OBJECTIVES:

1. Why use US for localization?
2. Review the US findings and features of parathyroid adenomas and locations
3. When to consider FNA biopsy?
4. Review the potential problems associated with biopsy and how to avoid them?

Dev Abraham MD, MRCP (UK), ECNU, FACE
Professor of Medicine (clinical), Division of Endocrinology
Asst Dean, Faculty Affairs, School of Medicine,
University of Utah, Salt Lake City, UT
**Historical perspectives**

1850–1900  Parathyroid glands discovered Sir Owen (Indian Rhino)
1877      In man - Uppsala anatomist - Ivar Sandström
1891      Bone disease - von Recklinghausen
1900–1925 Tetany after parathyroidectomy Gley and Bothy
1925      Active gland extract purified- Collip
1925 –1950s Pathophysiology of Hyper- and hypoparathyroidism- Virchow, Erdhim and Albright
1925      Mandl first parathyroid surgery - enlarged parathyroid tumor
1929      Bone mass increase in rats - Paradox (largely ignored)
1970s     Hormone structure and synthesis.
1970s     Multichannel analyzers – led to detection of hypercalcemia fortuitously – apparent increase in incidence
1980’s – 90’s – Tc99MIBI
Minimally invasive surgeries, the pendulum is swinging back

The success of minimal invasive surgery hinges on **LOCALIZATION**
PHPT

Most common cause of outpatient calcium elevation

3 fold common in women 1.5% of post menopausal women

Rule out FHH
24 hour urine calcium <100 mg
Mild elevation of Magnesium

Asymptomatic Diagnosed-Fortuitously 1970’s – Multichannel analyzers

More than 80% are single adenomas

MEN ESRD Multi-gland

SURGERY ONLY DEFINITIVE TX
### Indications for surgery

<table>
<thead>
<tr>
<th>Parameter</th>
<th>2002</th>
<th>2009</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum calcium</td>
<td>&gt;1 mg</td>
<td>&gt;1 mg</td>
<td>&gt;1 mg</td>
</tr>
<tr>
<td>Urine calcium</td>
<td>&gt;400 mg /day</td>
<td>Not recommended</td>
<td>&gt;400 mg /day &amp; nephro-lithiasis or risk</td>
</tr>
<tr>
<td>Creatinine clearance</td>
<td>Reduction of 30% or more</td>
<td>&lt;60 ml/min</td>
<td>&lt;60 ml /min</td>
</tr>
<tr>
<td>BMD-DXA</td>
<td>T score &lt;-2.5 at any site</td>
<td>T score &lt;-2.5 Same plus previous fracture</td>
<td>T score &lt;-2.5 any site and vertebral fracture by other imaging</td>
</tr>
<tr>
<td>Age</td>
<td>&lt;50 years</td>
<td>&lt;50 years</td>
<td>&lt;50 years</td>
</tr>
</tbody>
</table>
Essential to establish biochemical diagnosis first, prior to imaging or therapy - Serum Calcium, PTH and Urine calcium

Establish need for therapy, surgery

Localization studies – Neck US, (TC99MIBI, 4D CT): Do not apply as diagnostic studies

Surgical, ETOH ablation or medical treatment
Locate the adenoma

**WHY ULTRASOUND?**

**PHPT PA**

**Associated THYROID NODULES / CANCERS**

1. CHECK CALCIUM ON ANY PATIENT UNDERGOING THYROID SURGERY

2. ALWAYS EVALUATE FOR THYROID NODULES IN PATIENTS UNDERGOING PA SURGERY
Inferior pair undertake a longer migratory route along with the thymus gland.

Superior pair are more likely to be intra-thyroidal. Develop along with C-cells.
SUPERIOR PARATHYROID - Anatomic distribution and variations

- Upper pole of thyroid
- Mid portion of the thyroid lobe - Typical location

Carotid Sheath
Para-esophageal
ITA
RLN

11%
10%
1%
77%
INFERIOR PARATHYROID – Anatomical variations

- Undescended – Above ITA: 2%
- Inferior pole of thyroid: 3%
- Thyro-thymic ligament: 56%
- Mediastinal: 26%
- 9%
How common is ectopic location of adenomas?

- Autopsy series: Greece - 942 cadavers, 5% had supernumerary glands, 2% had 3 glands, 8.5% were ectopic within the neck, 0.2% intra-thyroidal, and 6% were within the mediastinum.
- Ectopic gland frequency varies from 5-20%.
- What is the reason for this wide variation?
Minimally invasive surgery

ADVANTAGES
- Most patients with PHPT have single adenomas that are easily accessible, in the vicinity of the thyroid gland
- Shortened hospital stay (same day surgery)
- Speedier recovery

HENCE THE NEED FOR LOCALIZATION STUDIES

DISADVANTAGES
- Requires accurate preoperative localization
- Requires intra-operative confirmation of successful removal (e.g. intra-operative rapid PTH, gamma probe)
- Associated thyroid disease may go unrecognized unless adequate pre-operative thyroid US.
Localization techniques

**Tc\textsuperscript{99} MIBI**
- "just a maybe scan"
- Later studies suggest 75% sensitivity
- Evaluation of thyroid gland not possible
- Protocol and institution dependent
- Less operator dependent
- Useful in intra-thoracic and posteriorly located Pas

