Joint CI-JAI advanced accelerator lecture series

Imaging and detectors for medical physics

Lecture 4: Radionuclides

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## Course layout

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<th>AM 09.30 – 11.00</th>
<th>PM 15.30 – 17.00</th>
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<td>Lecture 2: Detectors for medical imaging</td>
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</tr>
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<td><strong>Week 3</strong></td>
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</tr>
<tr>
<td>22nd June</td>
<td>Tutorial</td>
<td></td>
</tr>
</tbody>
</table>
Books & references

1. N Barrie Smith & A Webb
   Introduction to Medical Imaging
   Cambridge University Press

2. Edited by M A Flower
   Webb’s Physics of Medical Imaging
   CRC Press

3. A Del Guerra
   Ionizing Radiation Detectors for Medical Imaging
   World Scientific

4. W R Leo
   Techniques for Nuclear and Particle Physics Experiments
   Springer-Verlag

Nuclides live charts
- [https://www-nds.iaea.org/relnsd/vcharthtml/VChartHTML.html](https://www-nds.iaea.org/relnsd/vcharthtml/VChartHTML.html)
Nuclear medicine imaging

- Imaging of radioactive decay products of a radiopharmaceutical (radiotracer) introduced into the body → emission imaging (as opposed to X-ray imaging = transmission imaging)

- Spatial distribution depends on how radiopharmaceutical interacts with tissues in the body

- Administration of radiopharmaceutical:
  1. Intravenous injection into bloodstream
  2. Inhalation into lungs
  3. Subcutaneous administration
  4. Oral administration
Nuclear medicine imaging techniques

- SPECT = Single Photon Emission CT = Single Photon Emission Computed Tomography
- PET = Positron Emission Tomography
- Planar scintigraphy
Nuclide notation

Nucleus

• Formed of nucleons

- Nucleons:
  - proton = particle with positive charge
  - neutron = particle with zero charge

Notation

Element X

\[ \begin{align*}
A &= \text{mass number} = \text{number of protons} + \text{neutrons} \\
Z &= \text{atomic number} = \text{number of protons}
\end{align*} \]

Isotopes of an element = nuclides with same number of protons (same \( Z \)) but different number of neutrons (different \( A \))
Forces within the nucleus

- In stable nuclei forces are well balanced
- In unstable nuclei there are too many neutrons or protons → forces are not balanced → nucleus is prone to undergo nuclear rearrangement and decay
- Line of stability
  - For low $Z$: $N \approx Z$
  - For high $Z$: $N \approx 1.5 \times Z$
  - No stable nuclei for $Z > 82$ (Lead)
Radioactivity

- Intrinsic property of unstable nuclei that have too many neutrons or protons $\rightarrow$ unstable nuclei emit particles or $\gamma$-rays to become more stable

- Definitions:
  1. Radionuclide = nuclide that is unstable and undergoes radioactive decay
  2. Radioisotope = radioactive isotope
  3. Radioactive disintegration or decay = spontaneous change in nucleus composition with associated emission of energy to reach a more stable state
  4. Radiotracer = radiopharmaceutical
Radioactive decay law

- Number of radioactive atoms in a sample decreases with time:
  \[
  \frac{dN}{dt} = -\lambda t
  \]

- \( N(t) \) = number of atoms left at given time \( t \) decreases exponentially:
  \[
  N(t) = N_0 \exp(-\lambda t)
  \]
  
  \( N_0 \) = number of atoms at \( t = 0 \)
  
  \( \lambda [s^{-1}] = \) decay constant
  
  \( \exp(-\lambda t) = \) decay factor
Decay constant

- Probability that any individual radioactive atom will undergo decay per unit time
- Statistical definition → average rate of decay
- Exercise:
  Q: If $\lambda = 0.01 \text{ s}^{-1}$ on average how many atoms undergo radioactive decay per unit time?
(Radio)activity $Q$

Ref. 1 – Chapter 3.2 and Ref. 2 – Chapter 5.4.1

• (Radio)activity $Q = $ number of disintegrations per s = rate of change of number $N$ of radioactive nuclei

$$Q = - \frac{dN}{dt} = \lambda N$$

• Units for $Q$:

1. SI unit = Bequerel (Bq)
   1 Bq = 1 disintegration per second

2. Curies (Ci) = named after Pierre Curie and defined as number of disintegrations per second from 1 gramme of $^{226}Ra$
   1 Ci = $3.7 \times 10^{10}$ disintegrations per second = $3.7 \times 10^{10}$ Bq
(Radio)activity $Q$ decay law

- (Radio)activity $Q$ decreases with time too
- Exercise:
  Q: Determine the (radio)activity $Q$ decay law
Half-life

- Half-life $\tau_{1/2}$ = time required for $Q$ to drop to half (50%) of its initial value $\rightarrow \tau_{1/2}$ is independent of $N$
- Exercise: Calculate relation between $\tau_{1/2}$ and $\lambda$ and express $Q$ as function of $\tau_{1/2}$
Atomic half-lives

\[ Z = N \]

