Endocrine Nuclear Medicine

Outline of Lecture

Organs:

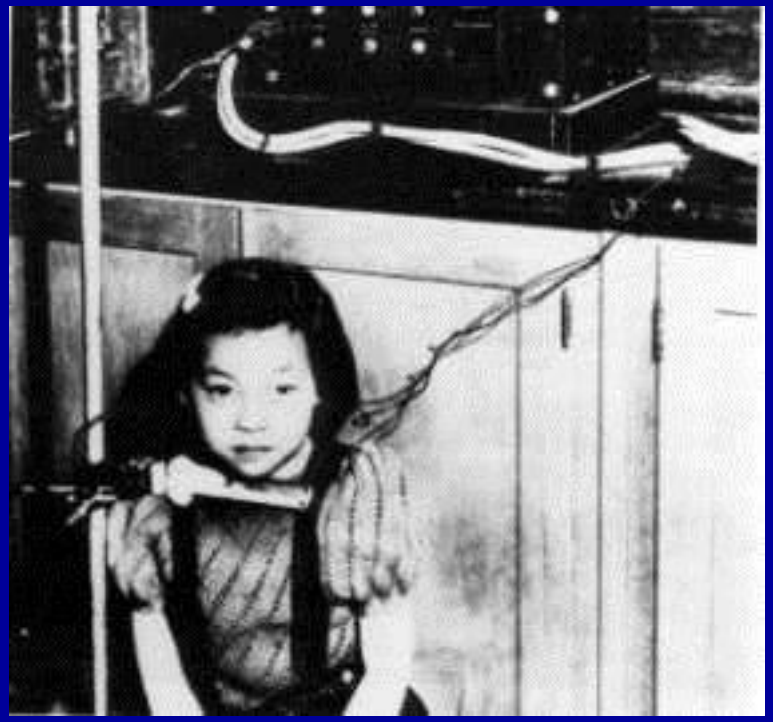
- Thyroid
- Parathyroid
- Adrenal Gland

Nuclear Medicine:

- Tracers, technical aspects
- Relationship to patient diagnostic pathways and other imaging modalities
- Contribution to management and treatment

Functional imaging

- Nuclear Medicine started with endocrinology
- I-131 used to exploit differences between the endocrine tissue and background
- Just need to find the right agent for the right adenoma



Functional imaging

- The aim of nuclear medicine is to identify and track physiological actions using a “tracer” labelled with a radioisotope
- Anatomical information may be inferred from the physiological image but this is secondary
- Imaging methods should be standardised-reproducible

The Thyroid Gland

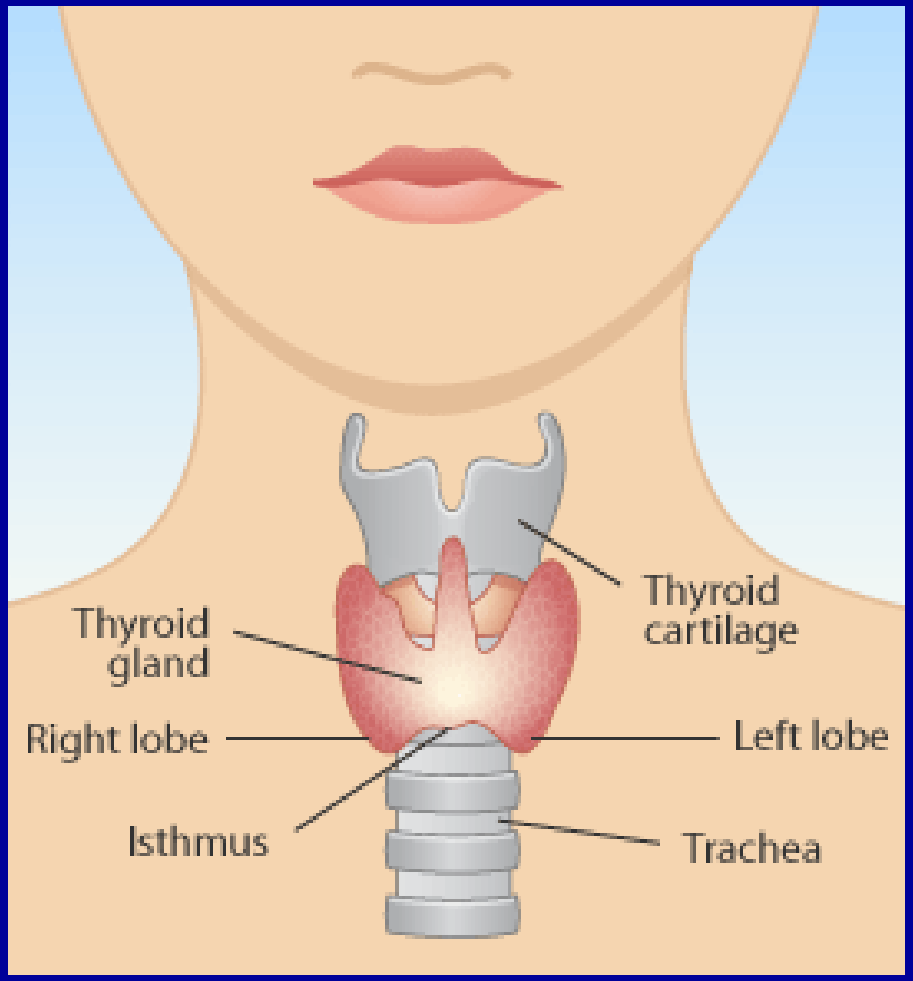


Image : ABC Health and Wellbeing Website

Thyroid Hormones

Negative Feedback System

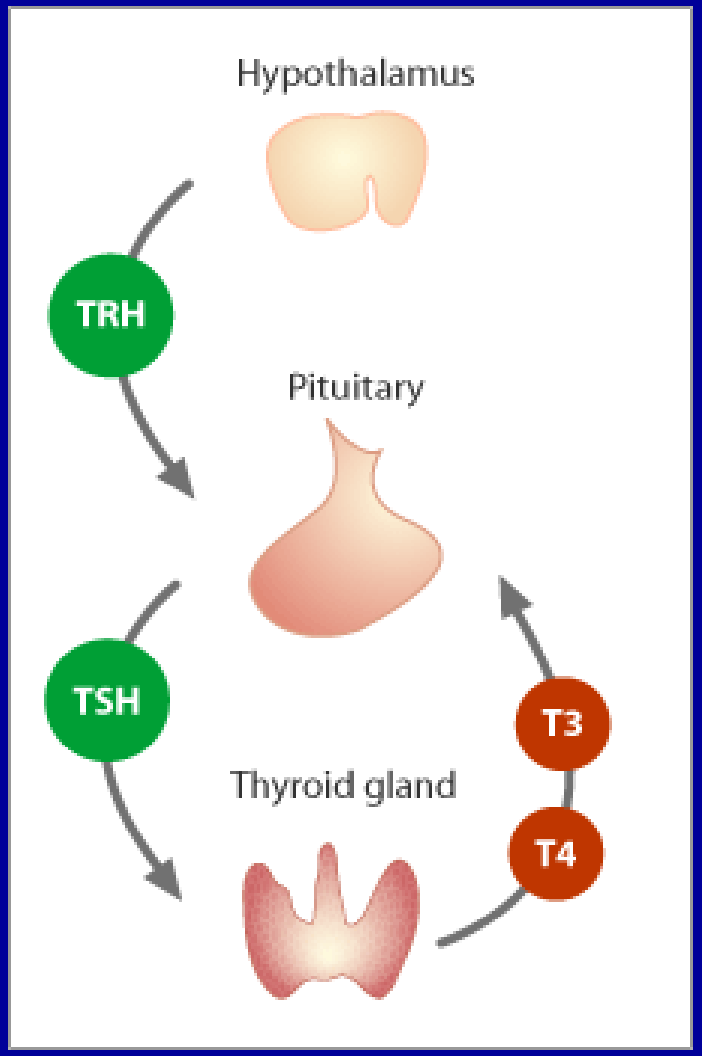
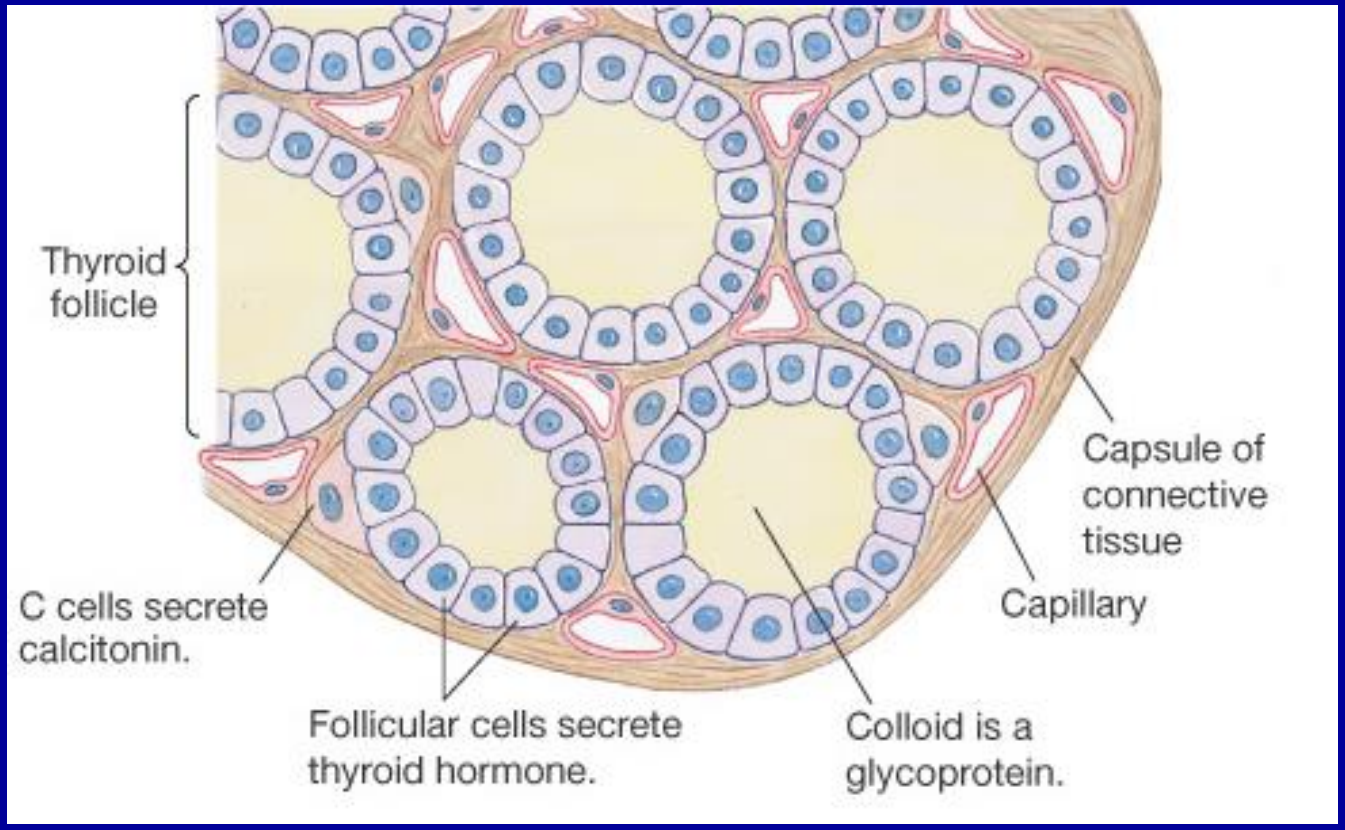
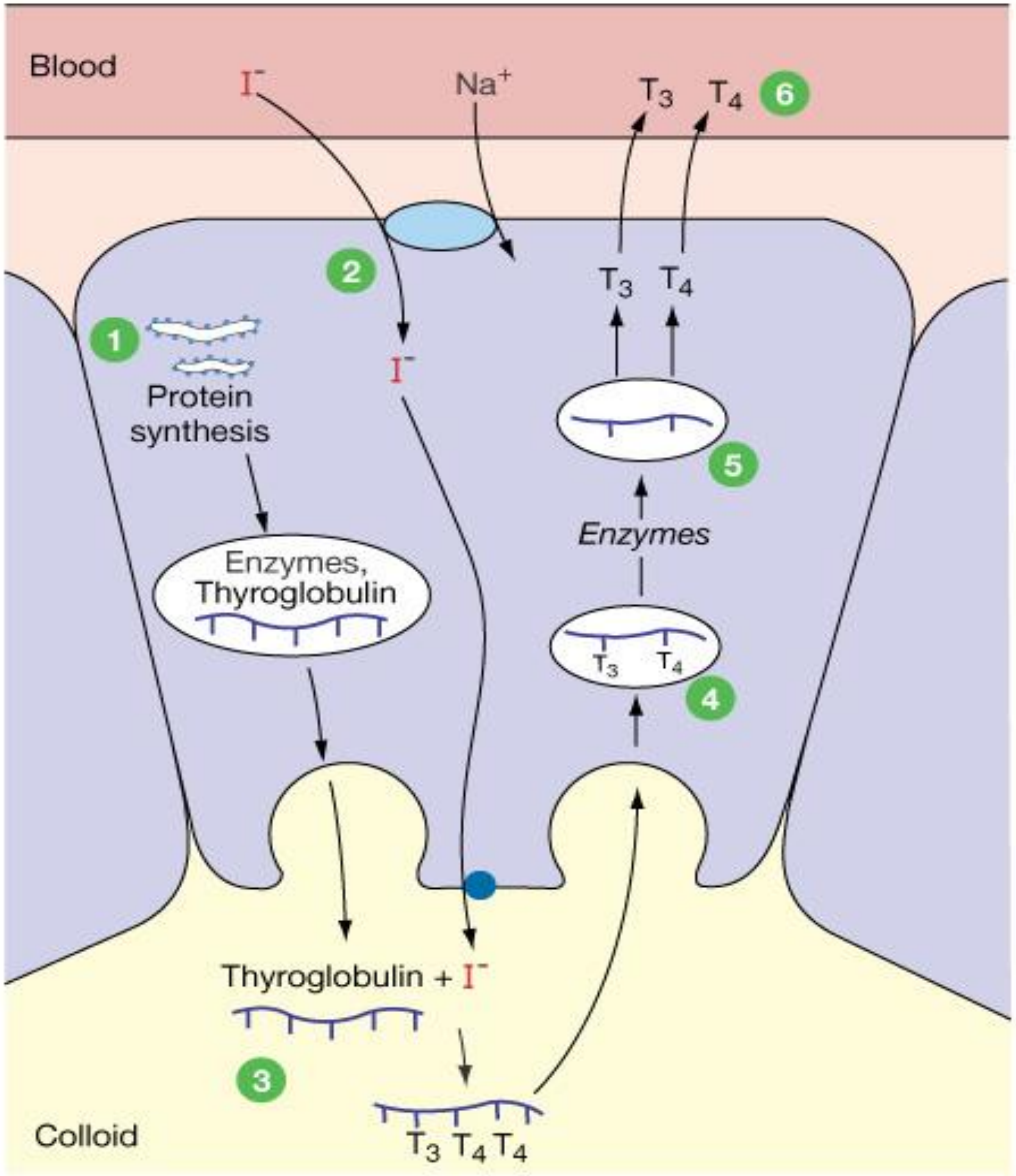


Image : ABC Health and Wellbeing Website

Thyroid Gland





1. Follicular cell synthesizes enzymes and thyroglobulin for colloid.
2. I^- is co-transported into the cell with Na^+ and transported into colloid.
3. Enzymes add iodine to thyroglobulin to make T_3 and T_4.
4. Thyroglobulin is taken back into the cell.
5. Intracellular enzymes separate T_3 and T_4 from the protein.
6. Free T_3 and T_4 enter the circulation.

Production of Thyroid Hormones T3 and T4

Thyroid imaging

- When should it be performed?
- How does it help diagnosis?
- What alternatives are there for imaging the thyroid?
- How do the results of the nuclear medicine scan affect treatment?

Functional Imaging of Thyroid

- Thyroid Gland
  - Overactive
  - Underactive
  - Malignancy

The Scan

Patient preparation:

- Patient letter/leaflet

- Stop relevant medication

  Carbimazole (CBZ) : 48 hrs
  Propothyruracil (PTU) : 48hrs
  T4 : 4-6 weeks
  T3 : 3 weeks

Other factors in patient history may affect scan

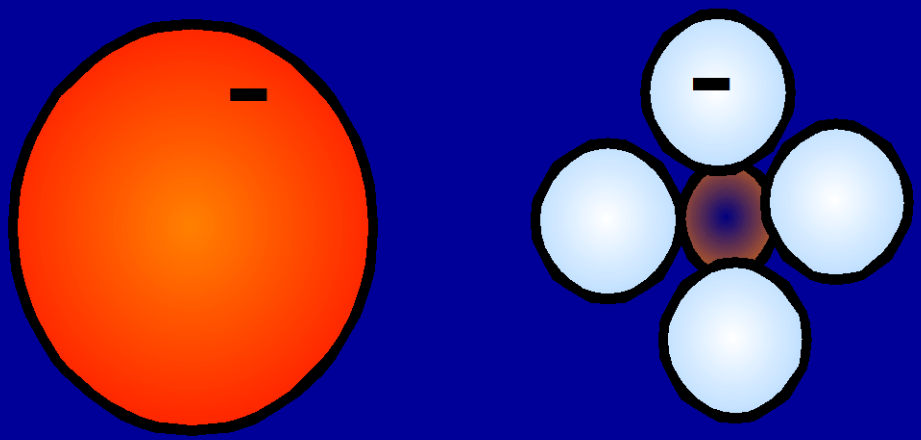
Factors affecting uptake of ^{123}I, ^{131}I and $^{99m}Tc\text{-}O_4^-$

- Exogenous thyroid hormone
- Medication (CBZ) and (PTU)
- Iodine containing radiological contrast agents (wait 6-8 weeks)
- High level of intake of Kelp products
- Amiodarone

All the above will decrease uptake : ASK the patient!!!!!!

Iodine and Pertechnetate

Both Iodine and pertechnetate have similar size and charge



The Scan

Radiopharmaceutical

- ^{99m}Tc pertechnetate: cheap, not organified scan that day (ARSAC DRL =80MBq). Scan 20 mins post injection
- ^{123}I: more expensive, scan next day if oral prep (ARSAC DRL= 20 MBq)

- Measure syringe activity before and after injection for % uptake calculation
- (accurate camera sensitivity required. Activities decay corrected etc)

The Scan

Scan Parameters

- Single or dual headed camera
- Camera: standard FOV
- Collimator: Pinhole, LEHR

Patient position

- Supine, neck extended, standard (eg 10 cms) from collimator. Optimise comfort!

