Thyroid Nodule Risk Stratification and FNA Guidelines

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Objectives

- Review features of benign and malignant nodules
- Highlight importance of pattern recognition for risk of malignancy assessment
- Discuss current guidelines for nodule FNA
Goals of Evaluation

- Determine if benign or cancer
- Manage nodules with compressive symptoms
- Identify autonomous nodules
- Determine if surgery is needed
Concerning Clinical Features

High clinical suspicion

- Rapid tumor growth
- Very firm nodule (rock hard)
- Fixation to adjacent structures
  - Vocal cord paresis
- Enlarged regional lymph nodes
- Family history of PTC or MEN 2
  - Distant metastases
  - High FDG on PET scan
  - “Hot” on Sestamibi scan
- History of radiation exposure to the head/neck

Positive Predictive Value (PPV) – high, clinically useful

Negative Predictive Value (NPV) – low, not helpful

Tests for Thyroid Nodules

- I-123 scan
- Thyroid ultrasound
- FNA biopsy
US Appearance of Nodules

- Composition (solid/cystic)
- Echogenicity (darkness on US)
- Margins
- Presence of calcifications
- Shape
- Vascularity
ATA 2015: Nodule Sonographic Pattern Risk of Malignancy

**High Suspicion** 70-90%
- microcalcifications
- hypoechoic nodule, irregular margins

**Intermediate Suspicion** 10-20%
- hypoechoic, regular margin
- hypoechoic, taller than wide

**Low Suspicion** 5-10%
- hypoechoic solid regular margin
- isoechoic solid regular margin
- partially cystic with eccentric solid area

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

**Benign** <1%
- cyst

Haugen et al. Thyroid; October 2015 (epub)
Fig. 1. Indications for FNA biopsy according to US findings. Suspicious US findings are markedly hypoechoic nodule, intranodular microcalcifications, more-tall-than-wide shape, and spiculated or lobulated margins. FNA = fine-needle aspiration; US = ultrasonography.
Characteristics Suggesting Low Risk Nodules

- Hyperechoic nodule (especially in autoimmune thyroiditis)
- Pure cyst without a solid component
- Thin Halo or a smooth margin
- Colloid within nodule “comet tails”
- Spongiform Echotexture
Hyperechoic with background of Hashi’s Nodule
Hyperechoic with background of Hashi’s
Giraffe Pattern in Hashimoto’s

Bonavita AJR 2009; 193:207-13
No Halo, but a Smooth Margin
Halo

Thin Halo
Benign Follicular Adenoma

Thick, Irregular Halo
Follicular CA
Subtle differences in halo

Irregular halo

Isoechoic Nodules

Thinner halo
Colloid within Nodule with "Comet Tails"
Colloid Within Nodule “Cat’s Eye” (Comet Tail, Stepladder or Ringdown artifact)
“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
Spongiform Echotexture

Note: Bright Linear Reflectors all posterior to the microcystic areas
Thin-walled Cyst
Thin-walled Cyst

Complex cyst
Suspicious Sonographic Features

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

NOT DOPPLER?
Hypoechoic

Compare to strap muscles and SCM
Hypoechoic
Hypoechoic
Markedly Hypoechoic

Compare to strap muscles and SCM
Calcifications

- **Macrocalcifications**: hyperechoic spots with acoustic shadowing ("dense calcifications")
  - Low-intermediate risk
- **Microcalcifications**: hyperechoic spots without acoustic shadowing (thought to represent psammoma bodies) (<1mm)
  - High Risk
- **Rim (eggshell) calcifications**: curvi-linear hyperechoic calcification along periphery
  - Higher risk if interrupted
Coarse Macrocalcification in PTC

Bonavita AJR 2009; 193:207-13
Eggshell Calcifications with Shadowing

Smooth Eggshell
Maybe Reassuring

Interrupted Eggshell
Not reassuring
PTC in Graves’

Left lobe showing background heterogeneity and a calcified nodule which proved to be papillary thyroid cancer on FNA biopsy in this patient with Graves’ Disease.
Microcalcification vs Comet Tail
Microcalcifications
Microcalcifications

Dense and Microcalcifications
Microcalcifications in Papillary Cancer

May be confused with comet tails

When in doubt - assume the worse
NOT microcalcifications!