Half-life (seconds)

- \( > 1e+15 \)
- \( 1e+10 \) 1e-01
- \( 1e+07 \) 1e-02
- \( 1e+05 \) 1e-03
- \( 1e+04 \) 1e-04
- \( 1e+03 \) 1e-05
- \( 1e+02 \) 1e-06
- \( 1e+01 \) 1e-07
- \( 1e+00 \) 1e-15
- unknown

Courtesy Piero Posocco (Imperial College)
Biological and effective half-life

• In many cases excretion of radiotracer from tissue follows an exponential decay law → biological half-life $\tau_{1/2,\text{bio}}$ used to characterise the decay → $\tau_{1/2,\text{bio}}$ gives a measure of how long radiotracer remains in the body

• Effective half-life $\tau_{1/2,\text{eff}}$ given by:

$$\tau_{1/2,\text{eff}} = \frac{\tau_{1/2} \cdot \tau_{1/2,\text{bio}}}{\tau_{1/2} + \tau_{1/2,\text{bio}}}$$

→ $\tau_{1/2,\text{eff}}$ always less than the shorter between $\tau_{1/2}$ and $\tau_{1/2,\text{bio}}$
Exercise

• Q: Two patients undergo nuclear medicine scans. One receives a dose of radiotracer A with $\tau_{1/2} = 6$ h and the other a dose of radiotracer B with $\tau_{1/2} = 24$ h. If dose of radiotracer A is $3 \times$ dose of radiotracer B and $\tau_{1/2,\text{bio}}$ of A is 6 h and of B 12 h, at what time the radioactivity in the body of the two patients is the same?
Radioactive decay modes

Ref. 2 – Chapter 5.4.3

• $\alpha^{+2}$ decay
• $\beta^-$ decay
• $\beta^+$ decay
• Electron Capture (EC)
• Isomeric transitions
  – Radiative $\alpha^{+2}$, $\beta^-$ and $\beta^+$ decays
  – Radiative EC
• Internal conversion (IC)
$\alpha^+2$ decay

- High A radionuclide emits $\alpha$-particle = helium nucleus = +2 charge
- Most energy distributed between:
  1. Daughter nucleus = recoil energy
  2. $\alpha$-particle = kinetic energy = $4\div8$ MeV → travels few $\mu$m in tissue
- If nucleus left in excited state → de-excitation is through emission of $\gamma$-rays
- Not use in medical imaging (shallow penetration in tissue) but as sealed X- or $\gamma$-rays sources in therapy
\( \beta^- \) decay

- Neutron-rich radionuclide ejects \( \beta^- \) particle = \( e^- = -1 \) charge in the process:
  \[
  n \rightarrow p + e^- + \bar{\nu}
  \]
- Three-body decay \( \rightarrow \) energy spectrum of \( e^- \) = continuum up to a maximum
- \( Z \rightarrow Z + 1, \ A \) and atomic weight remain the same
- \( e^- \) penetration in tissue < 2 mm \( \rightarrow \) not used in medical imaging

Example

\[
\frac{^{14}_6 C}{\beta^- \text{decay}} \rightarrow ^{14}_7 N + \beta^- + \bar{\nu} + E
\]

\( E \) = shared randomly between \( \bar{\nu} \) and kinetic energy of \( \beta^- \)
Radiative $\beta^-$ decay ($\beta^-, \gamma$)

- If following $\beta^-$ decay daughter nuclide is produced in excited state $X^* \rightarrow$ prompt de-excitation to more stable state through emission of $\gamma$ rays
- $Z \rightarrow Z + 1$, $A$ and atomic weight remain the same
- Typical energy of $\gamma$ rays = 50÷500 keV → useful for imaging
- Disadvantage: patient still exposed to $\beta^-$ particle → dose

Example

$$^{133}_{54}Xe \rightarrow ^{133}_{55}Cs^* \rightarrow ^{133}_{55}Cs$$

[Diagram showing the decay processes and energy levels]
Proton-rich or neutron deficient radionuclide ejects $\beta^+$-particle = $e^+ = +1$ charge in the process:
$$p \rightarrow n + e^+ + \nu$$

- Three-body decay → energy spectrum of $e^+$ = continuum up to a maximum
- $Z \rightarrow Z - 1, \ A$ and atomic weight remain the same
- $e^+$ travels $\sim 1$ mm in tissue → comes to rest → combines with atomic $e^-$ → 2 back-to-back 511 keV $\gamma$-rays
- If daughter nuclide is produced in excited state → de-excitation is through emission of $\gamma$-rays

Example

$^{15}_6O \beta^+ \text{decay} \rightarrow ^{15}_7N + \beta^+ + \nu + E$

$E = \text{shared randomly between } \nu \text{ and kinetic energy of } \beta^+$

Average kinetic energy $\langle E_{\beta^+} \rangle \approx \frac{E_{\beta^+}^{\text{max}}}{3}$

1.022 MeV

$E_{\beta^+}^{\text{max}} = 1.7 \text{ MeV}$
Electron Capture (EC) and radiative Electron Capture (EC, $\gamma$)

