An Overview of the Uses of Radioactive Substances in Medicine

Jim Thurston (with thanks to my colleagues in Physics at RMH)
Have a seat Kermit. What I'm about to tell you might come as a big shock...
Radionuclide Uses:

Nuclear Medicine and PET Imaging

Radionuclide Therapies

Laboratories (esp. In-Vitro Testing)

Radiotherapy (Sealed Sources)
A word on terminology

– You will see and hear the words “radioisotopes”, “radionuclides”, “radiopharmaceuticals”, and even “radio-nucleotides”.....

– They do all strictly mean different things

– Radioisotopes means the isotopes of one specific element, e.g. of Carbon, that are radioactive

– Radionuclides means a range of radioactive substances with the specific radiation properties – e.g. gamma emitters

– Radiopharmaceuticals are radioactive substances labelled to specific chemicals for administration to patients

– Radio-nucleotides refers to radioactive substances labelled to a range of specific chemicals used in laboratories
Nuclear Medicine - Imaging Physiology

– Use of radioactive materials in diagnosis and treatment of various diseases (physiology vs. anatomy)
Production of Radionuclides for Medical Uses

• Produced by Fission and Neutron Bombardment in Nuclear Reactors.

• Specifically in Research Reactors....

• ... But not in Reactors used for Generating Electricity in the UK!

• Radionuclides can also be produced in Cyclotrons (currently almost exclusively PET in the UK)

• Radionuclides are extracted in a hot cell, where they are chemically manipulated for purity.

• May also be put into “generators” as parent of useful daughter product – e.g. Molybdenum-99 for production of daughter Technetium-99m

• Resulting products are labelled onto chemicals/pharmaceuticals (Radiopharmacy)
Radiopharmaceutical

- Radiopharmaceutical = 
  Radionuclide + carrier molecule/pharmaceutical

- Radiopharmaceutical is administered to patient - carrier molecule travels to target cell, tissue, or organ system

- Therefore the radionuclide is concentrated in the target cell/tissue or organ

- Ideally there will be no dissociation of radionuclide and pharmaceutical over time
Requirements of the Radiopharmaceutical for Imaging

- The radiation must be penetrating - Gamma
- Short half-life
- Low radiation dose to patient
1957 – First Gamma Camera

- Availability of large sodium iodide crystals led Hal Anger to design and construct the first Gamma Camera
1961 – The “Wonder Radiopharmaceutical”!

- The development of a generator containing $^{99}$Molybdenum meant that hospitals had a ready supply of $^{99m}$Technetium, and the beginnings of Nuclear Medicine Imaging
Technetium-99m

- Half-life: 6 hours
- Energy: 140 keV
- TcO₄⁻ is pentavalent – “it sticks to anything”
- Produced using a generator (fairly cheap)

\[
\begin{align*}
\text{99Mo} & \rightarrow \text{99Tcm} \rightarrow \text{99Tc} \rightarrow \text{99Ru} \\
T_{1/2} &= 67h \quad T_{1/2} = 6h \quad T_{1/2} = 2 \times 10^6y
\end{align*}
\]

- Molybdenum is normally produced by fission of enriched U-235 in a reactor (but could be produced by neutron bombardment)
### Commonly used Pharmaceuticals - Tc-99m

<table>
<thead>
<tr>
<th>Pharmaceutical/Activity</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDP</td>
<td>Bone</td>
</tr>
<tr>
<td>MIBI</td>
<td>Myocardial Perfusion</td>
</tr>
<tr>
<td>MAA</td>
<td>Lung (Perfusion)</td>
</tr>
<tr>
<td>DMSA</td>
<td>Renal (Cortical cell uptake)</td>
</tr>
<tr>
<td>MAG3</td>
<td>Renal (Function)</td>
</tr>
<tr>
<td>DTPA</td>
<td>Renal (GFR measurement)</td>
</tr>
</tbody>
</table>
Other Radionuclides Available (not exhaustive!)

<table>
<thead>
<tr>
<th>Isotope</th>
<th>Application</th>
<th>Half-life</th>
</tr>
</thead>
<tbody>
<tr>
<td>I-123</td>
<td>Thyroid</td>
<td>13 hours</td>
</tr>
<tr>
<td>I-131</td>
<td>Thyroid metastases</td>
<td>8 days</td>
</tr>
<tr>
<td></td>
<td>NET imaging</td>
<td></td>
</tr>
<tr>
<td>Tl-201</td>
<td>Myocardial</td>
<td>73 hours</td>
</tr>
<tr>
<td>Ga-67</td>
<td>Tumour</td>
<td>78 hours</td>
</tr>
<tr>
<td></td>
<td>Infection/Inflammation</td>
<td></td>
</tr>
<tr>
<td>In-111</td>
<td>Somatostatin receptor</td>
<td>67 hours</td>
</tr>
<tr>
<td></td>
<td>Infection/Inflammation</td>
<td></td>
</tr>
</tbody>
</table>
Nuclear medicine Gamma Camera Imaging can be:

- Planar

- or

- Sectional

- SPECT – Single Photon Emission Computed Tomography
SPECT/CT - Imaging Physiology and Anatomy

I-131 uptake in lung metastasis
PET - Positron Emission Tomography
**PET**

<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>Half-life</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon-11</td>
<td>20.38 minutes</td>
</tr>
<tr>
<td>Nitrogen-13</td>
<td>9.96 minutes</td>
</tr>
<tr>
<td>Oxygen-15</td>
<td>2.01 minutes</td>
</tr>
<tr>
<td>Fluorine-18</td>
<td>109.8 minutes</td>
</tr>
<tr>
<td>Gallium-68</td>
<td>68 minutes</td>
</tr>
</tbody>
</table>