Small hyperechoic linear streaks just posterior to small cystic area → posterior acoustic enhancement!
Microcalcifications
Calcifications in PTC

Transverse

Longitudinal
Cystic PTC
Cystic PTC - UGFNA

4cm Left Cystic Nodule

FNA - PTC
Halos & Margins

- **Halo:** sonolucent rim around an iso/hyperechoic nodule representing capsule
  - Thin/regular – lower risk
  - Thick/irregular – higher risk

Hypoechoic Nodules ---- Margins:

- **Smooth and regular**
- **Poorly Defined:** interface between nodule and surrounding parenchyma is difficult to delineate
  - Lower risk, seen in hyperplastic nodules
- **Irregular:** the demarcation between the nodule and parenchyma is clearly visible but demonstrates an irregular, infiltrative or spiculated course.
  - Higher risk
Margins

Irregular

Poorly defined, but not infiltrative (spongiform)
Infiltrative/Irregular Borders
Invasion of Strap Muscle
Invasion of Carotid Sheath
Invasion of Larynx

Cystic Papillary carcinoma invading the Larynx. Note the classic intra-cystic Cauliflower appearance.
Taller than wide

Nodule is taller than wide on the transverse view

Kim AJR 2002; Cappelli Clin Endocrinol 2005; Moon Radiology 2008
What About Intranodular Flow?

NO LONGER CONSIDERED AN INDEPENDENT RISK FACTOR WHEN DECIDING ON FNA
Vascularity - What to do?

- Consider whether features are suspicious for papillary or follicular cancers.
  - Hypoechoic or features of papillary:
    - Vascularity may be less important
  - Iso or hyperechoic with variable thickness halo:
    - Consider intranodular vascularity as potential risk.

- AACE 2016 guidelines do consider vascularity – particularly with follicular process.
- Korean 2011 and ATA 2015 guidelines do not consider vascularity

**Don’t be reassured by absence of vascularity.**
PTC – lack of Doppler
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
Suspicious Lymph Node
Right Lateral Neck
Malignant Node
**US of Thyroid only.....**

**US of Entire Neck reveals.....**

LEFT Nodule -- PTC

LEFT Lateral Neck: Abnl LNs

<table>
<thead>
<tr>
<th>Feature</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microcalcifications</td>
<td>45%</td>
<td>85%</td>
</tr>
<tr>
<td>Absence of halo</td>
<td>66%</td>
<td>46%</td>
</tr>
<tr>
<td>Poorly defined margins</td>
<td>64%</td>
<td>77%</td>
</tr>
<tr>
<td>Hypoechoic</td>
<td>80%</td>
<td>45%</td>
</tr>
<tr>
<td>Increased Doppler flow</td>
<td>67%</td>
<td>81%</td>
</tr>
<tr>
<td>Taller than Wide</td>
<td>48%</td>
<td>92%</td>
</tr>
<tr>
<td>MicroCa$^{2+}$ + irreg margin</td>
<td>30%</td>
<td>95%</td>
</tr>
<tr>
<td>MicroCa$^{2+}$ + hypoechoic</td>
<td>28%</td>
<td>95%</td>
</tr>
<tr>
<td>Solid + hypoechoic</td>
<td>73%</td>
<td>69%</td>
</tr>
</tbody>
</table>

Interobserver variability of US features

Kappa values
Agreement
<0.2 slight
0.21-0.4 fair
0.41-0.6 moderate
0.61-0.8 substantial
>0.8 ~perfect!

Moon Radiology 2008 247:762; Choi Thyroid 2010 20:167
US Pattern Recognition

While individual features are suggestive, combining features and pattern recognition are the keys to US risk stratification of thyroid nodules.
<table>
<thead>
<tr>
<th>Category</th>
<th>US PATTERN</th>
<th>MALIGNANCY RISK %</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIRADS 1</td>
<td>Normal thyroid gland</td>
<td>0</td>
</tr>
<tr>
<td>TIRADS 2</td>
<td>Cyst with or without comet tail</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Spongiform</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mixed cystic/solid with solid portion mixed</td>
<td></td>
</tr>
<tr>
<td>TIRADS 3</td>
<td>Hashi’s pseudonodule</td>
<td>&lt;5</td>
</tr>
<tr>
<td>TIRADS 4</td>
<td></td>
<td>5-80</td>
</tr>
<tr>
<td>4A</td>
<td>Solid or mixed hyper/isoechoic with thin capsule</td>
<td>5-10</td>
</tr>
<tr>
<td>4B</td>
<td>Hypoechoic with irreg margins</td>
<td>10-80</td>
</tr>
<tr>
<td></td>
<td>Hyper/iso/hypo with thick capsule</td>
<td></td>
</tr>
<tr>
<td>TIRADS 5</td>
<td>Hypo/Iso nonencapsulated with microcalcals</td>
<td>&gt;80</td>
</tr>
</tbody>
</table>
## TIRADS-Kwak 2011

