PARATHYROID NUCLEAR MEDICINE IMAGING REVIEW

Miguel Hernandez Pampaloni, M.D., Ph.D.
Chief, Nuclear Medicine
Assistant Professor of Radiology
UCSF Department of Radiology and Biomedical Imaging

DISCLOSURES

Nothing to disclose
Parathyroid Glands

History

- 1852-first identified in rhinoceros.
- 1898-tetany first described in cats/dogs after removing parathyroid glands.
- 1898-histology described.
- 1903-relation between bone dis. & parathy.
- 1914-discovery of parathyroid hyperplasia in response to low Ca diet.
- 1921-Measure of serum calcium.
- 1926-first parathyroid surgery humans (Mandl).
- 1958-isolation of purified PTH (Rasmussen & Craig).
- 1960’s RIA for PTH.

ANATOMY OF PARATHYROID GLANDS

- Wt = 30 mg (10-70 mg).
- Size = 5x3x1mm.
- Develop from 3rd and 4th bronchial pouches at 6 wks gestation.
- Migrate to neck at 8 wks.
- Blood supply: Inferior thyroid artery.
- Inferior glands are more variable position.
ANATOMY OF PARATHYROID GLANDS

OVAL, BEAN SHAPED OR SPHERICAL 83%
ELONGATED 11%
BILOBATED 5%
MULTILOBATED 1%

Fig. 1. Different shapes of parathyroid glands and their frequencies.

Calcium Metabolism
Hyperparathyroidism

- About 27/100k in US
- Mostly middle age, female>male
- Due to ubiquitous serum biochemistry, most patients are asymptomatic
- Nephrolithiasis most common symptom, 15-20%
- Most solitary adenoma (80-90%)
  - multiple ~ 5%
  - hyperplasia 5 -10%
- may be associated with MEN syndromes
- carcinoma 1%

Hyperparathyroidism

- Primary: Adenoma, clear cell and chief cell hyperplasia, and carcinoma
- Secondary: (renal failure)
- Tertiary: Autonomous gland in a patient with treated secondary hyperparathyroidism
Biochemical Profile of Hyperparathyroidism

Primary  Secondary  Tertiary
• Parathormone  Increased  Increased  Increased
• Serum CA++  Increased  Normal  Increased
• Serum P04  Decreased  Increased  Decreased

Hyperparathyroidism
Relevance of Imaging

• Persistent disease post-surgery (5-8% of postsurgical patients)
• Re-operation carries higher morbidity and lower success rate due to 20-30% ectopia in this subpopulation.
• General agreement on value of scan in re-operative patients.
• Ectopic adenoma.
Morphologic Imaging

CT: Sensitivity 40-55% in preop, 25-55% postoperative neck
MR: Sensitivity 71-88%
Parathyroid may mimic small nodes
US: Sensitivity 51-78%; specificity 67-96%

Combine NM with US better than each alone

Chien et al. Otolaryngol Clin N Am 2010;43:399

Functional Imaging

• Shown to have greatest combined sensitivity and specificity
  Meta-analysis 1995-2003, 20,225 cases
  Sensitivity Sestamibi 88.9%; ultrasound 78.55%
  • For solitary adenoma
  • Multigland and hyperplasia lower
  • Especially good for postoperative patient looking for ectopic
Sestamibi Biodistribution

• Concentrates both in thyroid and parathyroid mitochondrial.
• Increased uptake secondary to increased vascularity and higher number of mitochondria in adenomas.
• Slower washout from parathyroids vs thyroids.
• With hyperparathyroidism, normal parathyroids suppressed.

Tomographic Imaging

• SPECT/CT based scans identified more tumors than planar or SPECT alone.
• Higher diagnostic performance
  
  *Wimmer et al. Langenbecks Arch Surg 2008;393:687
  Sensitivity 87%, specificity 97% fusion with CT
  Sensitivity 50%, specificity 92% SPECT alone

• Many different techniques
  Early and delayed SPECT-CT
  Combination of planar and/or I123 and/or subtraction
MIBI-Tc99 False Positives/Negatives

**False Positives:**
- Thyroid adenoma
- Thyroid cancer
- Thyroiditis
- Abscess
- Malignant or inflammatory LN
- Sarcoid
- Thymoma
- Esophageal Cancer

**False Negatives:**
- Multiglandular disease
- Ectopic
- Small adenomas
- Hypocellular
- Calcium channel blockers

Localize Hyperfunctioning Parathyroid Glands

- Surgery mainstay of treatment
- Experienced surgeon succeeds 95% time to detect abnormal gland in the first bilateral neck exploration
- But: Anatomic variations of parathyroid
- Size not a criteria to differentiate an adenoma from normal parathyroid
- Imaging pivotal in post-surgical patients
Hyperfunctioning Parathyroid Glands

- Persistent disease post-surgery.
- Recurrent hyperparathyroidism occurs in 5-8% of postsurgical patients.
- Re-operation carries higher morbidity and lower success rate due to 20-30% ectopia in this subpopulation.
- General consensus on value of scan in re-operative patients.