- In proton-rich radionuclide inner orbital (K-shell) $e^- = closer to nucleus, captured within nucleus:
  \[ p + e^- \rightarrow n + \nu + E \]
- $Z \rightarrow Z - 1$
- $e^-$ from outer orbital fills vacancy \( \rightarrow \) emission of X-ray characteristic of daughter nuclide = can be useful for imaging if high enough $E$
- The higher $Z$ the closer to the nucleus are the $e^-$ shells \( \rightarrow \) probability of EC increases with $Z$
- If daughter nuclide is produced in excited state $X^* \rightarrow$ de-excitation is through emission of $\gamma$-rays

Example

\[ \frac{^{125}_{53}I}{e^-} \rightarrow \frac{^{125}_{52}Te^*}{+ \nu + E} \rightarrow \frac{^{125}_{52}Te}{0.035 \text{ MeV}} \]
Feynman diagrams for $\beta^-$, $\beta^+$ decays and EC

\begin{align*}
A_X & \xrightarrow{\beta^-} z_{+1}A_Y + e^- + \bar{\nu}_e \\
A_X & \xrightarrow{\beta^+} z_{-1}A_Y + e^+ + \nu_e \\
A_X & \xrightarrow{EC} z_{-1}A_Y + \nu_e
\end{align*}

Courtesy Piero Posocco (Imperial College)
## $\beta$ emitters

### $(\beta^-, \gamma)$ emitters

<table>
<thead>
<tr>
<th>Nuclide</th>
<th>Half-life</th>
<th>$\langle E_\beta \rangle$ (MeV)</th>
<th>$E_\gamma$ (keV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{60}\text{Co}$</td>
<td>5.27 yrs</td>
<td>0.096</td>
<td>1173, 1332</td>
</tr>
<tr>
<td>$^{131}\text{I}$</td>
<td>8.04 days</td>
<td>0.192</td>
<td>364</td>
</tr>
<tr>
<td>$^{133}\text{Xe}$</td>
<td>5.24 days</td>
<td>0.101</td>
<td>81</td>
</tr>
<tr>
<td>$^{137}\text{Cs}$</td>
<td>30.00 yrs</td>
<td>0.173</td>
<td>662</td>
</tr>
</tbody>
</table>

### $\beta^+$ emitters

<table>
<thead>
<tr>
<th>Nuclide</th>
<th>Half-life (min)</th>
<th>$E_{\beta^+}^{\text{max}}$ (MeV)</th>
<th>$\langle \beta^+ \text{ range} \rangle$ in water (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{11}\text{C}$</td>
<td>20.30</td>
<td>0.961</td>
<td>0.103</td>
</tr>
<tr>
<td>$^{13}\text{N}$</td>
<td>10.00</td>
<td>1.190</td>
<td>0.132</td>
</tr>
<tr>
<td>$^{15}\text{O}$</td>
<td>2.07</td>
<td>1.720</td>
<td>0.201</td>
</tr>
<tr>
<td>$^{18}\text{F}$</td>
<td>110.00</td>
<td>0.635</td>
<td>0.064</td>
</tr>
</tbody>
</table>

¹Only dominant $\beta^-$ and $\gamma$ emissions shown
### EC radionuclides

<table>
<thead>
<tr>
<th>Nuclide</th>
<th>Half-life</th>
<th>$E_{X-ray}$ (keV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{125}I$</td>
<td>60.1 days</td>
<td>~30</td>
</tr>
<tr>
<td>$^{201}Tl$</td>
<td>3.04 days</td>
<td>~70</td>
</tr>
</tbody>
</table>

### (EC, $\gamma$) radionuclides

<table>
<thead>
<tr>
<th>Nuclide</th>
<th>Half-life</th>
<th>$E_{\gamma}$ (keV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{57}Co$</td>
<td>270 days</td>
<td>122, 136</td>
</tr>
<tr>
<td>$^{67}Ga$</td>
<td>78.3 h</td>
<td>93, 185</td>
</tr>
<tr>
<td>$^{111}In$</td>
<td>2.83 days</td>
<td>171, 245</td>
</tr>
<tr>
<td>$^{123}I$</td>
<td>13.2 h</td>
<td>159</td>
</tr>
</tbody>
</table>
Isomeric transitions (IT) and metastable states

- Excited state in which daughter nuclide can be produced called isomeric state
- Sometimes radiative decays from isomeric state to ground state are called isomeric transition
- Isomeric transitions can take from fractions of seconds (short-lived states) to many years (long-lived states)
- Long-lived isomeric states are called metastable states $\frac{A}{Z}X^m$

Example

- $^{99}Tc^m$ most common example of metastable isotope used in nuclear medicine
- Decay chain:
  $$^{99}Mo \xrightarrow{\beta^-} ^{99}Tc^m \xrightarrow{\gamma} ^{99}Tc$$
  - Half-life for $\beta^-$ decay = 66 h
  - Half-life for isomeric transition = 6 h
Internal Conversion (IC)

