HYPERPARATHYROIDISM AND MINIMALLY INVASIVE RADIO-GUIDED PARATHYROIDECTOMY

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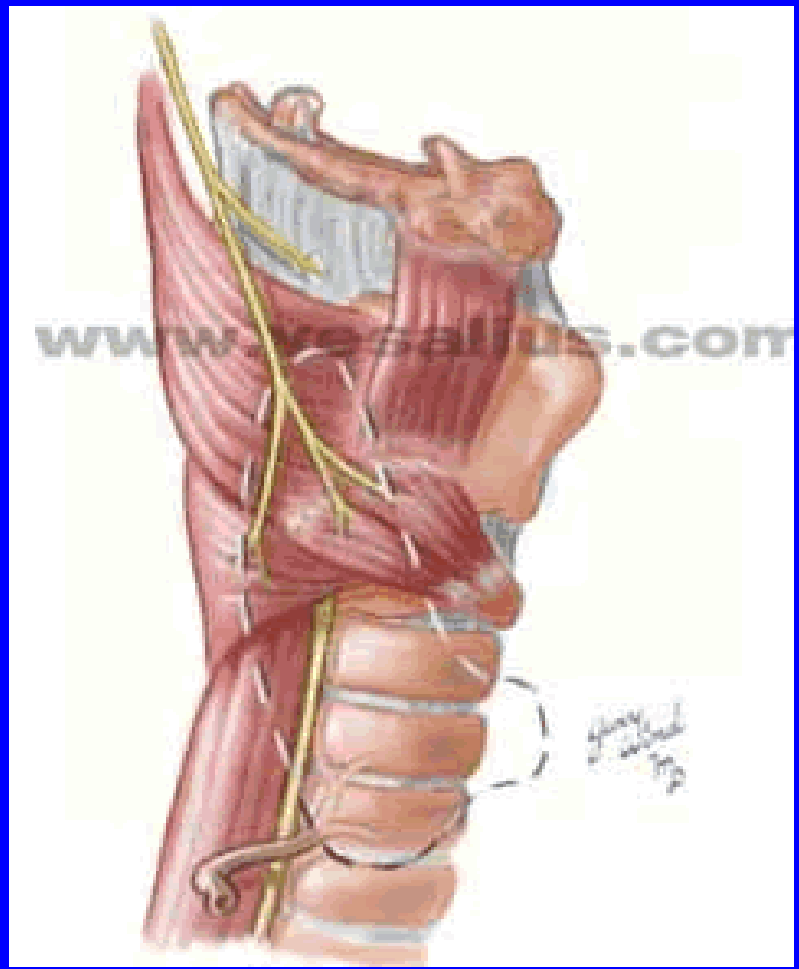
INTRODUCTION

