IAEA Regional Training Course (AFRA) on the Role of Nuclear Medicine in Endocrine Disease and Infection/Inflammation

Preoperative Localization and Radioguided Surgery of Parathyroid Adenomas

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Primary Hyperparathyroidism (PHPT)

- Inappropriate PTH secretion (relative to the plasma Ca^{++} levels) by adenoma(s), hyperplasia, or carcinoma (rare).
- Some genetic determinant (MEN 1 and 2, FHH, HPT-JT, familial isolated HPT).
- Disregulation of CaR (Ca^{++} "sensor") and of VDR (Vit D receptor).
- PHPT also linked to ionizing radiation.

Gene	Chromosome	Product	Clinical Phenotype
MEN1	11q13	MENIN	MEN1 20-40% sporadic adenomas familial isolated HPT[109,110]
RET	10q21	RET	MEN2A
CASR	3q13-21	CaR	FHH (heterozygotes) NSHPT (homozygotes) ADMH
HPC1/HRPT2	1q24-31 1q21-31	Unknown	Hereditary prostate CA HPT-JT syndrome Familial isolated HPT
RB	13q	Tumor suppressor	Parathyroid CA
p53	17p13	Tumor suppressor	Parathyroid CA
PRAD1	11q13 11p15	Cyclin	Sporadic adenoma
VDR	12q	Vitamin D receptor	Primary HPT

HPT, Hyperparathyroidism; *FHH*, familial hypocalciuric hypercalcemia; *NSHPT*, neonatal severe hyperparathyroidism; *ADMH*, autosomal dominant hypocalcemia; *CA*, carcinoma; *HPT-JT*, hyperparathyroidism-jaw tumor.

Kinder BK, Stewart AF. Hypercalcemia. Curr Probl Surg 2002; 39: 349-448.

Secondary Hyperparathyroidism

- Increased PTH secretion in response to reduced levels of Ca^{++} in the plasma.
- Most common cause: chronic renal failure (phosphor retention, reduced calcitriol levels, bone resistance to the the calcium-mobilizing activity of PTH, increased calcitonine levels).

Tertiary Hyperparathyroidism

- Persistence of hyperparathyroidism after correcting the cause of secondary HPT (e.g., successful kidney transplantation).
- Autonomy developing after prolonged secondary HPT, with hypercalcemia.

Persistent/Recurring HPT

Persistent HPT

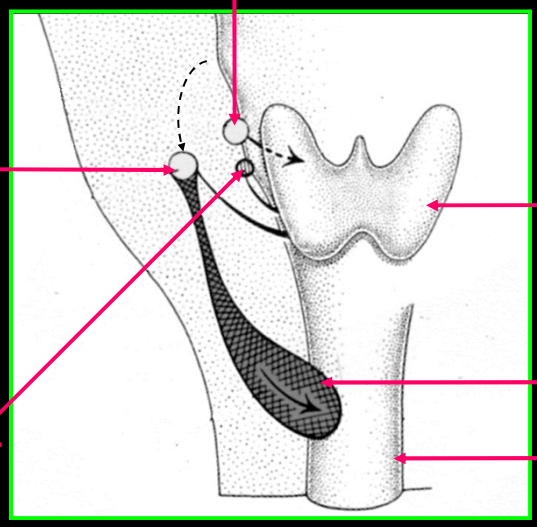
- Persistent abnormal plasma Ca^{++} levels immediately after surgery for PHPT.

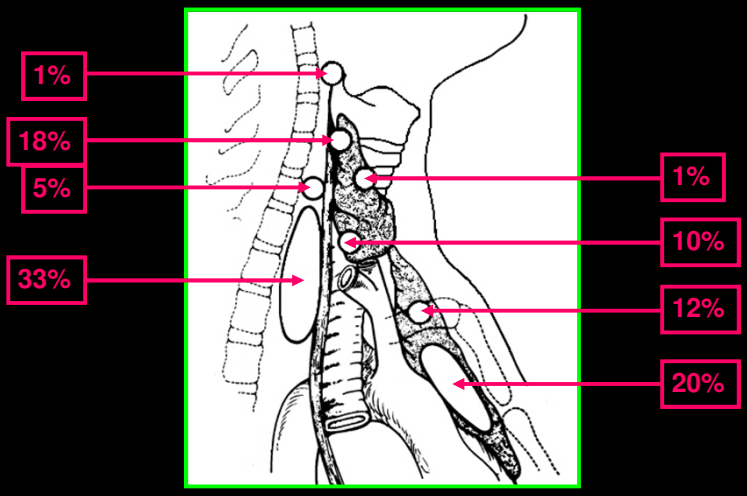
Recurring HPT

- Relapse of signs/symptoms of HPT after more than 6 months from normalization induced by surgery.

