US of pediatric thyroid nodules

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• No disclosures
• But...

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LaFranchi SH. Inaugural Management Guidelines for Children with Thyroid Nodules and Differentiated Thyroid Cancer: Children Are Not Small Adults. Thyroid 2015;25(7):713-715.


Jeong SH, Hong HS, Lee EH, Kwak JJ. The Diffuse Sclerosing Variant of Papillary Thyroid Cancer Presenting as Innumerable Diffuse Microcalcifications in Underlying Adolescent Hashimoto's Thyroiditis: A Case Report. Medicine 2016;95(12):e3141.


Larson SD, Jackson LN, Riall TS, Uchida T, Thomas RP, Qiu S, Evers BM. Increased Incidence of Well-Differentiated Thyroid Cancer Associated with Hashimoto Thyroiditis and the Role of the PI3k/Akt Pathway. Journal of the American College of Surgeons 2007;204(5):764-773.


Haugen BR, Alexander EK, Bible KC, et al. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. Thyroid 2016;26(1):1-33.


Objectives

• Provide information on the state of pediatric thyroid nodule guidelines
• Discuss differences between pediatric and adult population
• Illustrate malignant nodules and mimickers of malignancy
• Differentiate benign from malignant nodules based on US findings
• Present common mimickers of malignant thyroid nodular disease
2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer

The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer

<table>
<thead>
<tr>
<th>Sonographic pattern</th>
<th>US features</th>
<th>Estimated risk of malignancy, %</th>
<th>FNA size cutoff (largest dimension)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High suspicion</td>
<td>Solid hypoechoic nodule or solid hypoechoic component of a partially cystic nodule with one or more of the following features: irregular margins (infiltrative, microlobulated), microcalcifications, taller than wide shape, rim calcifications with small extrusive soft tissue component, evidence of ETE</td>
<td>&gt;70-90&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Recommend FNA at ≥1 cm</td>
</tr>
<tr>
<td>Intermediate suspicion</td>
<td>Hypoechoic solid nodule with smooth margins without microcalcifications, ETE, or taller than wide shape</td>
<td>10-20</td>
<td>Recommend FNA at ≥1 cm</td>
</tr>
<tr>
<td>Low suspicion</td>
<td>Isoechoic or hyperechoic solid nodule, or partially cystic nodule with eccentric solid areas, without microcalcification, irregular margin or ETE, or taller than wide shape.</td>
<td>5-10</td>
<td>Recommend FNA at ≥1.5 cm</td>
</tr>
<tr>
<td>Very low suspicion</td>
<td>Spongiform or partially cystic nodules without any of the sonographic features described in low, intermediate, or high suspicion patterns</td>
<td>&lt;3</td>
<td>Consider FNA at ≥2 cm</td>
</tr>
<tr>
<td>Benign</td>
<td>Purely cystic nodules (no solid component)</td>
<td>&lt;1</td>
<td>No biopsy&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

US-guided FNA is recommended for cervical lymph nodes that are sonographically suspicious for thyroid cancer (see Table 7). The estimate is derived from high volume centers, the overall risk of malignancy may be lower given the interobserver variability in sonography.

<sup>a</sup> Aspiration of the cyst may be considered for symptomatic or cosmetic drainage.

<sup>b</sup> ETE, extrathyroidal extension.
<table>
<thead>
<tr>
<th>Risk of malignancy</th>
<th>Sonographic patterns</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Suspicion &gt;70-90%</td>
<td>microcalcifications, hypoechoic nodule, irregular margin</td>
</tr>
<tr>
<td>Intermediate Suspicion 10-20%</td>
<td>hypoechoic, irregular margin</td>
</tr>
<tr>
<td>Low Suspicion 5-10%</td>
<td>hypoechoic solid, regular margin</td>
</tr>
<tr>
<td>Very low Suspicion &lt;3%</td>
<td>spongiform, partially cystic no suspicious features</td>
</tr>
<tr>
<td>Benign &lt;1%</td>
<td>cyst</td>
</tr>
</tbody>
</table>

Haugen et al. 2016

ATA nodule sonographic patterns and risk of malignancy
Table 7. Ultrasound Features of Lymph Nodes Predictive of Malignant Involvement