- Anatomy / Embryology
- Physiology
- Pathology
- Surgery

ANATOMY / EMBRYOLOGY

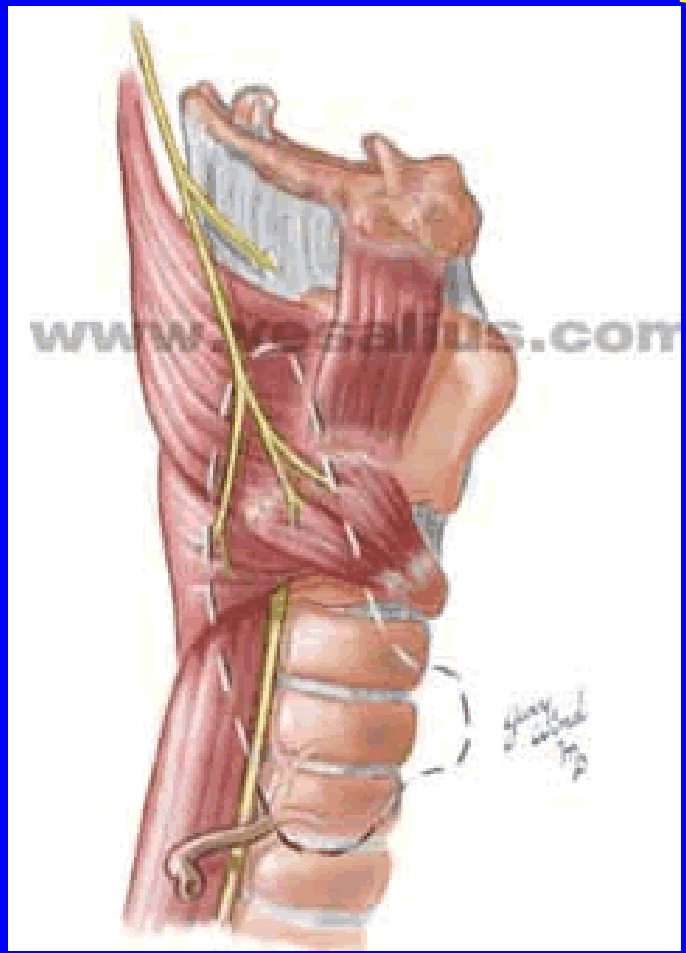
The third branchial pouch gives rise to the inferior parathyroid glands (dark blue) in close association with the primordia of the the thymus gland (orange). As the thymus descends to the anterior mediastinum, parathyroids III follow along, ultimately coming into contact with the developing thyroid caudal to parathyroids IV (yellow). The parathyroid glands derived from pouch IV take a more direct route to come in contact with the thyroid, and become the more cephalad or superior glands. A portion of pouch IV (light blue) contributes a lateral C-cell component to the thyroid. The parathyroids usually (~80%) lie near the posterolateral capsule of the thyroid lobes.

Anatomy / Embryology



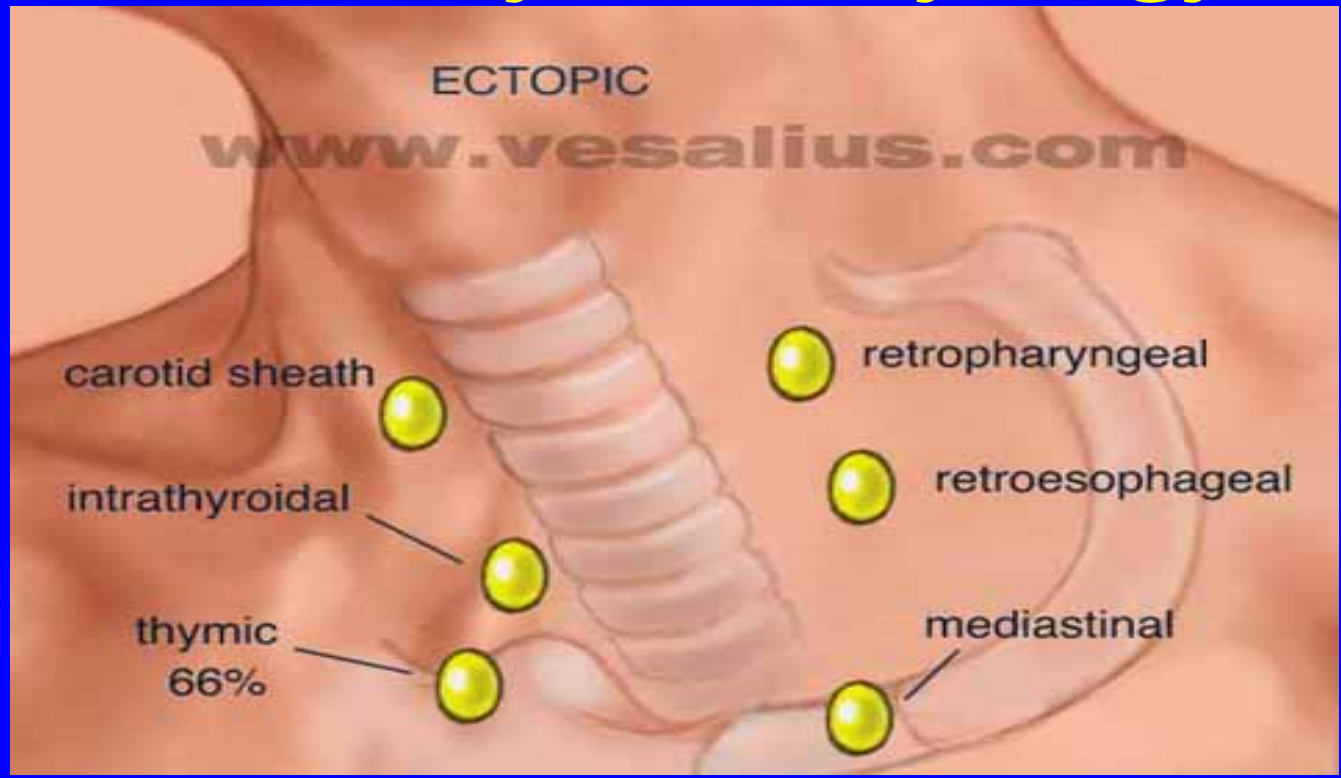
The superior parathyroid glands are most commonly found about the middle third of the thyroid lobe, at the level of the cricothyroid junction, and near the point where the recurrent laryngeal nerve passes beneath the inferior pharyngeal constrictor to enter the larynx

