

## Evaluation and Management of Hyperparathyroidism

Stanford Endocrine Head & Neck Surgery

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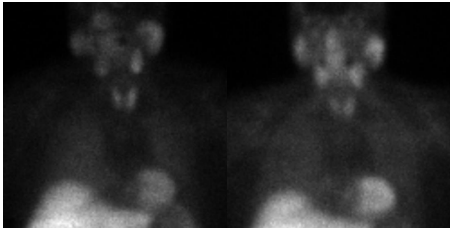
April 21, 2020

Patient: **DD**

- Elevated serum calcium for ~5 years prior (range 10.5 – 11.4mg/dL)
- PTH 159 – 204pg/mL
- Vit D 53ng/mL
- 2 episodes of nephrolithiasis
- Reports difficulty concentrating, memory loss, fatigue, headaches
- DEXA showed osteopenia

### Initial localization studies

- Sestamibi obtained outside and interpreted as negative



In-office ultrasound did not reveal a candidate  
 BUT! Also DID NOT show confluence of right common carotid and subclavian artery...

...so 4D CT was performed



### OR Findings

**IOPTH chronology:**

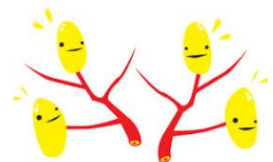
Pre-op: 104  
 Post-manipulation (pre-excision): 154  
 10 min post excision: 51  
 20 min post excision: 35.8  
 PTH aspirate: >5,000

LEFT RLN was recurrent, RIGHT RLN  
 not dissected but presumably non-recurrent



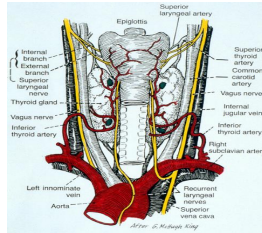
### The Parathyroid Glands

- Smallest endocrine glands
- Team of 4 (or more)
- Normally “grains-of-rice”, “lentils”
- Regulate calcium in blood and bones
- Benign tumors (adenomas): **too much** PTH
- Less common: hyperplasia: **too much** PTH
- Cancer extremely rare (<1%): **too much** PTH
- Effects: osteoporosis, kidney stones, “brain fog”, low energy, “I feel bad”
- **Too little** PTH: complication of thyroid surgery



## Parathyroid Hormone (PTH)

- 84 AA protein
- Increases serum calcium via:
  - osteoclast stimulation
  - GI absorption
  - renal resorption
  - Vit D activation
- Intact protein = current assay



## 2ary/3ary HPT

- Secondary HPT : Chronic hypocalcemia causes parathyroid hyperplasia; usually due to chronic renal failure; less commonly due to bone disease.
- Tertiary HPT: Persistent HPT/parathyroid hyperplasia after cause of secondary HPT resolved (e.g. after renal transplant)
  - Autonomous parathyroid glands
  - multigland disease, initial medical, ultimate surgical, management

## PHPT - Diagnosis

- Elevated serum Ca on at least 2 visits
- Elevated intact PTH
- Other labs: phosphate, alkaline phosphatase, urinary cAMP, urine Ca
- Radiographic studies: bone densitometry, KUB/renal US
- (Localization studies)

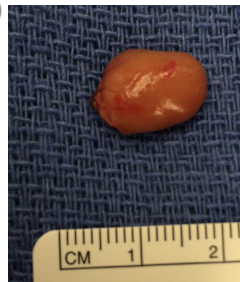
## Primary Hyperparathyroidism (PHPT)

- ~100,000 cases/year U.S.
- Mid-late life
- F:M - 3:1
- >50% “asymptomatic”
- Sx: bones, stones, groans, moans
- A SURGICAL DISEASE

## Primary HPT:

### Condition/Diagnosis vs Pathology/Source

Single adenoma: 85%  
 Multigland disease: 15%  
 (multiple adenomas vs hyperplasia)  
 Carcinoma: <1%



## PHPT: *Differential* Diagnosis

- Rule out Malignancy
- Other causes of hypercalcemia (esp meds)
- Normocalcemic HPT: High PTH, normal Ca
- Normohormonal HPT: High Ca, normal PTH (inappropriately normal or even low)
- Don't be fooled: FHH
- MEN – always ask about family history of HPT/endocrine neoplasms

# Management of PHPT

- Only chance for *cure* is surgery
- Adenoma (85%) : single gland excision
- Hyperplasia (15%) : 3.5 gland excision (± autotransplantation)
- Carcinoma (<1%) : wide local excision