<table>
<thead>
<tr>
<th>Category</th>
<th>Number of suspicious US features</th>
<th>CANCER RISK %</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIRADS 3</td>
<td>NONE</td>
<td>1.7</td>
</tr>
<tr>
<td>TIRADS 4A</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>TIRADS 4B</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>TIRADS 4C</td>
<td>3-4</td>
<td>44-73</td>
</tr>
<tr>
<td>TIRADS 5</td>
<td>5</td>
<td>88</td>
</tr>
</tbody>
</table>

**Suspicious US features:**
- solid
- marked hypoechochogenicity
- hypoechochogenicity
- microlobulated or irregular margins
- microcalcifications
- taller than wide shape

Kwak Radiology 2011;260:892
Kwak 2011 features – A – hypoechoic, B – microca, C – Markedly hypoechoic D – Irregular Margins
Suspect patterns

Highly suspect
Taller than wide
Irregular borders
Microcalcifications
Markedly hypoechoic
High stiffness with
sonoelastography (if available)

Mildly suspect
No sign of high suspicion
Mildly hypoechoic

3–5 signs
and/or
metastatic
lymph node

TIRADS
Score 5

1 or 2 signs
No metastatic
lymph node

TIRADS
Score 4B

TIRADS
Score 4A

Adapted TI-RADS based on Russ 2011.
Russ, Leboulleux, Leenhardt, Hegedus Eur Thyroid J. 2014 Sep;3(3):154-63
Benign patterns

Very probably
No sign of high suspicion:
- Regular shape and borders
- No microcalcifications
- Isoechoic or hyperechoic

TIRADS
Score 3

Constantly
- Simple cyst
- Spongiform nodule
- ‘White knight’
- Isolated macrocalcification
- Nodular hyperplasia

TIRADS
Score 2

Adapted TI-RADS based on Russ 2011.
Russ, Leboulleux, Leenhardt, Hegedus Eur Thyroid J. 2014 Sep;3(3):154-63
TIRADS - Interobserver

Kappa values - Agreement

- <0.2 slight
- 0.21-0.4 fair
- 0.41-0.6 moderate
- 0.61-0.8 substantial
- >0.8 ~ perfect!

Russ 2013

Thyroid incidentalomas (normal TSH level)

History of familial thyroid cancer or head/neck irradiation or focal FDG uptake

Yes

US risk stratification and size evaluation

Subcentimetric nodules

Size ≥10 mm
US-FNA

<10 mm
Follow-up is an option

TIRADS 4B or 5
Located near the capsule or at the upper pole of thyroid
US-FNA

Supracentimetric nodules

TIRADS 3
Follow-up

All TIRADS 4B, 4A
TIRADS 3 and >20 mm or growth

US-FNA
Otherwise: follow-up

95.7% Sensitivity
61% Specificity
ATA 2015: Nodule Sonographic Pattern Risk of Malignancy

Haugen et al. Thyroid; October 2015

High Suspicion 70-90%
- microcalcifications
- hypoechoic nodule, 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
HIGH Suspicion Pattern 70-90%

- hypoechoic, microcalcs, irreg margin
- hypoechoic, irreg margin (microlobulated/spiculated)
- hypoechoic, irreg margin, taller than wide
- hypoechoic, irreg margin, extrathyroidal extension
- hypoechoic, interrupted rim calcification with soft tissue extrusion
- irregular margins, suspicious left lateral lymph node
Intermediate Pattern 10-20%

HYPOECHOIC BUT WITHOUT OTHER SUSPICIOUS FEATURE
LOW Suspicion Pattern 5-10%

- Hyperechoic solid reg margins
- Isoechoic solid reg margins
- Partially cystic with eccentric solid areas

WITHOUT: MicroCa, Irregular Margin, Taller than Wide or Extra-thyroidal Extension
Isoechoic/Hyperechoic and Solid

- Benign Hürthle cell adenoma
- PTC follicular variant
- Follicular thyroid cancer
- Hyperplastic nodule
- Hyperplastic nodule

~20% of all cancers are Iso/hyperechoic: predominantly follicular/ Hürthle
Other Patterns

- Hyperechoic, microcalcs
- Isoechoic, coarse calc
- Isoechoic, margin lobulated smooth
- Eggshell calc
VERY LOW Suspicion Pattern
<3%

spongiform

partially cystic no suspicious features, note solid areas
Fig. 1. Indications for FNA biopsy according to US findings. Suspicious US findings are markedly hypoechoic nodule, intranodular microcalcifications, more-tall-than-wide shape, and spiculated or lobulated margins. FNA = fine-needle aspiration; US = ultrasonography.
**Benign - <1% ROM**

