Is Parathyroidectomy without Sestamibi Scan acceptable practice in 2018 ?

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Pretoria Controversies
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History

1880	Ivar Sandstrom	Discovered parathyroid in humans
1915	Friedrich Schlaugenhaufer	Link : bone disease & enlarged parathyroid

History

1925	→	Felix Mandl	→ First parathyroidectomy
1926	→	Concept of failed localisation realised	→ Neck exploration x 6 times from 1926 to 1932

History

Soon realisation

Primary Hyperparathyroidism

Not only

Solitary adenoma

Also

Multiple adenomas

Multiple gland hyperplasia

Founded on this knowledge,

Bilateral cervical exploration became the recommended routine procedure

History

Despite the growing success of surgery with advances in perioperative management, proper positioning of the patient & endotracheal intubation

Parathyroid surgeries were often prolonged, tedious & unsuccessful

The biggest challenge was still the precise location of the parathyroid glands

So, the search for a method for preoperative localization of patients' glands appeared as a need to avoid fruitless or inaccurately indicated explorations that could worsen patients' quality of life

History

1977	Roger Guillemin, Nobel prize	Sequencing of parathyroid hormone
1st localisation	Arteriography	Failed to demonstrate benefits
Next	Selective venous sampling	Superior to arteriography but > morbidity

Surgical anecdotes of the time, faced with the difficulties of location of the parathyroid glands, originated the quote:

"The only localization that a patient needs who has primary hyperparathyroidism is the localization of an experienced surgeon!"

Brennan MF. Lessons learned... Ann Surg Oncol. 2006;13(10):1322-8.

History

1980	Thallium 201 Scintigraphic imaging	For myocardial perfusion taken up by parathyroid gland
1987	Samuel Nussbaum	Detection of rapid PTH
1996	George Irvin	Rapid PTH available for commercial use

Tc 99 Sestamibi replaced Thallium,

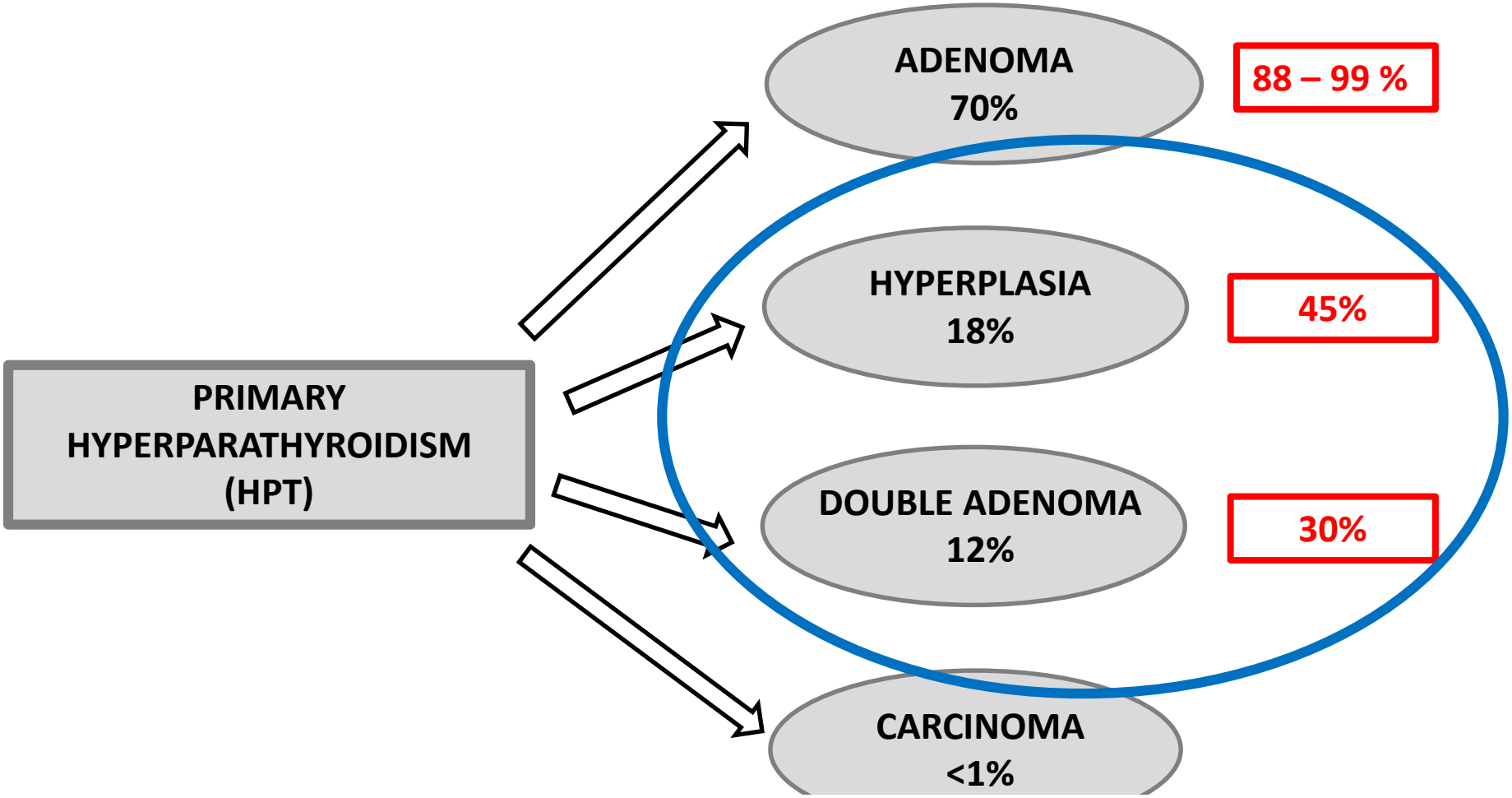
combination of pre op Sestamibi localisation & intra-op use of PTH, revolutionised surgery for the parathyroid resulting in a more focused approach !