# Parathyroidectomy: 20<sup>th</sup> Century

- 1928: first parathyroidectomy
- Through 1990's: gold standard = Bilateral Neck Exploration
- “The only localizing study is to locate an experienced parathyroid surgeon” Doppman 1991
- “Preop localization is of no value in patients with PHPT who have not undergone previous neck surgery” – NIH Consensus Panel, 1991
- Success rate of parathyroidectomy = 95% overall

## Parathyroidectomy in the 21<sup>st</sup> century

- Improvements in radiologic imaging and tools
- Development of rapid intraoperative PTH assay
- Demand/marketing of “minimally invasive” surgery, internet awareness of PHPT, aging population, routine calcium measurement and bone densitometry, earlier diagnosis and intervention

## Parathyroidectomy - Variations

- Bilateral neck exploration: 4 glands
- Unilateral neck exploration: 2 glands
- Focused = Directed exploration: 1 gland
- “Limited”/ “Minimally Invasive”/ “Small incision”...
- MIRP=Minimally invasive radioguided parathyroidectomy
- Endoscopic, video-assisted, robotic, transoral

## Localization studies

- High resolution Ultrasound\*
- Technetium<sup>99m</sup>Sestamibi
  - Thallium<sup>201</sup>/Technetium<sup>99</sup> subtraction
  - SPECT/CT Fusion
- CT (4DCT)
- MRI
- Selective venous sampling
- Selective arterial catheterization

\*surgeon-performed

## Preoperative Localization: Advantages

- Minimally invasive surgery (majority are single adenomas)
- Less time in OR
- Less risk
- Identify mediastinal/ectopic glands
- >80% sensitive or specific
- Greater success (?)

# Technetium<sup>99m</sup> Sestamibi

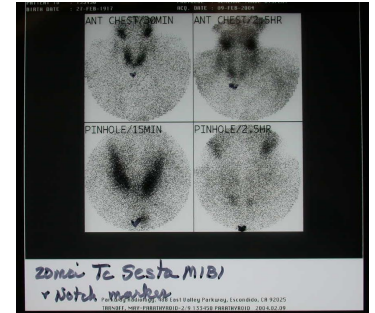
- Used alone, with <sup>123</sup>I subtraction, or Technetium<sup>99</sup> pertechnetate
- Most *consistently* sensitive available test
- Still operator/institution dependent
- 80-90% sensitivity/positive predictive value
- Poor for smaller or multigland disease (Sn<50%)
- Sensitivity refers to SIDE, not infer. v. super.
- Nonlocalizing scan still informative
- Oblique views helpful in isolating from thyroid
- SPECT/CT: cost v. benefit?
- Always look at the scan yourself!



## 2D sestamibi scan

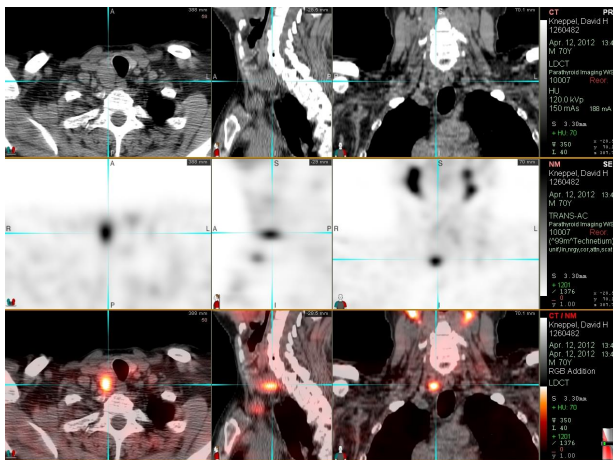


Parathyroid adenoma:  
Unilateral inferior uptake



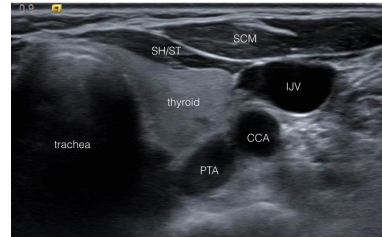
Parathyroid hyperplasia:  
Bilateral inferior uptake

## SPECT/CT Sestamibi Parathyroid Scan

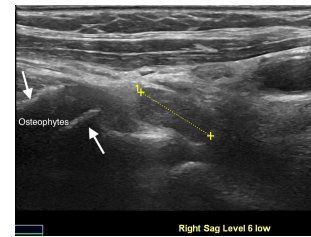


## Ultrasonography in PHPT

- 3D parathyroid localization
- Recognition of surrounding anatomy
- Identification of concomitant thyroid disease
- No radiation
- Surgeon-performed US: Accuracy for side *and* quadrant
- Operator experience/knowledge/motivation influential
- Patient education/rapport