- $\gamma$-ray emitted in isomeric transition interacts with atomic $e^{-} \rightarrow e^{-}$ is ejected = conversion electron
- Interaction is usually with K-shell $e^{-}$ as they are closest to nucleus
- Conversion $e^{-}$ has kinetic energy $E$:
  \[ E = E_{\gamma} - E_{\text{binding}} \]
- $e^{-}$ from outer shell fills vacancy $\rightarrow$ characteristic X-ray emitted
- X-ray emitted can interact with other outer shell $e^{-}$ $\rightarrow$ $e^{-}$ get ejected if $E_{X\text{-ray}} > E_{\text{binding}}$ = Auger $e^{-}$
Radioactive decay table

Z (protons) vs N (neutrons) diagram showing different decay modes:
- Stable
- EC, $\beta^+$
- $\beta^-$
- $\alpha$
- P
- N
- Unknown

Courtesy Piero Posocco (Imperial College)
Production of radionuclides

Ref. 2 – Chapter 5.4.2

• Man-made production:
  1. Neutron capture = neutron activation
  2. Nuclear fission
  3. Charged-particle bombardment
  4. Radioactive decay

• Naturally-occurring radionuclides
Man-made production technologies

• Nuclear reactors:
  1. Neutron capture = nuclear absorption
  2. Nuclear fission

• Accelerators:
  1. Charged-particle bombardment

• Radionuclide generators:
  1. Radioactive decay
Neutron capture / nuclear absorption

• Radionuclides produced when neutron absorbed by atomic nucleus
  \[\text{neutron} + \text{nucleus} \rightarrow \text{radionuclide}\]

• For neutron to be captured \(E_n\) needs to be low in the range \(0.03\div100\) eV = thermal neutrons

• Radionuclides produced predominantly neutron rich → decay mainly by \(\beta^-\)

• Production system:
  1. Nuclear reactor: creates thermal neutrons
  2. Target: placed inside field of thermal neutrons
Neutron capture reaction chain

• Neutron capture leaves nucleus excited → de-excitation via emission of $\gamma$-ray:

$$n + ^A X \rightarrow ^{A+1} X + \gamma$$

Notation: $^AX(n, \gamma)^{A+1}X$

• Radionuclide produced = isotope of target material = same $Z$ but $A + 1$ → very difficult to separate → low purity and activity

• Exception that can be easily separated: $^{125}I$ from decay of $^{125}Xe$ with half-life 17 h:

$$^{124}Xe(n, \gamma)^{125}Xe \overset{EC \text{ or } \beta^+}{\rightarrow} ^{125}I$$
Nuclear fission

- Nuclear fission process:
  1. Heavy nuclei \( {}_{232}^{\text{Th}}, {}_{235}^{\text{U}}, {}_{237}^{\text{U}}, {}_{239}^{\text{Pu}} \) and others with \( A > 92 \) are irradiated with thermal neutrons = neutron bombardment → absorb neutrons → become unstable
  2. Unstable nuclei undergo fission = break up into two lighter nuclei of approximately similar atomic weight

- Fission-produced nuclides have \( 28 < A < 65 \)

- Radionuclides produced predominantly neutron rich → decay mainly by \( \beta^- \)

- Fission products can be separated chemically with high specificity → high quality radiopharmaceuticals
Nuclear reactor

Main components:
1. Fuel cells: contain fissionable material
2. Moderator: commonly graphite or $D_2O$ surrounding fuel cells = slows down neutrons
3. Control rods: commonly boron exposing or shielding fuel cells = heavy neutron absorbers
4. Ports in reactor core: allow samples to be inserted for irradiation with neutrons

Position of fuel cells and control rods determine rate of chain reaction

Fission of $^{235}U$ or heavily enriched $^{235}U$ giving:
1. Fission products
2. Thermal neutrons $\rightarrow$ can be used to create radionuclide by neutron capture

Courtesy Piero Posocco (Imperial College)
Reactor-produced radionuclides

### Nuclear absorption

<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>Production reaction</th>
<th>$E_\gamma$ (keV)</th>
<th>Half-life</th>
<th>$\sigma$ (Barn)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{51}\text{Cr}$</td>
<td>$^{50}\text{Cr}(n,\gamma)^{51}\text{Cr}$</td>
<td>320</td>
<td>27.7 days</td>
<td>15.8</td>
</tr>
<tr>
<td>$^{59}\text{Fe}$</td>
<td>$^{58}\text{Fe}(n,\gamma)^{59}\text{Fe}$</td>
<td>1099</td>
<td>44.5 days</td>
<td>1.28</td>
</tr>
<tr>
<td>$^{99}\text{Mo}$</td>
<td>$^{98}\text{Mo}(n,\gamma)^{99}\text{Mo}$</td>
<td>740</td>
<td>66.02 h</td>
<td>0.13</td>
</tr>
<tr>
<td>$^{131}\text{I}$</td>
<td>$^{130}\text{Te}(n,\gamma)^{131}\text{Te} \rightarrow ^{131}\text{I}$</td>
<td>364</td>
<td>8.04 days</td>
<td>0.29</td>
</tr>
</tbody>
</table>

