CCAP
Centre for the Clinical Application of Particles

# Nuclear diagnostics and Magnetic Resonance Imaging

## Lecture 2: Nuclear diagnostics (II)

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# Outline

1. **Radionuclides for nuclear detection II**
   - Requirements
   - Branching ratios and decay chains
   - Production

Section 1

# Radionuclides for nuclear detection II

# A practical matter . . .

A "Goldilocks" problem:

- Lifetime: neither:
  Too long—too small a fraction of decays used for imaging;
  Too short—too small a fraction delivered for imaging
- Practical lifetimes for imaging: minutes (seconds) to days
  - Longer-lived isotopes have applications in therapy
- Decay products 'sufficiently' penetrating:
  - Imaging requires external detection of radiation
- Radiation must emerge from the body:
  - Without leaving an unacceptably large dose . . . and . . .
  - With properties that make it easy to detect . . . and . . .
  - Pointing back to the origin of the radiation

# Desirable properties of radioisotopes

- $\alpha$-emitters are not suitable for imaging;
  Range too small, deposit too much dose
- $\gamma$-emitters: $\gamma$ energy in range $50 < E_\gamma < 600\,\text{keV}$;
  Low-energy photons have large interaction probability so unlikely to leave body, simply deposit dose
- Beta emitters: $e^-$ absorbed or lose energy and scatter, not used for imaging;
  If absorbed, $e^-$ simply deposits dose, reducing rate that could be detected.
  Energy loss and scattering of high-energy $e^-$ destroys pointing accuracy and make $e^-$ hard to detect.
- $e^+$ emitters exploited in positron-emission tomography;
  Signal (back-to-back photons) from $e^+e^-$ annihilation.

# Radiopharmaceuticals – examples

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

# Branching ratio

Decay constant, $\lambda$, determines the decay rate. The 'lifetime', $\tau$ is defined to be:

$$\tau = \frac{1}{\lambda} \qquad \ldots \text{and so} \ldots \qquad \lambda = \frac{1}{\tau}$$

The decay rate for the transition of $X$ into $Y$ may be calculated using "Fermi's Golden Rule":

$$\lambda_{X \to Y} = \eta \left| M_{X \to Y} \right|^2 \rho_f$$

Where $\eta$ is a constant and $\rho_f$ is the density of final states. $M_{X \to Y}$ is the quantum-mechanical 'matrix element' for the transition $X \to Y$. Some radionuclides may decay via more than one route. For such nuclei:

$$\frac{dP}{dt} = \frac{dP_{X \to Y}}{dt} + \frac{dP_{X \to Z}}{dt} + \cdots = \lambda_{X \to Y} + \lambda_{X \to Z} + \cdots = \sum_i \lambda_i = \lambda_T$$

$\lambda_T$ is the 'total decay rate' (sometimes referred to as 'total width'). The $\lambda_i$ are the 'partial' decay rates, or 'partial widths'.

# Branching ratios; an additional constraint

'Branching ratio' ($BR$): fraction of all decays that result in a particular final state:

$$BR = \frac{\lambda_{X \to Y}}{\lambda_T}$$

Decay chain may include beneficial radiation, suitable for imaging, and harmful radiation.

Example: $^{131}$I decay — $^{131}\mathrm{I}(e^-, \gamma)^{131}\mathrm{Xe}$

- Some $\gamma$s in useful range for imaging, but
- $e^-$ and low-energy $\gamma$s simply deposit dose.

Has application in therapy, e.g., thyroid tumours.
Not widely used today for imaging.
So, consider $^{123}$I, which decays via EC.

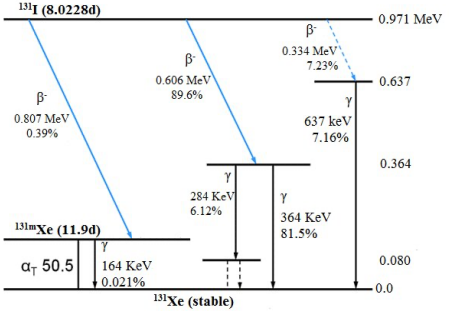
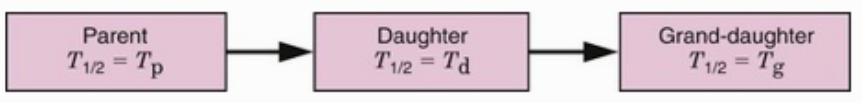



Figure from https://www.researchgate.net/publication/295919808_Radioiodine_I-131_for_Diagnosing_and_Treatment_of_Thyroid_Diseases