Diagnostic Imaging

- Virtually no role in primary differential diagnosis (complementary only).
- Important, crucial role for pre-operative localization, especially when planning mini-invasive surgery.





Wang CA. Parathyroid re-exploration. Ann Surg 1977; 186: 140-145.

Morphologic Imaging

- Ultrasound
- CT
- MR

Morphofunctional Imaging

- Scintigraphy

Ultrasound

Pros:

- low cost
- non-ionizing radiation

Cons:

- inter-operator variability
- variable sensitivity according to location (ectopic)
- does not explore mediastinum

CT or MR

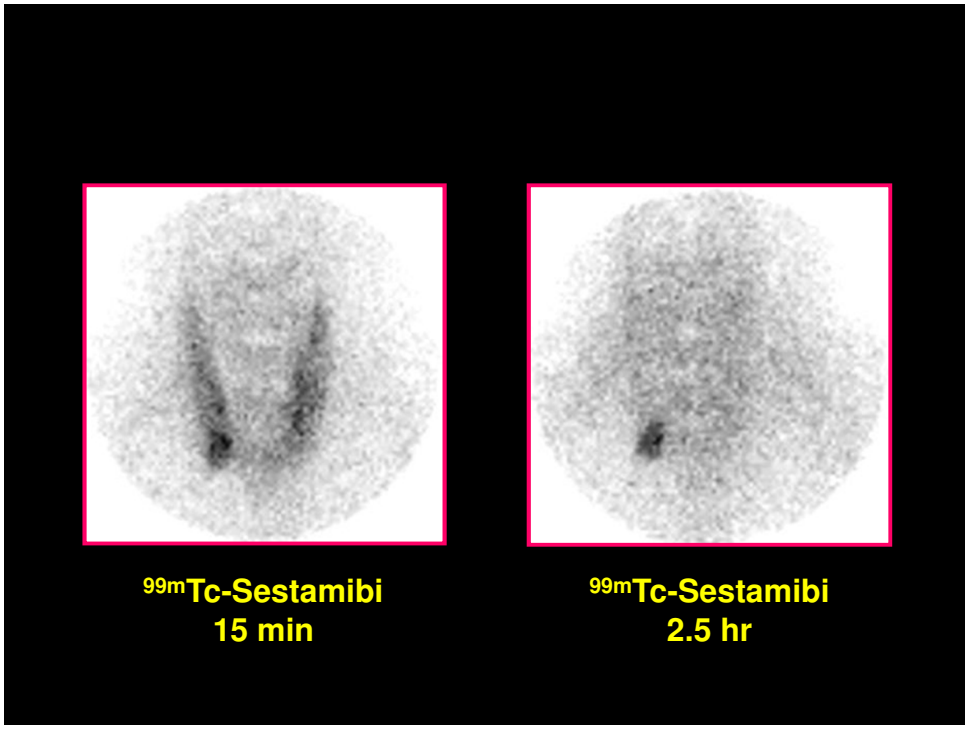
- **CT sensitivity :** 46%-80% (contrast)
  - 46-58% post-surgery.
- **MR sensitivity:** similar as scintigraphy, but wide variability
  - best employed in combination with scintigraphy (as for US)