### Nuclear fission

<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>$E_\gamma$ (keV)</th>
<th>Half-life</th>
<th>Fission yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{99}\text{Mo}$</td>
<td>740</td>
<td>66.02 h</td>
<td>6.1</td>
</tr>
<tr>
<td>$^{131}\text{I}$</td>
<td>364</td>
<td>8.05 days</td>
<td>2.9</td>
</tr>
<tr>
<td>$^{133}\text{Xe}$</td>
<td>81</td>
<td>5.27 days</td>
<td>6.5</td>
</tr>
<tr>
<td>$^{137}\text{Cs}$</td>
<td>662</td>
<td>30 yrs</td>
<td>5.9</td>
</tr>
</tbody>
</table>
Charged-particle bombardment

- Radionuclides produced through interaction of charged particles \((H^\pm, D^+, 3He^{2+}, 4He^{2+})\) with nuclei of stable atoms
  
  \[\text{charged particle} + \text{nucleus} \rightarrow \text{radionuclide}\]

- Radionuclides produced predominantly neutron deficient \(\rightarrow\) decay by \(\beta^+\) or EC

- Production system:
  1. Accelerator: kinetic \(E_{\text{charged particle}}\) needs to be high enough to overcome nucleus (+) electrostatic repulsion
  2. Target
Accelerators

- Two basic types used for medical imaging:
  1. Cyclotron → most commonly used and usually located near hospitals due to radionuclide short half-lives
  2. Linear accelerator

Cyclotron frequency: \[ f = \frac{qB}{2\pi m} \]
Path of +ve ion in cyclotron

+ve ion source

Magnetic field into page

$E_x(x)$

AC volts

Dees = vacuum chambers

Courtesy Piero Posocco (Imperial College)
Path of +ve ion in cyclotron

- +ve ion source
- Magnetic field into page
- Dees = vacuum chambers
- AC volts
- Ex(x)

Courtesy Piero Posocco (Imperial College)
Path of +ve ion in cyclotron

Magnetic field into page

+ve

E_x(x)

AC volts

-ve

Dees = vacuum chambers

Courtesy Piero Posocco (Imperial College)
Compact biomedical cyclotron

Power supplies and Target support unit

Retractable shields

Courtesy Piero Posocco (Imperial College)
## Accelerator-produced radionuclides

<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>Principal $\gamma$-ray $E_\gamma$ (keV)$^1$</th>
<th>Half-life</th>
<th>Production reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{11}C$</td>
<td>511</td>
<td>20.4 min</td>
<td>$^{14}N(p, \alpha)^{11}C$</td>
</tr>
<tr>
<td>$^{13}N$</td>
<td>511</td>
<td>9.96 min</td>
<td>$^{13}C(p, n)^{13}N$</td>
</tr>
<tr>
<td>$^{15}O$</td>
<td>511</td>
<td>2.07 min</td>
<td>$^{15}N(p, n)^{15}O$</td>
</tr>
<tr>
<td>$^{18}F$</td>
<td>511</td>
<td>109.7 min</td>
<td>$^{18}O(p, n)^{18}F$</td>
</tr>
<tr>
<td>$^{67}Ga$</td>
<td>93, 184, 300</td>
<td>78.3 h</td>
<td>$^{68}Zn(p, 2n)^{67}Ga$</td>
</tr>
<tr>
<td>$^{111}In$</td>
<td>171, 245</td>
<td>67.9 h</td>
<td>$^{112}Cd(p, 2n)^{111}In$</td>
</tr>
<tr>
<td>$^{120}I$</td>
<td>511</td>
<td>81 min</td>
<td>$^{127}I(p, 8n)^{120}Xe \rightarrow ^{120}I$</td>
</tr>
<tr>
<td>$^{123}I$</td>
<td>159</td>
<td>13.2 h</td>
<td>$^{112}Te(p, 2n)^{123}I$ $^{127}I(p, 5n)^{123}Xe \rightarrow ^{123}I$</td>
</tr>
<tr>
<td>$^{124}I$</td>
<td>511</td>
<td>4.2 days</td>
<td>$^{124}Te(p, n)^{124}I$</td>
</tr>
<tr>
<td>$^{201}Tl$</td>
<td>68÷80.3</td>
<td>73 h</td>
<td>$^{203}Tl(p, 3n)^{201}Pb \rightarrow ^{201}Tl$</td>
</tr>
</tbody>
</table>

$^1$511 keV $\gamma$-rays come from $\beta^+$ decay
Radioactive decay

- Radioactive decay of parent radionuclide can lead to:
  1. Unstable nuclide = radioactive nuclide = daughter radionuclide
  2. Stable nuclide

- \( Z \) of radionuclide daughter depends on decay type

- Good radionuclides for medical imaging:
  1. Daughter is short-lived and has \( Z \) different from parent → can be easily separated
  2. Parent has sufficiently long half-life for production, processing and shipment
Radionuclide generator