# Parent-daughter decay chain




Branching ratio [Parent $\rightarrow$ Daughter] $= \beta$

Rate of 'decay'of daughter nuclei:

$$\begin{aligned} \frac{dN_D}{dt} &= \lambda_P N_P \beta - \lambda_D N_D \\ &= \lambda_P N_{P0} \beta \exp(-\lambda_P t) - \lambda_D N_D \end{aligned}$$

I.e.:

$$\frac{dN_D}{dt} + \lambda_D N_D - \lambda_P \beta N_{P0} \exp(-\lambda_P t) = 0\,.$$

Solution:

$$N_D = \frac{\lambda_P}{\lambda_D - \lambda_P} \beta N_{P0} \left[\exp(-\lambda_P t) - \exp(-\lambda_D t)\right] + N_{D0} \exp(-\lambda_D t)$$

Or in terms of activation:

$$A_D = \frac{\lambda_D}{\lambda_D - \lambda_P} \beta A_{P0} \left[\exp(-\lambda_P t) - \exp(-\lambda_D t)\right] + A_{D0} \exp(-\lambda_D t) \quad (1)$$

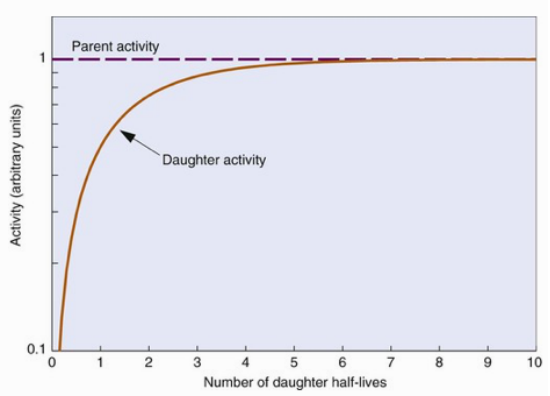
# $T_P >> T_D$; secular equilibrium

$T_P >> T_D \Rightarrow \frac{\lambda_P}{\lambda_D} << 1$ and $\exp(-\lambda_P t) \sim 1$.

So, equation 1 becomes:

$$A_D = \beta A_{P0}\left[1 - \exp(-\lambda_D t)\right] + A_{D0}\exp(-\lambda_D t)$$

If $A_{D0} = 0$ and $\beta = 1$, then the build up of $N_D$ reaches 'secular equilibrium after 5–6 $T_D$.



# $T_P > T_D$; transient equilibrium

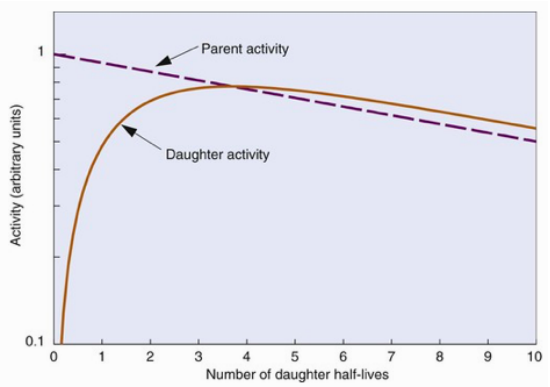
Transient equilibrium occurs at $t_{\mathrm{eq}}$ given by:

$$t_{\mathrm{eq}} = \frac{\ln\left[\frac{\lambda_P}{\lambda_D}\right]}{\lambda_P - \lambda_D}$$

At this time the activity of the daughter is a maximum, so one may write:

$$t_{\mathrm{max}} = t_{\mathrm{eq}} = \frac{1.44\,T_P\,T_D}{T_P - T_D}\ln\left[\frac{T_P}{T_D}\right]$$

If $A_{D0} = 0$, $\beta = 1$, and $T_P = 0.1\,T_D$, then build up and decay of $N_D$ reaches 'transient equilibrium' after $\sim 3.5\,T_D$.



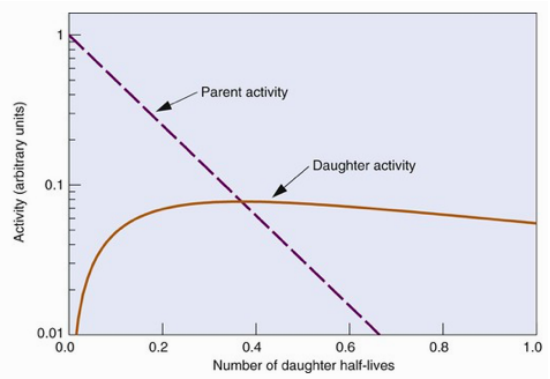
# $T_D > T_P$; no equilibrium

Maximum activity of daughter is still given by:

$$t_{\max} = t_{\text{eq}} = \frac{1.44\, T_P\, T_D}{T_P - T_D} \ln\left[\frac{T_P}{T_D}\right]$$

The daughter activity grows until $t_{\max}$ and then decreases. The parent activity 'falls away' and therefore fails to replenish the daughter.

