Sonographic Features of Thyroid Nodules & Guidelines for Management

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Objectives

- Review ultrasound imaging characteristics for assessment of risk of malignancy in thyroid nodules
- Discuss current guidelines for UGFNA of thyroid nodules
- Incorporate clinical status into thyroid nodule FNA decision making
Goals of Thyroid Nodule Evaluation

- Identify and treat the small group of patients with malignancy while avoiding unnecessary procedures in the majority with benign nodules
- Evaluate for compressive symptoms of dysphagia, dysphonia and dyspnea
- Identify nodules that impact thyroid function
How common are nodules?

Mazzaferri, NEJM 1993
Epidemic of Nodules

- Can no longer FNA all nodules >1cm
- Current ATA, AACE and Korean guidelines rely on recognition of sonographic features of low-risk and high-risk nodules
Thyroid Ultrasound

R2 Thyroid sonography should be performed in all patients with known or suspected thyroid nodules (A)

ATA guidelines, Cooper DS, Thyroid, 2009

- Is the palpable abnormality a thyroid nodule?
- Are other nodules present?
- Size?
- Suspicious features?
- > 50% cystic?
- Posterior?
- Associated abnormal lymph nodes?
Which Nodules need FNA??

0.8cm

2.0 cm
Which to FNA?

Frates MC et al, Radiology 2005
# 2009 ATA Guidelines

## Table 3. Sonographic and Clinical Features of Thyroid Nodules and Recommendations for FNA

<table>
<thead>
<tr>
<th>Nodule sonographic or clinical features</th>
<th>Recommended nodule threshold size for FNA</th>
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<tbody>
<tr>
<td><strong>High-risk history</strong>&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Nodule WITH suspicious sonographic features&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&gt;5 mm</td>
</tr>
<tr>
<td>Nodule WITHOUT suspicious sonographic features&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&gt;5 mm</td>
</tr>
<tr>
<td>Abnormal cervical lymph nodes</td>
<td>All&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Microcalcifications present in nodule</td>
<td>≥1 cm</td>
</tr>
<tr>
<td><strong>Solid nodule</strong></td>
<td></td>
</tr>
<tr>
<td>AND hypoechoic</td>
<td>&gt;1 cm</td>
</tr>
<tr>
<td>AND iso- or hyperechoic</td>
<td>≥1–1.5 cm</td>
</tr>
<tr>
<td><strong>Mixed cystic–solid nodule</strong></td>
<td></td>
</tr>
<tr>
<td>WITH any suspicious ultrasound features&lt;sup&gt;b&lt;/sup&gt;</td>
<td>≥1.5–2.0 cm</td>
</tr>
<tr>
<td>WITHOUT suspicious ultrasound features</td>
<td>≥2.0 cm</td>
</tr>
<tr>
<td>Spongiform nodule</td>
<td>≥2.0 cm&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Purely cystic nodule</td>
<td>FNA not indicated&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Refers to individuals with a personal or familial history of thyroid cancer, or head and neck irradiation. 

<sup>b</sup> Suspicious sonographic features are defined as irregular, hyperechoic, or hypoechoic nodule margins, increased vascular flow, or microcalcifications. 

<sup>c</sup> All refers to all high-risk features and suspicious sonographic features. 

<sup>d</sup> Refers to solid or mixed cystic–solid nodules. 

<sup>e</sup> Refers to purely cystic nodules. 

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Cooper, et al, Thyroid 19(11), 2009
NCCN Version 2.2013

US Findings

- Solid Nodule
  - With Suspicious Features
  - Without Suspicious Features
- Mixed Solid-Cystic Nodule
  - With Suspicious Features
  - Without Suspicious Features
- Spongiform
- Simple Cyst
- Suspicious Lymph Node

Threshold for FNA

- Solid Nodule
  - ≥1.0cm
  - ≥ 1.5cm
- Mixed Solid Cystic
  - ≥ 1.5 – 2.0cm
  - ≥ 2.0cm
- ≥ 2.0 cm
- Not Indicated
- FNA LN and/or Nodule

Also recommend lowering thresholds with high risk clinical history. Allow for informed patient decision making for surgery in patients with nodules >4 cm and/or high risk history.
High Risk History

- History of thyroid cancer in one or more first degree relatives
- History of external beam radiation as a child
- Exposure to ionizing radiation in childhood or adolescence
- Prior hemithyroidectomy with discovery of thyroid cancer
- 18-FDG avidity on PET scanning
- MEN2/FMTC-associated RET protooncogene mutation
  - Calcitonin >100 pg/mL.
AACE / AME Guidelines 2010