Centres and Surgeons universally continued performing bilateral neck explorations without pre operative localisation !

WHY ?????

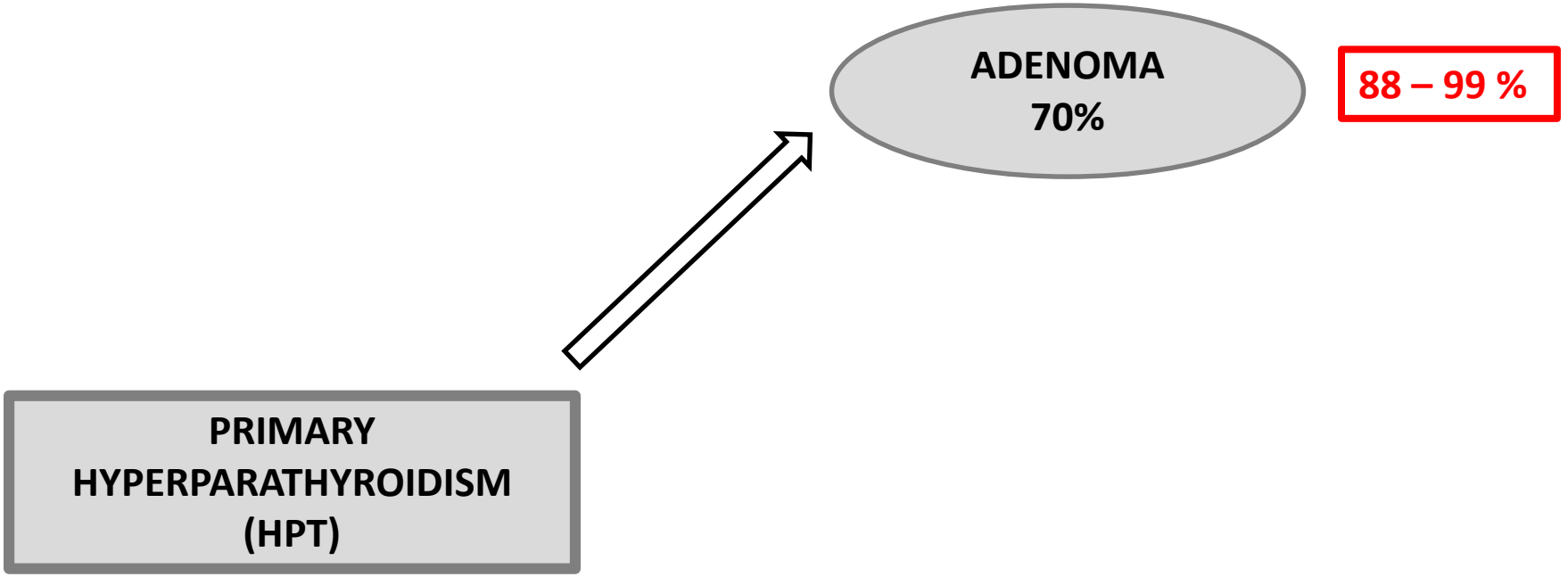
Was it the accuracy of sestamibi in localising the offending gland ?