<table>
<thead>
<tr>
<th>Sign</th>
<th>Reported sensitivity, %</th>
<th>Reported specificity, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microcalcifications</td>
<td>5–69</td>
<td>93–100</td>
</tr>
<tr>
<td>Cystic aspect</td>
<td>10–34</td>
<td>91–100</td>
</tr>
<tr>
<td>Peripheral vascularity</td>
<td>40–86</td>
<td>57–93</td>
</tr>
<tr>
<td>Hyperechogenicity</td>
<td>30–87</td>
<td>43–95</td>
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<tr>
<td>Round shape</td>
<td>37</td>
<td>70</td>
</tr>
</tbody>
</table>

*Adapted with permission from the European Thyroid Association guidelines for cervical ultrasound (20).*
Thyroid Ultrasound Reporting Lexicon: White Paper of the ACR Thyroid Imaging, Reporting and Data System (TIRADS) Committee

Edward G. Grant, MD, Franklin N. Tesler, MD, Jenny K. Hoang, MBBS, Jill E. Langer, MD, Michael D. Beland, MD, Lincoln L. Berland, MD, John J. Cronan, MD, Terry S. Deser, MD, Mary C. Frates, MD, Ulrike M. Hamper, MD, William D. Middleton, MD, Carl C. Reading, MD, Leslie M. Scutt, MD, A. Thomas Stavros, MD, Sharlene A. Teeffy, MD

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Management Guidelines for Children with Thyroid Nodules and Differentiated Thyroid Cancer

The American Thyroid Association Guidelines Task Force on Pediatric Thyroid Cancer

Gary L. Francis,¹,* Steven G. Waguespack,²,* Andrew J. Bauer,³,⁴,* Peter Angelos,⁵ Salvatore Benvena,⁶ Janete M. Cerutti,⁷ Catherine A. Dinauer,⁸ Jill Hamilton,⁹ Ian D. Hay,¹⁰ Markus Luster,¹¹,¹² Marguerite T. Parisi,¹³ Marianna Rachmial,¹⁴¹⁵ Geoffrey B. Thompson,¹⁶ and Shunichi Yamashita¹⁷

CHILDREN ARE NOT JUST SMALL ADULTS
**Background- why pediatric guidelines are needed?**

- Prevalence of thyroid nodules in children 0.05-5% (adults 5-10%)
- Children ~25% ➔ malignant (adults: 5-10%)
- Differentiated thyroid ca (DTC) < 20 y.o ➔ 1.8% of all thyroid malignancies in the US... incidence is increasing!
- Girls 15-19 y.o ➔ DTC 2nd most common malignancy
- Adolescents 10 fold greater incidence than young children with 5:1 female preponderance (not in younger kids)
- Cases present at advanced stages with greater rates of lymph nodal (~80%) and pulmonary metastasis (~30%)
- “Hot/autonomous nodules” ➔ 30% malignancy (adults: typically benign)
- Recurrence rate after total thyroidectomy ~30% (adults: 4.7-8%)
- Papillary TC – 90% (adults: 70-80%)
  - Classic
  - Follicular
  - Diffuse sclerosing (no microcalcs?)
- Follicular TC - uncommon
- Medullary TC,
- Poorly differentiated tu
- Anaplastic tu

Rare in children
Special populations at high risk for thyroid neoplasia – screening?

- Radiation exposure, especially those <5 years of age, are the most sensitive
- Iodine deficiency
- History of autoimmune thyroiditis
- Genetic disorders that predispose to thyroid neoplasia

**Recommendation 4**

Annual physical exam
Additional imaging if:
- Palpable nodules
- Thyroid asymmetry
- Cervical lymphadenopathy

**Recommendation rating: B**
(Fair evidence that service or intervention can improve outcome)
All FNA should be performed under US guidance
No FNA of hyperfunctioning nodules \(\rightarrow\) surgery
Diffusely infiltrative form of PTC \(\rightarrow\) diffuse enlargement of a lobe or the entire gland (rarely microcalcifications)
Indeterminate cytology \(\rightarrow\) surgery
US characteristics and clinical context - not only size!!