The Scan:

Views:

- Anterior (include salivary glands) 100-200K counts
- Obliques
- +/- Lateral (vital in infant if looking for lingual thyroid)
- +/- Large FOV 100K counts
- Suprasternal notch (SSN) – Co source marker 60 secs to check for retrosternal extension

Causes of Hyperthyroidism

- Graves
- Solitary or Multiple Autonomous Nodules
  (toxic adenoma, Plummer's Disease)
- Thyroid Hormone 'Leak'
  thyroiditis, Hashimotos thyroiditis (early), subacute(=De Quervains) thyroiditis, post partum thyroiditis
- XS thyroid hormone ingestion eg thyroxine, 'slimming' drugs
- Thyroid hormone or TSH secreting tumour eg some ovarian
- Pituitary gland malfunction

Grave's

- Primary diagnosis by history, examination
- Diagnosis established by biochemistry and immunology
- Functional imaging confirmatory
- May be of particular use if thyroid abnormal:
  - Nodules
  - Previous surgery
  - ^{131}I Therapy being considered

Graves Disease

- Autoimmune disease ie antibodies made to ‘self’
- Up to 10 different Abs described so far
- Abs to TSH receptor on thyroid cell stimulates hormone production
- Abs stimulating thyroid growth (or other tissues e.g. front of shins, retro-orbital fat)
- Clinical manifestations depend on Abs present

Graves Disease

- Women>>men
- 20-40 years
- Genetic predisposition (other auto-immune conditions may co-exist)

  HLA B81, DR2 and DR3 in Caucasians

  BW35 and BW 36 in Asians
- 50% have family history

Graves Disease: Clinical Picture

- Increased metabolic rate: weight loss, increased bowel transit
- Sweating
- Sympathomimetic effects: fast heart rate, palpitations, tremor, anxiety
- Immune mediated effects: dysthyroid eye disease, pretibial myxoedema
- Other: e.g. proximal muscle wasting

Pretibial Myxoedema

Skin is thickened and inelastic due to deposition of excess glycosaminoglycans

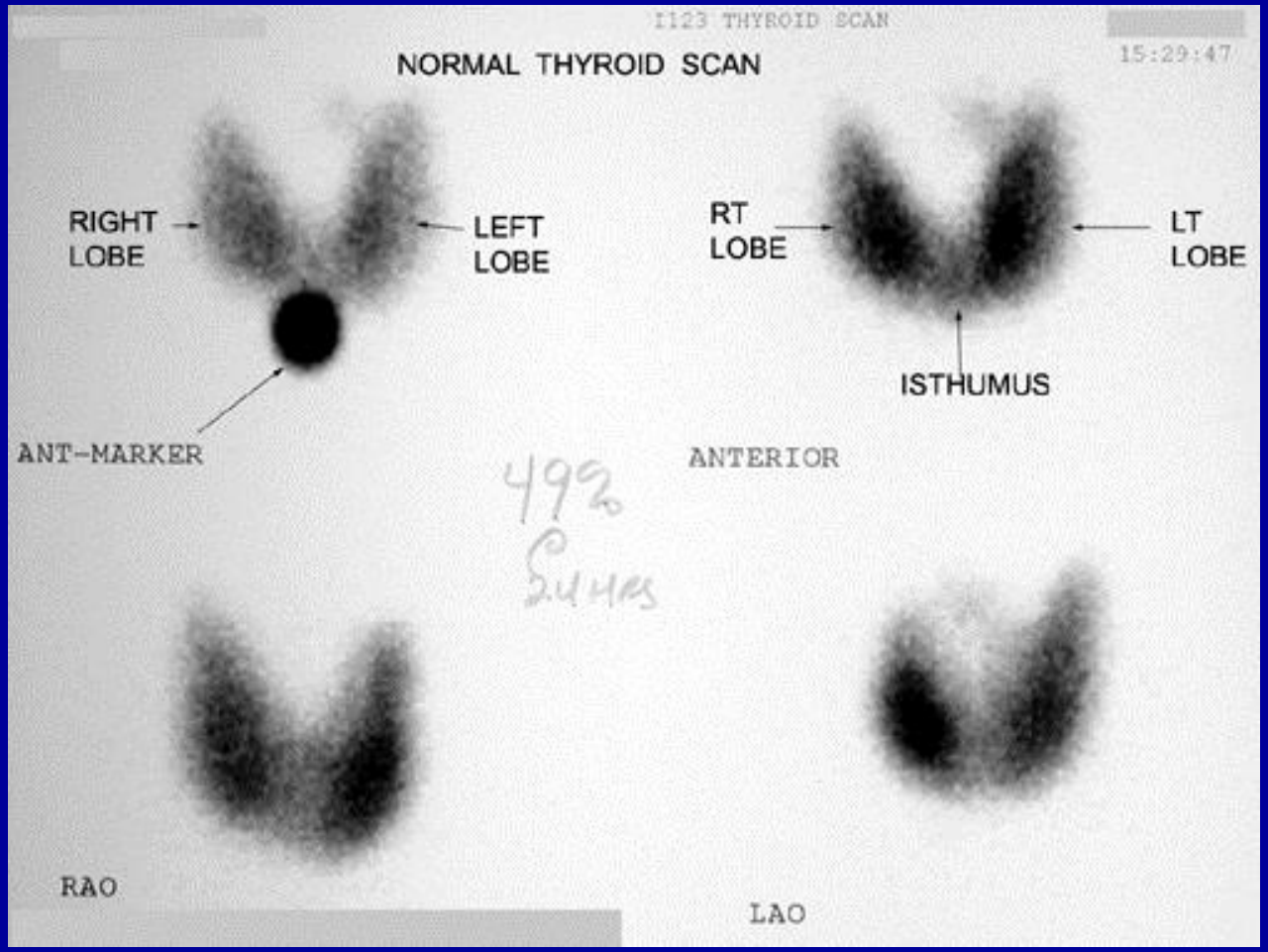
Image: DermNet NZ

Graves Dysthyroid Eye Disease

- Affects up to 50% of patients
- Proptosis, diplopia and compression of optic nerve
- Infiltration of fat and occular muscles with muccopolysaccharides

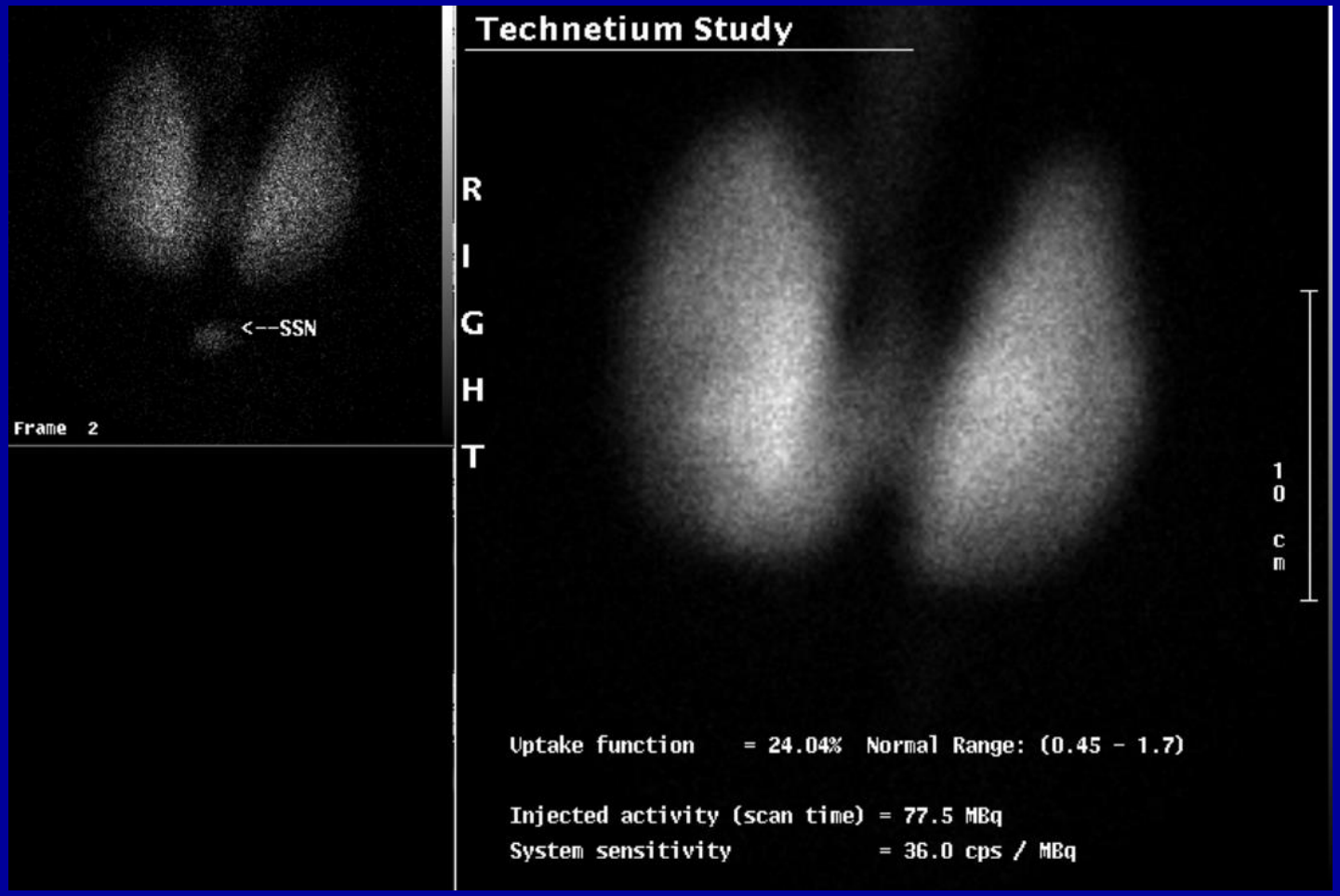
Images: Handbook of Ocular Disease Management
www.revoptom.com
Visitech Eye Centre

Normal Thyroid Gland



Graves disease

Graves Disease



Hypothyroidism

- NM: Not so useful as uptake low
- Especially difficult to see nature of nodes
- Ultrasound is probably better

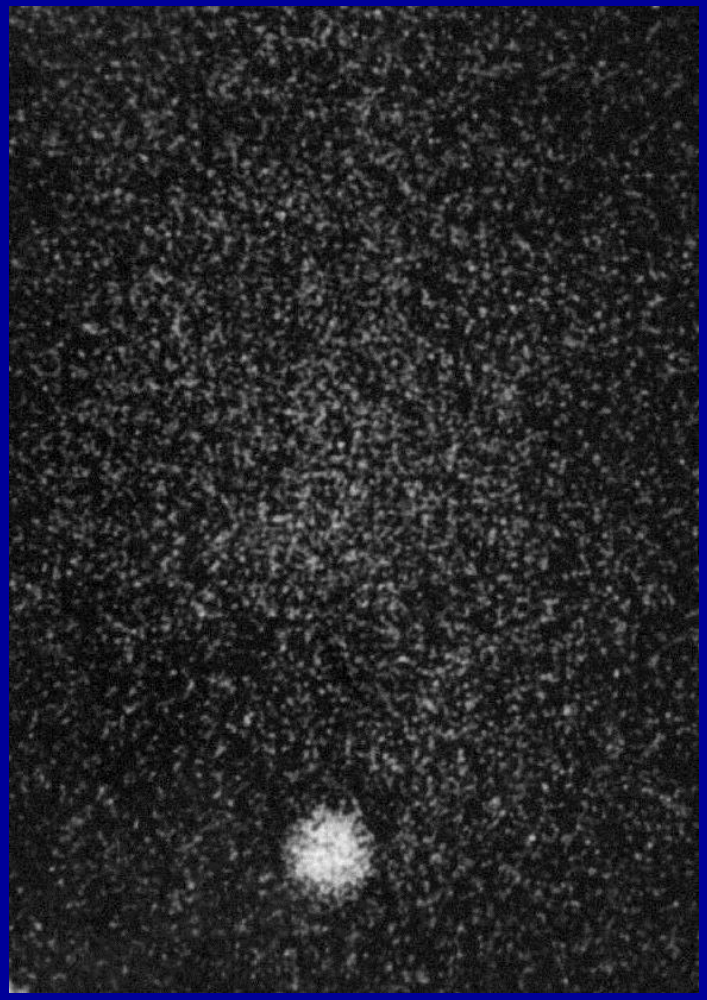
- Hashimoto's Thyroidtis is most common cause of hypothyroidism - autoimmune condition (can be toxic in very early stage)
  - scan appearances vary with stage
  - chronic : inhomogeneous tracer uptake

Thyroiditis

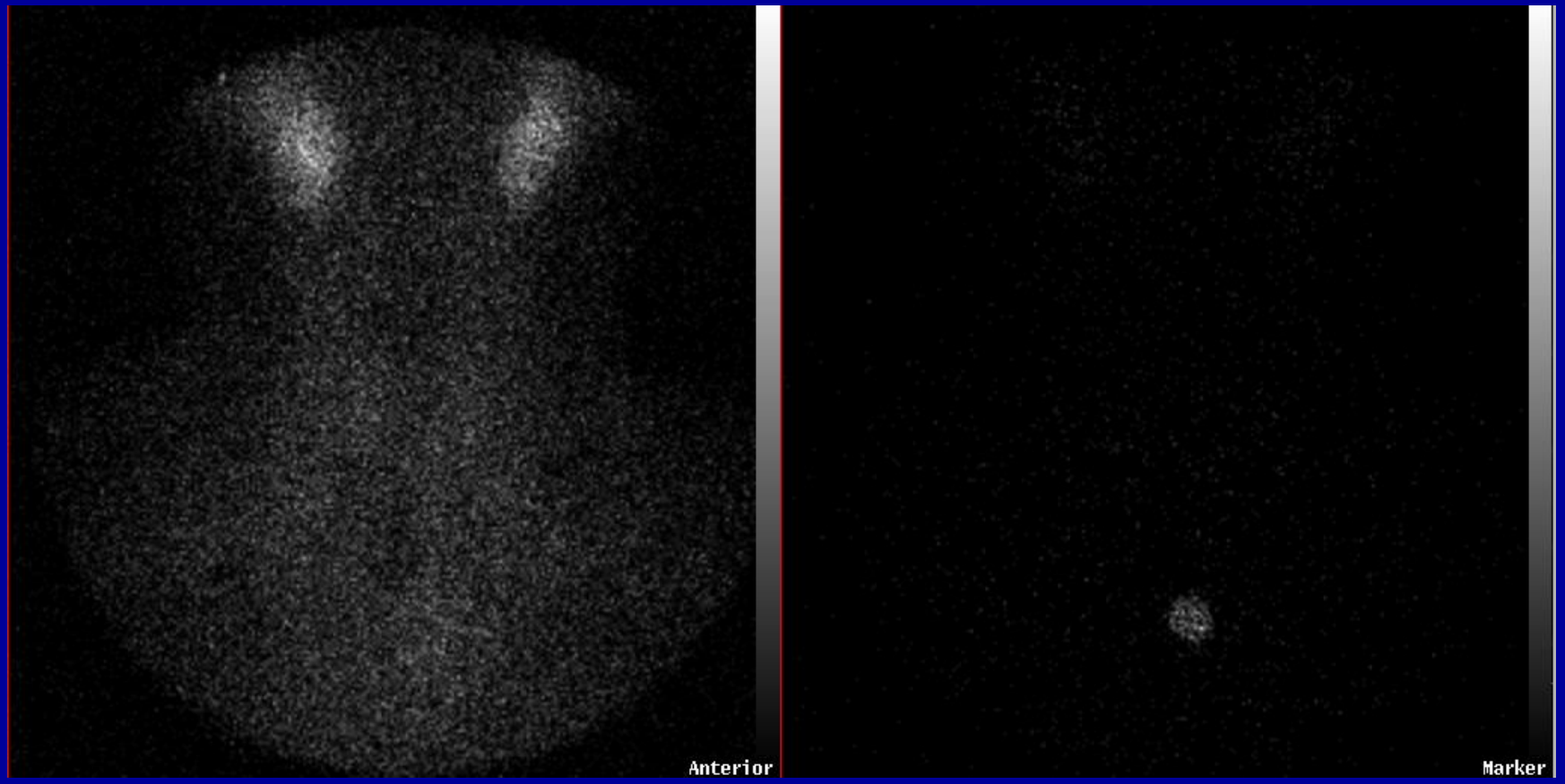
Subacute thyroidits (also known as de Quervains)

- NM: Very good test as Iodine and pertechnetate are not taken up in acute phase (first 4 weeks after onset of symptoms)
- Patient initially toxic
- Reduced uptake persists 4-8 weeks
- Tends to be normal by 12 weeks
- Scan these within 10 days of request
- NB This patient is NOT treated with ^{131}I for 'toxic' state

Thyroiditis



Thyroiditis

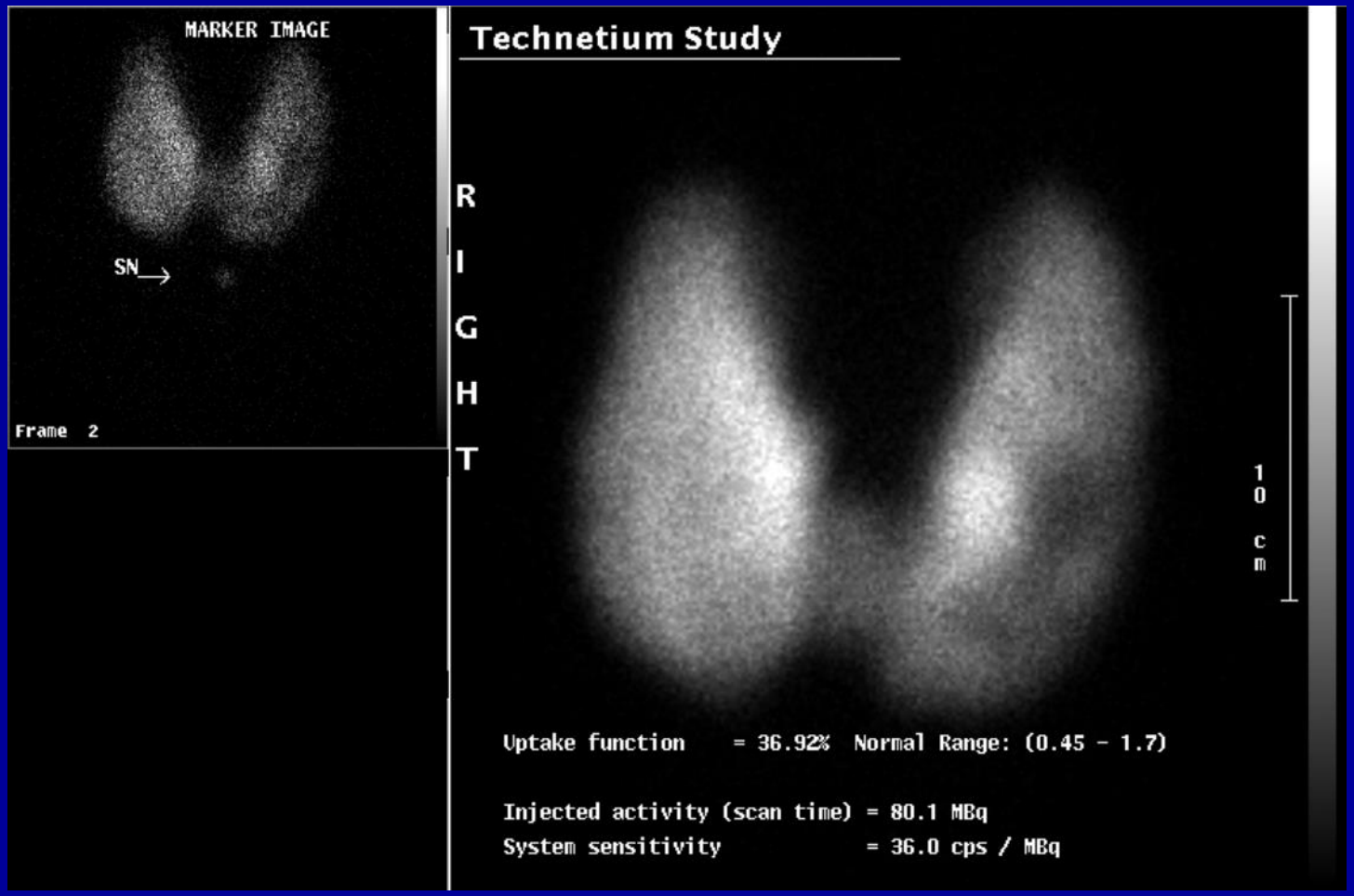


Thyroid Nodules

- Common – F>>M and ↑ with age
- 95% of nodules are cold ('nonfunctioning')
- Cold nodule is not normally cancer however risk of malignancy 1.5-38%, most quoted value ≈ 10%