– F-18 FDG – (FluoroDeoxyGlucose) is still the most common PET radiopharmaceutical used in medicine today
PET/CT
Radionuclide Therapy
Long before Nuclear Medicine Imaging there were therapeutic uses of radionuclides:

- **1936** - P-32 to treat leukaemia
- **1942** - Metabolic studies of bone tumours with Sr-89
- **1944** - P-32 for treatment of polycythemia vera
- **1949** - I-131 became much more readily available for treatment of thyroid cancer
Radionuclide Therapy

– Aims to target tumour cells whilst sparing normal tissue
– Systemic or intracavitary
– Non-invasive
– Few immediate or late side effects
Requirements of a Therapy Radiopharmaceutical

- Fairly long half-life
- Alpha or Beta emissions
- High and specific tumour uptake
- Prolonged retention by tumour
<table>
<thead>
<tr>
<th>Radiopharmaceutical</th>
<th>Application</th>
</tr>
</thead>
<tbody>
<tr>
<td>I-131 NaI</td>
<td>Ca thyroid, Thyrotoxicosis</td>
</tr>
<tr>
<td>I-131 mIBG</td>
<td>Neuro-endocrine tumours</td>
</tr>
<tr>
<td>Lu-177 peptide</td>
<td>Neuro-endocrine tumours</td>
</tr>
<tr>
<td>Y-90 peptide</td>
<td>Neuro-endocrine tumours</td>
</tr>
<tr>
<td>Y-90 Ibritumomab</td>
<td>NHL</td>
</tr>
<tr>
<td>Y-90 colloid</td>
<td>Intracranial cysts</td>
</tr>
<tr>
<td>P-32 Phosphate</td>
<td>Polycythemia vera</td>
</tr>
<tr>
<td>Sr-89 chloride</td>
<td>Bone metastases</td>
</tr>
<tr>
<td>Sm-153 EDTMP</td>
<td>Bone metastases</td>
</tr>
<tr>
<td>Ra-223 dichloride</td>
<td>Bone metastases</td>
</tr>
<tr>
<td>Radionuclide</td>
<td>Emission</td>
</tr>
<tr>
<td>--------------</td>
<td>----------</td>
</tr>
<tr>
<td>I-131</td>
<td>$\beta &amp; \gamma$</td>
</tr>
<tr>
<td>Lu-177</td>
<td>$\beta &amp; \gamma$</td>
</tr>
<tr>
<td>Y-90</td>
<td>$\beta$</td>
</tr>
<tr>
<td>P32</td>
<td>$\beta$</td>
</tr>
<tr>
<td>Sr89</td>
<td>$\beta$</td>
</tr>
<tr>
<td>Sm-153</td>
<td>$\beta &amp; \gamma$</td>
</tr>
<tr>
<td>Ra-223</td>
<td>$\alpha$</td>
</tr>
</tbody>
</table>
Prior to Treatment

- Establish whether any contra-indications to therapy exist, such as:
  - Pregnancy & breast-feeding
  - Myelosuppression
  - Renal impairment

- Provide information to patient on radiation safety
Requirements of Patient

- Reasonably ‘self-caring’
- No open wounds
- Continent
- Written consent to remain in room (inpatients) or comply with restrictions (outpatients)
A Note on RNT and Patient Dosimetry / Planning / Verification

• It would be remiss for me to not take the opportunity to point out that Nuclear Medicine administrations for Therapeutic purposes is defined in the European Directive (from which we get IRMER) as “radiotherapy”.

• This requires treatment planning individualised to the patient

• It requires verification that the prescribed dose has been delivered to the tumour(s)

• HOWEVER, we and many other countries still prescribe in terms of fixed activity to adults, irrespective of the individual uptake in the tumour(s)

• There has been no precedent in a Court of Law to determine whether this approach is appropriate...... yet!!
Use of Radionuclides in Laboratories - In-Vitro testing
In-Vitro Testing in Laboratories

- Taking tissue and/or blood samples, and labelling them with a radionuclide

- Measuring the uptake/activity in the cells

- Using the result to determine the physiology – whether it is within a normal expected range

- The patient does not receive a radiation exposure!
In-Vitro Testing in Laboratories

- Range of Radionuclides used for many years in laboratories:
  - H-3
  - C-14
  - I-125
  - P-32 (and P-33)
  - S-35
- In the past 20-30 years many of these techniques have been replaced by non-radioactive alternatives
Radioactive Sources Used in Radiotherapy (Sealed Sources)
Sealed Sources in Radiotherapy

– Used in Teletherapy Machines (Co-60 or Cs-137) – almost all now replaced by LINACS

– Used in High Dose Rate Brachytherapy (Ir-192, etc)

– Use in Low Dose Rate Brachytherapy (I-125 Seeds)

– (Such therapeutic practice is planned and verified in compliance with the Directive and IRMER)
So, what happens to the radioactivity used...?
Ordering / Receipt and Use of Radioactive Substances

- The use of radioactive substances must be in compliance with the limitations and conditions set down in the Environmental Permit issued by the Environment Agency.
- When ordering there must be checks in place such that on the day of delivery the total activity on site does not exceed a limit.
- When receiving the order, further checks must be carried out to ensure that what has been delivered was what was ordered.
- Records must be kept of the stock and use of all radioactive substances, decay-corrected as necessary.
It leads to Radioactive Waste!

- The use of radioactive substances will generate waste in different forms, which in turn will have limitations and conditions for final disposal.
- Radioactivity administered to patients doesn’t just stay in the body (even as sealed sources....!)
- Some is excreted (normal and abnormal physiology)
- Some radioactivity is lost in the process of preparing radiopharmaceuticals
- We need to manage and account for this radioactive waste
- See later talk!
Thank you for listening -

Any questions?