If $A_{D0} = 0$, $\beta = 1$, and $T_P = 10\, T_D$, then build up of $N_D$ reaches maximum activity at $\sim 0.3\, T_D$.



# Methods for the production of radionuclides; overview

Nuclear reactor:

- Neutron capture
- Fission fragments

Radionuclide generators:

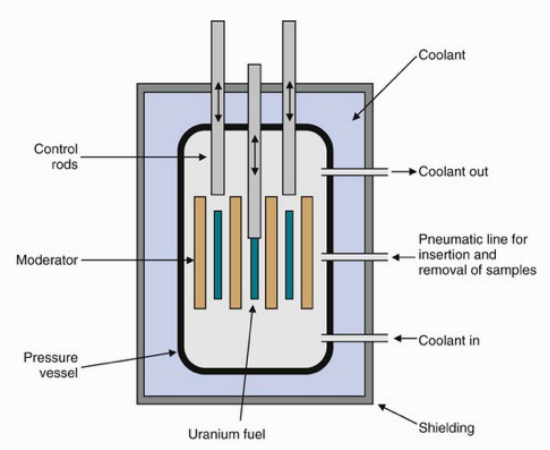
- Portable devices widely used in hospitals
- Require materials produced in nuclear reactors or accelerators

Accelerator:

- Cyclotron
- Active area of research; may return to this if there is time

# Nuclear reactor; one-slide outline

- Graphite or $D_2O$ moderator surrounds fissionable fuel cells
- Control rods, commonly boron, shield or expose fuel cells
- Position of fuel cells & control rods determine rate of chain reaction
- Ports in core allow insertion of samples for irradiation




Used to generate fission products or perform neutron activation

# Nuclear reactor: radionuclides produced by 'neutron activation'

Fission of $^{235}$U produces neutrons which bombard samples introduced into the core.

Neutron activation produces:

- Neutron-rich radionuclides, which usually undergo beta decay
- Product is chemically identical to parent material:
  - Product therefore can not be separately chemically;
  - Results in lower purity and lower activity than other production methods

Example reactions:

- $^{31}\mathrm{P}(n,\gamma)^{32}\mathrm{P}$
  - Capture of $n$ produces $^{32}\mathrm{P}^{*}$ which decays to $^{32}\mathrm{P}$ emitting a $\gamma$
- $^{50}\mathrm{Cr}(n,\gamma)^{51}\mathrm{Cr}$

# Nuclear reactor: production of $^{125}$I

$^{125}$I *is* produced via neutron activation and *can* be chemically separated, vis:

$$^{124}\mathrm{Xe}(n,\gamma)^{125}\mathrm{Xe} \underbrace{\xrightarrow{\text{EC or } \beta^-}}_{T_{\frac{1}{2}}=17\,\mathrm{hr}} {}^{125}\mathrm{I}$$

# Nuclear reactor: production via fission fragments

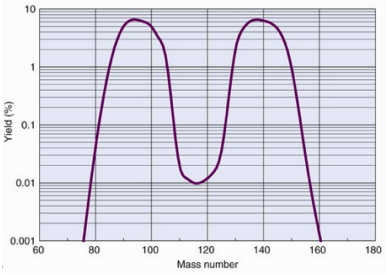
Fission fragments:

- Have bimodal distribution in $A$
- Excess of neutrons, hence tend to undergo $\beta^-$ decay until stable nucleus is produced

If long-lived isotope is produced it can be chemically extracted, e.g.:

$$^{99}_{39}\mathrm{Y} \xrightarrow{\beta^-(1.5\,\mathrm{s})} {}^{99}_{40}\mathrm{Zr} \xrightarrow{\beta^-(21\,\mathrm{s})} {}^{99}_{41}\mathrm{Nb} \xrightarrow{\beta^-(15\,\mathrm{s})} {}^{99}_{42}\mathrm{Mo}$$

Halflife of $^{99}$Mo is 65.9 hr, long enough to allow it to be extracted and incorporated in radionuclide generator to produce $^{99\mathrm{m}}$Tc



# Radionuclide generators

Parent-daughter radionuclide pair in an apparatus that permits separation and extraction of the daughter from the parent

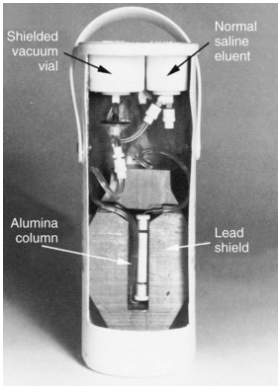
$T_P > T_D$ so that daughter product is replenished continuously by the decay of the parent and may be extracted repeatedly