So just how accurate is it ?



If sensitivity is so low in multiple gland disease,
"Why localise , just bilateralise" your exploration ?

So why this variable sensitivity ?



Factors affecting rates of uptake

The exact reason for uptake of the radiotracer in pathological parathyroids remains debatable; however, higher mitochondrial activity remains the major factor

Reasons for decreased rates of uptake

Biochemical

- A low serum calcium
- Low serum pth
- Normal vitamin b levels
- The use of calcium channel blockers

Biological

- A small size gland,
- An adenoma with low oxyphil cell content
- P-glycoprotein membrane positivity
- Multiple gland disease

Factors affecting rates of uptake

The exact reason for uptake of the radiotracer in pathological parathyroids remains debatable; however, higher mitochondrial activity remains the major factor

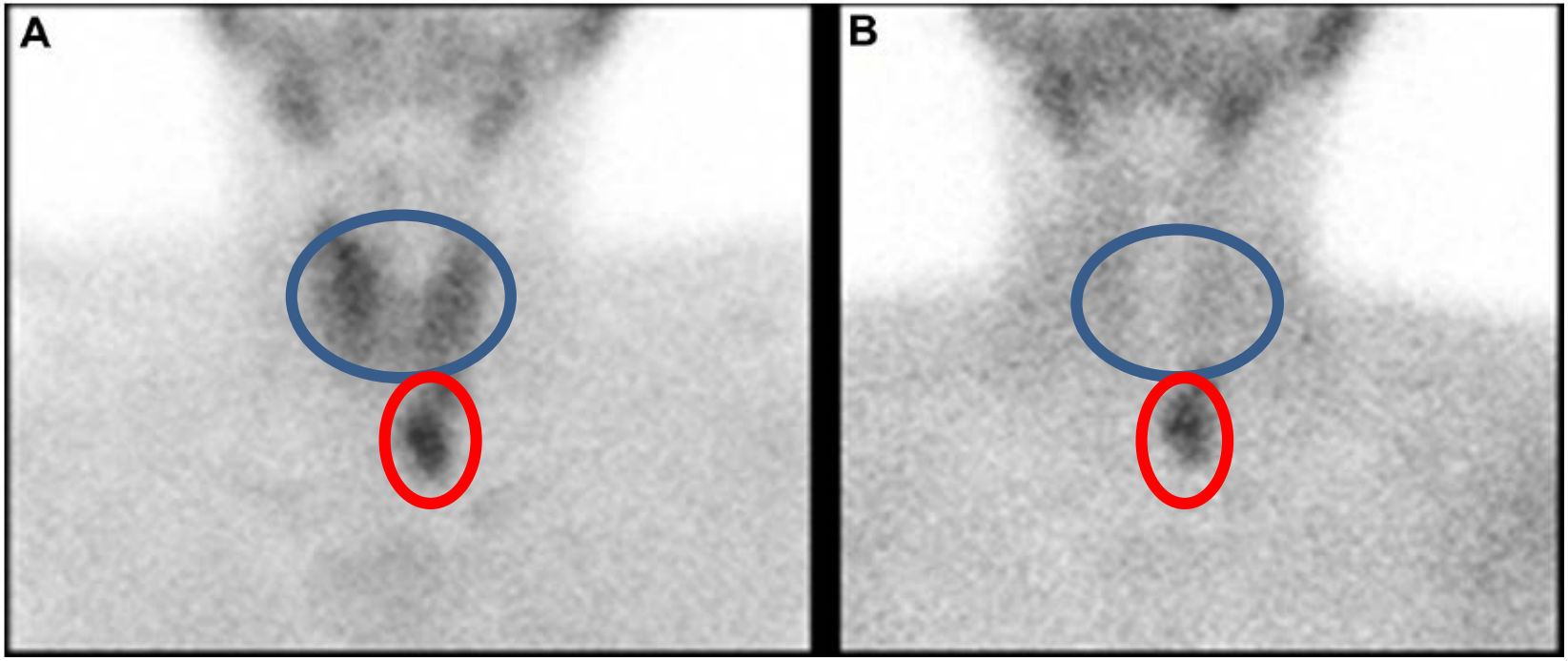
However uptake rates can be improved with

