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

- 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
Thyroid Hormones

Negative Feedback System

Image: ABC Health and Wellbeing Website
Thyroid Gland

- Thyroid follicle
- C cells secrete calcitonin.
- Follicular cells secrete thyroid hormone.
- Colloid is a glycoprotein.
- Capsule of connective tissue.
- 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 $^{123}$I, $^{131}$I and $^{99m}$Tc-$O_4^-$

- 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!!!!!!!
Both Iodine and pertechnetate have similar size and charge.
The Scan

Radiopharmaceutical

- **99mTc pertechnetate**: cheap, not organified scan that day (ARSAC DRL = 80 MBq). Scan 20 mins post injection

- **123I**: 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
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
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

Technetium Study

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

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
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’
- $^{201}$Tl
$^{111}$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
$^{123}$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?

<table>
<thead>
<tr>
<th>Ultrasound</th>
<th>Nuclear Medicine</th>
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<tbody>
<tr>
<td>• Readily available</td>
<td>• May not be so readily available (in UK)</td>
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<tr>
<td>• Needs skilled operator</td>
<td>• Skilled reader required</td>
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<tr>
<td>• Local (neck) imaging only</td>
<td>• Regional : whole chest easily surveyed</td>
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<tr>
<td>• No radiation dose</td>
<td>• Less affected by other thyroid pathology</td>
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<tr>
<td>• Other thyroid pathology may be found</td>
<td>• Small radiation dose – 4mSv</td>
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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 (TI-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, $^{99}$mTc 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
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 in small adrenal adenoma in medial limb of right adrenal
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 $^{123}$IMIBG scan is positive