  -patient should have USS +/- FNA
- Less than 1% hot ('functioning') nodules are malignant

Cold Nodule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10 cm
Uptake function = 36.92% Normal Range: (0.45 - 1.7)
Injected activity (scan time) = 80.1 MBq
System sensitivity = 36.0 cps / MBq

Thyroid Nodules

Cold Nodule

- Colloid Nodule
- Cyst
- Adenoma
- Haemorrhage
- Focal Thyroiditis
- Abscess
- Parathyroid adenoma

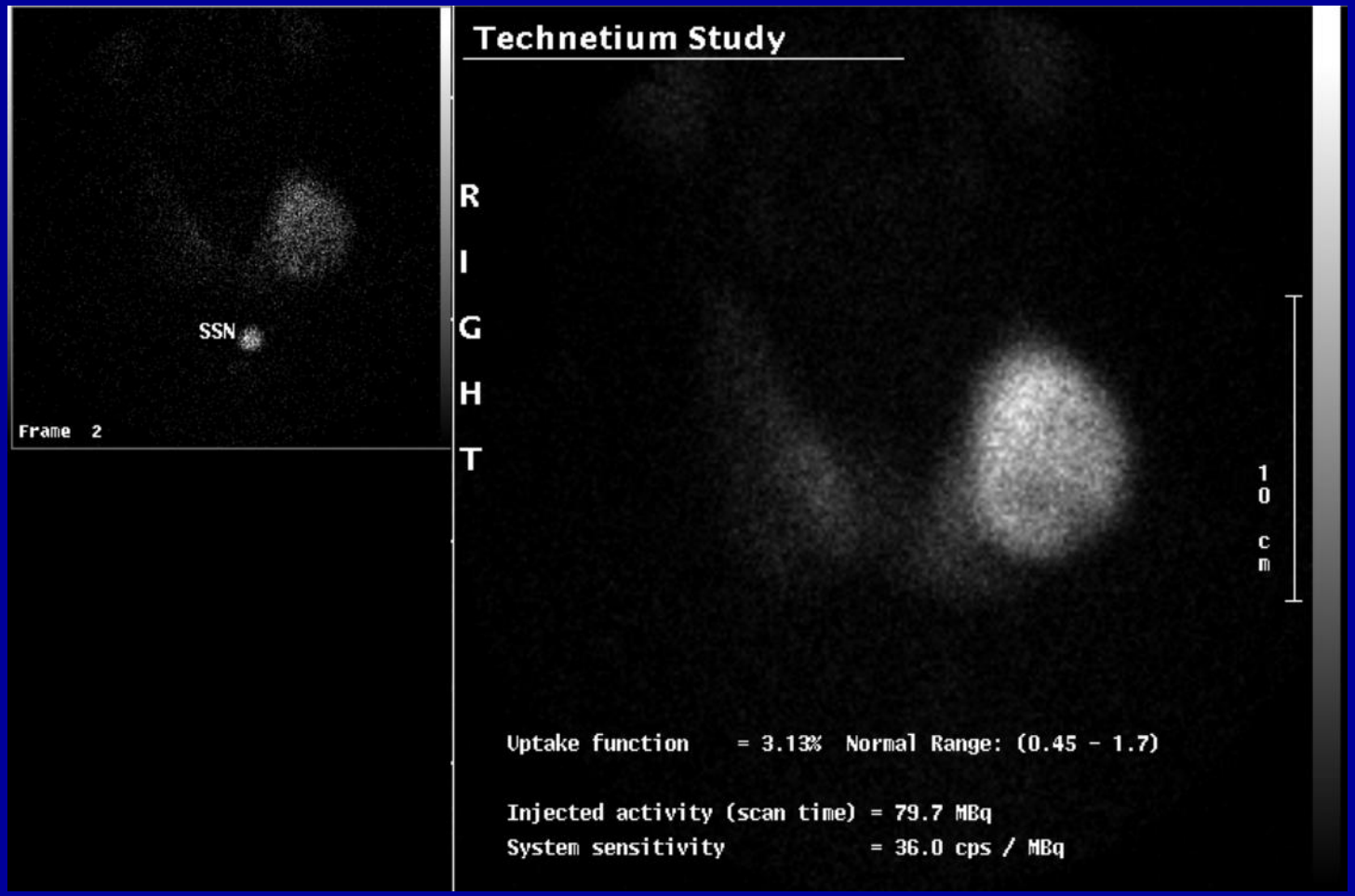
Hot Nodule

Adenoma

Hot Nodule

- May become autonomous (not responsive to feedback loop)
- Rest of gland suppressed
- If patient ‘toxic’ (i.e. ↑T4 and/or ↓TSH) due to functioning nodules, then they have ‘Plummers Disease

Hot Nodule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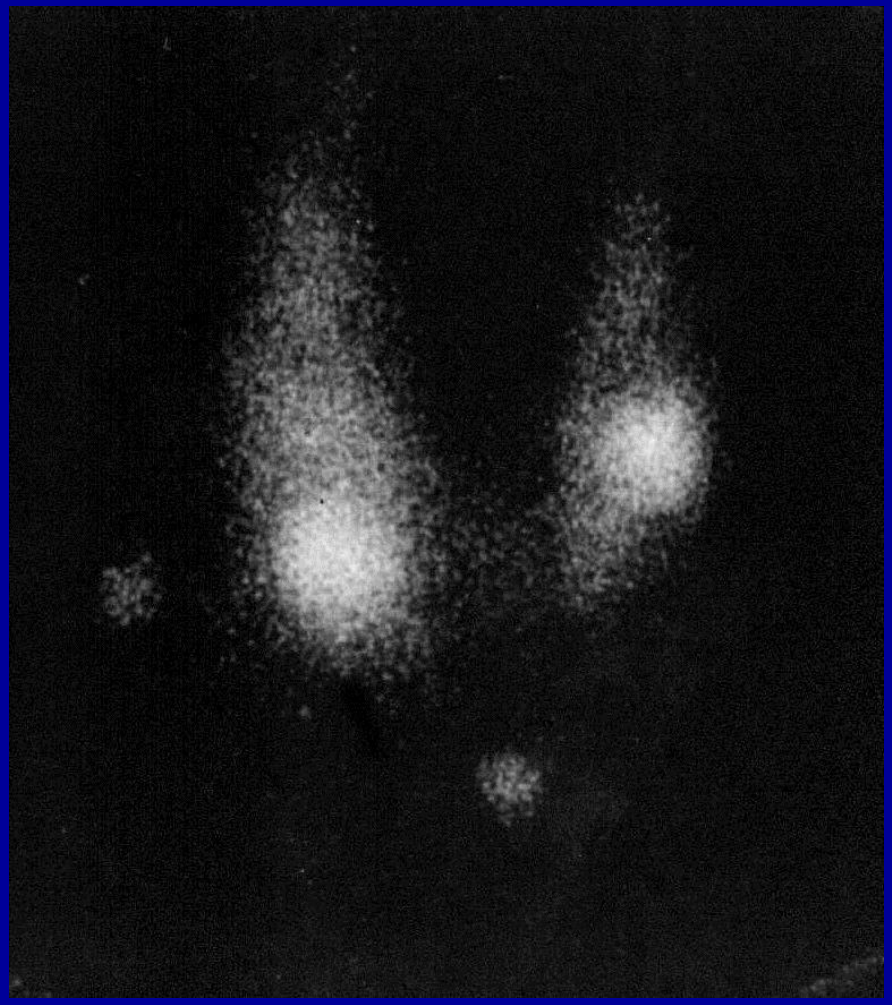
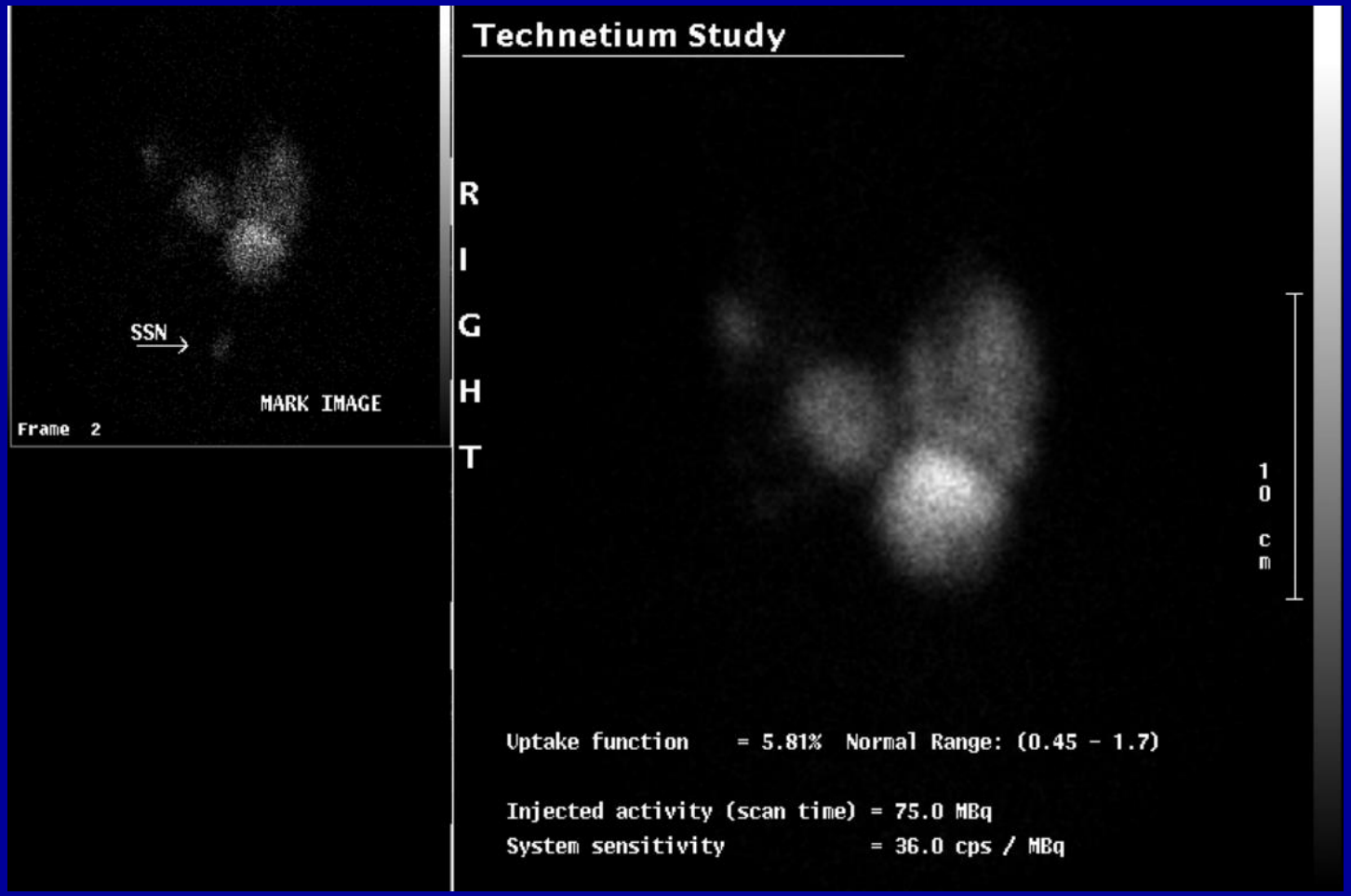
10 cm
Uptake function = 3.13% Normal Range: (0.45 - 1.7)
Injected activity (scan time) = 79.7 MBq
System sensitivity = 36.0 cps / MBq

?HOT nodule



MNG


SSN
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10 cm
Uptake function = 5.81% Normal Range: (0.45 - 1.7)
Injected activity (scan time) = 75.0 MBq
System sensitivity = 36.0 cps / MBq

Treatment of Benign Thyroid Disease

Conditions

- Graves
- Toxic Nodules – high activity required (600MBq)
- MNG – high activity required (600MBq)

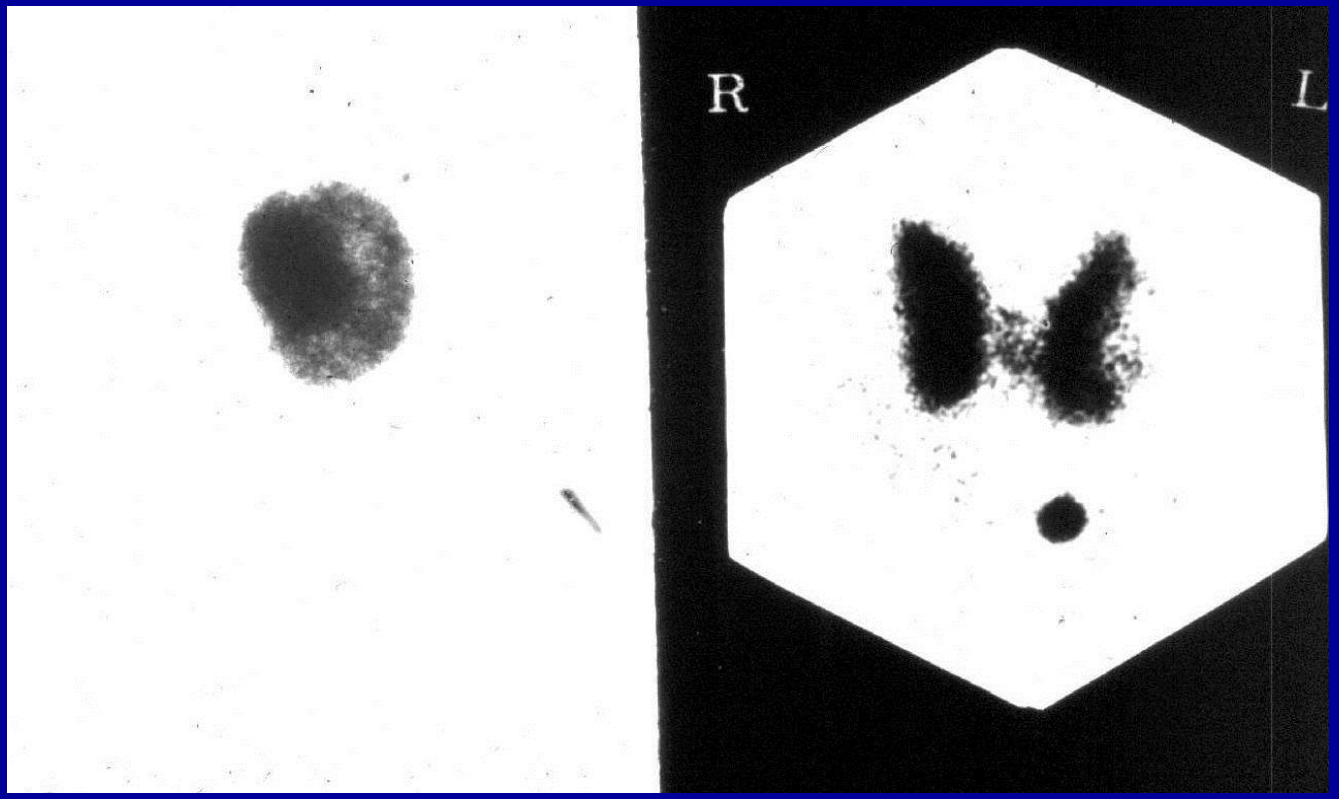
Treatment : ^{131}I

- Discuss with patient: treatment options e.g. surgery
- Informed consent – risk of hypothyroidism
- Radiation protection issues: exposing family members and public (time and distance!!)

  Restrictions last up to ≈ 3 weeks e.g. separate bed from partners, avoid pregnancy for 6 months

Lifelong follow up (regular thyroid blood tests)

Treating an Adenoma



Before I-131 After I-131

Image: courtesy Dr AJW Hilson

Thyroid Cancer

Types

- Papillary - 50 to 80%
- Follicular - 10 to 40%
- Hurtle Cell (follicular variant) - 5%
- Medullary (from ‘C’ cells , type of NET) - 10%
- Anaplastic (very aggressive) - 5 to 15%
- (Lymphoma)