Technical

Reduces the false postive findings associated with concomitant thyroid disease

- **Dual isotope tracer subtraction imaging (to subtract the thyroid and exclude thyroid pathology)**
- **Single-isotope dual-phase imaging (for thyroid uptake to washout)**

SINGLE-ISOTOPE (tc 99) DUAL-PHASE IMAGING (15 min AND 120 min)



15 MIN

120 MIN

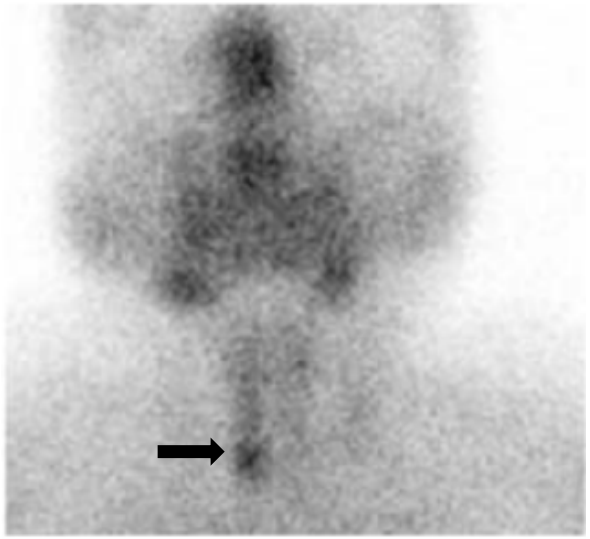
Advancements

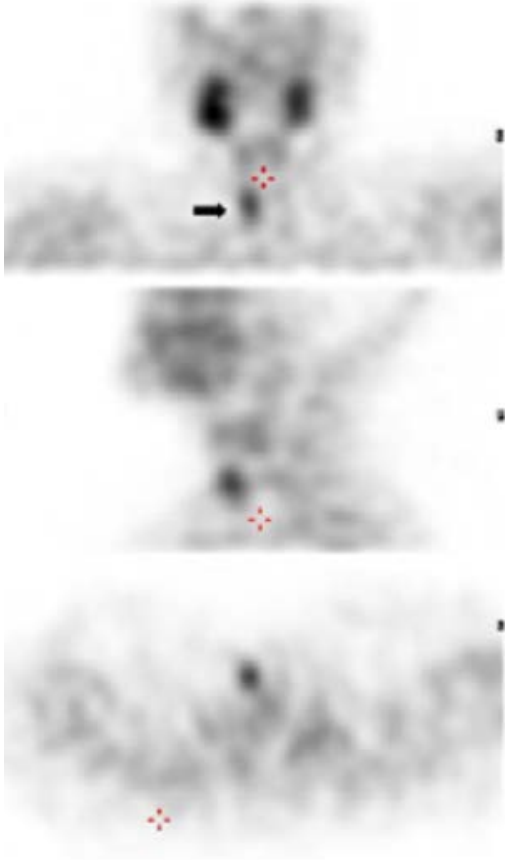
With the turn of the century, sestamibi sensitivities improved with advancements