Transverse view

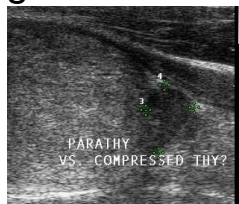


Sagittal view

## Challenging Cases

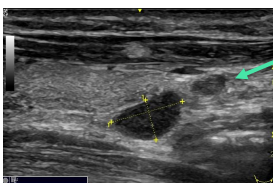


Nonlocalizing MIBI s/p failed exploration

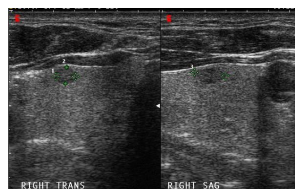


Coexisting thyroid nodules

LEFT SAG INFER TO DOM. NOD.

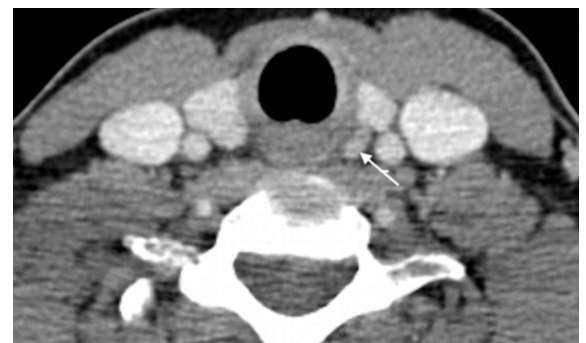


Hashimoto's thyroiditis



Intrathyroidal parathyroid adenoma

## 4DCT



Arterial phase: parathyroid enhancement  
Venous phase (30 seconds later): parathyroid washout, lymph nodes enhance

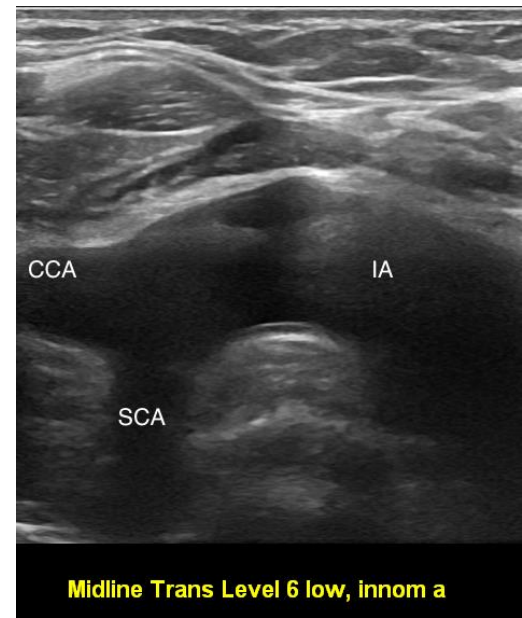
# Invasive Parathyroid Localization Procedures

- USGFNA
  - PTH concentration
  - Simultaneous serum PTH
  - (Cytology)
- US-guided IJV sampling
- Selective venous sampling (IR/catheter-based)

You've Recommended Surgery - Now What?

Additional Preop Considerations

- Vocal fold mobility
- Chvostek sign
- TSH, Vit D (TPO Abs)
- Thyroid nodules
- Lymph nodes
- Ectopic?
- Supranumerary?
- Nerve anatomy
- Prior neck surgery



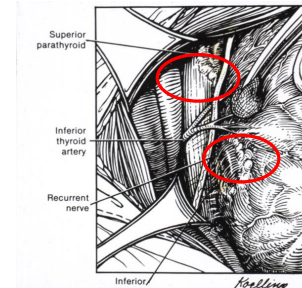
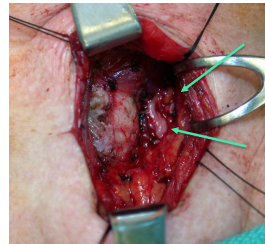
## Parathyroidectomy: Operation

- General vs. local anesthesia
- Paralysis vs. not (for IONM)
- Patient supine, neck extended
- Incision: 2 fingers above clavicles, extendable (vs. customized for US findings, skin creases)
- Midline vs. lateral to strap muscles
- Mobilize thyroid (traditional)
- Preserve thyroid blood supply as able
- Always watch for (though may not see) laryngeal nerves (unlike thyroidectomy)
- Bipolar cautery/suture ligation