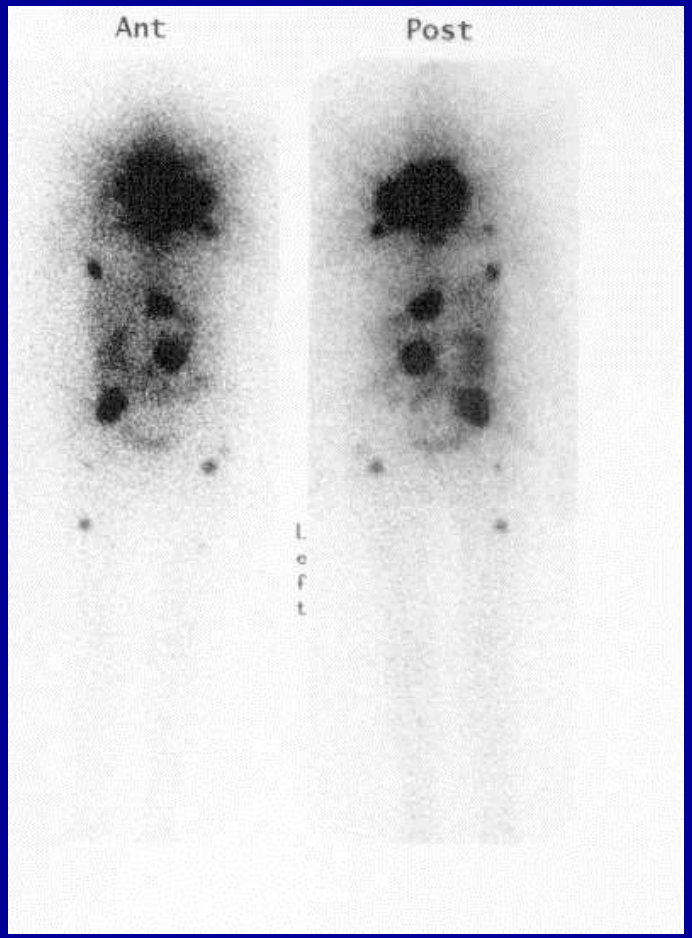
Thyroid cancer

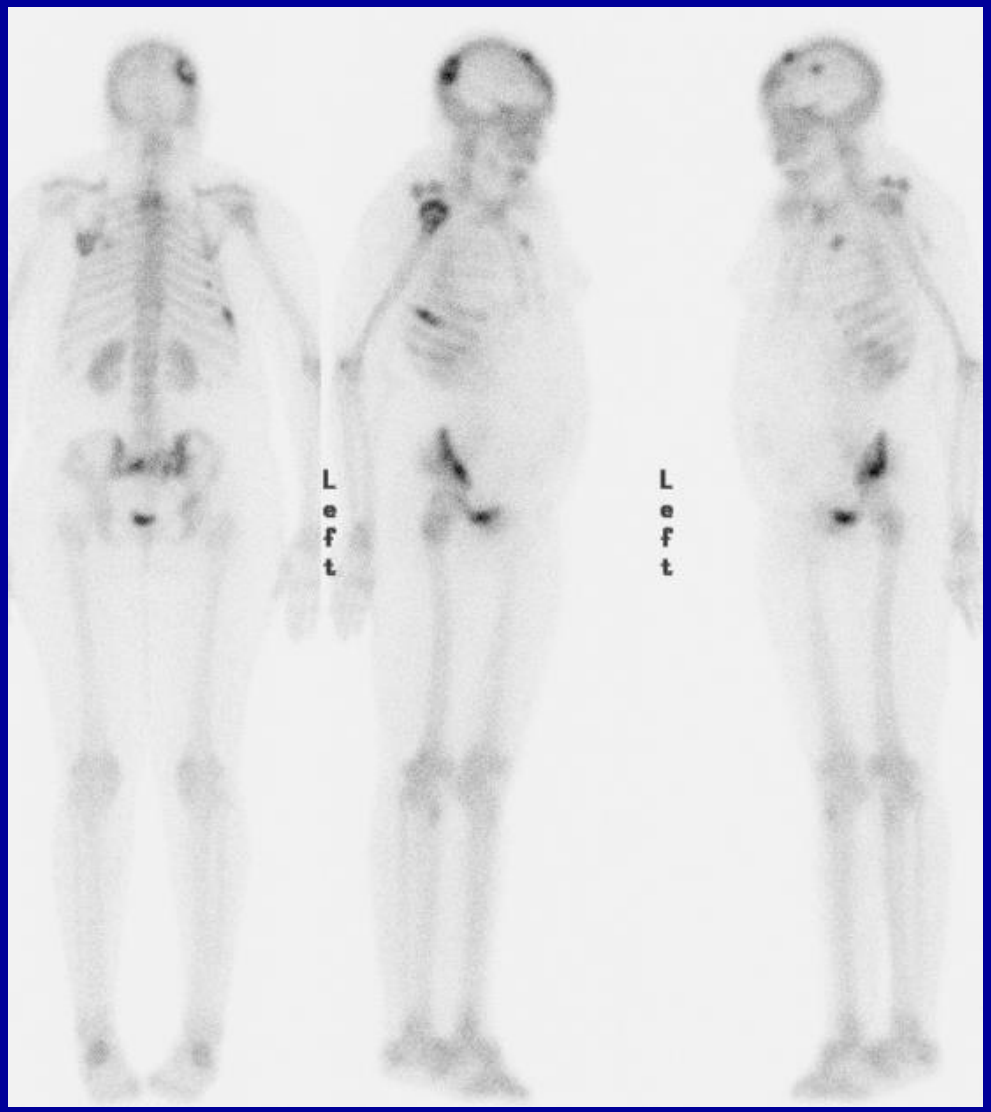
- Ablation Therapy: 6 weeks post thyroidectomy (papillary and follicular ca, T2 and above) give 3-5GBq ^{131}I ablation therapy
- Have to stop T4 for 4weeks, T3 for 10 days
- Can be given with TRH, rTSH (£1000)
- Scan at 48-72 hours

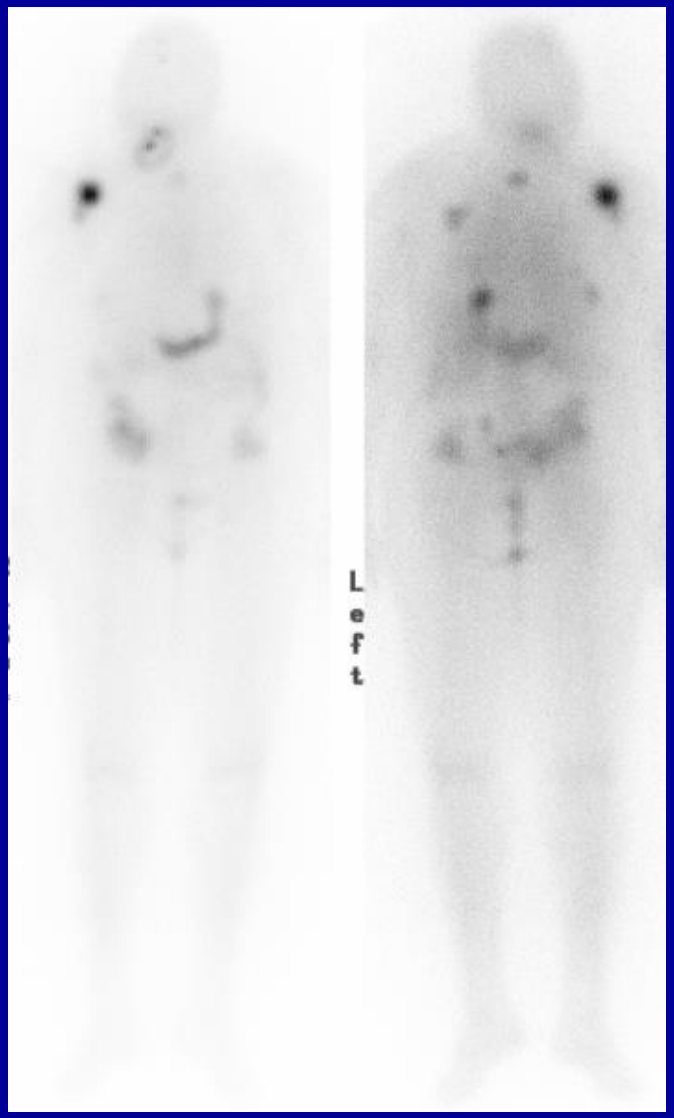
- Repeat therapies till thyroid bed and any mets disappear 3-6 monthly intervals
- Post treatment image is used to stage patient.
- If uptake is low, consider 'tracer' dose (^{123}I prior to next therapy – 400MBq)

NB: has NO role in anaplastic ca or lymphoma

Multiple Metastases on 1st Dose ^{131}I





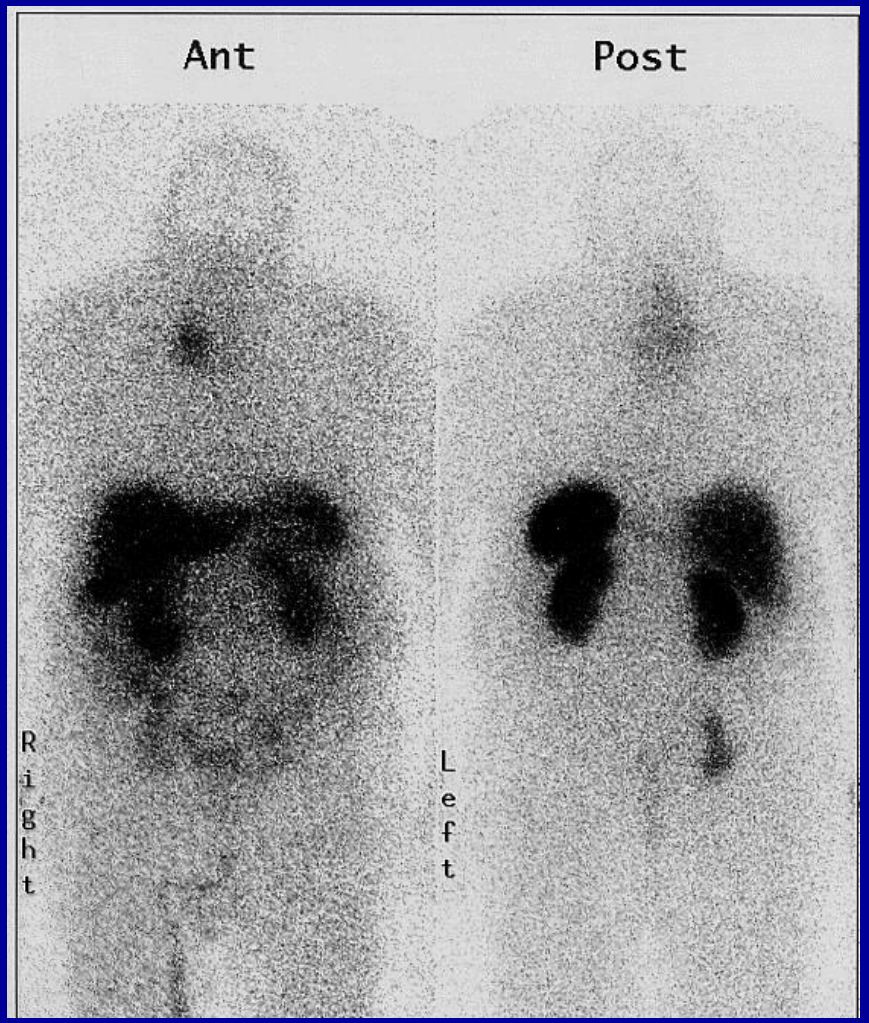


Thyroid Ca: Multiple Metastases

Other Tracers Used for Detecting Ca Thyroid (if Iodine Scan Negative)

- ^{99m} Tc MIBI or tetrafosmin
  useful with SPECT of neck
- ^{18}F FDG
- ^{111}In octreotide
- ^{99m}TcDMSA(V) – ‘pentavalent DMSA’
- ^{201}Tl

^{111}In Octreotide in papillary Ca Thyroid



F-18 FDG in thyroid cancer

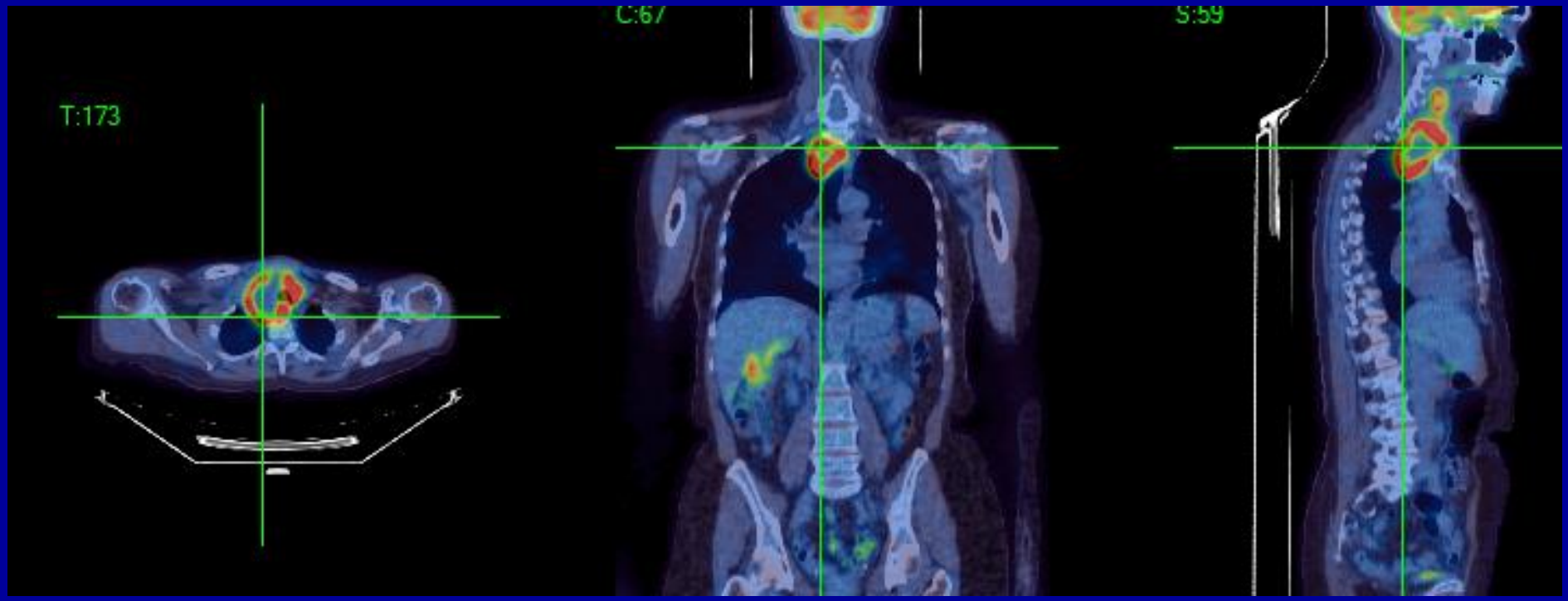


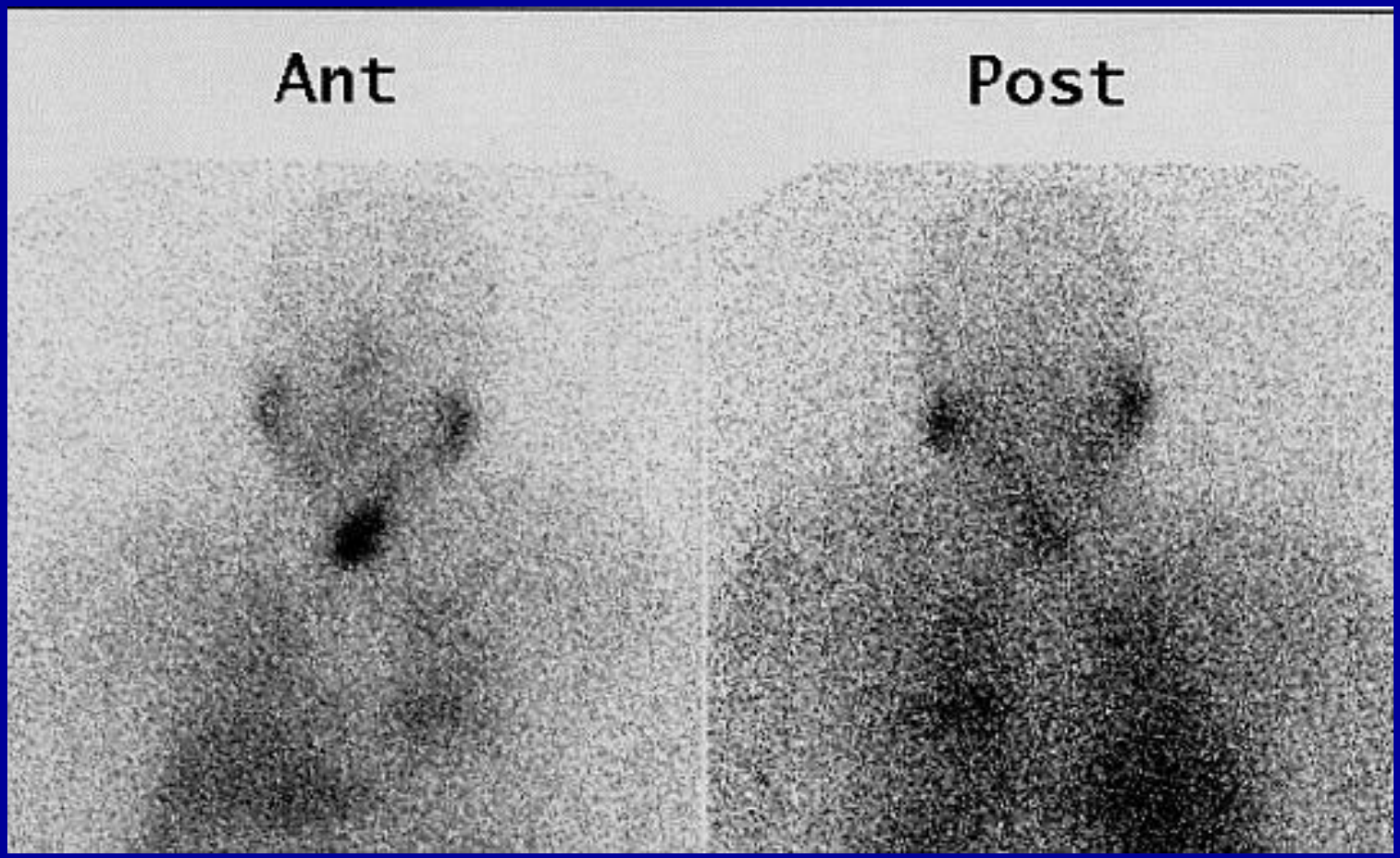
Image: Atlas of Clinical PET, 2006, Eds Barrington et al

Imaging Medullary Carcinoma of the Thyroid (MCT)

- Tc-99m DMSA (V)
- ^{123}I mIBG - Therapy version available with ^{131}I mIBG
- ^{111}In Octreotide - Therapy version available with ^{90}Y Octreotide
- ^{18}F- FDG PET/CT

Mainly used for staging

^{123}I-MIBG in MCT



Parathyroid Glands : Role of Nuclear Medicine

- Diagnosis
  - Renal patients: primary vs secondary
- Localisation
  - Assist surgeon in reducing surgical operating times
  - May help reduce morbidity
  - Aids use of minimally invasive techniques
- ‘Second look’ !
  - Missed adenoma
  - Ectopic adenoma

What Imaging Methods are Available ?

