDG-PET

- Focal uptake in a nodule of 1cm or larger should have FNA done
- Diffuse uptake in a patient with chronic lymphocytic thyroiditis does not require further imaging or FNA.
- Not routinely recommended for evaluation of indeterminate cytology.
  - Sensitivity: 89%; Specificity: 55%; PPV: 41%; NPV: 93%

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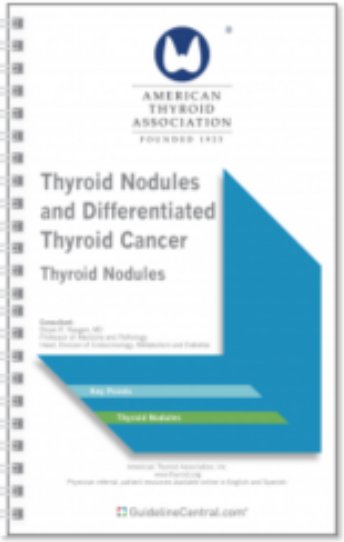
Thyroid Hormone Therapy

- Routine TSH suppression for benign thyroid nodules in iodine sufficient populations is NOT recommended.
- "There are no data to guide recommendations on the use of thyroid hormone therapy in patients with growing nodules that are benign on cytology."
- TSH suppression
  - ↑ risk of cardiac arrhythmias, osteoporosis, and adverse symptomatology.
  - Risks outweigh the benefits

Haugen BR, et al. ***Thyroid*** 2016;26:1-132

Summary/Conclusions

- If you suspect at thyroid nodules, request TSH and Thyroid Ultrasound
  - Know your radiologist to assure they will sent you a useful report and cervical lymphadenopathies will be evaluated if necessary.
- Risk stratify the nodules
  - High or Intermediate suspicion do FNA if 1.0cm or larger
  - Low suspicion do FNA if 1.5cm or larger
  - Very low suspicion FNA if 2.0cm or larger is optional
- Know your cytopathologist
- Molecular marker should be selected according to the evaluation and management planed with the patient.



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