Provides a local supply of short-lived radionuclides without needing a cyclotron or nuclear reactor

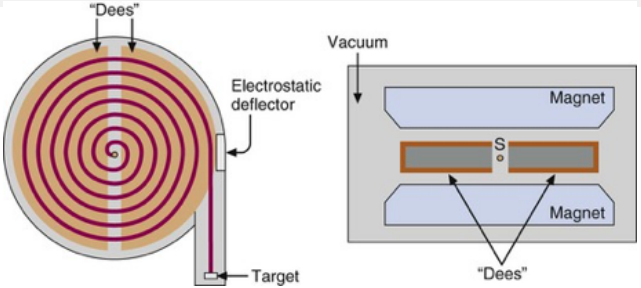
# Radionuclide generator: $^{99m}Tc$ for imaging

$$^{99}\text{Mo} \xrightarrow{\beta^-;\ T_{\frac{1}{2}}=66\ hr} {}^{99m}\text{Tc} \xrightarrow{\gamma;\ T_{\frac{1}{2}}=6\ hr} {}^{99}\text{Tc}$$

- $^{99}$Mo bound to an alumina column in form of molybdate ion ($MoO_4^-$)
- $^{99m}$Tc, the decay product, is not bound to column; it is chemically different
- $^{99m}$Tc is eluted from column with 5–25 ml saline
- 75–85% of available $^{99m}$Tc can be extracted
- Typically used for one week
- Often refereed as a 'Molly' or a 'Cow'



# Accelerator: cyclotron



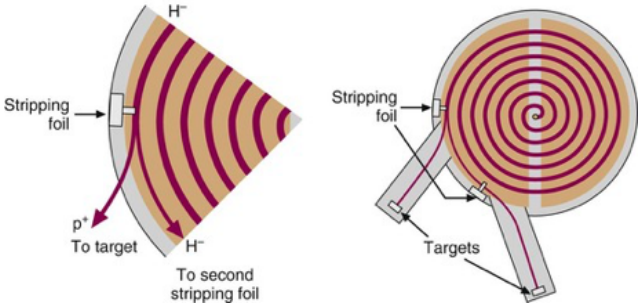

Cyclotron frequency, $f$:

$$f = \frac{qB}{2\pi m}$$

where $q$ is ion charge, $B$ the magnetic field strength, and $m$ is ion mass.

Extraction is at a single, pre-determined, energy.

# Accelerator: cyclotron




Schematic of $H^-$ ion cyclotron showing stripping foils and targets.

# Compact biomedical cyclotron

Medical cyclotrons usually located near PET scanner due to short lifetimes of radionuclides that are produced.

# Examples of cyclotron-produced radionuclides

| Product | Decay Mode | Common Production Reaction | Natural Abundance of Target Isotope* (%) | Energy Threshold (MeV)† |
|---|---|---|---|---|
| $^{11}C$ | $\beta^+$, EC | $^{14}N(p,\alpha)^{11}C$ | 99.6 | 3.1 |
| | | $^{10}B(d,n)^{11}C$ | 19.9 | 0 |
| $^{13}N$ | $\beta^+$ | $^{16}O(p,\alpha)^{13}N$ | 99.8 | 5.5 |
| | | $^{12}C(d,n)^{13}N$ | 98.9 | 0.35 |
| $^{15}O$ | $\beta^+$ | $^{14}N(d,n)^{15}O$ | 99.6 | 0 |
| | | $^{15}N(p,n)^{15}O$ | 0.37 | — |
| $^{18}F$ | $\beta^+$, EC | $^{18}O(p,n)^{18}F$ | 0.20 | 2.57 |
| | | $^{20}Ne(d,\alpha)^{18}F$ | 90.5 | 0 |
| $^{67}Ga$ | (EC,$\gamma$) | $^{68}Zn(p,2n)^{67}Ga$ | 18.8 | 5.96 |
| $^{111}In$ | (EC,$\gamma$) | $^{109}Ag(\alpha,2n)^{111}In$ | 48.2 | — |
| | | $^{111}Cd(p,n)^{111}In$ | 12.8 | — |
| $^{123}I$ | (EC,$\gamma$) | $^{122}Te(d,n)^{123}I$ | 2.6 | — |
| | | $^{124}Te(p,3n)^{123}I$ | 4.8 | — |
| $^{201}Tl$ | (EC,$\gamma$) | $^{201}Hg(d,2n)^{201}Tl$ | 13.2 | — |

Radioisotopes produced using cyclotron beams.
Decay schemes and production reactions are given.