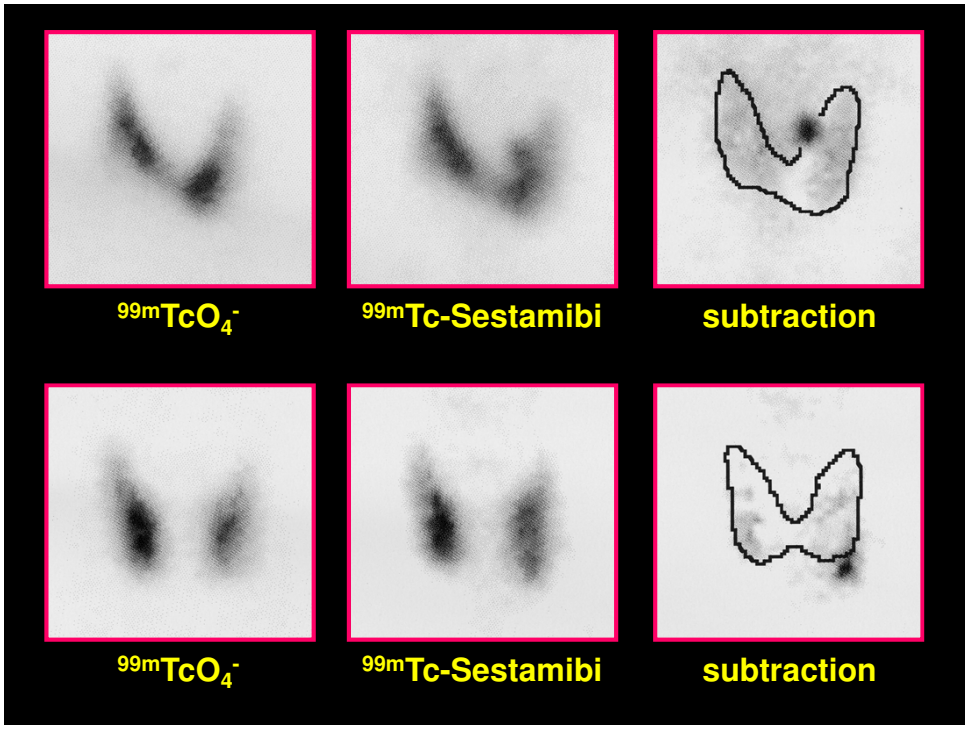
Parathyroid Scintigraphy

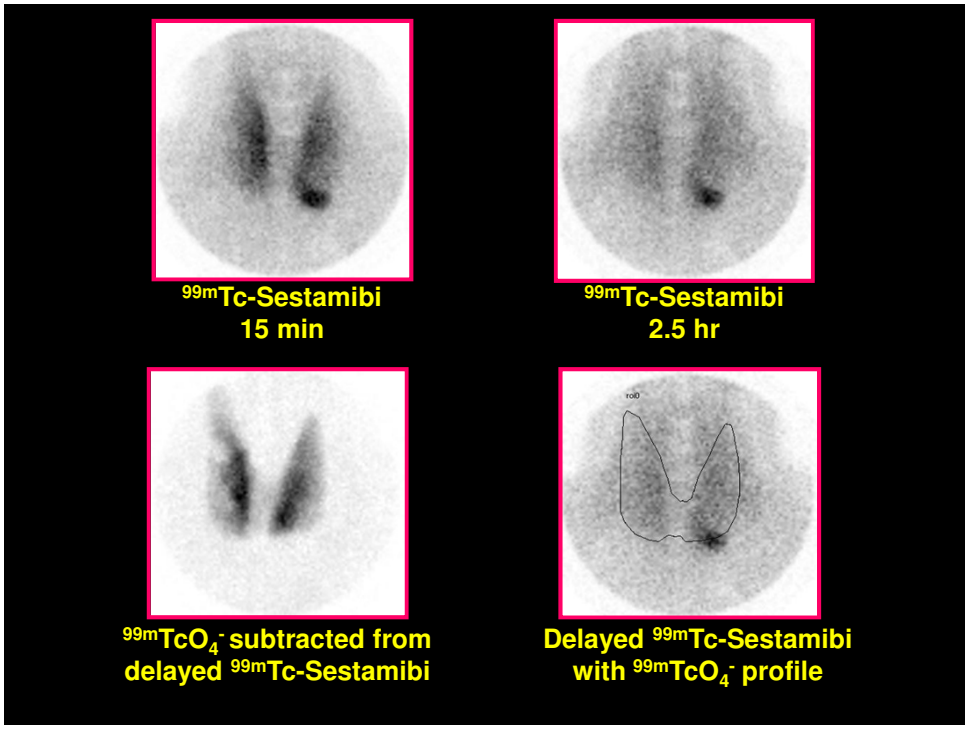
- There is no radiopharmaceutical that specifically accumulates in parathyroid tissue.
- Dual-tracer procedures were originally developed to take advantage of different uptake in the thyroid and in parathyroid (^{75}Se-methionine-$^{131}I^-$, ^{201}Tl-$^{99m}TcO_4^-$/$^{123}I^-$).