Evidence that service or intervention can improve outcome

Francis GL et al - 2015
<table>
<thead>
<tr>
<th>Study name</th>
<th>Intranodular vascularity</th>
<th>Microcalcifications</th>
<th>Hypoechogeticity</th>
<th>Subcapsular location</th>
<th>Taller than wide</th>
<th>Irregular margins</th>
<th>Abnormal lymph nodes</th>
<th>Heterogenous echotexture</th>
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<tbody>
<tr>
<td>Goldfarb et al 2002</td>
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<td>Lyschik et al 2005</td>
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<td>Corrias et al 2010</td>
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<td>Gupta et al 2013</td>
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<td>Mussa et al 2015</td>
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<td>Al Nofal et al 2016</td>
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<td>Koltin et al 2016</td>
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Thyroid Nodule Characterization

- Echogenicity
- Microcalcifications
- Margins
- Elastography
- Vascularity
Echogenicity

- **Hypoechogenicity** commonly associated with malignancy in both adults and children
- **20-30% of all cancers are Iso/hyperechoic:** predominantly follicular/ Hürthle cell (adults)
- **Sensitivity 75.9%  Specificity 55.8%**  

17 year old female originally seen for ovarian teratoma. Areas of increased uptake seen on follow up imaging. Suspicious features included **hypoechoic echotexture**, largest 7.5 x 6.9 x 8.8 mm in posteromedial inferior pole of the right lobe, and **calcifications**

FNA: Papillary Carcinoma
• **Follicular adenomas** can mimic malignant nodules
• Typically solitary, but can be multinodular
• Well defined with hyper-, isoechogenic
• Thick/smooth hypoechoic halo
• Peripheral vascularity but **relatively hypovascular**

Peripheral vascularity +/- central vascularity is independent predictor of benignity

16 year old female
Nodule was incidental finding on spine MRI
US: 4.4 x 2.2 x 2.6 cm complex mass in left thyroid lobe with peripheral vascularity
FNAC: Bethesda III (lesion of undetermined significance)
Due to size, patient underwent left lobectomy
Final pathology: **follicular variant papillary cancer**
Follow up care was complete thyroidectomy
**Microcalcifications**

- **Sensitivity 44.8% & Specificity 97.3%**  
- Multiple bright punctate (under 1 mm) echoes without shadowing
- Most specific sign of malignancy (85-95%)
- **Pitfall:** colloid in a hyperplastic nodule-reverberation artifacts

16 year old female with Graves Disease  
Asymptomatic with nonpalpable nodule  
US was suspicious due to microcalcifications (red arrows), irregular and ill defined margins and hypoechoic echotexture  
FNA: Papillary Carcinoma Diffuse Sclerosing Variant
**Pitfall:** Colloid nodules
- Iso-hypoechoic
- Internal cystic or heterogenous change
- Echogenic foci with comet tail/reverberation artifacts
15 y.o. girl with a history of thyroid nodule
1 year later
FNA: PTC
11 y.o. girl with Hashimoto’s thyroiditis
2 years later...
17 year old female presented with fatigue and thyromegaly.

Suspicious US findings included **complex mixed echotexture, irregular margins, extrathyroidal extension and increased vascularity**.

FNA: Papillary Carcinoma

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**Margins**

- **Irregular** margins are concerning for malignancy.
- Extrathyroidal extension is highly suspicious.
- However **smooth borders are found in 33-93%** of adult malignant nodules.

17 year old female presented with fatigue and thyromegaly. Suspicious US findings included complex mixed echotexture, irregular margins, ETE and increased vascularity. FNA: Papillary Carcinoma.

Koltin et al: Pediatric Thyroid Nodules
- Presence of microcalcifications, size > 35 mm and ill defined margins together was most predictive of malignancy in children
- Sensitivity 80.7% & Specificity 79.2%

Elastography

- **Increased stiffness** is suggestive of malignancy
- Useful in non-diagnostic or indeterminate aspirates
  - **Sensitivity 94.9% & Specificity 90.3%**

16 year old female - 2x2 cm palpable thyroid nodule

**Nodule (red arrows)** was suspicious for malignancy due to presence of **extrathyroidal extension, chaotic vascularity, incomplete hypoechoic halo** and **increased stiffness**

**FNA:** Left Nodule: Papillary Carcinoma classic variant, Right Nodule: Colloid Nodule
**Vascularity**

- Chaotic or irregular central vascularization is suggestive of malignancy
- **Sensitivity 80% & Specificity 86.4%**