• The generator:
  1. Receives in input radionuclides produced from nuclear reactors or accelerators
  2. Contains:
     a) Chemical separation system of daughter radionuclide from parent radionuclide: chromatographic techniques most common
     b) Extraction system

• Main features:
  1. Portable → provides local supply of short-lived radionuclides without a nearby accelerator or nuclear reactor
  2. Daughter product replenished continuously by decay of parent → can be extracted repeatedly
## Generator-produced radionuclides

<table>
<thead>
<tr>
<th>Parent P</th>
<th>Parent half-life</th>
<th>Mode of decay P → D</th>
<th>Daughter D</th>
<th>Daughter decay mode</th>
<th>Daughter half-life</th>
<th>Daughter γ Eγ (keV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>⁶²Zn</td>
<td>9.1 h</td>
<td>β⁺ EC</td>
<td>⁶²Cu</td>
<td>β⁺ EC</td>
<td>9.8 min</td>
<td>511 1173</td>
</tr>
<tr>
<td>⁶⁸Ge</td>
<td>280 days</td>
<td>EC</td>
<td>⁶⁸Ga</td>
<td>β⁺ EC</td>
<td>68 min</td>
<td>511 1080</td>
</tr>
<tr>
<td>⁸¹Rb</td>
<td>4.7 h</td>
<td>EC</td>
<td>⁸¹Kr</td>
<td>IT</td>
<td>13 s</td>
<td>190</td>
</tr>
<tr>
<td>⁸²Sr</td>
<td>25 days</td>
<td>EC</td>
<td>⁸²Rb</td>
<td>EC β⁺</td>
<td>76 s</td>
<td>777 511</td>
</tr>
<tr>
<td>⁹⁹Mo</td>
<td>66.02 h</td>
<td>β⁻</td>
<td>⁹⁹Tcᵐ</td>
<td>IT</td>
<td>6.02 h</td>
<td>140</td>
</tr>
<tr>
<td>¹¹³Sn</td>
<td>115.1 days</td>
<td>EC</td>
<td>¹¹³Inᵐ</td>
<td>IT</td>
<td>1.66 h</td>
<td>392</td>
</tr>
<tr>
<td>¹⁹⁵Hgᵐ</td>
<td>40 h</td>
<td>IT EC</td>
<td>¹⁹⁵Auᵐ</td>
<td>IT</td>
<td>30.6 s</td>
<td>262</td>
</tr>
</tbody>
</table>
\[ {^{99}Mo} - {^{99}Tc}^{m} \text{ generator} \]

Ref. 1 – Chapters 3.4 and 3.5

- \(^{99}Tc^{m}\) most common radioisotope used in nuclear medicine:
  \[ {^{99}Mo} \quad \text{Half-life=66 h} \quad \xrightarrow{} \quad {^{99}Tc}^{m} \quad \text{Half-life=6.02 h} \quad \rightarrow \quad {^{99}Tc} + 140 \text{ keV } \gamma \]

- Also called a Molly or Cow
- Typically used for one week
- \(^{99}Mo\) bound to alumina column as molybdate ion \((\text{NH}_4)_2\text{MoO}_4^{-}\)
- \(^{99}Tc^{m}\) :
  - Chemically different → not bound to column → eluted from column with 5±25 ml saline
  - 75±85% of available \(^{99}Tc^{m}\) extracted
Equation for number of $^{99}Tc^m$ atoms produced with generator

$^{99}Mo \xrightarrow{\lambda_1} ^{99}Tc^m \xrightarrow{\lambda_2} ^{99}Tc$

$\left( N_1 \right) \quad \left( N_2 \right) \quad \left( N_3 \right)$

- Number $N_1$ of $^{99}Mo$ atoms decreases with time from $N_0$ due to decay:
  \[ N_1 = N_0 e^{-\lambda_1 t} \]

- Number $N_3$ of $^{99}Tc$ atoms increases with time due to decay of $^{99}Tc^m$

- Number $N_2$ of $^{99}Tc^m$ atoms has two components = one decreases with time due to $^{99}Tc^m$ own decay, other increases with time due to $^{99}Mo$ decay → first order differential equation for $N_2$:
  \[ \frac{dN_2}{dt} = \lambda_1 N_1 - \lambda_2 N_2 \rightarrow \frac{dN_2}{dt} + \lambda_2 N_2 = \lambda_1 N_1 \]

With boundary condition: $N_2 = 0$ at $t = 0$
Solution of first order differential equation for $N_2$

• Solution of first order differential equation for $N_2$ made of two terms:

$$N_2 = Ce^{-\lambda_2 t} + De^{-\lambda_1 t}$$

1. Homogeneous: $N_2 = Ce^{-\lambda_2 t}$
2. Particular: $N_2 = De^{-\lambda_1 t}$

• From boundary condition $\rightarrow C = -\frac{\lambda_1 N_0}{\lambda_2 - \lambda_1}$

• Solving particular solution for $D \rightarrow D = \frac{\lambda_1 N_0}{\lambda_2 - \lambda_1}$