Anatomy / Embryology



The inferior glands are usually found near the lower pole of the thyroid lobe or below the lobe in the thyro-thymic ligament. They commonly lie below the inferior thyroid artery and anterior to the recurrent laryngeal nerve.

Anatomy / Embryology

- 

- Blood supply = inferior thyroid artery for both the superior & inferior thyroid glands

Aberrant parathyroid locations

- Thymus gland (most common)
- Carotid sheath
- Vertebral body
- Thyroid gland

- Location identified by sestimibi

Anatomy

- **Superior Laryngeal** nerve adjacent to the superior thyroid vascular pedicle, controls motor to the cricothyroid muscle, injury usually asymptomatic, but can cause loss of vocal projection & high pitch

- **Recurrent laryngeal** nerve posterior to the inferior thyroid artery, motor for vocal cord abductors, unilateral injury causes hoarseness, bilateral injury causes airway occlusion (pt needs tracheostomy)

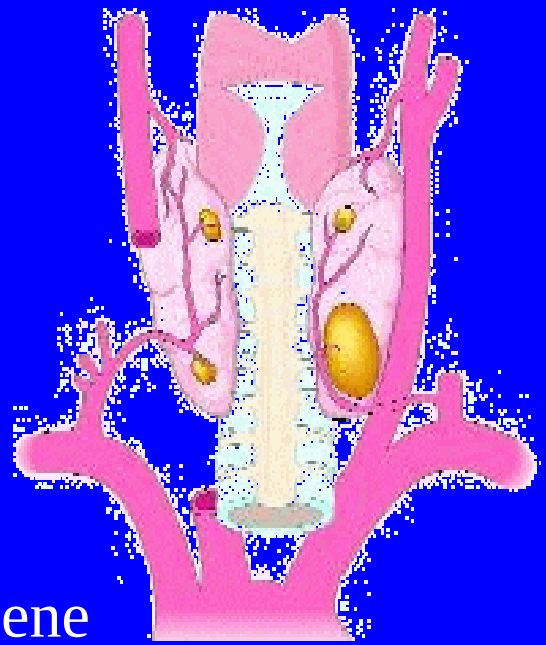
PHYSIOLOGY

- Parthyroid Hormone (PTH)
  - Secreted by the Chief cells
  - Levels are inversely conrolled by [Ca^{2+}]

- Effects:
  - Tubular reabsorption of Ca^{2+}
  - Osteoclastic resorption of bone
  - Intestinal absorption of Ca^{2+}
  - Synthesis of 1-25DHCC (active Vit. D)
  - Excretion of phosphate