Hyperfunctioning Parathyroid Glands

- Of value to identify the uncommon ectopic adenoma in presurgical patients and for facilitating operative planning.
- Can save time and do limited exploration.
Imaging

- CT: Sensitivity 40-55% in preop, 25-55% postoperative neck.
- MRI: Sensitivity 71-88%; Parathyroid may mimic small nodes.
- Scintigraphy higher sensitivity in one series with direct comparison (86 vs 71%).
- US: Sensitivity 51-78%; specificity 67-96%
- Combine NM with US better than each alone

Chien et al. Otolaryngol Clin N Am 2010;43:399

Functional Imaging

- Greatest combined sensitivity and specificity
- Sensitivity Sestamibi 88.9%; ultrasound 78.55%
- For solitary adenoma.
- Multigland and hyperplasia lower.
- Especially good for postoperative patient looking for ectopic.
Imaging Protocols

- Dual Isotope
- T1-201 / Tc-99m: phasing out
- Tc-MIBI / I-123
- Dual Phase
- Tc-MIBI early and delay

Dual Isotope Technique

- I-123 / Tc-99m MIBI
- 300-600 μCi I-123 orally
- Four hour delayed images
- Patient should not move
- 20-25 mCi Tc-99m MIBI IV
- 10 minute delayed images
- Subtraction
Dual Phase Tc-99mMIBI

- 20-25 mCi Tc-99m MIBI IV
- 10 Min images
- Two hour delayed images
Planar Imaging Tc-MIBI Early and Delay
Planar Imaging Tc-MIBI Early and Delay
Planar Imaging Tc-MIBI Early and Delay
Multiple Adenoma

Early

Delay

No Clear Cut Which is Better

- Subtraction
- May be more sensitive
- But technically demanding
- Motion may cause artifact not easily recognized and decrease specificity

- Dual phase less technically demanding
- Less chance of something going wrong
- May be good enough especially with SPECT-CT
When to use Which

- Dual isotope:
- Prior thyroid surgery and pathology
- Dual phase:
- New cases of primary hyperparathyroidism
- Patient is on suppressive dose of thyroxine

Pitfall

- Imaging only the neck will miss 5% of adenomas
- Imaging thorax is a must
Planar Imaging Tc-MIBI Early and Delay Mediastinal Adenoma

Planar  ______________  SPECT

SPECT Improvement Over Planar Imaging

- Pinhole improvement over parallel hole collimator alone
- SPECT improvement over both, though not statistically significant across all series
Tc-99 m  Mibi 10 min  Mibi 3 hrs

10 min subtraction

SPECT/CT
Planar Imaging Tc-MIBI Early and Delay

Tc-99m 10 min  Mibi 10 min  Mibi 3hrs

SPECT/CT
Fusion Imaging

- SPECT/CT based scans identified more tumors than planar or SPECT alone.
- Higher diagnostic performance and/or confidence.
  Wimmer et al. Langenbecks Arch Surg 2008;393:687
- Sensitivity 87%, specificity 97% fusion with CT
- Sensitivity 50%, specificity 92% SPECT alone

SPECT/CT

- 110 patients with primary hyperparathyroidism
- Different combination of planar, SPECT, SPECT-CT
- Early SPECT-CT with any delayed imaging best combination
- 72-73% sensitivity; >99% specificity; 86.3-90.7% PPV
- If no SPECT-CT, dual phase with planar or SPECT
- Planar alone: 56.5% sensitivity; 98.7% specificity; 79% PPV
- SPECT: 64.5%-66 sensitivity; 99% specificity; 79-80% PPV
SPECT/CT

Thyroid

US

Left thyroid lobe
Persistently Elevated PTH after two Surgeries
PTH persisted after surgery
Parathyroid Adenoma Adjacent to the Right Atrium

Ectopic Parathyroid Tissue

FIGURE 2. Anatomic locations of abnormal parathyroid glands found at reoperation by single group. Most common ectopic sites mirror routes of descent of upper parathyroid glands (short migration path) and of lower parathyroid glands (longer migration path in association with thymus) (modified from [116]).
Ectopic Retrotracheal Adenoma

- Missed at Original Surgery
- Mass in tracheo-esophageal groove
- Surgery correlated with imaging
- Intraoperative PTH went down
- Patient did well post-surgery
- Describe position well using surgical anatomy

Ectopic Parathyroid Adenoma

*Better Localized with SPECT/CT*
PET Imaging

- F-18 FDG PET-CT.
- Parathyroid adenomas have increased mitochondrial content.
- Relatively increased FDG uptake.
- C-11 Methionine

Causes of False Positive

- UPTAKE of Tc-99m MIBI
  - In The Neck
    - Thyroid adenoma
    - Thyroid cancer
    - Thyroiditis
    - Abscess
  - Malignant or inflammatory Lymph Node
- In The Chest
  - Malignant Lymph Node
  - Sarcoïd
  - Thymoma
  - Esophageal Cancer
  - Inflammation
  - Abscess
Tc-99m MIBI / I-123 Subtraction Images

Patient s/p removal of 3 parathyroids and implant in the arm
Causes of False Negative

• Multiglandular disease.
• Ectopic.
• Small adenomas.
• Hypocellular.
• Calcium channel blockers.
• Some report thyroid suppression improves detection.