Ultrasound

- Readily available
- Needs skilled operator
- Local (neck) imaging only
- No radiation dose
- Other thyroid pathology may be found

Nuclear Medicine

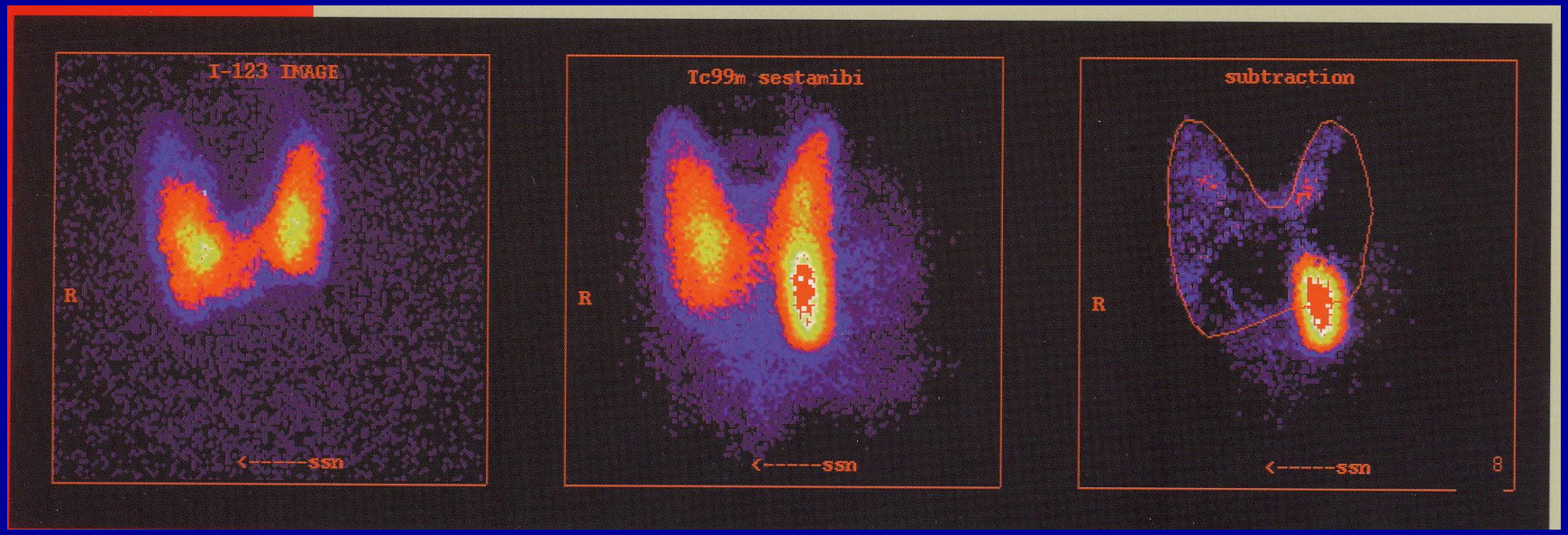
- May not be so readily available (in UK)
- Skilled reader required
- Regional : whole chest easily surveyed
- Less affected by other thyroid pathology
- Small radiation dose – 4mSv

Nuclear Medicine

- Exploits functional aspects of tumour
- Ideally need an agent taken up only by parathyroids but no such agent currently available
- Some agents only have uptake in thyroid and others in both thyroid and parathyroid
- Others have initial uptake in both organs but “washout” of normal thyroid

Subtraction technique

- Inject agent: taken up by thyroid and parathyroid (Tl-201 or Tc-99m MIBI/TF)
- Wait 30 minutes, then scan neck
- Keep patient under camera, inject agent taken up by only thyroid (^{123}I, ^{99m}Tc pertechnetate)
- Wait 15 minutes, then rescan
- Subtract images



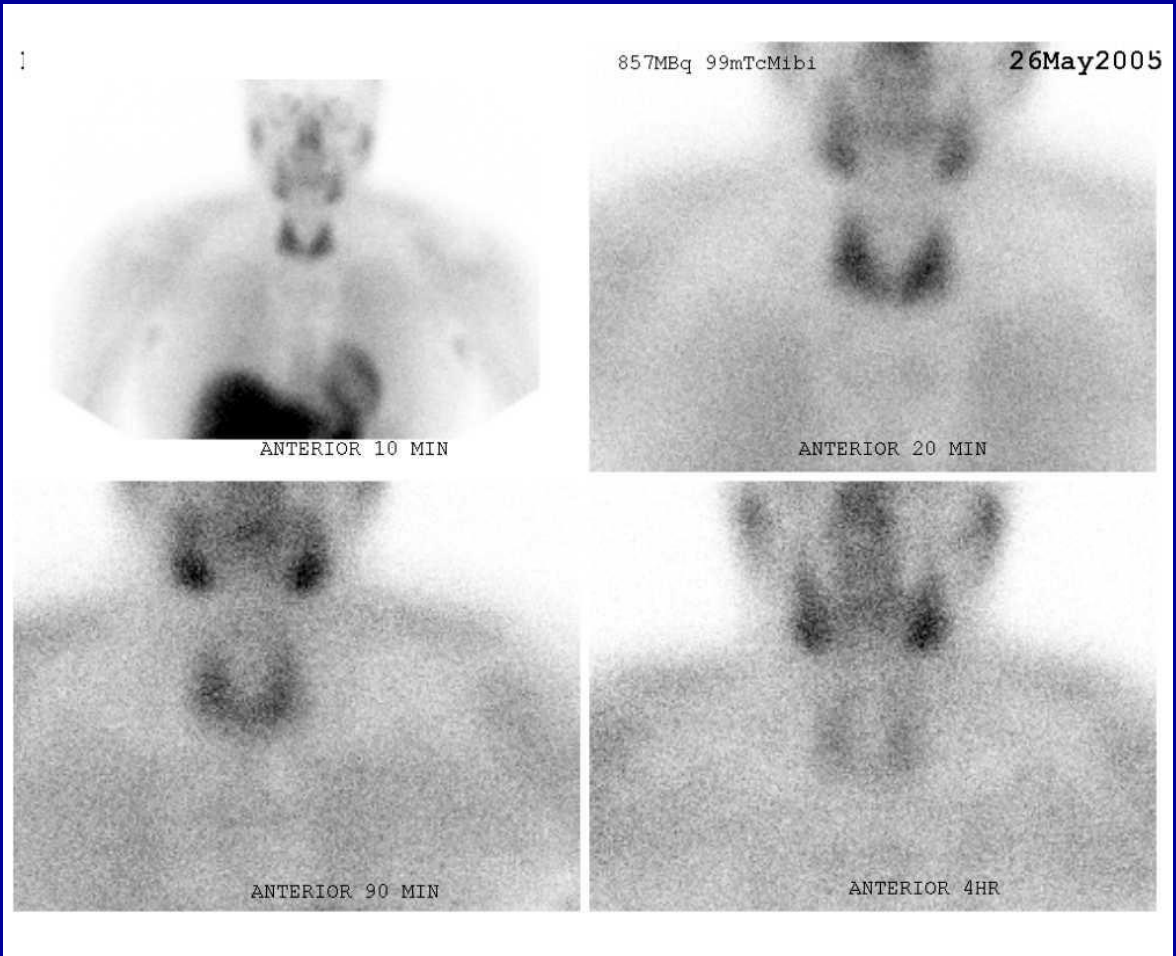
Washout technique

- Inject agent which washes out of thyroid but not parathyroid (^{99m} Tc MIBI)
- Wait 15 minutes
- Perform planar and/or SPECT images
- Wait a further 2 hours
- Repeat planar and/or SPECT images
- Review images.

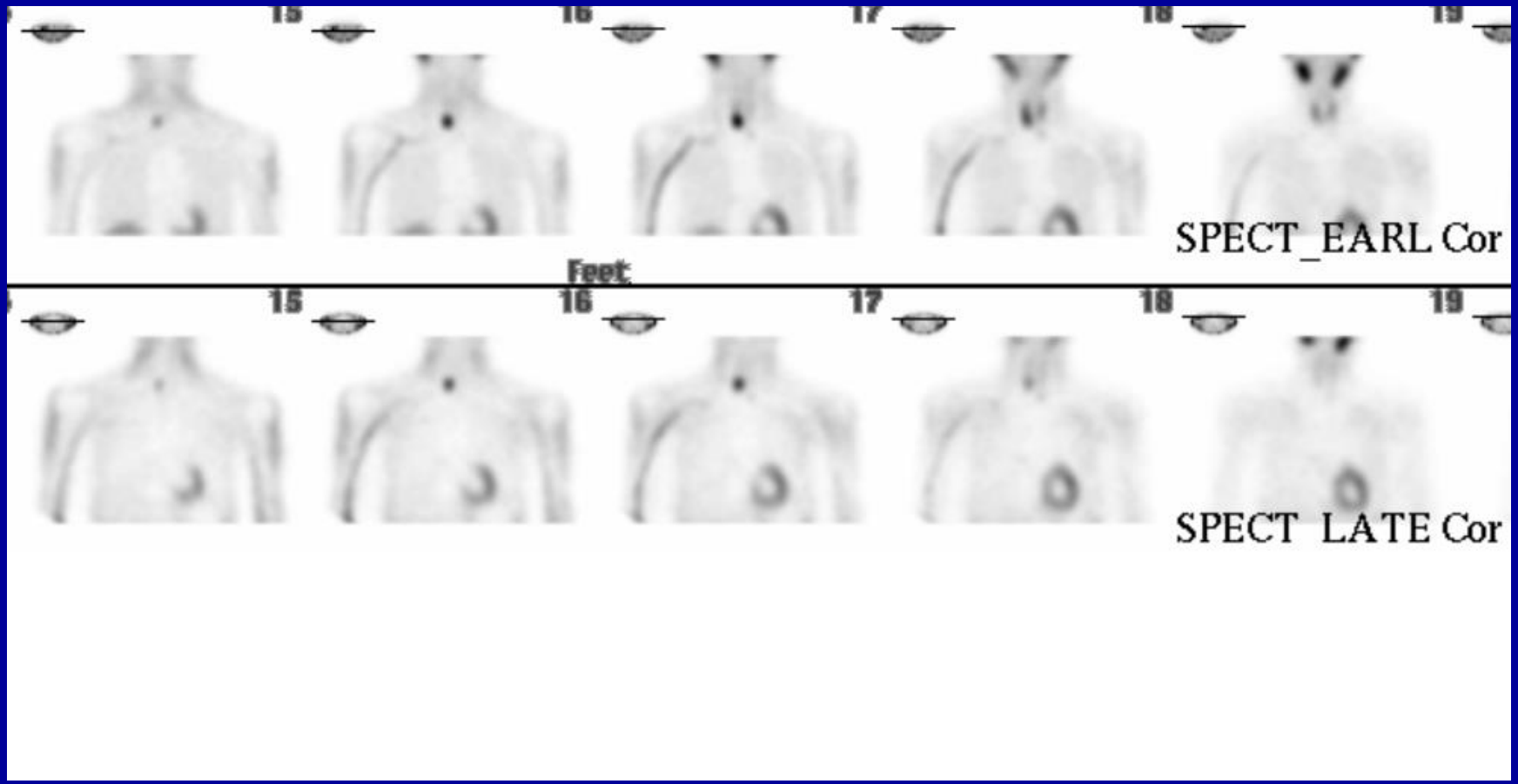
Normal (Negative) Washout Scan

Early

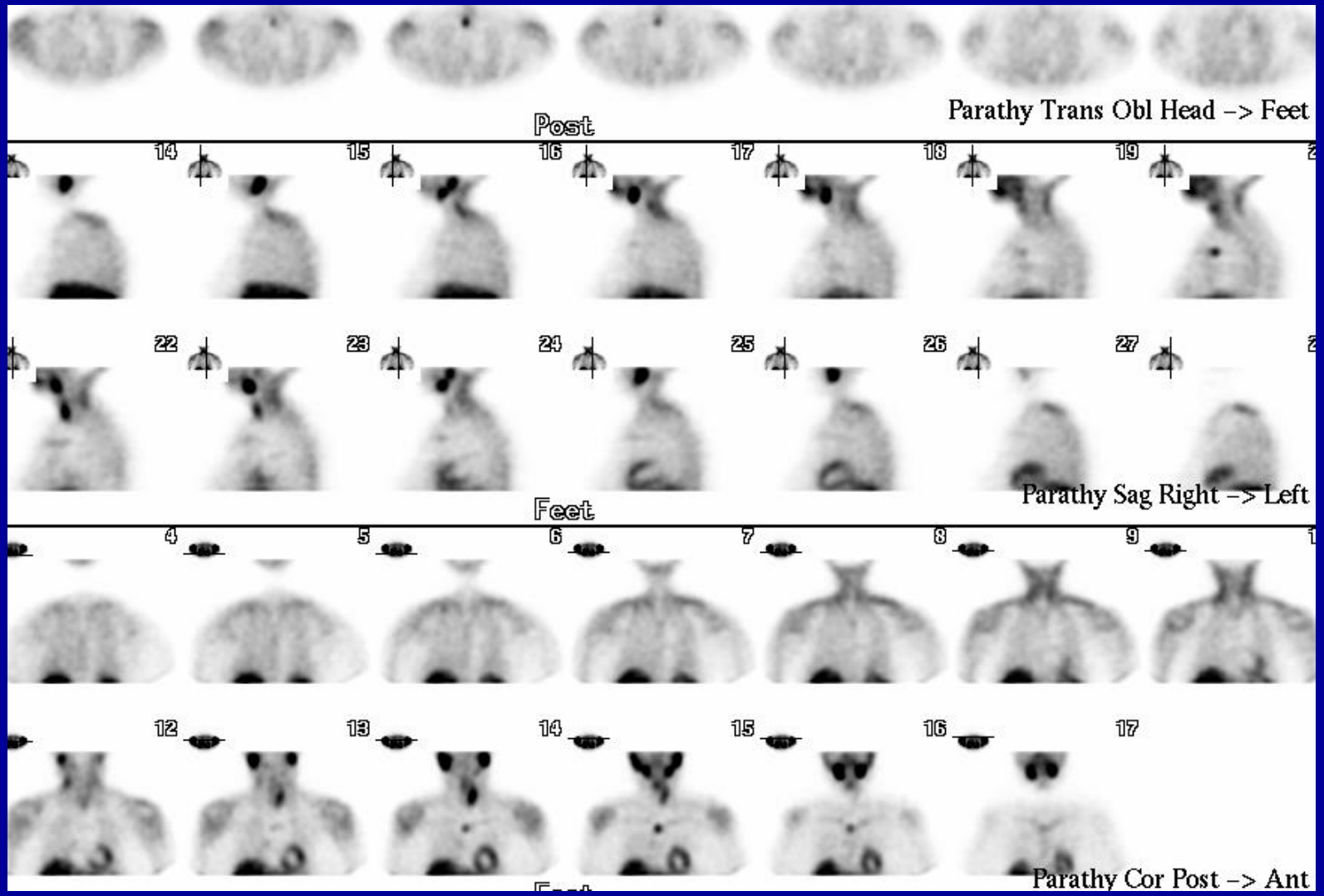
Late



Parathyroid Adenoma

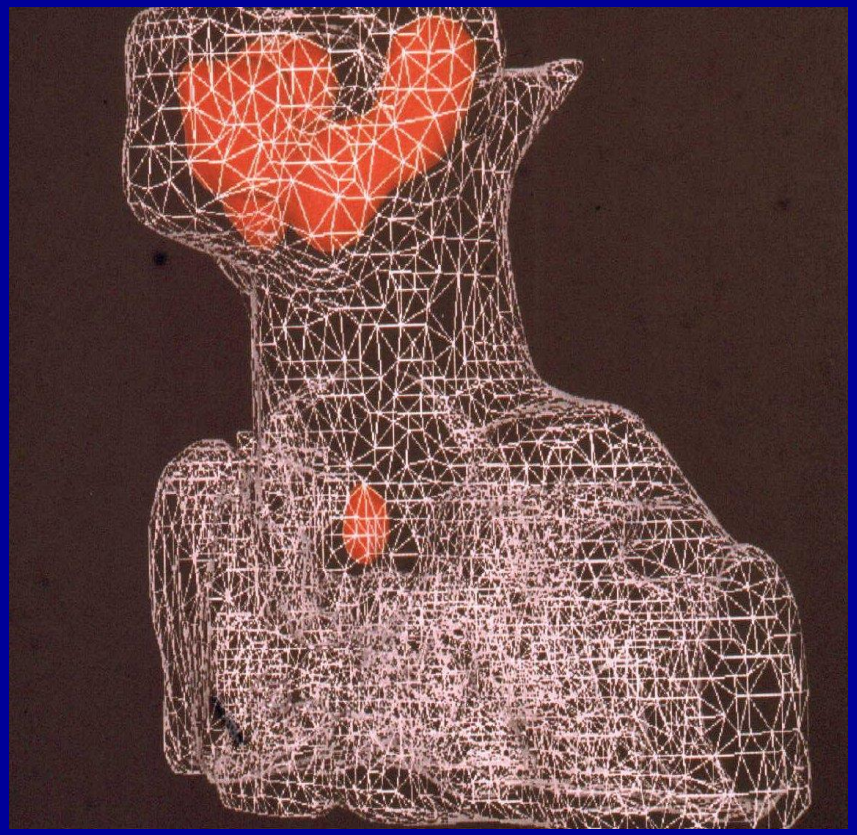


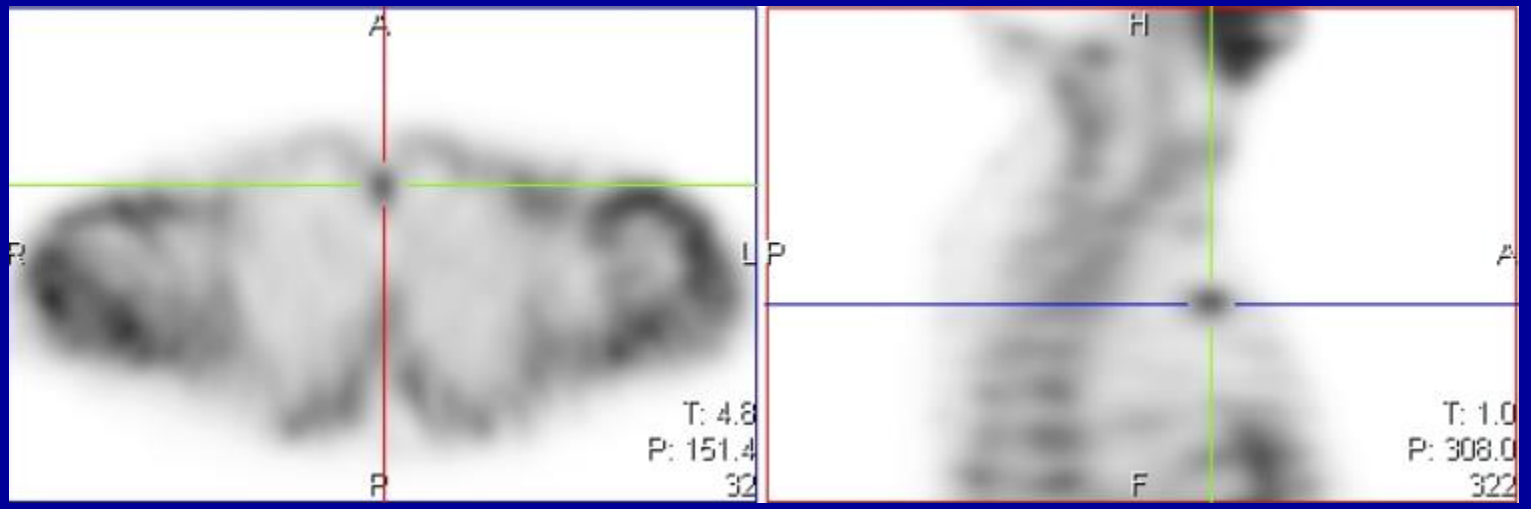
Ectopic Parathyroid Adenoma



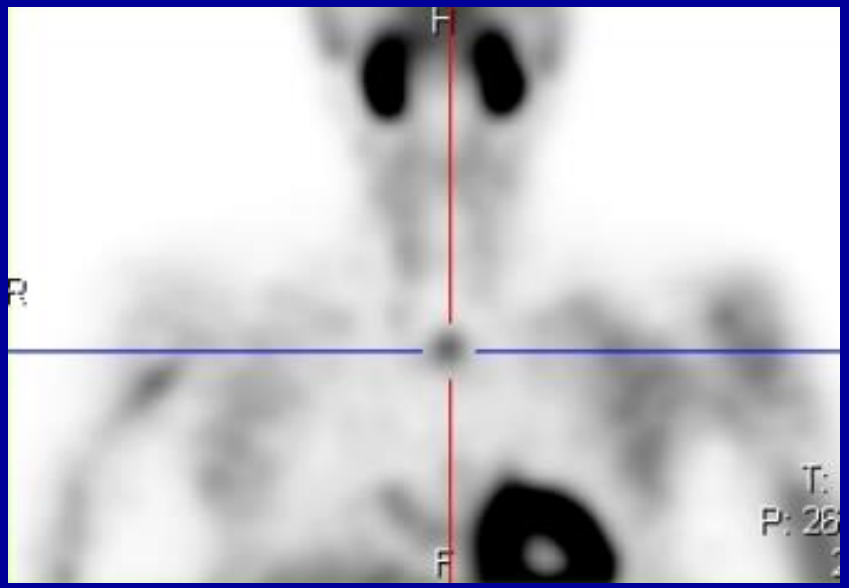
Advantages of SPECT in parathyroid imaging

