Objectives

- FNA in thyroid nodule diagnosis
- FNA technique
- FNA Interpretation and Reports
- Core biopsy and frozen section

The palpable thyroid nodule

- Usually means >1.0 cm.
- If <8mm, FNA necessary?
- Common: 5% of population
- Usually benign: 90-95%.
- Pre-test probability cancer - low

Malignant neoplasms

- Papillary carcinoma: 75-80%
- Follicular carcinoma: 10-15%
- Medullary carcinoma: 5%
- Other: <1%
  - including anaplastic carcinoma, lymphoma, metastatic malignancy, rare tumor types
Pre-FNA assessment

- History: duration, growth rate, radiation exposure, family history
- Exam: size, fixation, nodes
- TSH
- Ultrasound - confirm and assess for high risk features
  - Complex cyst
  - Increased vascularity
  - Micro calcification
  - Irregular margins

Who should do FNA?

Any trained and interested physician with sufficient intensity of practice.

FNA Technique

Informed Consent
- bleeding
- nerve injury
- tracheal puncture
- needle track seeding of tumor
Palpation or Ultrasound-guided
Fine needle: #25 or #27 gauge needle
Local anaesthetic is nice!

FNA Technique

- Needle passes: minimum of 2; 3-6 to adequately sample
- Non-aspiration (capillary method) is best.
- Don’t wander the needle! You will come out of the target.
- Be Quick! 10 seconds is enough. Blood in the hub – quit!
- Smears if possible but Liquid based collection is ok
- Post biopsy care: pressure, observation, acetaminophen
FNA – Simple not Trivial

FNA technique

Blood, Blood!!
Dx: Unsatisfactory
- Excess suction
- Large bore needle
- Excess time

Slide preparation

- Express the material as a drop on the slide.
- Air dried smear and Alcohol fixed smear (Cytology spray)
- Rinse the needles into balanced salt solution, RPMI or Cytolyte and send to lab.
- Cell blocks: usually not necessary or helpful
  - need 1-2 passes to get adequate material
  - nice for special stains

FNA: Palpation or Ultrasound?

- Palpation:
  - Convenient, inexpensive, office procedure.
  - Nodule: >1.0cm, confirmed by ultrasound, mostly solid
  - No contraindications or recent previous FNA

- Ultrasound:
  - more complex and costly
  - more accurate and higher satisfactory rate.

- All nodules should have Ultrasound before FNA
  - 15-20% of "palpable" nodules are <1.0 cm. on US
  - 25-50% of "solitary" nodules are in multinodular gland (most <1.0cm)
  - 2-3% of US detected nodules >1.0 cm are not palpable.
**Ultrasound - indications**
- Non-palpable or difficult location (posterior-inferior)
- Nodule in background of Hashimoto’s thyroiditis
- Difficult neck exam (thick, short, previous surgery)
- Complex cystic nodules
- Unsatisfactory repeat
- Surveillance: known nodule, follow up for lymph nodes

**Is a repeat FNA helpful?**
- Studies vary: ‘not helpful’ to >50% diagnostic on second biopsy
- Most report is helpful for unsatisfactory or non-specific cases (e.g., cyst, nodular)
- Wait at least 3 months to avoid false positive atypia from reparative change.
- Repeat with ultrasound

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**What about core biopsy?**
- Increasingly being offered in some USA centres.
- Usually #20 gauge needle.
- Single action spring needle
- May be useful as a second test in some patients
- Not helpful in follicular lesions

**FNA vs core biopsy?**
*Renshaw and Pinnar AJCP 2007; 128: 370-4*

<table>
<thead>
<tr>
<th>Adequacy</th>
<th>FNA</th>
<th>CB</th>
<th>Combined</th>
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<tr>
<td>70%</td>
<td>70 cases</td>
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<td>82%</td>
<td>25 cases</td>
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<td>90%</td>
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- 377 patients, 6 years
- Concurrent FNA and one pass Core biopsy
- NB. FNA atypical in 21 cases of Core bx negative: 14 biopsies revealed 9 malignancies (8 PTC)
Interpretation and Reporting

- **Purpose**: identify who should have surgery
- Many reporting systems from 2 to 6 categories

Benign - Thyroiditis

- Hashimoto Thyroiditis
- Granulomatous Thyroiditis

Follicular Lesion – Favor Goiter

Follicular Lesions – Favor Neoplasm

- Microfollicular pattern
- Hurthle Cell lesion
What are the problems?

- No sample: Missed the target / poor technique
- Sample quality: few cells, fixation poor, only histiocytes (no follicular cells)
- Interpretation – inexperience, borderline nuclear changes, reactive change (HT, recent FNA). 2nd opinion may be helpful?
- Diagnostic criteria – overlap of diagnostic criteria for follicular lesions
- Unhelpful or useless reports – 2nd opinion

Microfollicular lesions
Insufficient for diagnosis

- The major cause of diagnostic error is the interpretation of suboptimal samples leading to false-negative and false-positive diagnosis.