- >1 cm solid and hypoechoic.
- US-FNA nodules any size if radiation, FH of MEN/MCT, history of thyroid cancer, or elevated calcitonin (>100)
- US-FNA nodules of any size with either marked hypoechoenicity, irregular or microlobulated margins, taller than wide shape, microcalcifications, or “chaotic arrangement or intranodular vascular images” (sic).
- FNA independent of size if US suggestive of metastatic node or extracapsular growth.
- FNA (solid component) of complex cystic nodules
- Do not biopsy nodules “hot on scintigraphy”.

US CRITERIA FOR FNA THRESHOLD

Purely cystic
Spongiform
Mixed cystic/solid
Solid hypoechoic
Microcalcifications, irregular margins
Abnormal cervical lymph nodes, extracapsular invasion
High risk history with suspicious US features

Adapted from AACE/AME/ETA Guidelines (2010)
Divides nodules into three categories:

- **Probably benign**
  - Spongiform
  - Completely cystic or predominately cystic with comet tails

- **Suspicious for malignancy – Any feature present**
  - Taller than wide, irregular
  - Marked hypoechoic
  - Calcifications – microcalcifications or macrocalcifications
  - Extracapsular extension (spiculated margin)

- **Indeterminate – Neither benign or suspicious features**
  - Iso, hypo or hyperechogenic
  - Ovoid to round or irregular shape
  - Smooth or ill-defined margin
  - Rim calcification
Korean Endocrine Society 2011

Biopsy based on category (and size)

- **Probably benign**
  - \(< 1\text{cm} - \text{no f/u US needed}\)
  - \(> 1\text{cm} - \text{f/u US 2y and 3-5y}\)
  - \(> 2\text{cm} - \text{Selective FNA biopsy}\)

- **Suspicious for malignancy – Any feature present**
  - FNA biopsy all
  - \(< 5\text{mm} - \text{Selective FNA based on risk factors and experience}\)
  - \(> 5\text{mm} - \text{All if feasible}\)

- **Indeterminate – Neither benign or suspicious features**
  - \(< 1\text{cm} - \text{f/u US}\)
  - \(> 1\text{cm} - \text{FNA biopsy}\)
  - Growth – \((20\% \text{ diam or 50\% volume}) \text{ FNA biopsy}\)
Korean Guidelines 2011

Moon et al,
Korean J Radiology 2011
INITIAL FNA – BENIGN……What next?

Table 3

<table>
<thead>
<tr>
<th>Benign Cytologic Result</th>
<th>No. of Nodules</th>
<th>No. of Ultimately Benign Nodules</th>
<th>Likelihood of Nodule Being Benign (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>At first aspiration</td>
<td>1343</td>
<td>1317</td>
<td>98.1</td>
<td>0.9718, 0.9873</td>
</tr>
<tr>
<td>At least twice</td>
<td>545</td>
<td>545</td>
<td>100</td>
<td>0.9933, 1.0000</td>
</tr>
<tr>
<td>At first aspiration + positive US result ***</td>
<td>93</td>
<td>74</td>
<td>79.6 **</td>
<td>0.6995, 0.8723</td>
</tr>
<tr>
<td>At first aspiration + negative US result</td>
<td>1250</td>
<td>1243</td>
<td>99.4</td>
<td>0.9885, 0.9977</td>
</tr>
<tr>
<td>At first aspiration + negative US + no interval change at follow-up US</td>
<td>1111</td>
<td>1106</td>
<td>99.5</td>
<td>0.9895, 0.9985</td>
</tr>
<tr>
<td>At first aspiration + negative US + increased in size at follow-up US</td>
<td>139</td>
<td>137</td>
<td>98.6</td>
<td>0.9490, 0.9983</td>
</tr>
</tbody>
</table>

Figure 4

a. US (a, transverse; b, longitudinal) scans in 49-year-old woman show 1.0-cm irregular, hypoechoic nodule (arrows) with microcalcifications (arrowheads) in right lobe of thyroid gland. Initial cytologic result was adenomatous hyperplasia; surgical results confirmed papillary carcinoma.
ATA 2015: Nodule Sonographic Pattern Risk of Malignancy