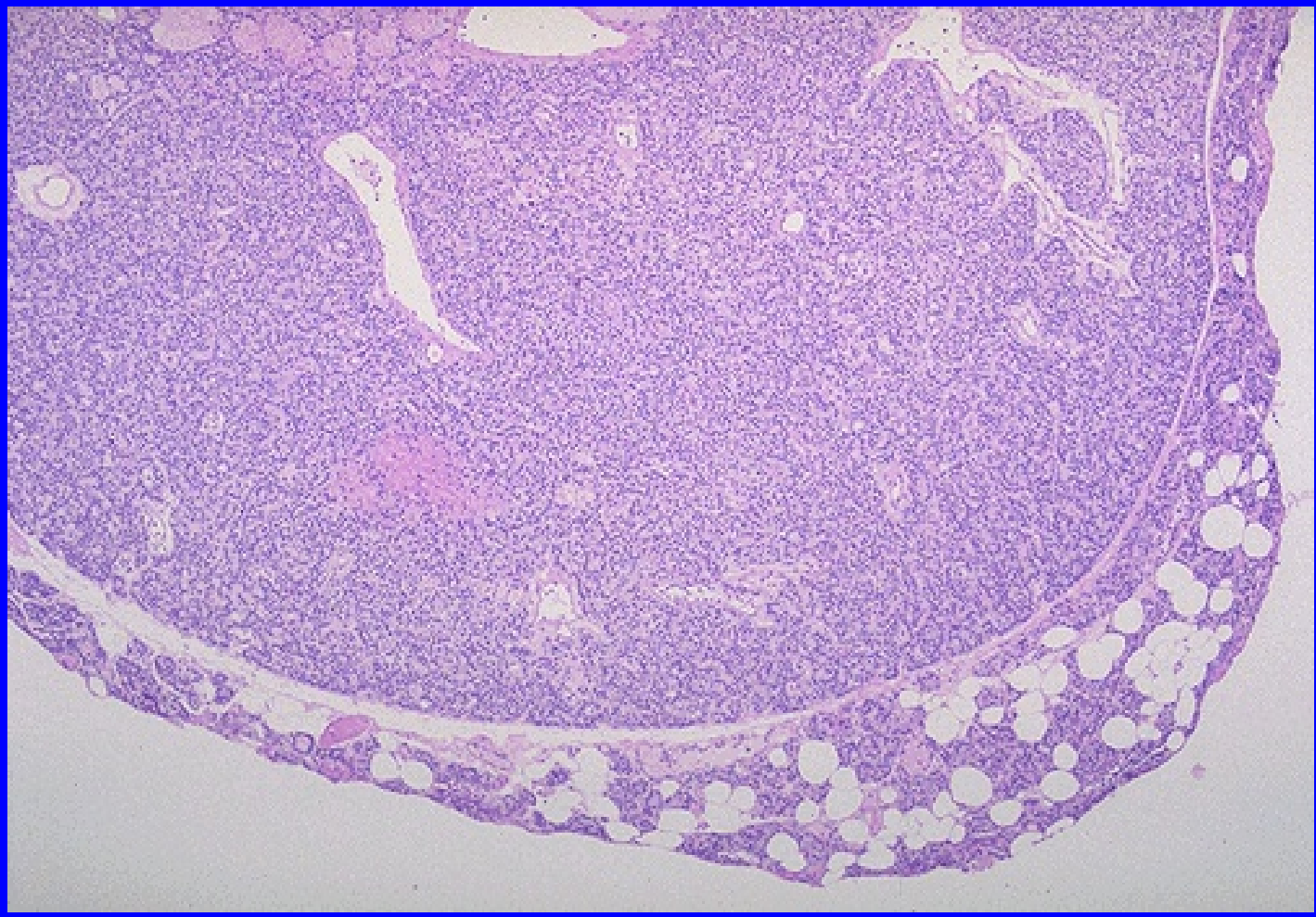
Incidence

- HYPERPARATHYROIDISM
  - 1 : 1,000 prevalence
  - F : M 2 : 1
  - Usually mild / asymptomatic
  - Primary assoc. w/ PRAD-1 oncogene



