The evaluation of nodular thyroid disease

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Primary providers should know how to manage the thyroid nodule

- It is an "epidemic"
- Incidence - 5% of the general population
- Incidence of nodular goiter (females)
  - Physical exam 6.4%
  - Ultrasound 49-72%
- Autopsy 57%
- Incidence of thyroid cancer: 5-6%

SEER Data

- Incidence rates for thyroid cancer
  - 1975 4.8/100,000
  - 2007 11.99/100,000
  - 2009 14.25/100,000
- Incident rates for death of thyroid cancer
  - 1975 0.55/100,000
  - 2009 0.52/100,000
“Thyroid Nodule Assessment: Are There New Ways to Identify Malignancies?”
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Evaluation of the thyroid nodule epidemic
- Evaluation of the patient with a thyroid nodule
- Role of ultrasound
- “Suspicious” US findings
- FNA results
- Molecular gene expression testing
- TSH and thyroid hormone suppressive tx

The history: who has an increased risk of thyroid cancer?
- Sex
  - Female 4.2% Male 8.2%
- Age
  - <20 6.5%
  - 31-40 2.9%
  - 51-60 3.9%
  - 71-80 16.4%
- Rapid growth/childhood XRT/total body irradiation for transplant
- Family hx of thyroid cancer

Physical examination
- Learn to do a good exam
- However, PE is limited and findings can differ substantially from ultrasound imaging
- 173 pts referred to thyroid clinic MGH
- PE different from US in 63% of cases
- Of 114 pts with solitary nodule, 24% had multiple nodules and 20% did not have a nodule >1 cm.
- (Marquesse Ann Intern Med 2000)
Work up

- 45 year old female complains of tightness in her neck. PE is unrevealing. Thyroid US reveals a 1.6 cm right and 1.2 cm left thyroid nodule.
- You should order which of the following?
  - Thyroid scan and uptake
  - TSH
  - Free T4/T3
  - Anti-thyroglobulin AB
  - Anti-peroxidase AB
  - Serum thyroglobulin
  - Fine needle aspiration biopsy of the 1.6 cm right nodule
  - CT of the neck
  - Refer to surgeon

We look smart because we do this all the time
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![Image of Autonomous Thyroid Nodule Appearance on Thyroid Scintigraphy](image1.png)

123I-thyroid scan demonstrating an autonomous (“hot”) nodule with suppression of isotope uptake elsewhere. The total 24-hour dose uptake was normal (12 percent).

![Image of Nonfunctioning Thyroid Nodule Appearance on Thyroid Scintigraphy](image2.png)

123I-thyroid scan demonstrating typical appearance of a large, 3.6 cm nonfunctioning (“cold”) nodule in the left, upper lobe of the thyroid. The position of the nodule is outlined in white.

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**Initial Evaluation of a Patient with a Thyroid Nodule**

- Thyroid nodule found clinically or incidentally on imaging
  - TMR elevated
  - TMR normal or elevated
    - Radium thyroid scan
      - Nodule is functional
        - Check FNAC for malignancy
        - Nodule is nonfunctional
          - Consider further imaging and clinical course
      - Nodule is incompletely resected or not amenable to surgery
        - Observe in thyroid cancer
        - Treat

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TMR: thyroid stimulating hormone (thyrotrpin). FNAC: fine needle aspiration. Refer to topics on subclinical hyperthyroidism and toxic adenoma.
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Hypoechoic Nodule

Microcalcification
Benign Peripheral Vascularity

Central Vascularity in Malignant Nodule

Table: Computed and Ultrasound Features of Thyroid Nodules and Recommendations for Management

<table>
<thead>
<tr>
<th>Feature of Nodule</th>
<th>Ultrasound Features</th>
<th>Management Recommendations</th>
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</thead>
<tbody>
<tr>
<td>Benign</td>
<td>Central vascularity</td>
<td>Biopsy or follow-up</td>
</tr>
<tr>
<td>Malignant</td>
<td>Peripheral vascularity</td>
<td>Biopsy or surgical resection</td>
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</tbody>
</table>

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Nodules < 1cm, low risk

- Follow up US
  - 6-12 months
  - 3-5 years
- BX if increased growth and fits criteria above
- (low evidence)

Thyroid biopsy

- Technique
  - FNA
  - Core-needle biopsy
- Accuracy >95% with false negative rate 0-3%
- Positive predictive value of a malignant interpretation 97-99%
- Multiple nodules
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FNA biopsy

Ultrasound guided FNA biopsy
Ultrasound guided FNA biopsy

Management of thyroid nodules based upon results of fine needle aspiration

FNA benign
adenomatoid/hyperplastic nodules, colloid nodules, nodular goiter, Hashimoto’s

- Observe with US 6-18 months and less often if no change.
- Do you need to re-biopsy a benign nodule?
  - If no or minimal growth -> no
  - Consider re-biopsy if >20% growth in 2 diameters of at least 2 mm
- Should you start the patient on thyroxine suppressive therapy?
  - Prevents new nodules after partial thyroidectomy in pts with hx of neck XRT (Fogelfield NEJM 1989)
- Other studies
- Adverse effects of suppressive therapy
Follow the arrows

Perhaps we're overthinking the situation.

Management of thyroid nodules based upon results of fine needle aspiration

FNA nondiagnostic

- This does not mean "negative!"
- Repeat bx in 2-3 months (use US if not done initially)
- Consider core-needle biopsy
- If still nondiagnostic-observation vs surgery
Abnormal FNA

- Follicular lesion of undetermined significance
- Follicular neoplasm
- Atypical cells of undetermined significance

- 5-32% are malignant and many patients undergo surgery for what ultimately turns out to be benign disease
Abnormal FNA-molecular characterization of FNA samples

- Mutational analysis: BRAF, RAS, RET/PTC
  - If positive, 80+% chance of malignancy
  - But high false negative rate
- mRNA gene expression classifier—measures activity level of 167 genes within the nodule
  - NPV of 95%
  - PPV 38%
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