High Suspicion 70-90%
- microcalcifications
- hypoechoic nodule, irregular margin
- hypoechoic, irregular margins
- hypoechoic, taller than wide
- hypoechoic, irregular margins, extrathyroidal extension
- hypoechoic, interrupted rim calcification with soft tissue extrusion
- nodule with irregular margins, suspicious left lateral lymph node

Intermediate Suspicion 10-20%
- hypoechoic solid regular margin
- hypoechoic solid regular margin

Low Suspicion 5-10%
- hyperechoic solid regular margin
- isoechoic solid regular margin
- partially cystic with eccentric solid area
- partially cystic with eccentric solid areas

Very low Suspicion <3%
- spongiform
- partially cystic no suspicious features
- partially cystic no suspicious features

Benign <1%
- cyst

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HIGH Suspicion Pattern 70-90%

- Hypoechoic, microcalcifications, irregular margin
- Hypoechoic, irregular margin (microlobulated)
- Hypoechoic, irregular margin, taller than wide
- Hypoechoic, irregular margin, extrathyroidal extension
- Hypoechoic, interrupted rim calcification with soft tissue extrusion
Suspicious Sonographic Features

- Hypoechoic
- Microcalcifications
- Infiltrative margins
- Taller than wide on transverse view
- Abnormal cervical lymph nodes
Hypoechoic

Compare to strap muscles and SCM
What About Intranodular Flow?

NO LONGER CONSIDERED AN INDEPENDENT RISK
Microcalcifications

- Punctate (<1mm) echogenic lesions without shadowing
  - Differentiate from “comet tail” ringdown artifact
- Microcalcifications are felt to be 85% specific for cancer but only 50% sensitive
Microcalcification vs Comet Tail
Comet Tail Artifact

Benign Colloid Nodule
Microcalcifications
Diffuse Microcalcifications
Invasion of Strap Muscle
Shape of Nodule

Taller than Wide (AP > transverse)
INTERMEDIATE Suspicion Pattern
10-20%

Hypoechoic solid with regular margins

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LOW Suspicion Pattern 5-10%

hyperechoic solid reg margins

isoechoic solid reg margins

partially cystic with eccentric solid areas
Halo

Thin Halo
Benign Follicular Adenoma

Thick, Irregular Halo
Follicular CA
Subtle differences in halo

Irregular halo

Thinner halo
VERY LOW Suspicion Pattern

<3%

spongiform
pure cyst
Characteristics Suggesting Low Risk Nodules

- Spongiform Echotexture
- Hyperechoic nodule (especially in autoimmune thyroiditis)
- Pure cyst without a solid component
- Thin Halo or a smooth margin
  - Thick and Irregular Halo in Follicular Neoplasms
- Colloid within nodule “comet tails”
- Intact eggshell calcifications
Spongiform echotexture
“Spongiform” nodules

- aggregation of multiple microcystic components in more than 50% of the volume of the nodule
- “honeycomb of internal cystic spaces”
- Only 1 in 360 spongiform nodules malignant
  - 99.7% Specificity (Moon)

Moon Radiology 2008; 247: 762-70
Bonavita AJR 2009; 193:207-13
Spongiform Echotexture

Note: Bright Linear Reflectors all posterior to the microcystic areas
The “White Knight”
Hyperechoic with background of Hashi’s
Colloid within Nodule with “Comet Tails”
Small Mural Component – Low Risk
Cystic PTC
# R8 US Pattern and suggested FNA cutoffs

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<tr>
<th>Sonographic Pattern</th>
<th>Estimated malignancy risk</th>
<th>Consider biopsy</th>
<th>Strength of rec</th>
<th>Quality of evidence</th>
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<tr>
<td>High suspicion</td>
<td>&gt;70-90%</td>
<td>≥ 1 cm</td>
<td>Strong</td>
<td>Moderate</td>
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<td>≥ 1 cm</td>
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<td>5-10%</td>
<td>≥ 1.5 cm</td>
<td>Weak</td>
<td>Low</td>
</tr>
<tr>
<td>Very low suspicion</td>
<td>&lt; 3%</td>
<td>≥ 2 cm</td>
<td>Weak</td>
<td>Moderate</td>
</tr>
<tr>
<td>Benign</td>
<td>&lt; 1%</td>
<td>No biopsy</td>
<td>Strong</td>
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<td>FNA is not recommended for nodules that do not meet the above criteria, including all nodules &lt; 1 cm</td>
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<td></td>
<td>Strong</td>
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### R8 US Pattern and suggested FNA cutoffs