Etiology

- Primary (↑ PTH, ↑ Ca^{2+}, ↑ renal cAMP, ↓ Phos)
  - Adenoma 90% (5% multiple)
  - Hyperplasia 10% assoc w/ MEN I & IIa
  - Carcinoma < 0.1%
- Secondary (↑PTH appropriate to low Ca^{2+})
  - Chronic Renal Failure
  - Vitamin D Deficiency
- Tertiary
  - Continued excess PTH secretion following prolonged secondary hyperparathyroidism.



Parathyroid Adenoma : inferior rim of normal parathyoid tissue admixed with adipose tissue cells

Electrolytes

- Hyperchloremic metabolic acidosis can occur in patients with primary metabolic acidosis

- Renal failure – ↓ Ca → ↑ PTH,
↓ Mag ↓ Na ↑ K ↑ Phos

Secondary Hyperparathyroidism

- Decreased serum Ca & increased PTH
- Associated with ESRD & vitamin D deficiency
- Aluminum build up from ESRD increased osteomalacia
- Tx - Dietary – Ca & Vit D supplements
- Surgery only if symptomatic

Tertiary Hyperparathyroidism

- Secondary hyperparathyroidism refractory to renal transplantation
- Treated with surgery frequently

Signs / Symptoms

- Asymptomatic (mild, < 2.99)

- "*Bones, stones, abdominal groans, psychic moans*"

Bones	Bone pain, #'s, arthralgia
Renal	Stones, polyuria
G.I.	Pain, duodenal ulcer, pancreatitis
Neuro.	Depression, apathy
Cardiac	Hypertension, heart block

Clinical Presentation

Symptom	%
Asymptomatic hypercalcaemia	50
Renal stones	28
Arthralgia	5
Peptic Ulcer	4
Hypertension	4
Bone disease / MEN 1 / others	9

Indications for Surgery

- Symptomatic hyperparathyroidism (stones, bone pain, peptic ulcers)
- Serum Ca 2+ >1.0mg/dl above normal
- Creatinine clearance < 30 % for age
- Renal stone on PFA
- Hypercalciuria (>400mg/day)
- Bone marrow T-score <-2.5 @hip, L-spine or distal radius
- Young patient (< 50 y.o.)
- Poor follow up

SURGERY

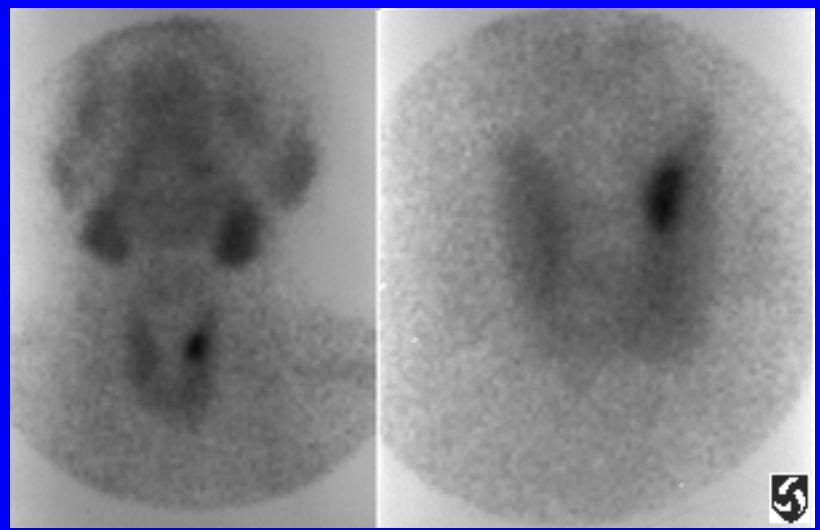
- Success rate for surgical cure of primary hyperparathyroidism should exceed 95%
- Until 10 years ago – bilateral neck exploration.
- Radiological localization of hyperfunctioning PTH tissue was reserved for re-exploration surgery.