• Final solution of first order differential equation for $N_2$:

$$N_2 = -\frac{\lambda_1 N_0}{\lambda_2 - \lambda_1} e^{-\lambda_2 t} + \frac{\lambda_1 N_0}{\lambda_2 - \lambda_1} e^{-\lambda_1 t}$$

$$N_2 = \frac{\lambda_1 N_0}{\lambda_2 - \lambda_1} (e^{-\lambda_1 t} - e^{-\lambda_2 t})$$
Radioactivity $Q$ of $^{99}Tc^m$ produced with the generator

- Radioactivity $Q$ of $^{99}Tc^m$ produced with the generator given by:
  \[ Q = \lambda_2 N_2 \]

- Using solution for $N_2$ the radioactivity $Q$ is finally given by:
  \[ Q = \lambda_2 \frac{\lambda_1 N_0}{\lambda_2 - \lambda_1} (e^{-\lambda_1 t} - e^{-\lambda_2 t}) = \frac{\lambda_1 \lambda_2 N_0}{\lambda_2 - \lambda_1} (e^{-\lambda_1 t} - e^{-\lambda_2 t}) \]

  $N_0$ = number of $^{99}Mo$ at $t = 0$

  $\lambda_1$ = $^{99}Mo$ decay constant = $\frac{\ln 2}{\tau_{1/2}^1} = \frac{\ln 2}{66} = 0.0105 \text{ h}^{-1}$

  $\lambda_2$ = $^{99}Tc^m$ decay constant = $\frac{\ln 2}{\tau_{1/2}^2} = \frac{\ln 2}{6} = 0.116 \text{ h}^{-1}$

- Radioactivity proportional to difference of two exponentials = one governing increase in $^{99}Tc^m$ due to $^{99}Mo$ decay and other decrease in $^{99}Tc^m$ due to its decay
Naturally-occurring radionuclides

- Very long-lived elements
- Mainly very heavy elements

<table>
<thead>
<tr>
<th>Nuclide</th>
<th>Abundance (%)</th>
<th>Half-life (yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{40}K$</td>
<td>0.01</td>
<td>$1.26 \times 10^9$</td>
</tr>
<tr>
<td>$^{87}Rb$</td>
<td>27.8</td>
<td>$4.88 \times 10^{10}$</td>
</tr>
<tr>
<td>$^{232}Th$</td>
<td>100</td>
<td>$1.40 \times 10^{10}$</td>
</tr>
<tr>
<td>$^{235}U$</td>
<td>0.7</td>
<td>$7.04 \times 10^8$</td>
</tr>
<tr>
<td>$^{238}U$</td>
<td>99.3</td>
<td>$4.46 \times 10^9$</td>
</tr>
</tbody>
</table>

- → Not useful for imaging
Choice of radionuclides for imaging

Ref. 2 – Chapter 3.4.4

• Desirable physical characteristics of radionuclides for nuclear medicine imaging:

1. Physical half-life:
   a. Long enough to allow:
      1) Preparation of radiopharmaceuticals
      2) Completion of imaging procedures
   b. Short enough to ensure dose to patient and staff is minimised

2. Decay via isomeric transition = produces $\gamma$ rays with:
   a. High photon yield $\rightarrow$ good counting statistics
   b. Suitable $E_\gamma$

3. Absence of particulate emission ($\alpha$ or $\beta$ particles) $\rightarrow$ no unnecessary dose to patients
Emitted photon energy

• Emitted photon energy critical and chosen as “compromise” for various reasons:

1. High enough $E_\gamma$ so that:
   a. Photon is able to efficiently escape the body
   b. Photopeak is easily separated from scattered radiation

2. Low enough $E_\gamma$ so that:
   a. Detection efficiency is still good
   b. Do not penetrate thin collimator septa → thickness of collimator septa not too big
   c. Photons are not too difficult to shield and to handle
Commonly used radionuclides for imaging