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<td>&gt; 1.5 cm</td>
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Modify cutoffs by:
- patient risk factors
- presence of sonographically suspicious LNs

US FNA of sono susp LNs

FNA is not recommended for nodules that do not meet the above criteria, including all nodules < 1 cm
Sonographically Suspicious Lymph Nodes

- Suspicious lymph node features:
  - Rounded Shape
  - (Loss of Hilar Line)
  - Calcifications
  - Cystic Necrosis
  - Peripheral or Chaotic Vascularity

- Biopsy node for cytology and TG analysis
Why use Size Criteria?

- Numerous studies confirm poor or no correlation between size and malignancy.
- However, the risk of metastasis (and therefore mortality) does have an association with size.
- “...attempts to diagnose and treat all small thyroid cancers in an effort to prevent these rare outcomes would likely cause more harm than good.” (ATA 2009 guidelines)
When multiple nodules $\geq 1\text{cm}$ are present, FNA based upon US pattern (R8)
- Strong recommendation, Moderate quality evidence

If multiple sonographically similar low or very low suspicion pattern nodules, the likelihood of malignancy is low and it is reasonable to FNA the largest nodule ($\geq 2\text{cm}$) and observe others
- Weak recommendation, Low quality evidence
Multinodular Goiter

Enlarged thyroid with multiple sonographically similar nodules with little or no normal parenchyma
A patient with multinodular thyroid has a similar risk of malignancy as a patient with a single thyroid nodule.
Benign Nodule Follow-up

- **ATA 2009**
  - Ultrasound 6–18 months after the initial FNA
  - If same size or smaller, may follow-up @ 3-5 years (C)
  - If increase size by > 50% in volume or >20% in 2 dimension repeat FNA and f/u 6-18mos (B)

- **AACE/AME/ETA 2010**
  - Perform repeated clinical and US examination and TSH measurement in 6 to 18 months (D)
  - Perform repeated UGFNA biopsy in cases of appearance of clinically or US suspicious features (B)
  - Perform repeated UGFNA biopsy in cases of a greater than 50% increase in nodule volume (B)
  - Consider routine repeated UGFNA biopsy in 6 to 18 months, even in patients with initially benign cytological results (D)
Given the low false negative rate of US FNA cytology and the higher yield of missed malignancies based upon nodule sonographic features rather than growth, the follow up of thyroid nodules with benign cytology diagnoses should be determined by risk stratification based upon **sonographic pattern**.

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### R22 Follow-up of nodules with benign cytology

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<th>Quality of evidence</th>
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<td>Repeat US and US FNA within 12 months</td>
<td>Strong</td>
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<td><strong>Intermediate/ Low suspicion</strong></td>
<td>Repeat US at 12-24m If growth, repeat FNA OR continued observation</td>
<td>Weak</td>
</tr>
<tr>
<td><strong>Very low suspicion</strong></td>
<td>Utility of surveillance US and assessment of nodule growth as an indicator for repeat FNA is not known. If repeat US, it should at &gt; 24 months</td>
<td>NO rec</td>
</tr>
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</tbody>
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| **Intermediate/ Low suspicion** | **Repeat US at 12-24m**  
**If growth, repeat FNA OR continued observation** | **Weak** | **Low** |
<p>| <strong>Very low suspicion</strong> | <strong>Utility of surveillance US and assessment of nodule growth as an indicator for repeat FNA is not known. If repeat US, it should at ≥ 24 months</strong> | <strong>NO rec</strong> | <strong>Insufficient</strong> |
| <strong>IF 2\textsuperscript{nd} US FNA done with benign cyto, US surveillance for continued risk of malignancy is no longer indicated</strong> | <strong>Strong</strong> | <strong>Moderate</strong> |</p>
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<td>Utility and time interval of repeat US for risk of malignancy is not known. If repeated, do at ≥ 24 months</td>
<td>NO rec</td>
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<td>Utility and time interval of repeat US for risk of malignancy is not known. If repeated, do at ≥ 24 months</td>
<td>NO rec</td>
<td>Insufficient</td>
</tr>
<tr>
<td>Nodules &lt; 5 mm without high suspicion US pattern do not require routine sonographic FU and if repeated, the US should be performed at 24 months or later</td>
<td>Weak</td>
<td>Low</td>
</tr>
</tbody>
</table>