16 year old female - 2x2 cm palpable thyroid nodule

**Nodule** was suspicious for malignancy due to presence of **extrathyroidal extension, chaotic vascularity, incomplete hypoechoic halo** and **increased stiffness**

**FNA**: Left Nodule: Papillary Carcinoma classic variant, Right Nodule: Colloid Nodule
Additional Suggested Malignant Features

- **Subcapsular location**
  - Sensitivity 76.3% & Specificity 63.7%

- **Taller vs Wide Orientation**
  - Well established predictor in adults
  - Proven individual predictor of malignancy in pediatrics in only 1 paper
  - TIRADS Definition: AP to horizontal diameter ratio in transverse plane > 1

- **Lymph Node Alterations**
  - Including: rounded profile, calcifications, cystic change, absent hilum, heterogeneous echotexture, eccentric cortical thickening, increased vascular flow (with normal TSH), Longitudinal vs transverse axes ratio < 1.5
  - Sensitivity 48.3%, Specificity 95.9%
Mimickers of Malignancy
Traditionally Benign US Features

- **Hyperechogenicity (???)**

- **Cystic features**

- **Smooth, well defined margins, colloid**

16 year old female with history of nodules, none palpable
US findings included heterogeneous glandular echotexture and large hypoechoic nodule (2.9 x 1.0 cm) with well defined margins
FNA: No malignant cells, likely inflammatory

16 year old female with history of thyromegaly and palpable nodule
Suspicious findings included a large complex cystic lesion involving the mid and inferior poles and vascular internal septations
FNA: No malignant cells, likely degenerative benign cyst/nodule
• US findings seen in Graves’ Disease and Hashimoto’s Thyroiditis (HT) mimic diffusely infiltrative hypervascular tumors

• Shared findings include:
  – Thyroid gland enlargement
  – Hypoechoogenicity
  – Heterogeneous appearance
  – Hypervascularity

18 year old female with history of syncope and mild thyromegaly
US demonstrated 2.3 x 1.2 x 0.9 cm hypoechoic nodule in left lower pole
FNA: Hashimoto Thyroiditis

Findings specific to HT include:
- Multiple discrete hypoechoic micronodules
- Coarse septations

Malignancy suggested by:
- Irregular and nodular thyroid enlargement
- Nodal metastasis
- Infiltrative growth patterns

14 year old female with history of Hashimoto’s and hypothyroidism
Maternal history of Papillary Carcinoma
US demonstrated multiple hypoechoic nodules (red arrows): Right upper pole 7.4 x 3.9 x 5.2 mm, subtle anterior mid pole 1.3 x 0.5 x 0.1 cm
FNA: Hashimoto Thyroiditis

Ectopic Thymic Tissue (ETT) is commonly mistaken for malignant nodules.

Misdiagnosis leads to invasive procedures in children.

US Appearance of Thymic Tissue:
- Hypoechoic pattern
- Multiple linear and punctate bright internal echoes
  - “dot and dash – starry sky appearance”

Versus Papillary Cancer, findings suggestive of Ectopic Thyroid Tissue include:

- **Starry sky**- brighter intranodular echogenic foci compared to microcalcifications
- **Not prominent intranodular vascularity**
- **Longitudinal elongated appearance**
- **Well defined, geographic margins**
- **MC in lower poles**
McCune-Albright Syndrome

- Café au lait spots
- Polyostotic fibrous dysplasia
- Endocrinopathies

Case courtesy
Dr. Alan Daneman
Additional Pseudonodules

- Inflammatory Pseudonodules
- Nodular Subacute Thyroiditis
- Intraglandular Fatty Tissue / Lipoma
- Regression of Benign Cystic Nodule after FNA or Ethanol Ablation
- Perithyroidal Esophageal Diverticulum

Summary

• Children are not small adults! Size doesn’t matter…
• Look for: microcalcifications, extrathyroidal extension, intranodular vascularity and nodal composition
• We need more studies on echogenicity and taller vs wide
• Continuing retrospective and prospective studies may allow for further amendments to current guidelines – such as repeating US months later rather than subjecting the child to FNA or surgery
• In addition, further studies with common lexicon will solidify the predictive power of US findings in the pediatric population and improve the diagnostic process
Thank you for your attention!

Special Thanks to Dr. Alex Essenmacher and the Pediatric Radiology group from the University of Iowa Hospitals and Clinics