- Most pathologists want to see at least 6-10 groups of follicular epithelial cells (10 cells/group) on 2 slides.

Insufficient for diagnosis

Inadequate aspirates should be <15%.

- Variable amongst practitioners

- BCCA unsatisfactory rates for physicians sending in samples 15-55%

FNA Performance

- Reported sensitivities (57-99%) and specificities (55-99%)
- Dutch national survey: false negative rate 30%
  - Cancer Cytopathol 2000;90:330-334
- BCCA: false negative rate (PTC only) in clinic 4/18 = 22%
  referred in 18/54= 33%
  - Unpublished data 1995-2003

1. Effectiveness of Toyota Process Redesign in reducing Thyroid Gland Fine-Needle Aspiration Errors
Raab et al. Am J Clin Pathol 2006;126:585-592

1. Specimen adequacy was standardized
2. Immediate Interpretation encouraged
3. Standard reports established
   - Unsatisfactory
   - Non-specific
   - Benign
   - Atypical
   - Follicular neoplasm
   - Suspicious
   - Malignant
2. Effectiveness of Toyota Process Redesign in reducing Thyroid Gland Fine-Needle Aspiration Errors
Raab et al. Am J Clin Pathol 2006;126;585-592

Standardized terminology for adequacy
- Pre-standard 5.8% unsatisfactory
- Post-standard 19.8% unsatisfactory

Immediate interpretation
- Yes: 7.8% unsatisfactory
- No: 23.8% unsatisfactory

3. Effectiveness of Toyota Process Redesign in reducing Thyroid Gland Fine-Needle Aspiration Errors
Raab et al. Am J Clin Pathol 2006;126;585-592

Accuracy characteristics from Standard reports
- Sensitivity: 70.2% to 90.6%
- Specificity: 67.0% to 55.1%
- False Neg rate: 41.8% to 19.1%
  ● (benign only, more unsatisfactory)
- False Pos rate: 22.6 to 26.3%
  ● (follicular neoplasms, suspicious and malignant included in calculation of positive)

Standardized FNA Report (probable)
- Malignant: PTC, MC, ACA, NHL, other
- Suspicious for (specify eg. papillary carcinoma)
- Follicular patterned lesion:
  - indeterminate type
  - favour hyperplastic nodule
  - favour Follicular or Hurthle cell neoplasm
- Benign: Colloid cyst, Thyroiditis - Hashimoto or Sub acute (granulomatous) types
- Suboptimal cellularity/preservation but suggestive of ....
- Unsatisfactory: no cells or poor slide preparation

Standardized FNA Reports – Predictive values
- Malignant ~100%
- Suspicious ~ 65-70%
- Follicular patterned lesion:
  - indeterminate type: ?
  - favour hyperplastic nodule: 15-20% neoplasm
  - favour Follicular or Hurthle cell neoplasm: ~50% neoplasm
- Benign: <1% will be neoplasms
- Suboptimal cellularity/preservation but suggestive of .... ?
- Unsatisfactory: ? Perhaps 5-10% neoplastic
Management - Unsatisfactory

- Clinical/Ultrasound follow up
- Repeat FNA
- Consider Core Biopsy if available

Management - Suboptimal

- Follow and repeat under Ultrasound.
- Cystic change only
  - Clinical and Ultrasound follow up.
  - Repeat FNA with Ultrasound
  - Most are degenerate adenomas or hemorrhagic cysts
  - Cancer risk low; increases with size (>4cm.)
  - If cyst disappears with FNA risk of cancer is very low.
  - If residual lesion after FNA – reaspirate the remnant

Management - Follicular Lesions

- 80% are benign (Neoplasm risk ~20%)
- Assess predictive value of report
- Follicular carcinoma risk increases with:
  - Size >4cm (40% vs. 13%)
  - Male vs. Female (43% vs. 16%)
  - Solitary vs. Multinodular (25% vs. 6%)
  - Nuclear atypia (60% vs. 6%)

Frozen section useful?

Yes!!

- Margins
- Tissue type: lymph node, parathyroid
- Suspicious for papillary carcinoma: 25-40% are diagnostic.
  - (Some reports up to 75% but false positive rate increased.)
Frozen section useful?

- **No!**
  - If FNA report is follicular pattern lesion then
    - FS unlikely to find adenoma vs. carcinoma features
    - Post FNA pseudo-invasion may give false positive diagnosis on FS.

Is Frozen section useful?

- **No!**
  - FNA report is malignant

Summary

- FNA the best test but far from perfect.
- FNA technique is simple but not trivial!
- Better technique gives better samples and more accurate diagnosis.
- Ultrasound-guided FNA may be indicated.
- Core biopsy may be useful.
- Frozen section definite but limited role.
- New standard reporting pending.

Thanks!!