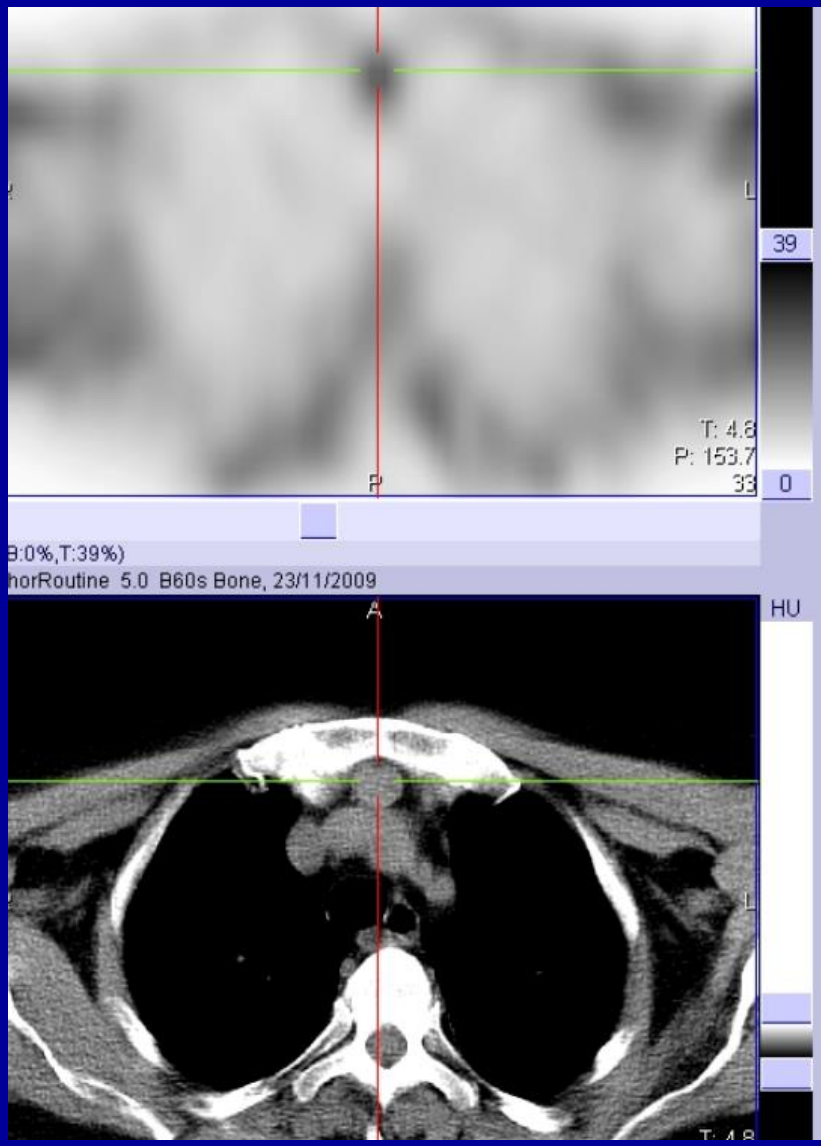
- Allows increased contrast (fewer overlapping structures)
- Better localisation
- Should find lesions 7mm and above
- Interactive display possible





SPECT alone

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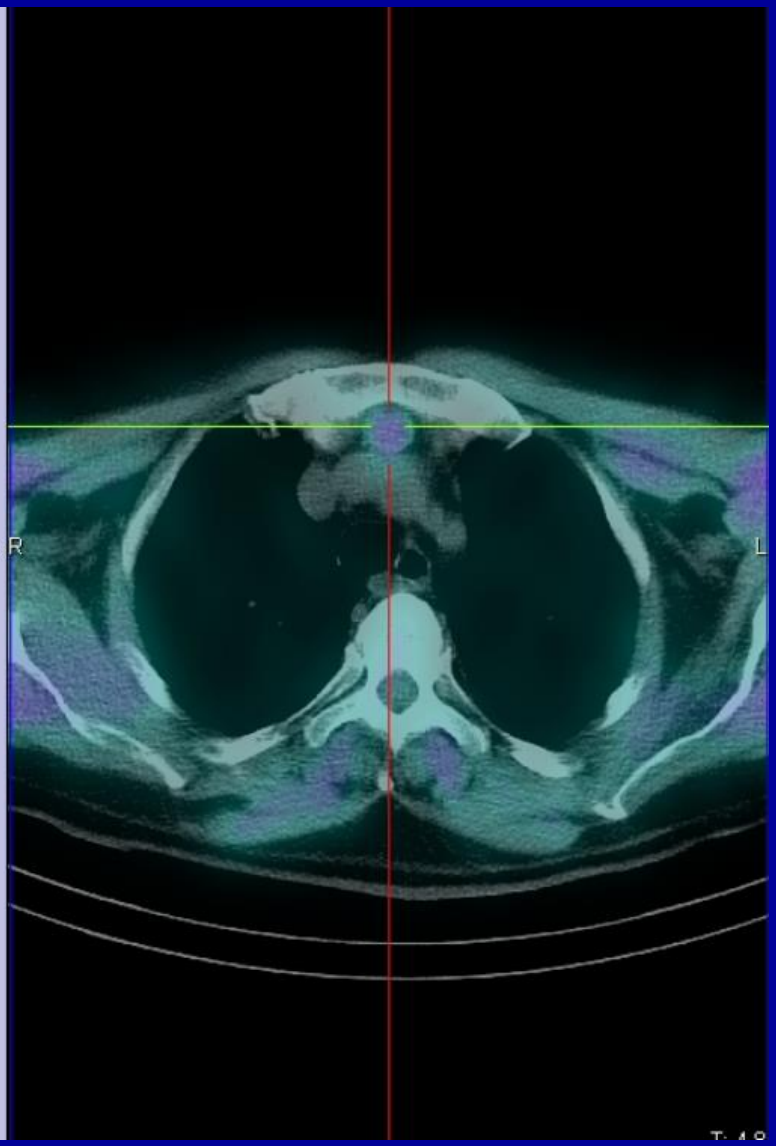
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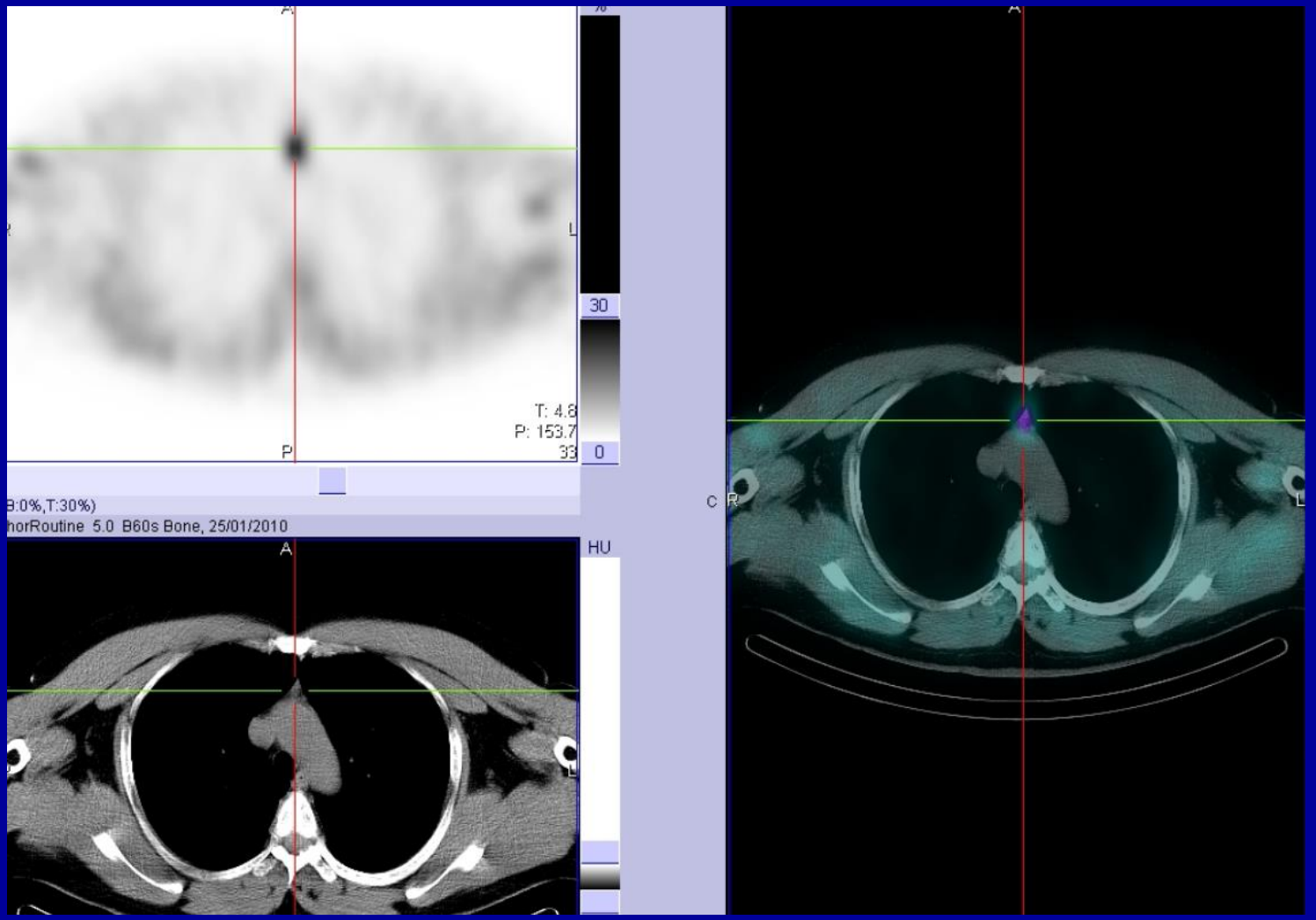
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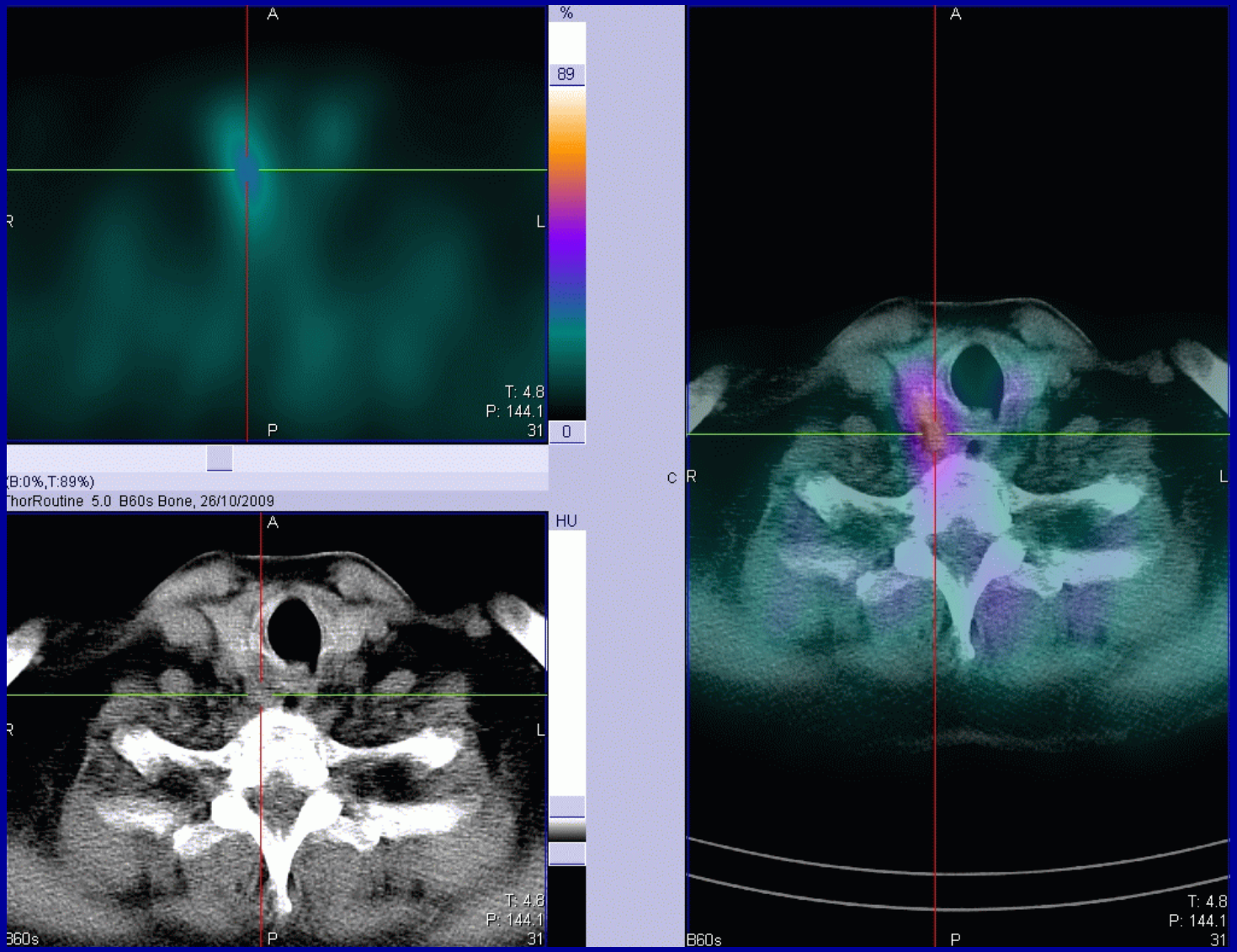
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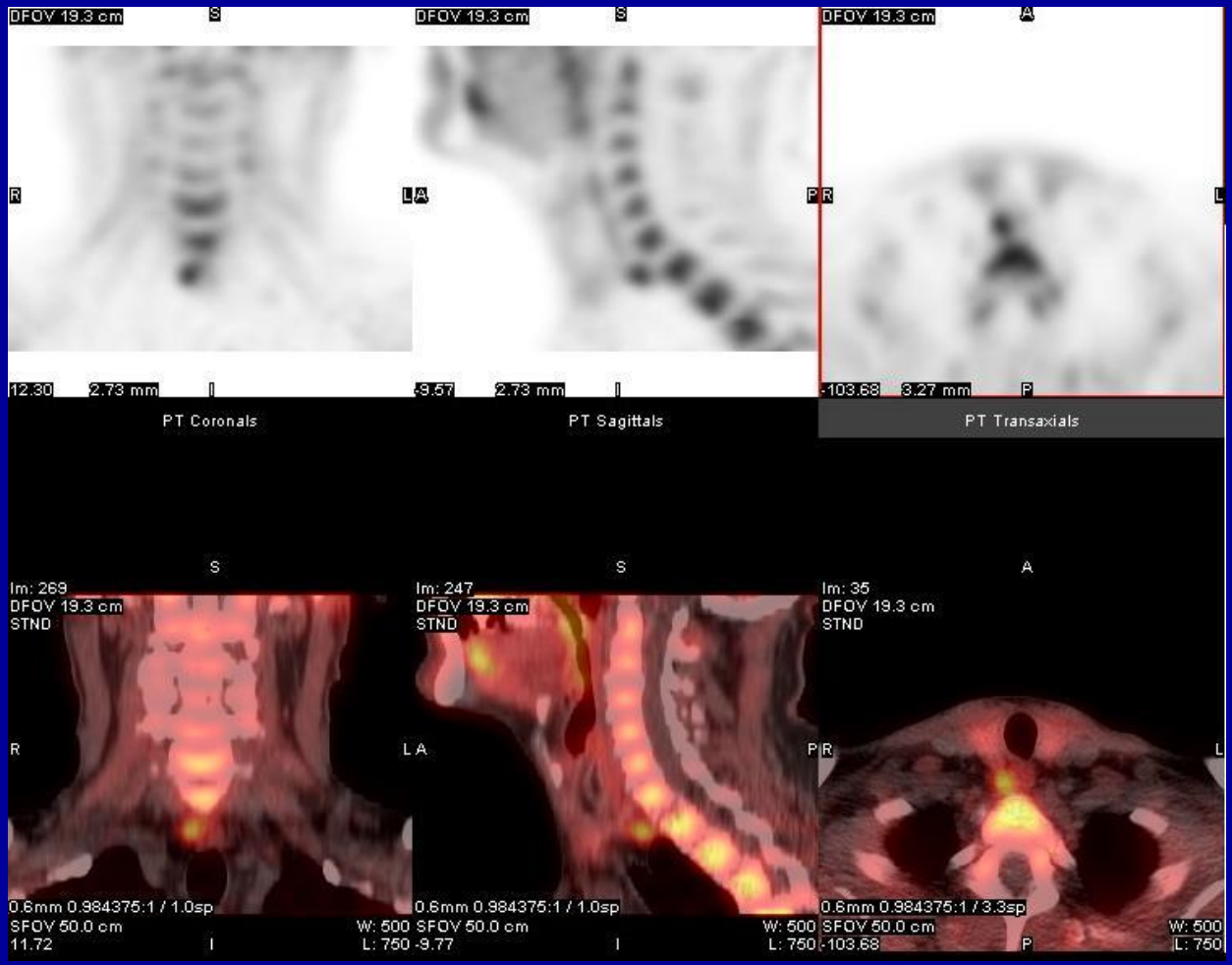
C-11 methionine in hyperparathyroid adenoma



Other uses of ^{99m}Tc MIBI

Peri-Operative Use

- Inject 50MBq of ^{99m}Tc MIBI (10% of usual activity)
- Localise uptake with gamma probe in theatre at time of surgery to localise adenoma
- Surgery can be pre-planned e.g. just one side explored
- Scar size and surgery time are reduced
- Ugar et al Ankara (2006) showed significantly improved surgical localisation using probe in 35 patients vs usual imaging protocol then surgery

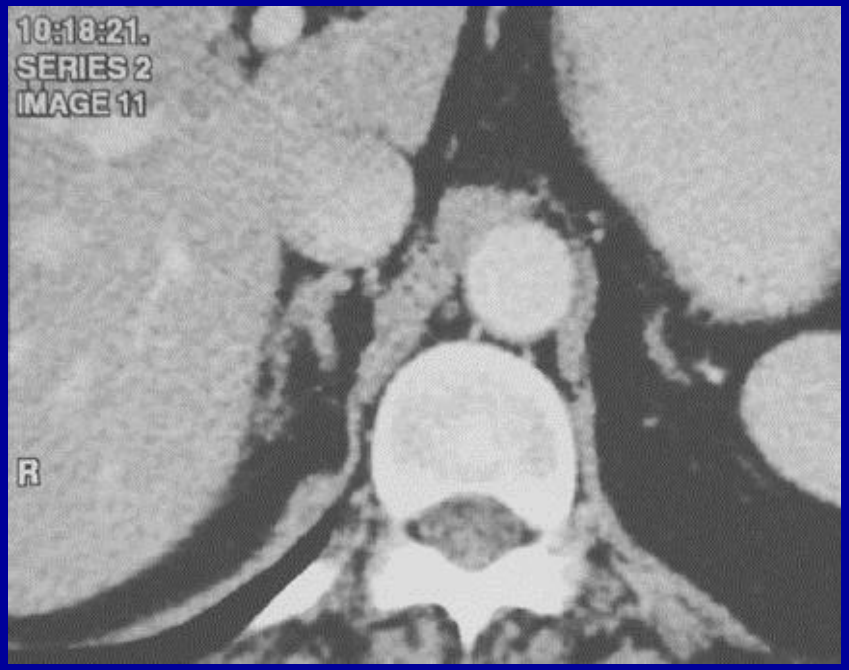
Adrenal Imaging

- Adrenal gland lies in retroperitoneal space
  - Right – above right kidney
  - Left – superomedial to left kidney
- Gland is divided into two anatomical and functional regions:

  Cortex – produces hormones derived from cholesterol (aldosterone, steroids and androgens)

  Medulla – produces catecholamines (adrenaline and noradrenaline). Sympathetic control