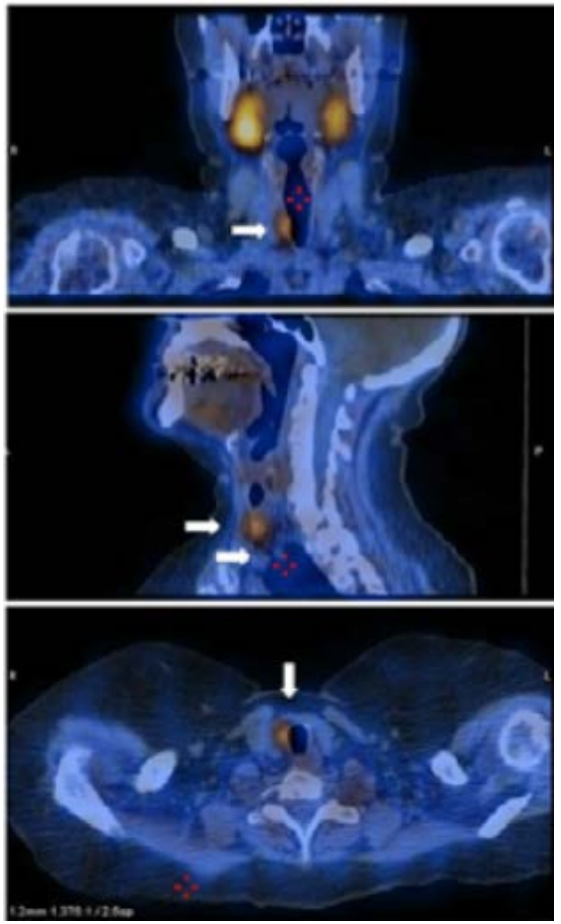
Planar imaging	→	2d imaging
Single photon emission computed tomography (spect)	→	3d imaging
Spect combined with ct (spect/ct)	→	Better anatomical defining localisation
Spect with ct & iv contrast (4d-ct)	→	Excellent anatomy of gland and surrounding structures

INCREASING SENSITIVITY

Example of right lower parathyroid adenoma in same patient using different Sestamibi scans







PLANAR IMAGING **SPECT** **SPECT / CT**

CLEARLY DEMONSTRATING MORE ACCURATE ANATOMICAL LOCALISATION

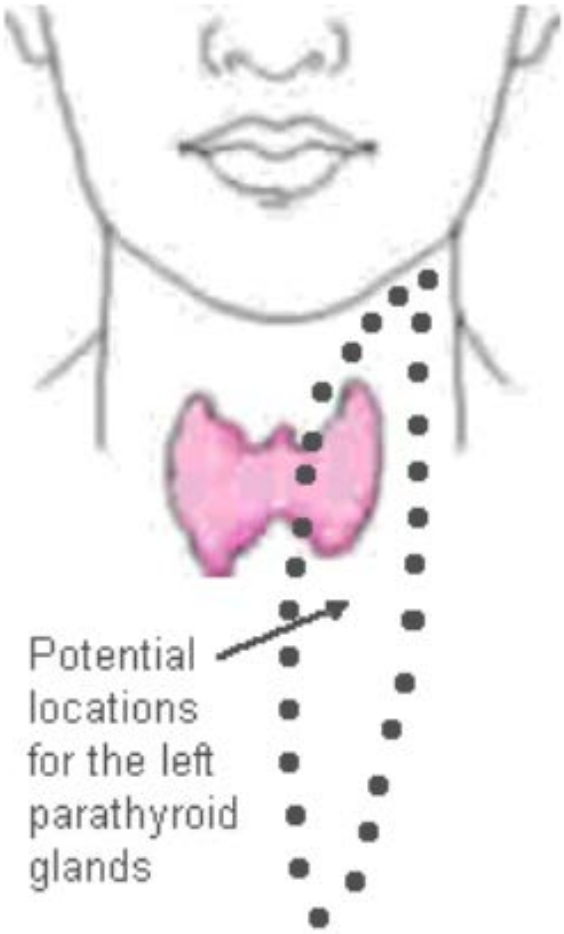
Advantages: SPECT / CT

Differentiates thyroid from non thyroidal tissue

Relationship of adenoma to surrounding structures

Precise localisation of ectopic adenomas (6-16% incidence):

- **Paraoesophageal (28%)**
- **Mediastinal (26%)**
- **Intrathymic (24%)**
- **Intrathyroid (11%)**
- **Carotid sheath (9%)**
- **High cervical (2%)**



The accuracy will continue to improve as CT components with higher resolution are incorporated into SPECT cameras