<table>
<thead>
<tr>
<th>Nuclide</th>
<th>Decay mode</th>
<th>Product</th>
<th>$E$ (keV)</th>
<th>Half-life</th>
<th>Imaging system</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{11}C$</td>
<td>$\beta^+$</td>
<td>$\gamma$</td>
<td>511</td>
<td>20 min</td>
<td>PET</td>
<td></td>
</tr>
<tr>
<td>$^{13}N$</td>
<td>$\beta^+$</td>
<td>$\gamma$</td>
<td>511</td>
<td>10 min</td>
<td>PET</td>
<td></td>
</tr>
<tr>
<td>$^{15}O$</td>
<td>$\beta^+$</td>
<td>$\gamma$</td>
<td>511</td>
<td>2 min</td>
<td>PET</td>
<td></td>
</tr>
<tr>
<td>$^{18}F$</td>
<td>$\beta^+$</td>
<td>$\gamma$</td>
<td>511</td>
<td>110 min</td>
<td>PET</td>
<td>~80% of all PET imaging (FDG)</td>
</tr>
<tr>
<td>$^{67}Ga$</td>
<td>EC</td>
<td>$\gamma$</td>
<td>93, 185, 300</td>
<td>3.3 days</td>
<td>$\gamma$-camera, SPECT</td>
<td></td>
</tr>
<tr>
<td>$^{82}Rb$</td>
<td>$\beta^+$</td>
<td>$\gamma$</td>
<td>511</td>
<td>1.25 min</td>
<td>PET</td>
<td></td>
</tr>
<tr>
<td>$^{99}Tc^m$</td>
<td>IT</td>
<td>$\gamma$</td>
<td>140</td>
<td>6.0 h</td>
<td>$\gamma$-camera, SPECT</td>
<td>&gt; 80% of all nuclear medicine imaging</td>
</tr>
<tr>
<td>$^{111}In$</td>
<td>EC</td>
<td>$\gamma$</td>
<td>172, 247</td>
<td>2.8 days</td>
<td>$\gamma$-camera, SPECT</td>
<td>Used for longer term studies</td>
</tr>
<tr>
<td>$^{123}I$</td>
<td>EC</td>
<td>$\gamma$</td>
<td>159</td>
<td>13 h</td>
<td>$\gamma$-camera, SPECT</td>
<td></td>
</tr>
<tr>
<td>$^{201}Tl$</td>
<td>EC</td>
<td>X-ray</td>
<td>68÷80</td>
<td>3.0 days</td>
<td>$\gamma$-camera, SPECT</td>
<td></td>
</tr>
</tbody>
</table>
Radiopharmaceuticals

Ref. 2 – Chapter 5.4.5

• Radiopharmaceutical = radioactive compound (biomolecule or drug) of suitable quality to be safely administered to humans for diagnosis, therapy or research

• Radiopharmaceutical composition:
  1. Usually radionuclide + pharmaceutical compound
  2. Some exceptions:
     a. No associated pharmaceutical compound, for ex. $^{133}\text{Xe}$ gas
     b. Pharmaceutical component = counter ion, for ex. NaI

Courtesy Piero Posocco (Imperial College)
Radiopharmaceutical chemistry and biology

Ref. 2 – Chapters 5.4.5, 5.4.6 5.4.7 and 5.4.8

• Radiolabelling = “attach” the radionuclide to the pharmacological compound

• Distribution of radiopharmaceutical within living system depends on various factors including:
  1. 3D structure and size of the molecule
  2. Blood flow

• Quality control:
  1. Biological purity: toxicity, sterility and apyrogenicity
  2. Radiopharmaceutical purity: radionuclide, radiochemical and chemical purity
Choice of radiopharmaceuticals for imaging

- Characteristics of radiopharmaceuticals for nuclear medicine imaging:
  1. Accumulation / rate of uptake or clearance of radiopharmaceutical should be related to a physiologic, biochemical or molecular process, target or function
  2. No pharmacological or toxicological effects on system / organ under study → concentration usually subpharmacological (micromolar to nanomolar)
  3. High uptake in target tissue compared with non-target tissue = specificity → lower required dose + increase image contrast
  4. Half-life appropriate for the duration of the study
  5. Easily synthesised or labelled
  6. Sufficiently long shelf life before and after radiolabelling
  7. Be of required pharmaceutical quality
# Some common radiopharmaceuticals

<table>
<thead>
<tr>
<th>Compound</th>
<th>Nuclide</th>
<th>Measurement</th>
<th>Example of clinical use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ammonia</td>
<td>$^{13}N$</td>
<td>Myocardial perfusion</td>
<td>Coronary artery disease</td>
</tr>
<tr>
<td>Fluorodeoxyglucose (FDG)</td>
<td>$^{18}F$</td>
<td>Glucose metabolism</td>
<td>Cancer, neurological disorders and myocardial diseases</td>
</tr>
<tr>
<td>Gallium citrate</td>
<td>$^{67}Ga$</td>
<td>Sequestered in tumours</td>
<td>Tumour localization</td>
</tr>
<tr>
<td>$^{99}Tc^{m}$-methylene diphosphonate (MDP)</td>
<td>$^{99}Tc^{m}$</td>
<td>Bone metabolism</td>
<td>Metastatic spread of cancer</td>
</tr>
<tr>
<td>Sestamibi, Tetrofosmin</td>
<td>$^{99}Tc^{m}$</td>
<td>Myocardial perfusion</td>
<td>Coronary artery disease</td>
</tr>
<tr>
<td>MAG3, DTPA</td>
<td>$^{99}Tc^{m}$</td>
<td>Renal function</td>
<td>Kidney disease</td>
</tr>
<tr>
<td>HMPAO, EDC</td>
<td>$^{99}Tc^{m}$</td>
<td>Cerebral blood flow</td>
<td>Neurologic disorders</td>
</tr>
<tr>
<td>Labelled white blood cells</td>
<td>$^{111}In$</td>
<td>Sites of infection</td>
<td>Detecting inflammation</td>
</tr>
<tr>
<td>Sodium Iodide</td>
<td>$^{131}I$</td>
<td>Thyroid function</td>
<td>Thyroid disease</td>
</tr>
</tbody>
</table>