SURGERY

- 99mTc sestamibi: A new agent for parathyroid imaging.
  - Coakley et al, Nucl Med Commun, 1989
- Clinical usefulness of intraoperative “quick parathyroid hormone” assay.
  - Irvin,GL, Surgery, 1993
- Intraoperative identification of parathyroid gland pathology. A new approach utilizing a hand held gamma probe.
  - Martinez DA, J Paedr. Surg, 1995

SESTEMIBI SCANNING

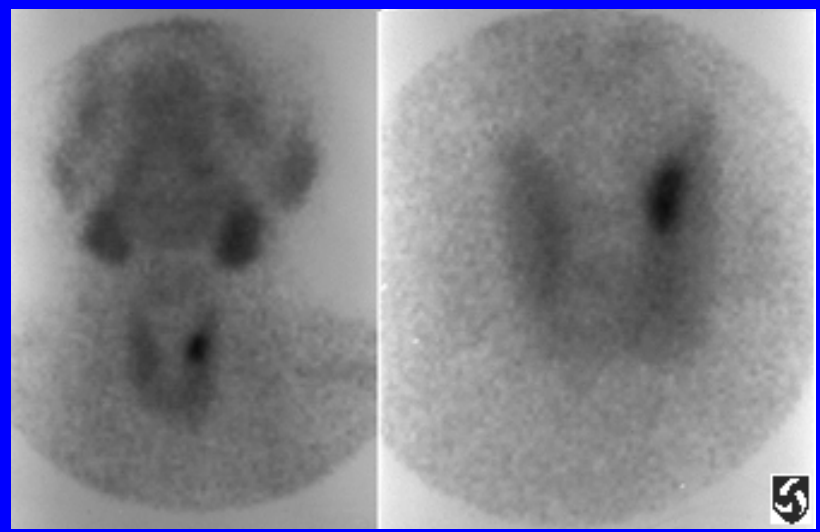
- 99mTc 2-methyl-isobutyl-isonitrile radionuclide (Tc-sestemibi)
- Discovered in 1989 to be useful in imaging of parathyroid glands.
- Radioisotope uptake increases with gland weight.
- MIBI concentrated in tissues rich in mitochondria.
  - Heart
  - Salivary glands
  - Thyroid glands
  - Parathyroid glands



- Denham et al, J Am Coll Surg, 1998

- Meta-analysis of 784 patients having preoperative sestemibi scans for exploration of primary HPT

  – Sensitivity 91%
  – Specificity 99%

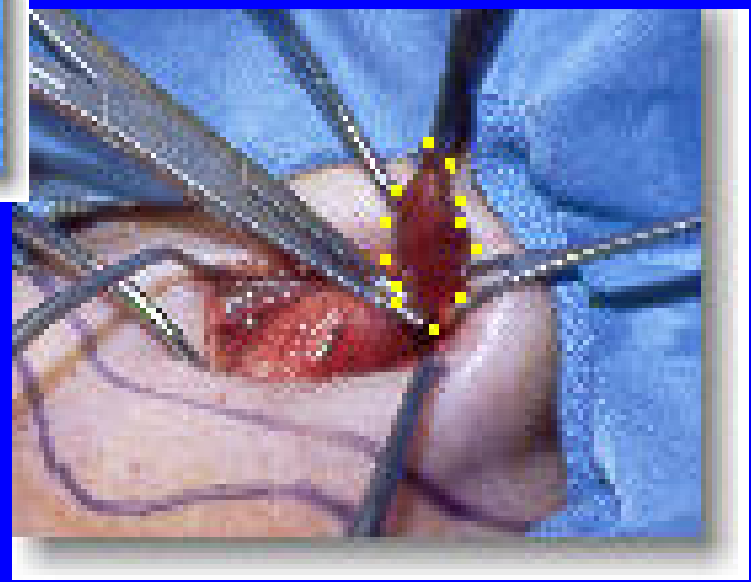


Clinical usefulness of intraoperative "quick parathyroid hormone" assay. Irvin,GL, Surgery, 1993