54 year old male

Primary HPT

No pre op localisation

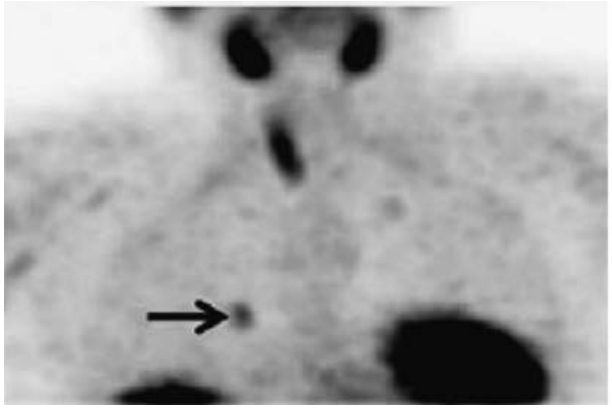
Bilateral neck exploration

Failed localisation even with common ectopic sites

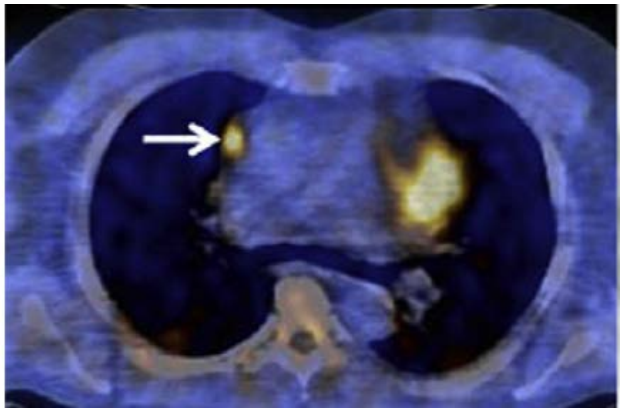
Right inferior PT + left thyroid removed

Persistant hypercalcaemia

POST OP SESTAMIBI SCAN



SPECT demonstrating location in mediastinum



SPECT CT more accurate localisation lateral to ascending aorta

Correlation with MRI

What about other localisation techniques, how does sestamibi fair against them ?

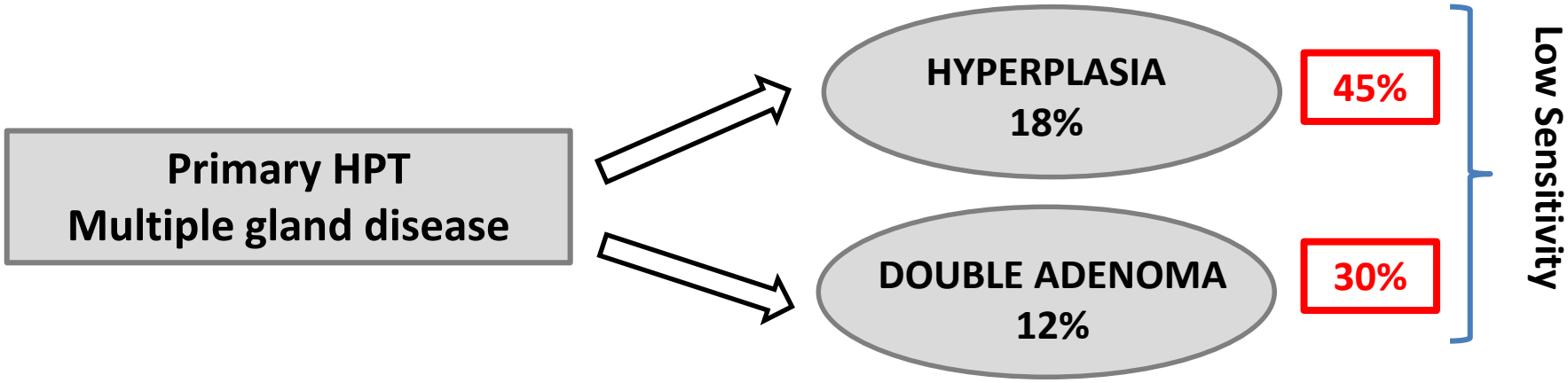
Comparison with other pre op localisation studies

Single adenoma
Typical position
Absent thyroid pathology
Operator dependant

IMAGING MO	RCENT)
SESTAMIBI – P	
SESTAMIBI – SPECT	70-81
SESTAMIBI – SPECT CT (4D)	-95
ULTRASOUND	64-91
MRI	40-85
PET-CT	79-90

***Sestamibi** especially in the form of SPECT/CT remains the **gold standard** of pre operative localisation studies*

But what about the low sensitivity in multiple gland disease?