<table>
<thead>
<tr>
<th>US features indicative of a benign nodule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoechoic spongiform appearance (microcystic spaces comprising &gt;50% of the nodule)</td>
</tr>
<tr>
<td>Simple cyst with thin regular margins</td>
</tr>
<tr>
<td>Mostly cystic (&gt;50%) nodules containing colloid (hyperechoic spots with comet-tail sign)</td>
</tr>
<tr>
<td>Regular “eggshell” calcification around the periphery of a nodule</td>
</tr>
</tbody>
</table>
Intermediate – 10-15% ROM

Indeterminate US features

- Isoechoic or hyperechoic nodule with hypoechoic halo
- Mild hypoechoic (relative to surrounding parenchyma) nodule with smooth margin
- Peripheral vascularization
- Intranodular macrocalcification
Suspicious – 50-90% ROM

<table>
<thead>
<tr>
<th>US features indicative of a malignant nodule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Papillary carcinoma</td>
</tr>
<tr>
<td>Solid hypoechoic (relative to prethyroid muscles) nodule, which may contain hyperechoic foci without posterior shadowing (i.e., microcalcifications)</td>
</tr>
<tr>
<td>Solid hypoechoic nodule, with intranodular vascularity and absence of peripheral halo</td>
</tr>
<tr>
<td>“Taller-than-wide” nodule (AP&gt;TR diameter when imaged in the transverse plane)</td>
</tr>
<tr>
<td>Hypoechoic nodule with spiculated or lobulated margin</td>
</tr>
<tr>
<td>Hypoechoic mass with a broken calcified rim and tissue extension beyond the calcified margin</td>
</tr>
<tr>
<td>Follicular neoplasm (either follicular adenoma or carcinoma)</td>
</tr>
<tr>
<td>Isoechoic or mildly hypoechoic homogeneous nodule with intranodular vascularization and well-defined halo</td>
</tr>
<tr>
<td>Sonographic Pattern</td>
</tr>
<tr>
<td>--------------------------</td>
</tr>
<tr>
<td>High suspicion</td>
</tr>
<tr>
<td>Intermediate suspicion</td>
</tr>
<tr>
<td>Low suspicion</td>
</tr>
<tr>
<td>Very low suspicion</td>
</tr>
<tr>
<td>Benign</td>
</tr>
<tr>
<td>FNA is not recommended for nodules that do not meet the above criteria, including all nodules &lt; 1 cm</td>
</tr>
</tbody>
</table>

**One option is surveillance**

Haugen et al. Thyroid; January 2016
# US Risk and suggested FNA cutoffs

<table>
<thead>
<tr>
<th>Sonographic Pattern</th>
<th>Estimated malignancy risk</th>
<th>FNA size cutoff</th>
<th>AACE Level of Evidence</th>
<th>AACE Strength of Rec</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Risk US</td>
<td>50-90%</td>
<td>≥ 1 cm</td>
<td>2</td>
<td>A</td>
</tr>
<tr>
<td>Intermediate Risk US</td>
<td>5-15%</td>
<td>≥ 2 cm</td>
<td>2</td>
<td>A</td>
</tr>
<tr>
<td>Low Risk US</td>
<td>&lt;1%</td>
<td>≥ 2 cm or growing</td>
<td>2</td>
<td>A</td>
</tr>
<tr>
<td>Sonographic Pattern</td>
<td>Strength of rec</td>
<td>Quality of evidence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>---------------------</td>
<td>-----------------</td>
<td>---------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>High suspicion</strong></td>
<td><strong>Strong</strong></td>
<td><strong>Moderate</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Repeat US and US FNA within 12 months</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Intermediate/ Low suspicion</strong></td>
<td><strong>Weak</strong></td>
<td><strong>Low</strong></td>
<td></td>
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</tr>
<tr>
<td>Repeat US at 12-24m If growth or new suspicious US feature, repeat FNA OR continued observation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Very low suspicion</strong></td>
<td><strong>Weak</strong></td>
<td><strong>Low</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Utility of surveillance US and assessment of nodule growth as an indicator for repeat FNA is not known. If repeated, US should at ≥ 24 months</td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>IF 2nd US FNA done with benign cytology, US surveillance for continued risk of malignancy is no longer indicated</strong></td>
<td><strong>Strong</strong></td>
<td><strong>Moderate</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Haugen et al. Thyroid; January 2016