## Parathyroid Glands

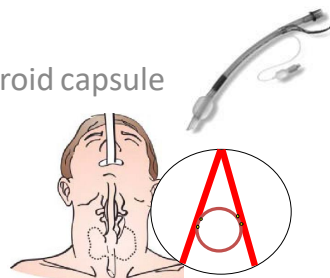
Superior (4<sup>th</sup> pouch): posterior (dorsal) to plane of RLN

Inferior (3<sup>rd</sup> pouch): anterior (ventral) to plane of RLN  
Near inferior thyroid artery entrance



## Avoiding Complications

- Watch for RLN (and EBSLN)
- Preserve normal parathyroid glands with blood supply
- Don't remove glands until you are convinced...
- Ensure meticulous hemostasis
- Ensure preservation of parathyroid capsule
- Nerve Integrity Monitoring



## Intraoperative aids

Ultrasonography  
Magnification  
Palpation  
Esophageal intubation

IOPTH

Radioguidance  
Endoscopy  
Robotics  
Methylene blue  
**Autofluorescence**

# Intraoperative PTH Assay (IOPTH)

- Serial “rapid” intact PTH levels in OR:
  - Baseline
  - Pre-excision of adenoma
  - 10 min post-excision, (20 min post)
- Expect >50% drop in PTH for single adenoma, and into normal range

# Minimally Invasive Radioguided Parathyroidectomy (MIRP)

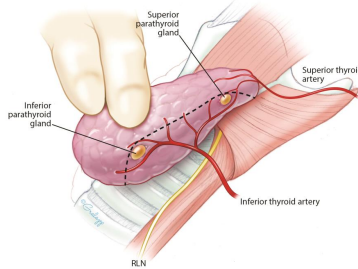
- Injection of sestamibi 1.5-2.5h preop
- Directional gamma probe
- “20% rule”: specimen >20% of neck background

No frozen section/No IOPTH/No other glands identified

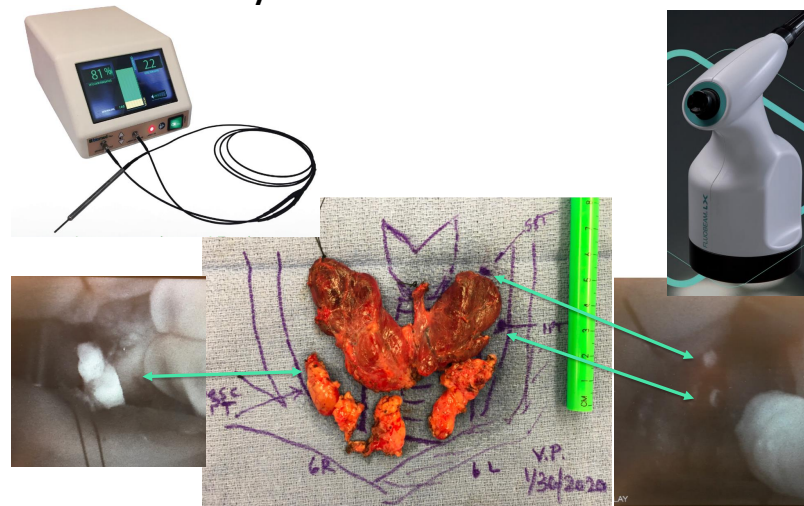
Enthusiasm has waned due to:  
 no increased success rate  
 no decreased OR time  
 no smaller incision  
 added expense and complexity

## Parathyroid Gland Identification: New Optical Technologies

- Autofluorescence
  - Spectroscopy
  - Imaging
- Fluorescence
  - Methylene blue (old)
  - 5-ALA (newer)
- Optical coherence tomography
- Dynamic optical contrast imaging
- VIABILITY assessment
- Other techniques...