How will we know we **excluded multiple gland disease** on pre operative scintigraphy & terminate surgery with confidence ?

How will we know we **missed multiple gland disease** on pre operative scintigraphy & proceed to bilateral exploration to minimize risk of operative failure ?

Answer = Intra op PTH or Intra op Scintigraphy

Intra op scintigraphy

Better than the frozen section can, and much better than intraoperative PTH hormone assay can

Use of a gamma probe in the operating room can distinguish the difference between a

NORMAL GLAND	HYPERPLASTIC GLAND	ADENOMA
Do not become radioactive over that of fat. Will read zero.	Will become radioactive, but NEVER more than 15% of background	Will become very radioactive & will almost always be more radioactive than 20% of background

"The 20% Rule..."

If the removed parathyroid has > 20% of background radioactivity it MUST be an adenoma and it does NOT require a frozen section to diagnose it

Murphy C, Norman J. The 20% rule: a simple, instantaneous radioactivity measurement defines cure and allows elimination of frozen sections and hormone assays during parathyroidectomy. Surgery. 1999;126(6):1023-8

Not reproduced by other centres!

Confirmation of one adenoma removal doesn't exclude the presence of another !

Intra op pth

How will we know we excluded multiple gland disease on pre operative scintigraphy & terminate surgery with confidence ?

Can confirm complete removal of all hyper functioning parathyroid tissue, which allows for termination of surgery with confidence

How will we know we missed multiple gland disease on pre operative scintigraphy & proceed to bilateral exploration to minimize risk of operative failure ?

Can identify patients with additional hyper functioning parathyroid tissue following the incomplete removal of diseased parathyroid/s, which necessitates extended neck exploration

Is localisation imperative ?