- Intact PTH molecule has a half life measured in minutes
- Pre-op, pre-excision and 10 minute post-incision
- QPTH Assay should reduce by > 50%

Assay completion time	12 mins
Sensitivity	96%
Specificity	100%
Positive predictive value of post-op calcium	97%

Intra-operative Gamma probe



Intra-operative Gamma probe

“Minimally invasive parathyroidectomy facilitated by intraoperative nuclear mapping”

Norman J, Surgery, 1997

15 patients with clearly a solitary adenoma on Sestemibi

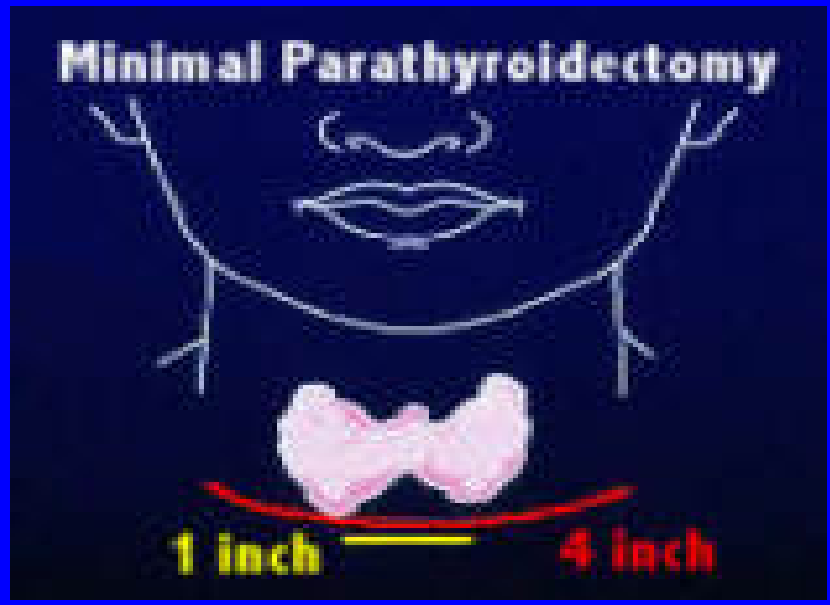
Average incision	2.4 cm
Mean operating time	24 minutes