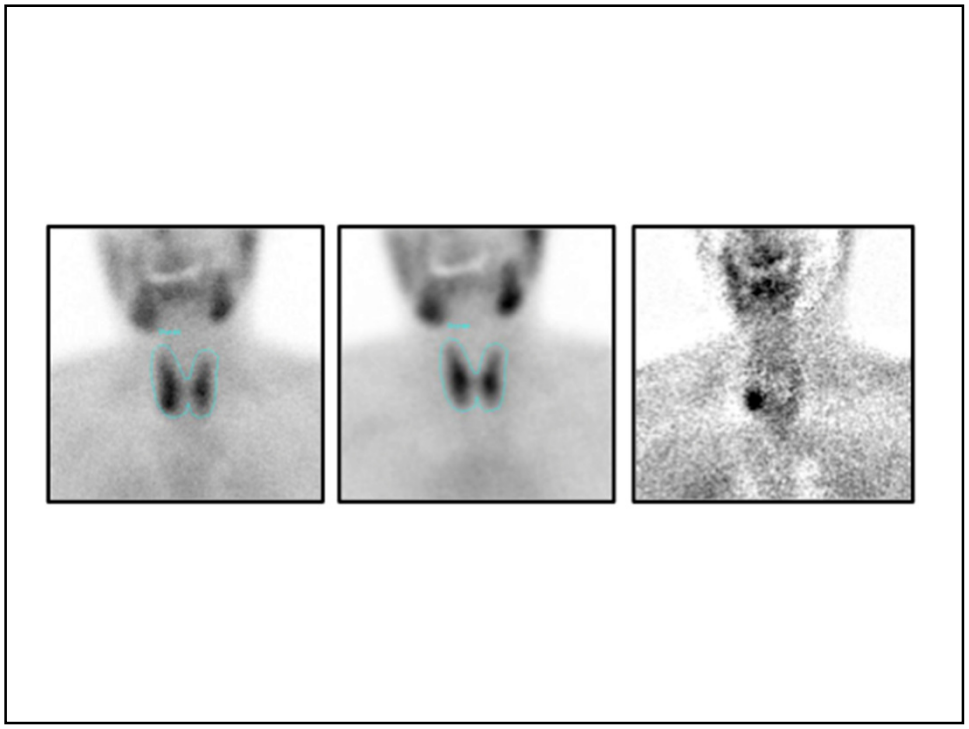
Parathyroid Scintigraphy

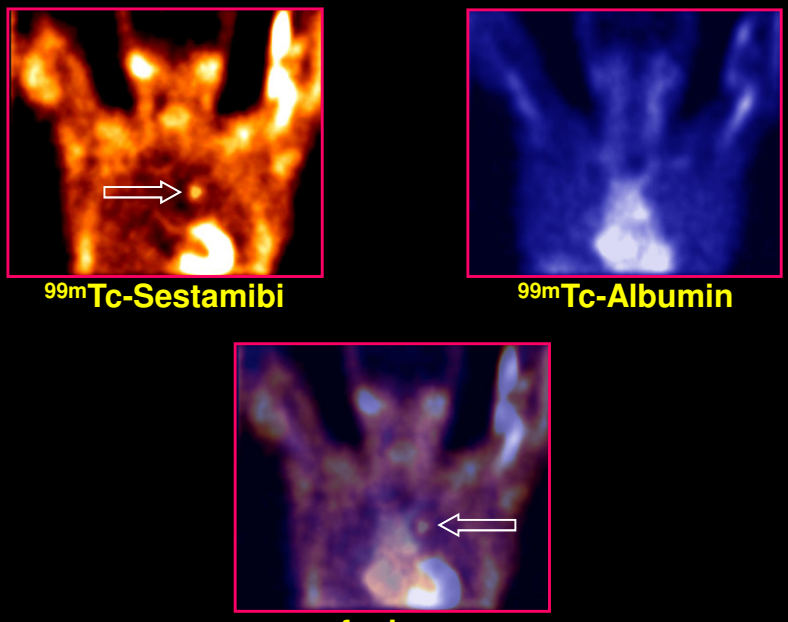
- ^{99m}Tc-Sestamibi: after rapid uptake in both the thyroid and parathyroid tissue, it exhibits different retention/washout times (early and delayed acquisitions).
- Adding a second tracer that solely accumulates in the thyroid ($^{99m}TcO_4^-$ or ^{123}I-iodide) facilitates interpretation of the scintigraphic patterns.