**Ultrasound**
- Greater sensitivity
- Lower cost
- No ionizing radiation
- Less time for examination
- Evaluation of thyroid possible
- Operator dependent
- Non-operator dependent limitations: posterior and intrathoracic locations

**4D CT**
- Not practical in most centers
- High radiation exposure
LOW FREQUENCY TRANSDUCER SETTING 7-10 MHz

NECK EXTENSION WITH SUPPORT TO SHOULDERS

HAVE A SYSTEM TO COVER THE ‘USUAL SUSPECT’ NECK AREAS

COUGHING BREATHE VALSALVA TURNING HEAD SIDE TO SIDE
Proper patient positioning

Adequate extension of the neck is essential with pillows placed under the shoulders.
Ultrasound Characteristics of Parathyroid Adenoma – HYPERCALCEMIC SUBJECT

1. Homogenously-hypoechoic
2. Variable Shapes:
   Conforms to surrounding structures
3. Adjacent to but separate from posterior thyroid
   • May indent the posterior capsule
   • Echogenic line of separation from the thyroid capsule
4. Vascular pedicle from polar artery
5. Can be mobile
5 D’s

US Features of Parathyroid Adenoma

1. ‘DARK’ - Hypoechoic
2. Variable shapes Conforms to the anatomical space available
3. ‘DENTING’ The thyroid capsule indentation, capsular separation
4. ‘DOPPLER’ Look for vascular pedicle
5. ‘DIVING’ - Mobile into the posterior neck and thorax
ECHOGENIC LINE

NOTE THE INDENTATION OF THE THYROID CAPSULE

Cranio-caudal
Indentation

Cranio-caudal axis
Note the following: Extrathyroidal, hypoechoic – indentation and echogenic line of separation (capsule)
TE groove lesions

- Smaller, posterior located lesion is usually hard to be seen with US
- More mobile
- Valsalva, cough, movement of neck can also 'bring out' the lesion into vision
Mobile TE groove
right upper adenoma
T-E groove left upper mimicking esophagus
Vascular pedicle / flow
Polar Artery
Coincidental thyroid pathology
MNG/FVPCT and PA
Multiple lesions / hyperplasia

- Relatively uncommon in general population – 15%
- ESRD – 50% or more chance that multiple glands are involved
- MEN 1 – multi-gland hyperplasia
- Limited role for localization in ESRD and MEN 1 patients
Multiple lesions

CRC

THYROID

LCC

+ Length 1.5cm
× Length 1.7cm
∩ Length 0.7cm
□ Length 0.8cm
Cystic parathyroid adenoma
Cystic lesion

PTH – >50,000 pg/ml
When and how to biopsy

- The more typical a lesion appears, less the necessity for biopsy
- Caution in patients on warfarin or anti-platelet agents
- Use 27 g needles
- One or two attempts, using rotation of the syringe & aspiration
- Avoid jabbing technique
Parathyroid FNA

- Avoid vigorous jabbing and multiple passes
- Avoid puncture of posterior capsule
- Fewer passes, one to two - rotate and aspirate
- Parathyroid lesions yield bloody tap
- ‘Dry’ tap – usually a LN

Parathyroid FNA

Indications:
- Typical imaging phenotype – no FNA
- Unusual location
- Intra-thyroidal
- Failed surgery
- Multiple lesions (FNA the less typical appearing lesion)
- Prior to ETOH ablation

Contraindications:
- Jaw Tumor syndrome CDC-73
- Family history of jaw tumors + PHPT
- Relative – anticoagulation
- Obscuration by blood vessels
- Respiratory excursions
- Morbid obesity
When to suspect Parathyroid carcinoma?

- Acute, massive calcium elevation
- Massive elevation of PTH
- Palpable mass
- Jaw tumor history
- US findings – non specific – But, suspect when tumors are large
- Calcification
- Fibrous bands
How to process parathyroid FNA specimen?
Perform FNA – 27 g needle one or two passes

Make one or two smears

Rinse the syringe and needle into 1 cc saline

Ideally, spin and separate supernatant fluid

Freeze fluid prior to transportation to lab

Save the cell pellet, this serves as a duplicate specimen

If the PTH FNA level is low, submit the smears for cytological analysis
Cytology of Parathyroid Aspirates

- Cytology is not useful in the identification of PA
- Thyroid follicular cells and colloid can be seen
- But recommend at least 1-2 smears to be made
  - Save the slides until PTH results become available
  - If PTH level from the syringe washing is elevated, discard slide. Only perform cytology in cases with negative PTH analysis

What is the rationale to making smears?

- Small but finite probability that lesion is a pathological lymphnode as a result of coincidental cancers.

One of the following is a typical finding of parathyroid adenoma

a. Isoechoic texture in relation to the thyroid gland
b. Indentation of the posterior thyroid capsule and echogenic line of separation
c. Multiple penetrating capsular blood flow
d. Cystic generation
e. Internal calcification
UA – Primary Hyperparathyroidism

Conclusions:

• Useful in preoperative localization of parathyroid adenoma and hyperplasia
  • Biochemical diagnosis should be established prior to imaging
• Understanding the anatomical variations in the location of parathyroid glands is essential.
• Proper patient positioning
• Remember the 5 D’s
• Parathyroid ca – clinical suspicion – do not FNA
• FNAB for PTH analysis in select patients