97% of patients discharged within 2 hours of surgery

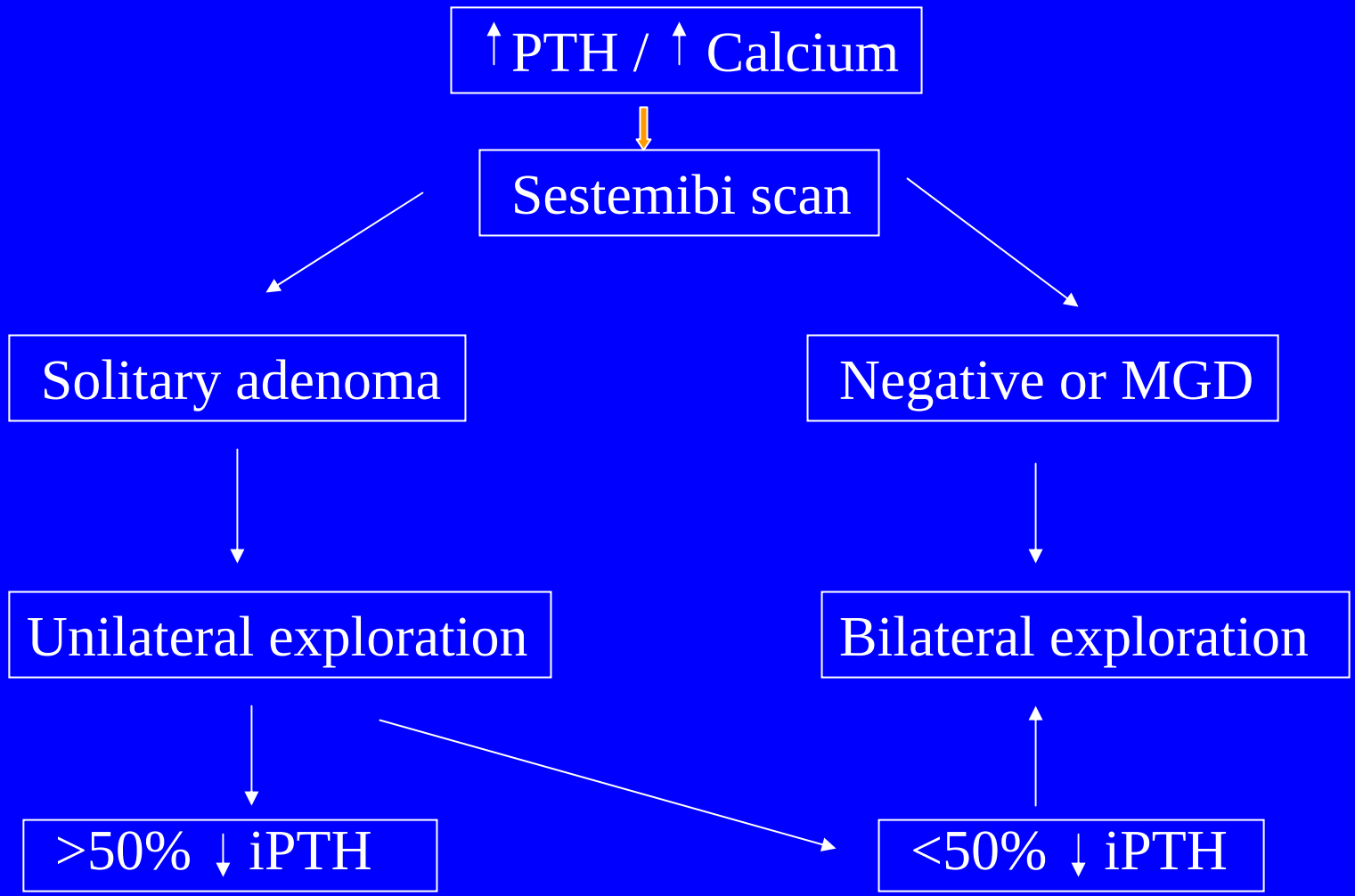
Ex-vivo counts of 32% of background

Advantages of MIRP

- Smaller incision
- 25 minutes
- Localization
- Pain
- Cost
- Haematoma
- Recurrent laryngeal nerve injury
- Tissue planes
- Contralateral structures
- Less post-op hypocalcaemia



Algorithm for MIRP



Summary

- Pre-operative quality imaging is essential for successful unilateral parathyroidectomy.
- Sestemibi is the gold standard
  - 91% specificity
  - Allows intra-op Gamma probe confirmation
- Minimally invasive parathyroidectomy has revolutionised adenoma surgery.

Familial Hypercalcemia Hypocaliuria

- PTH receptor abnormality w/n the kidney causing Ca resorption
- Most common cause of hypercalcemia
- PTH normal & Urine Calcium is low

- No treatment needed

Parathyroid Carcinoma

- Rare
- Very high calcium level with a palpable mass
- Treatment:
  En bloc resection of the tumor with thyroid lobe and any associated lymph nodes

Medical treatment of Hypercalcemia

- **Increase Calcium excretion** –
  Loop diuretics, IVF hydration, dialysis if renal impairment
- **Inhibit bone resorption** -
  Bisphosphates (3-6 day onset, lasts weeks)
  Calcitonin (rapid onset & short-lived)
  Mithramycin (hepatotoxic & nephrotoxic)
- Exogenous PTH production from Squamous Cell Carcinoma of the lung is most common cancer related hypercalcemia

? QUESTIONS ?