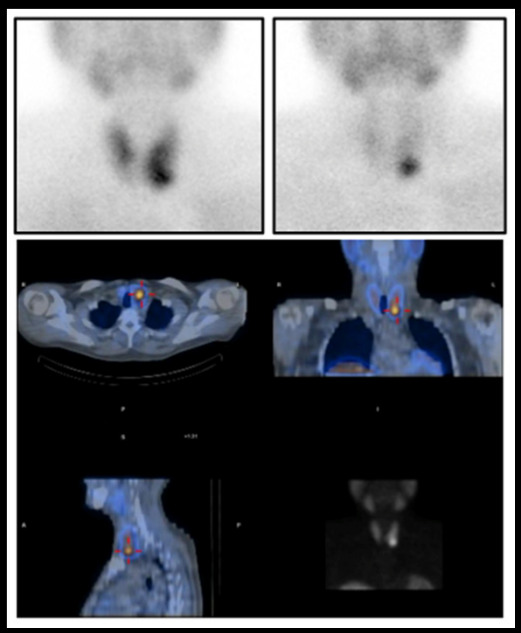

^{99m}Tc-Sestamibi
15 min
^{99m}Tc-Sestamibi
2.5 hr

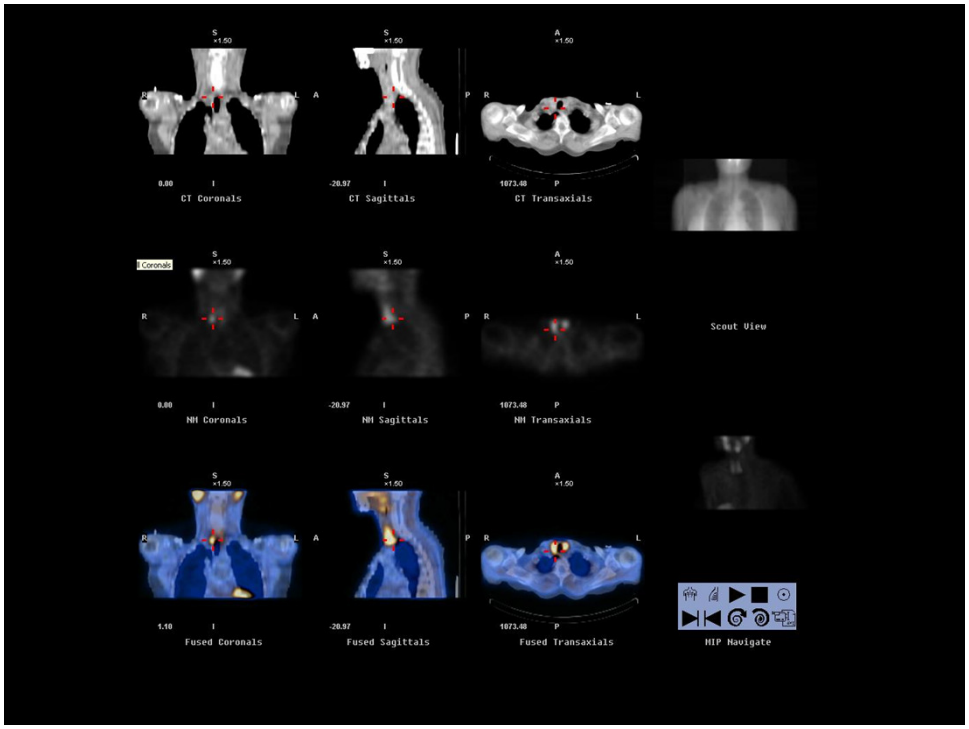

$^{99m}TcO_4^-$
^{99m}Tc-Sestamibi
subtraction
$^{99m}TcO_4^-$
^{99m}Tc-Sestamibi
subtraction