PARATHYROIDECTOMY OPERATIVE APPROACHES

DIRECTED

- UNILATERAL NECK EXPLORATION
- FOCUSED PARATHYROIDECTOMY
- MINIMALLY INVASIVE RADIOGUIDED PARATHYROID (MIRP) SURGERY

PRE OPERATIVE LOCALISATION REQUIRED

NON-DIRECTED

- BILATERAL NECK EXPLORATION

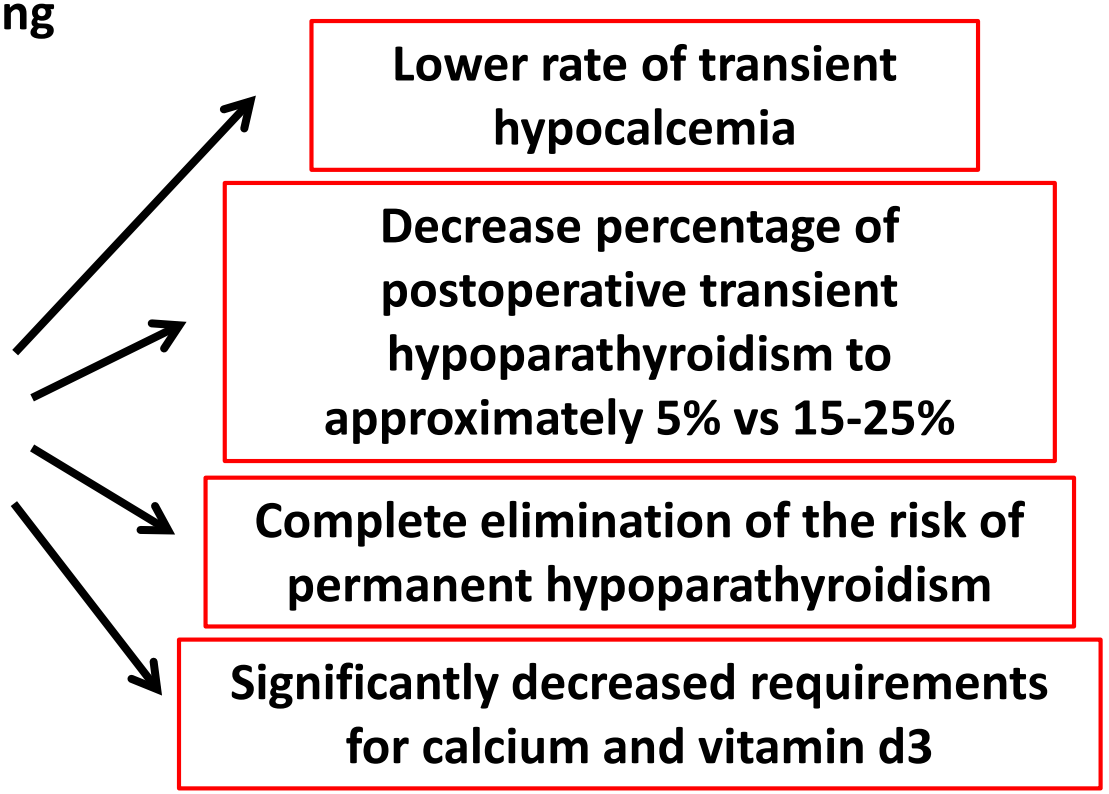
NO PRE OPERATIVE LOCALISATION REQUIRED

Directed vs Non-directed

The so called "gold standard" bilateral neck exploration, an attractive option that has an impressive cure rate of >95%

What happens when compared with focused parathyroidectomy

- Equally effective in restoring normocalcemia
- Better cosmetic effects
- Less pain
- Less nerve injuries
- Preserves intact blood supply of normal parathyroids, because no unnecessary exposure
- Shorter hospitalization
- ? Cost



Barczyński M, Cichoń S, Konturek A, et al. Minimally invasive video-assisted parathyroidectomy versus open minimally invasive parathyroidectomy for a solitary parathyroid adenoma: a prospective, randomized, blinded trial. World J Surg 2006;30:721-31

Directed vs Non-directed costs

Table 2. Risk of Surgical Failure Following the Initial Operation Total Charges (for the Initial Operation Plus a Subsequent Operation, If Needed), and Charges for a Subsequent Operation for Each Localizing Strategy

Strategy*	Risk of Surgical Failure, %	Average Charge, $	Incremental Cost of a Subsequent Operation, $
Bilateral neck exploration	5.0	17 358	918
IOPTH	1.6	14 962	600
Preoperative technetium Tc 99m sestamibi scanning			
Alone	2.3	13 380	125
Plus IOPTH	0.7	13 854	388
Plus IORG	1.2	13 158	270

*IOPTH indicates intraoperative parathyroid hormone assay; IORG, intraoperative radioguidance.

Fahy BN, Bold RJ, Beckett L, Schneider PD. Modern Parathyroid Surgery: A Cost-benefit Analysis of Localizing Strategies. Arch Surg. 2002;137(8):917-923.

Directed vs Non-directed costs

Directed parathyroidectomy

Cost effective

Cost benefit

Due to

- **Reduced operative charges**
- **Immediate hospital discharge**

Not due to

- **Lower need for re exploration**
- **Persistent hpt**

Fahy BN, Bold RJ, Beckett L, Schneider PD. Modern Parathyroid Surgery: A Cost-benefit Analysis of Localizing Strategies. Arch Surg. 2002;137(8):917-923.

CONCLUSION
Is Parathyroidectomy without Sestamibi Scan acceptable practice in 2018 ?

Prompted by better understanding in parathyroid physiology currently

Improvements in imaging modalities and imaging techniques

Increase in sensitivity of sestamibi scan in combination with ct scan

The pre-operative use of Sestamibi scanning for localisation in primary HPT

Has to be encouraged !

Is Parathyroidectomy without Sestamibi Scan acceptable practice in 2018 ?
KEY POINTS

For focused exploration	with intra operative PTH assays, has shown to decrease the rates of proceeding to bilateral neck and the resultant complications
For routine bilateral exploration	plays a role in identifying ectopic glands and thus facilitates operative accuracy
for pt's with non localising imaging / imaging demonstrating more than one focus	can be planned for bilateral neck exploration upfront, preparing both surgeon and patient alike
for recurrent / persistent disease or concomitant thyroid disease	pre-operative localisation with a sestamibi scan is invaluable as it increases success rates from 60% to 95%

The skewed notion that Sestamibi scanning will improve outcome in the hands of inexperienced surgeons should also be discouraged

praemonitus, praemunitus

Forewarned, forearmed; to be prepared is half the victory.

(Miguel de Cervantes)

If you haven't changed to using Sestamibi scans, the time is now !