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
Thyroid Hormones

Negative Feedback System
Thyroid Gland

Thyroid follicle

C cells secrete calcitonin.

Follicular cells secrete thyroid hormone.

Capsule of connective tissue

Colloid is a glycoprotein.

Capillary
Production of Thyroid Hormones T3 and T4

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.
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 $^{123}\text{I}$, $^{131}\text{I}$ and $^{99m}\text{Tc}-\text{O}_4^-$

- 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

- $^{99m}\text{Tc}$ pertechnetate: cheap, not organified scan that day (ARSAC DRL = 80 MBq). Scan 20 mins post injection

- $^{123}\text{I}$: 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 ocular muscles with mucopolysaccharides

Images: Handbook of Ocular Disease Management
www.revoptom.com
Visitech Eye Centre
Normal Thyroid Gland
Graves disease
Graves Disease

Technetium Study

Uptake function = 24.04% Normal Range: (0.45 - 1.7)

Injected activity (scan time) = 77.5 MBq
System sensitivity = 36.0 cps / MBq
Hypothyroidism

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

- **Hashimoto’s Thyroiditis** 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 thyroiditis (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

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. $\uparrow$T4 and/or $\downarrow$TSH) due to functioning nodules, then they have ‘Plummers Disease’
Hot Nodule

Technetium Study

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

Technetium Study

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 $\approx$ 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 4 weeks, 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’
- $^{201}$TI
In Octreotide in papillary Ca Thyroid
F-18 FDG in thyroid cancer

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
$^{123}\text{I}$-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 \(^{99m}\text{Tc MIBI}\)
- 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
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.
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
Malignant Metastatic Phaeochromocytoma

Treatment

High dose (5GBq) x3 $^{131}$I-MIBG if $^{123}$I-MIBG 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