99mTc-Sestamibi
15 min
99mTc-Sestamibi
2.5 hr
99mTcO4- subtracted from
delayed 99mTc-Sestamibi
Delayed 99mTc-Sestamibi
with 99mTcO4- profile

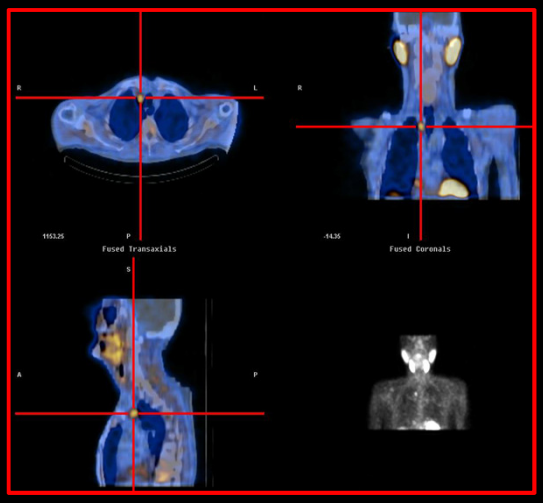



99mTc-Sestamibi
99mTc-Albumin
fusion

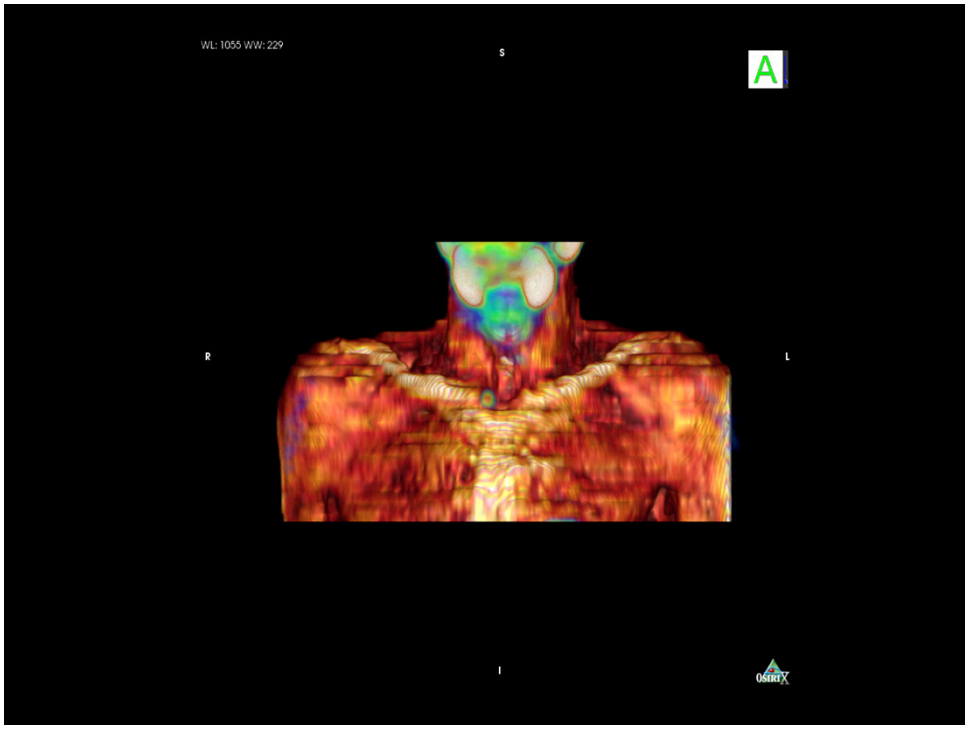




SPECT/CT with ^{99m}Tc-Sestamibi in patient with recurrent PHPT



Ectopic adenoma in upper mediastinum



Debate on Radioguided Surgery

- Preoperative radioguidance only?
- Intraoperative radioguidance?
- Quick intraoperative PTH assay?
- Intraoperative ultrasound?
- “Single-day” high-dose protocol?
- Separate-day low-dose protocol?