Adrenal Glands on CT



RIGHT

LEFT

Imaging of Adrenal Gland

Adrenal Cortex

- Nuclear medicine very rarely used in imaging of the adrenal cortex.
- Biochemical tests e.g. serum cortisol levels, together with anatomical imaging (CT or MRI) usually used.
- Tracers – limited availability

  ^{131} I-19 Iodocholesterol

  (^{75}Se-6-beta-selenomethyl –norcholesterol)

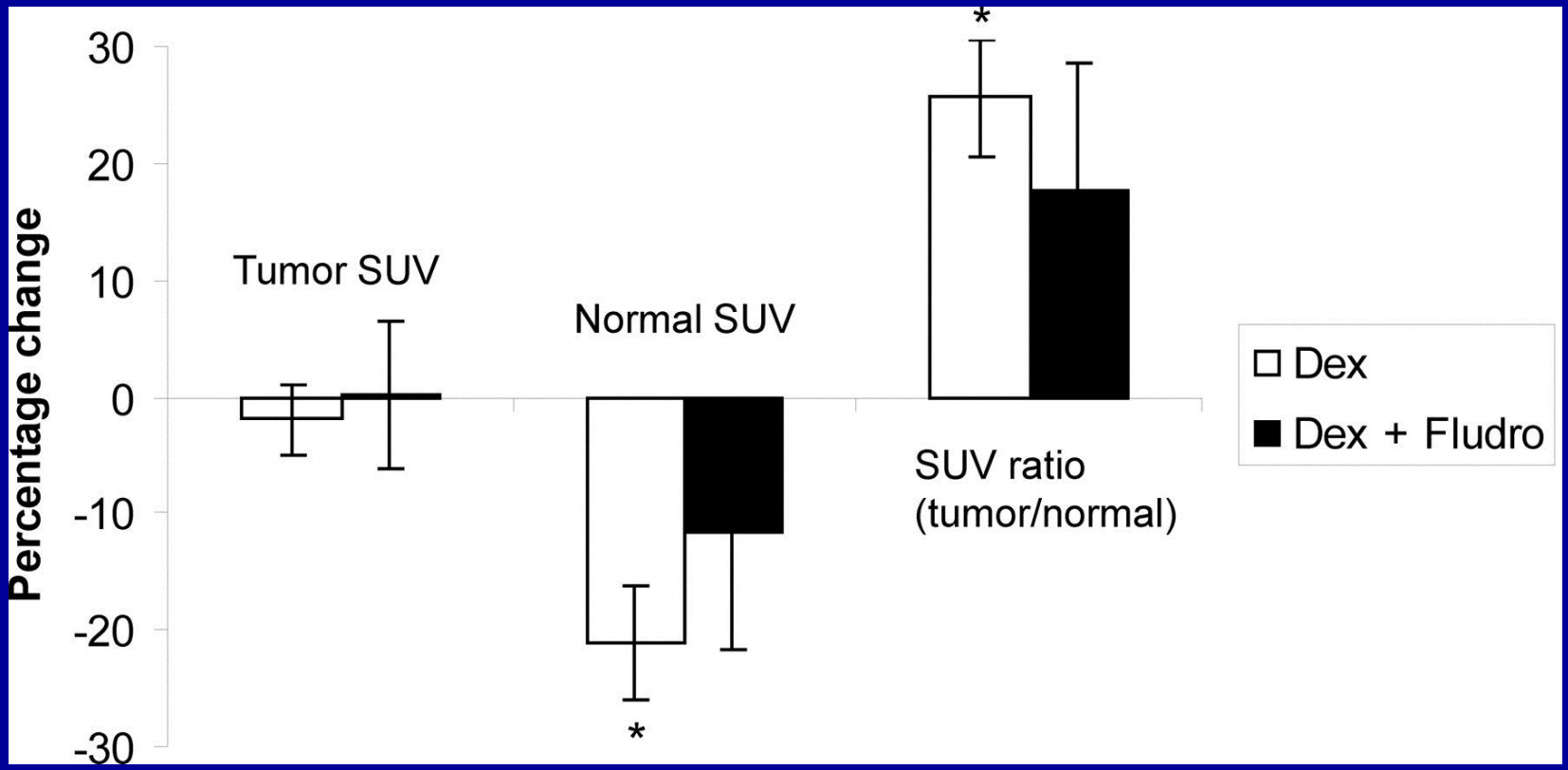
  ^{11}C metomidate

  Incorporated into synthesis pathway
- Imaged at 5 days
- High(ish) dose to patient 6mSv

C-11 Metomidate

- Burton et al JCEM 2012
- 39 patients studied some with Conn's some with incidentalomas
- Dexamethasone +/- fludrocortisone 3 days before C-11 metomidate increased TBR
- SUVmax of tumour 22, normal adrenal 14
- Incidentalomas same as normal adrenal or less

Effect of pretreatment on SUV. Mean ± sem values are shown in six subjects.



Burton T J et al. JCEM 2012;97:100-109

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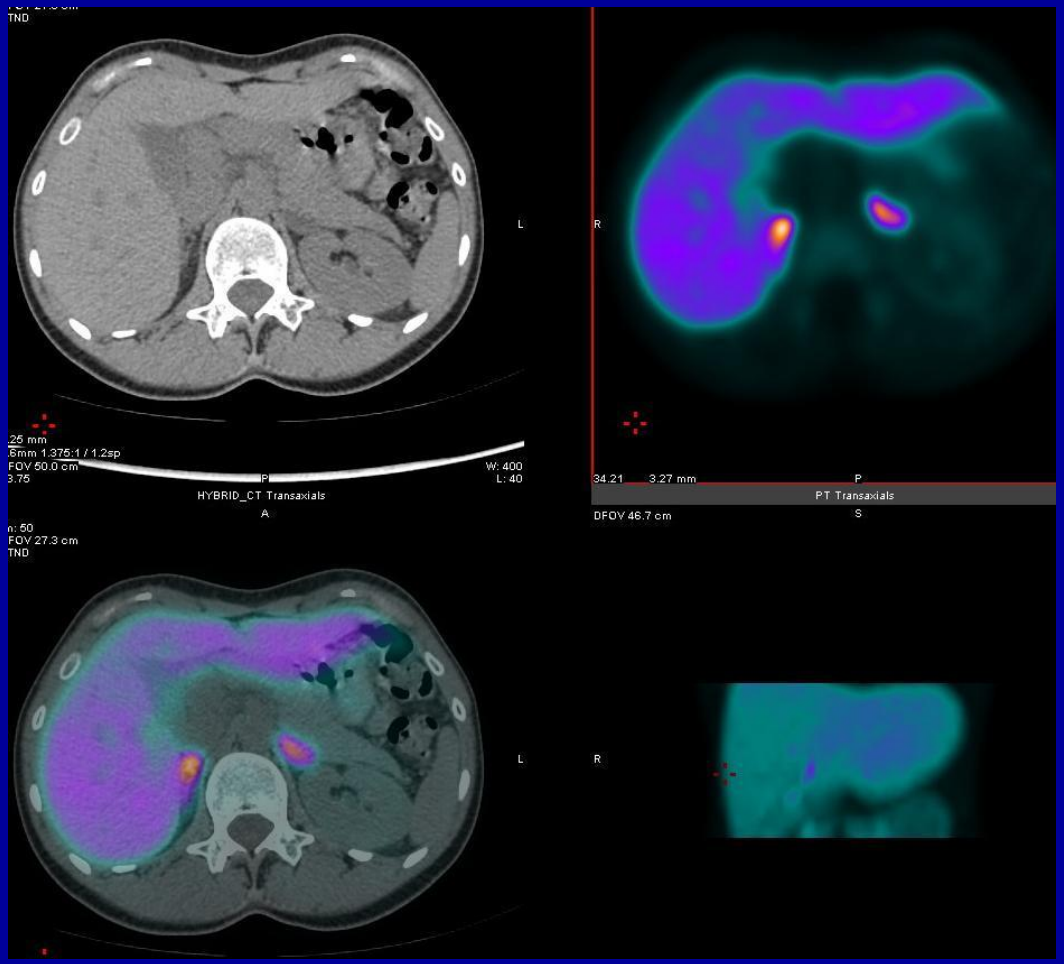
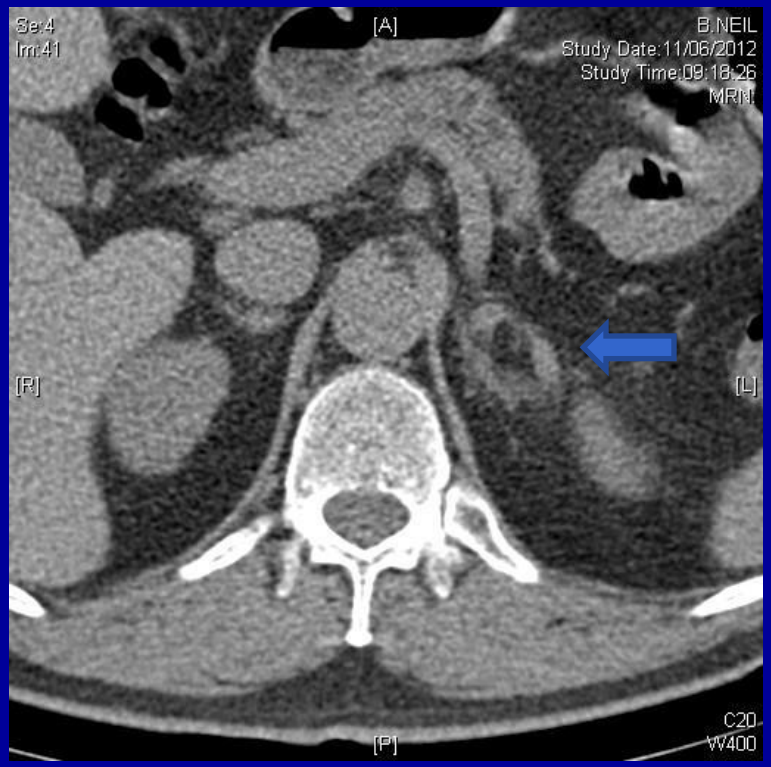
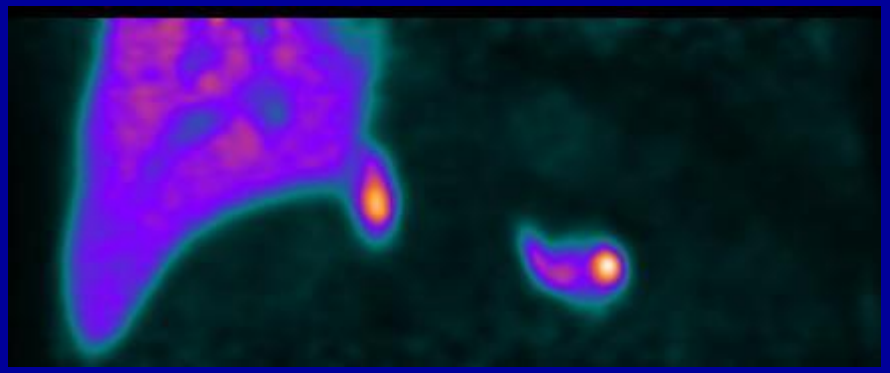
Normal uptake

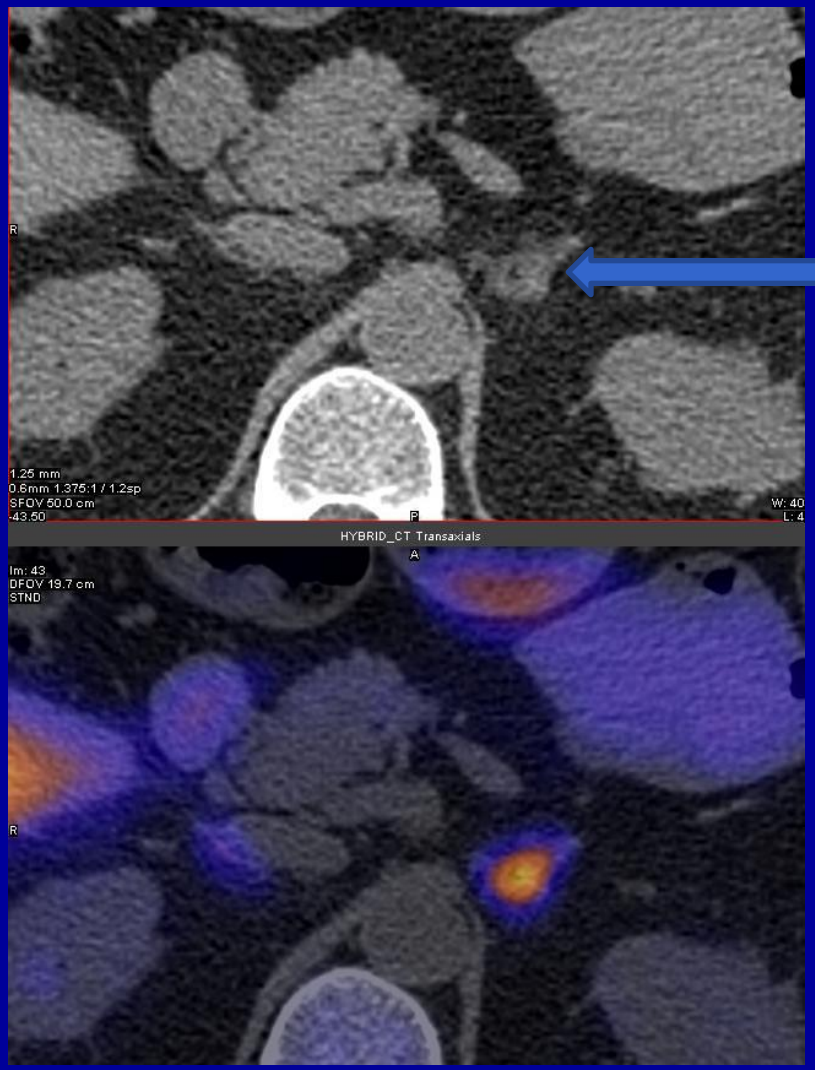


Conn’s tumour





Small tumour



6mm tumour

Imaging of the Adrenal Gland

Adrenal Medulla

- Indication: localisation of phaeochromocytoma (should have +ve catecholamine in urine)
- Tracer: ^{123}I MIBG
- Method of uptake: amine uptake transporter mechanism present in neuroectodermal tissue
- May need to stop drugs which reduce uptake of ^{123}I MIBG - reserpine, cocaine(!) and labetolol and some anti-depressants

- Give thyroid blockade: e.g. potassium iodide 60mg bd for 3 days. Start at least 1hr prior to injection

The Scan

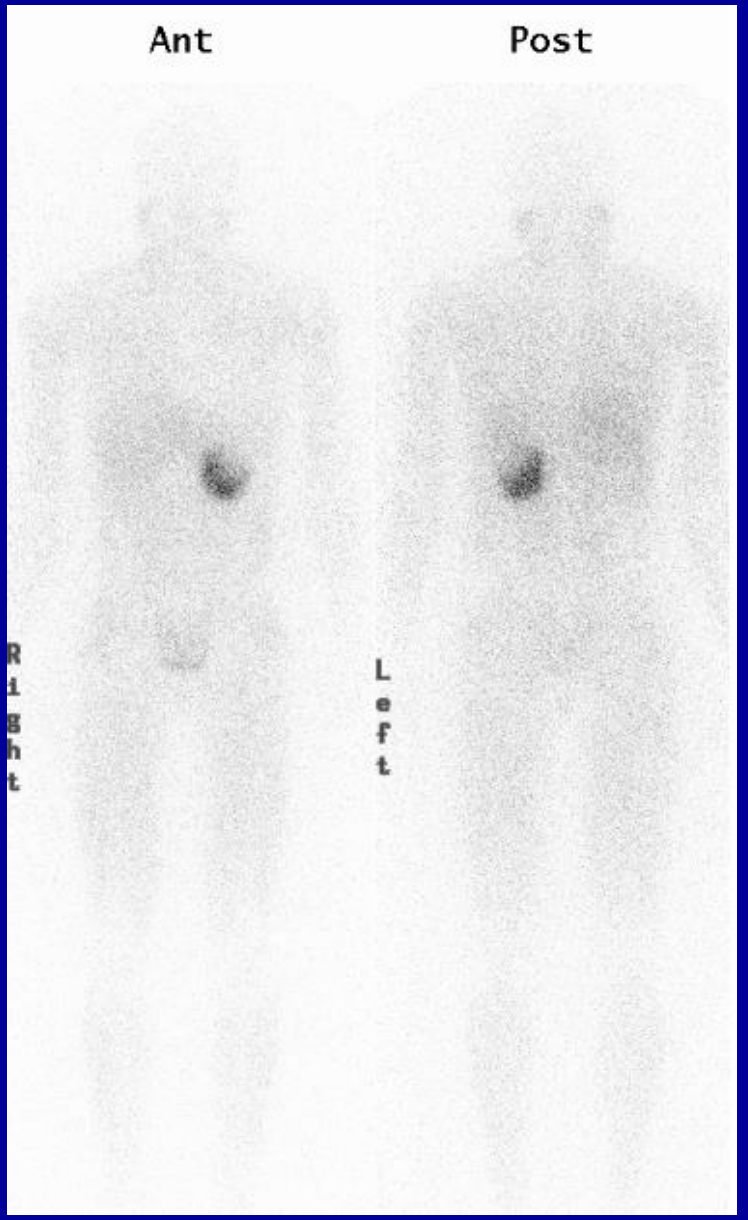
- Inject up to 400MBq ^{123}I MIBG
- Image at 24 hrs
- Parameters: LEHR
- Planar
- SPECT images e.g 2 headed camera
  60 projections at 3°
  20-30 secs per projection

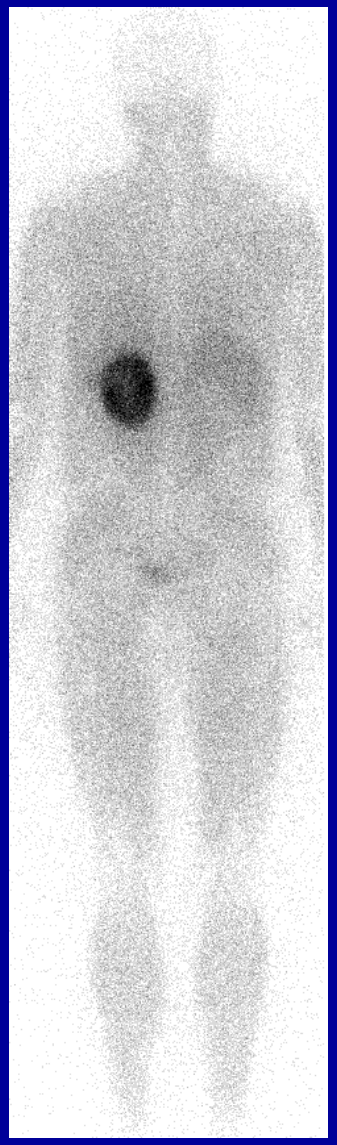
Phaeochromocytoma

- Neoplasm arising from adrenal medulla
- Triad (paroxysmal headache, ↑BP, palpitations)