## Parathyroid Autofluorescence



## KM, 57yo M MD

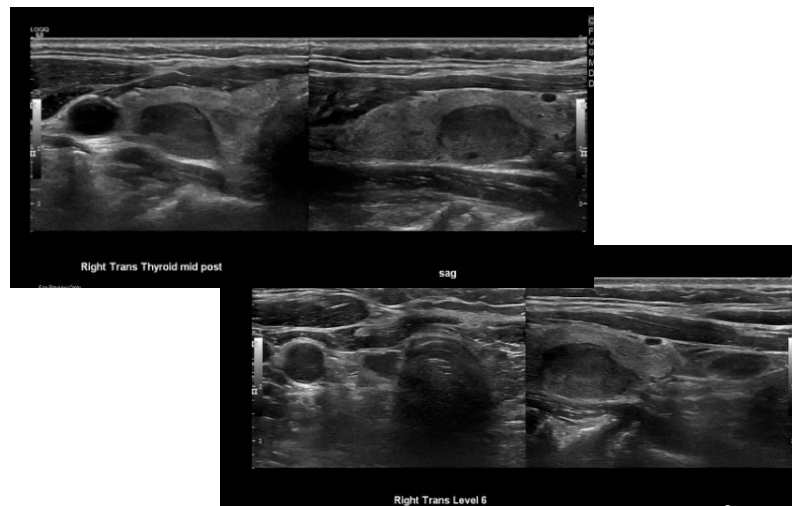
- CT chest for cough and chest pain : incidental 12 mm right thyroid nodule.
- dedicated neck ultrasound: 1.8 cm TI-RADS 4 nodule right lower thyroid
- USGFNA : ATYPIA OF UNDETERMINED SIGNIFICANCE (Bethesda III)

ROS: Still has an occasional cough. Somewhat fatigued, sx of burnout (ER work x 30 years).

FAMILY HISTORY: Negative for thyroid or parathyroid disease.

RADIATION HISTORY: Negative for therapeutic but years of incidental exposure during work in the ER, unknown dose.

## KM: In-office Ultrasonography



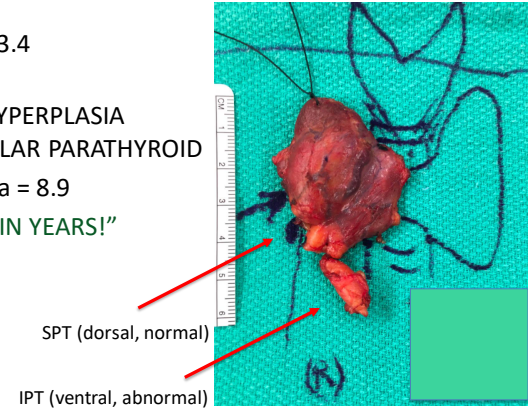
# KM: Thyroid *and* Parathyroid

- In summary,
  - 57 Y male with R thyroid AUS (Bethesda III)
  - US and hx suggestive of possible hyperparathyroidism.
  - He reports that in fact he has had a borderline high serum calcium for many years.
  - Labs obtained:

TFTs normal, **Ca 10.3**, **PTH 147**, 25OHD=29

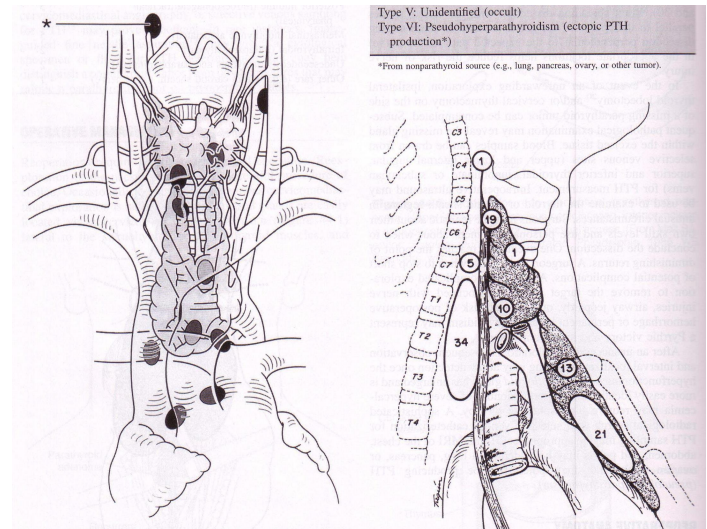
# Surgery: R thyroid lobectomy and Parathyroidectomy

- IOPTH: 226 -> 23.4
- Pathology:
  - NODULAR HYPERPLASIA
  - HYPERCELLULAR PARATHYROID
- 5 days postop Ca = 8.9
- "BEST I'VE FELT IN YEARS!"



## Postoperative Course

- 😊 • Immediate normalization of Ca<sup>++</sup> (within 24h.)
- 😬 • Rapid hypocalcemia (Hungry Bone)
- 😬 • Persistent hypercalcemia...



Missed glands : locations



Questions?

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