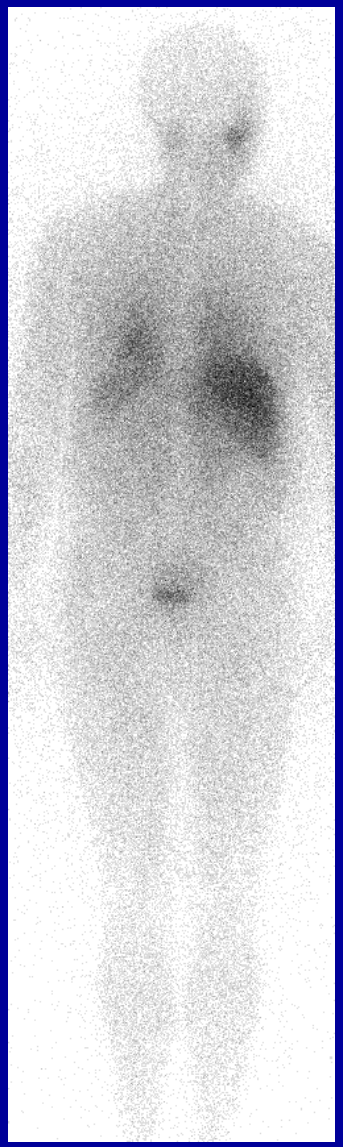
‘10%’

- 10% malignant
- 10% bilateral
- 10% ectopic
- 10% found in children
- 10% associated with syndrome
- 10% neg MIBG scan

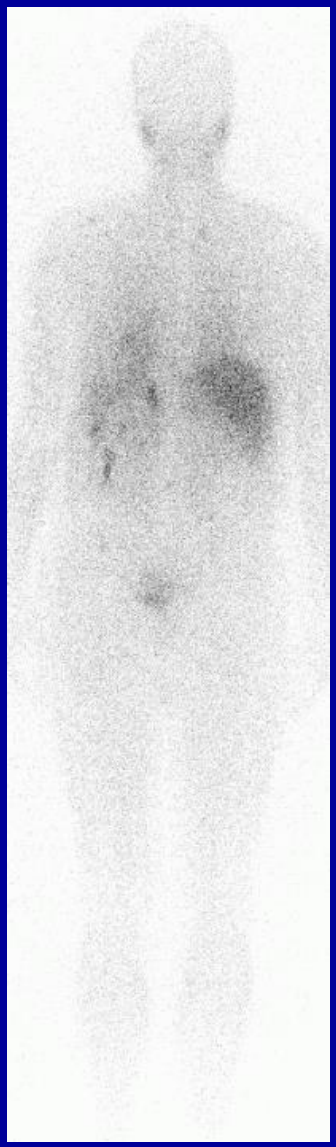




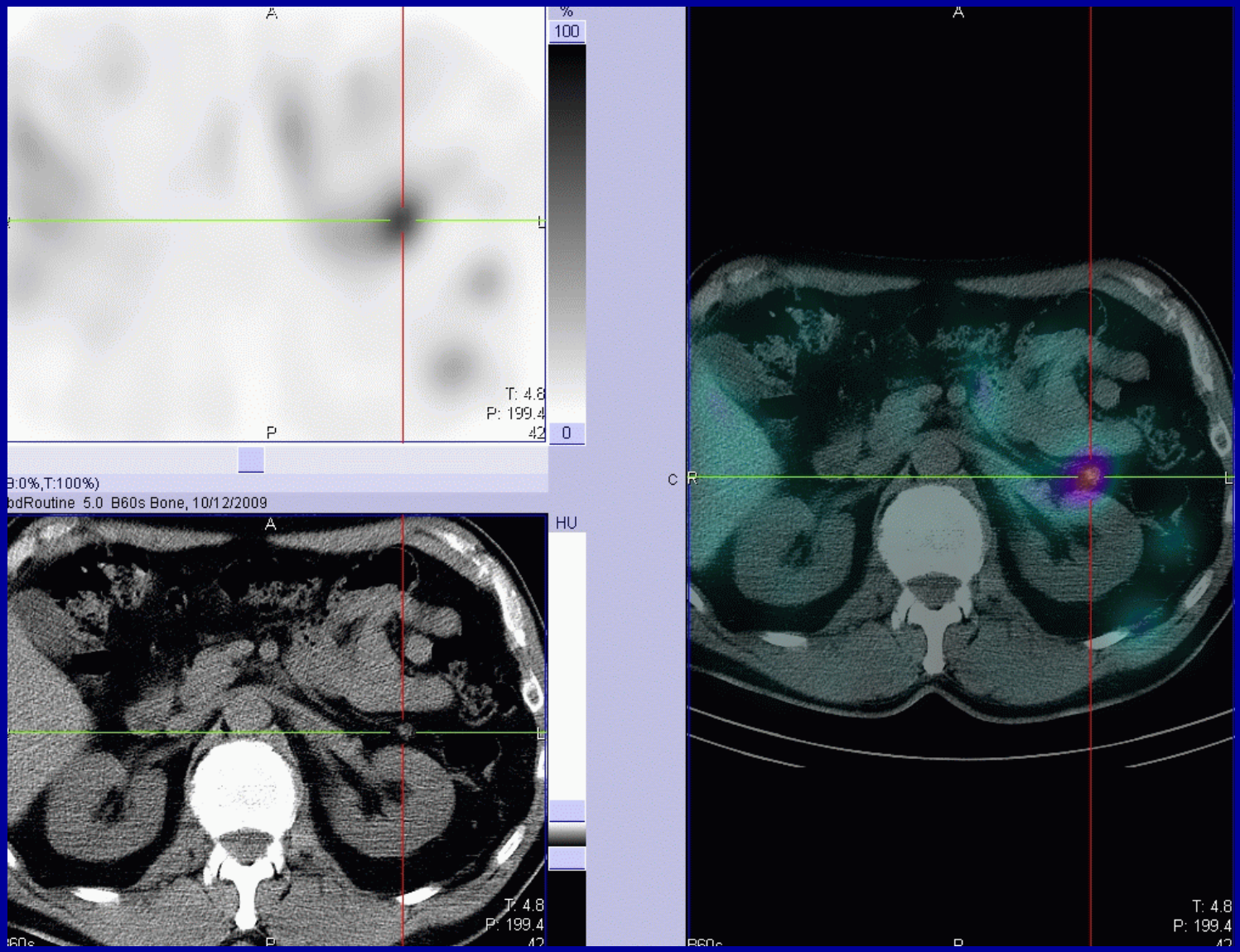
Pre Surgery



Post Surgery



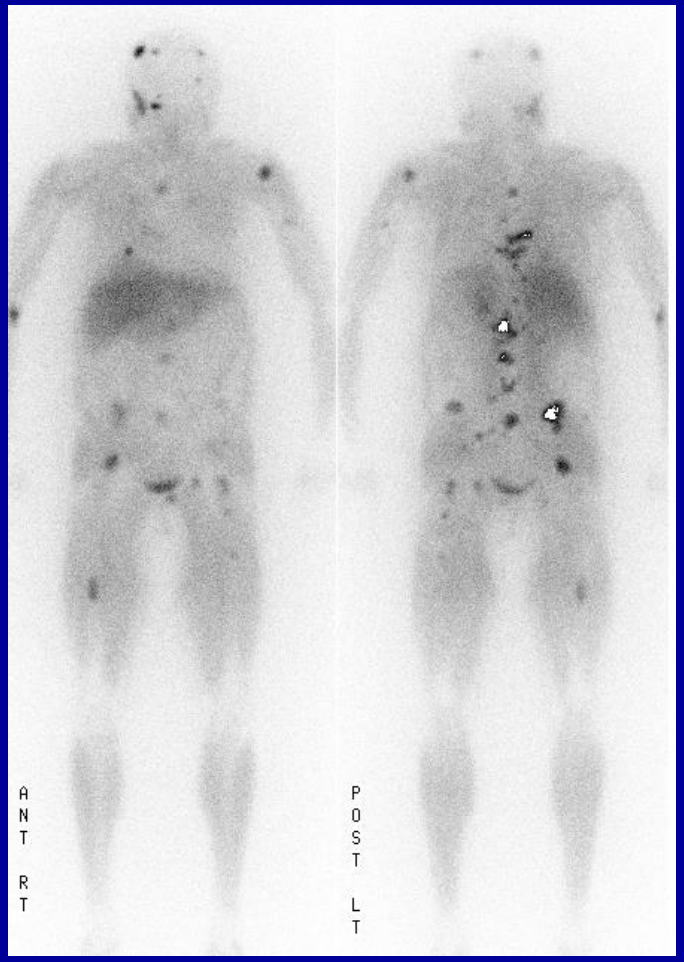
Recurrence


A
%
100
T: 4.8
P: 199.4
42
P
0
B:0%,T:100%)
bdRoutine 5.0 B60s Bone, 10/12/2009
A
HU
T: 4.8
P: 199.4
42
P
C
A
R
L
T: 4.8
P: 199.4
42
P

Malignant Metastatic Phaeochromocytoma

Treatment

High dose (5GBq) x3 ^{131}I-MIBG if ^{123}IMIBG scan is positive



C-11 methionine

- Used to identify tumours
- Uptake related to cell growth
- In brain only malignant cells grow and divide
- So high TBR with normal brain c/w F-18 FDG
- Used to image brain tumours
- Developed use in post surgery recurrence
- Similar role in pituitary tumour

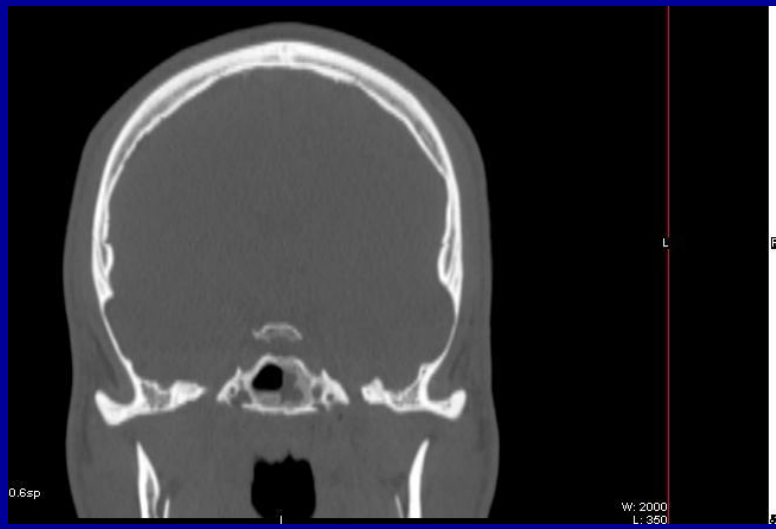
Pituitary tumours

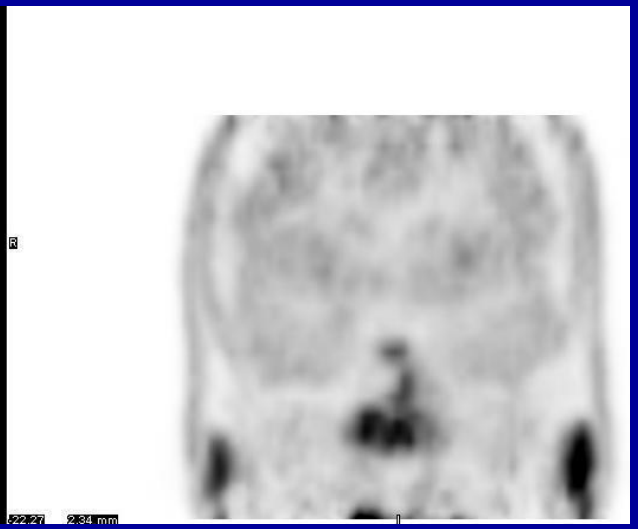
- Either productive
  - TSH
  - ACTH
  - GH
- Non productive tends to lead to syndromes of reduced uptake as replaces working cells
- Normal treatment surgery trans-sphenoidal
- However if symptoms persist ?residual

Finding recurrent tumour

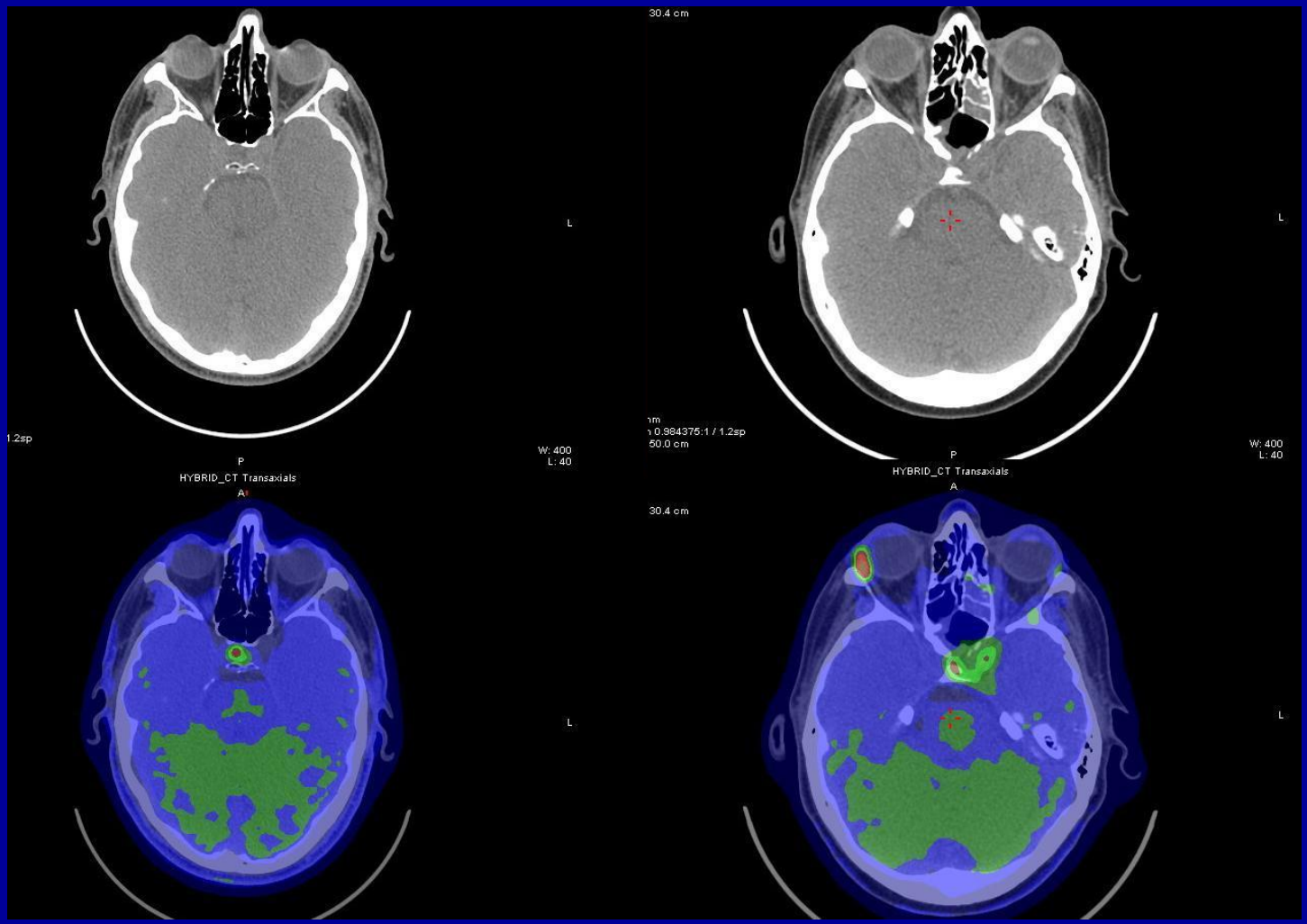
- Normally use MRI
- Look for hypointense on T1 and hyperintense on T2
- Enhances on Gd
- However changes can be non-specific

How may C-11 methionine help?

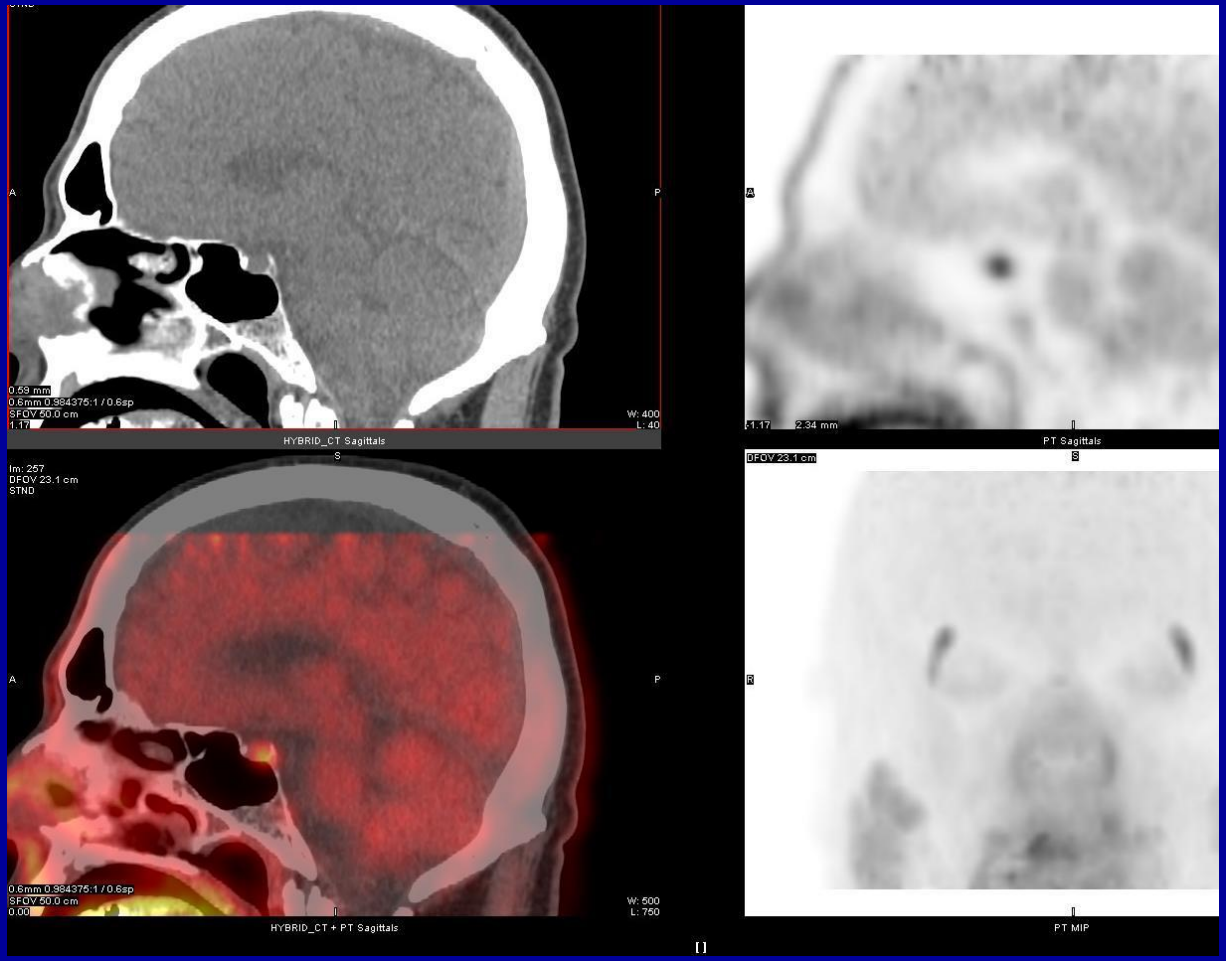




Different size recurrent tumours



Localize in pit fossa



C-11 methionine

- Tang et al EJNMMI Brussels 2005
- 33 patients post surgery with /recurrent tumour
- 24 functional
- 30/33 found with MET PET
- 19/33 found with MRI