Lecture 10 – Radiotracer

This lecture will cover: *(CH3.1-3.5)*

- Nuclear Medicine
- Radioactive decay
- Radiotracer

(*Supplementary reading: The Essential Physics of Medical Imaging CH15-16*)

Nuclear Medicine

- Measure the concentration of radiotracer molecules which are involved in a metabolic process.
- Detecting γ-ray emitted from unstable isotopes
- Functional imaging to visualize physiological process
- Difference from Angiography
  - Isotope with radioactivity *vs* non-radioactive contrast agent
  - Biological and metabolic process *vs* physical process
- Imaging techniques
  - Gamma camera
  - Emission CT (ECT) : SPECT, PET
  - Combined scanner : SPECT/CT, PET/CT, PET/MR

Nuclear medicine scan

The images from nuclear medicine comparing to radiography and CT:

- Lower SNR
- Lower spatial resolution
- Slow image acquisition
- High sensitivity and specificity

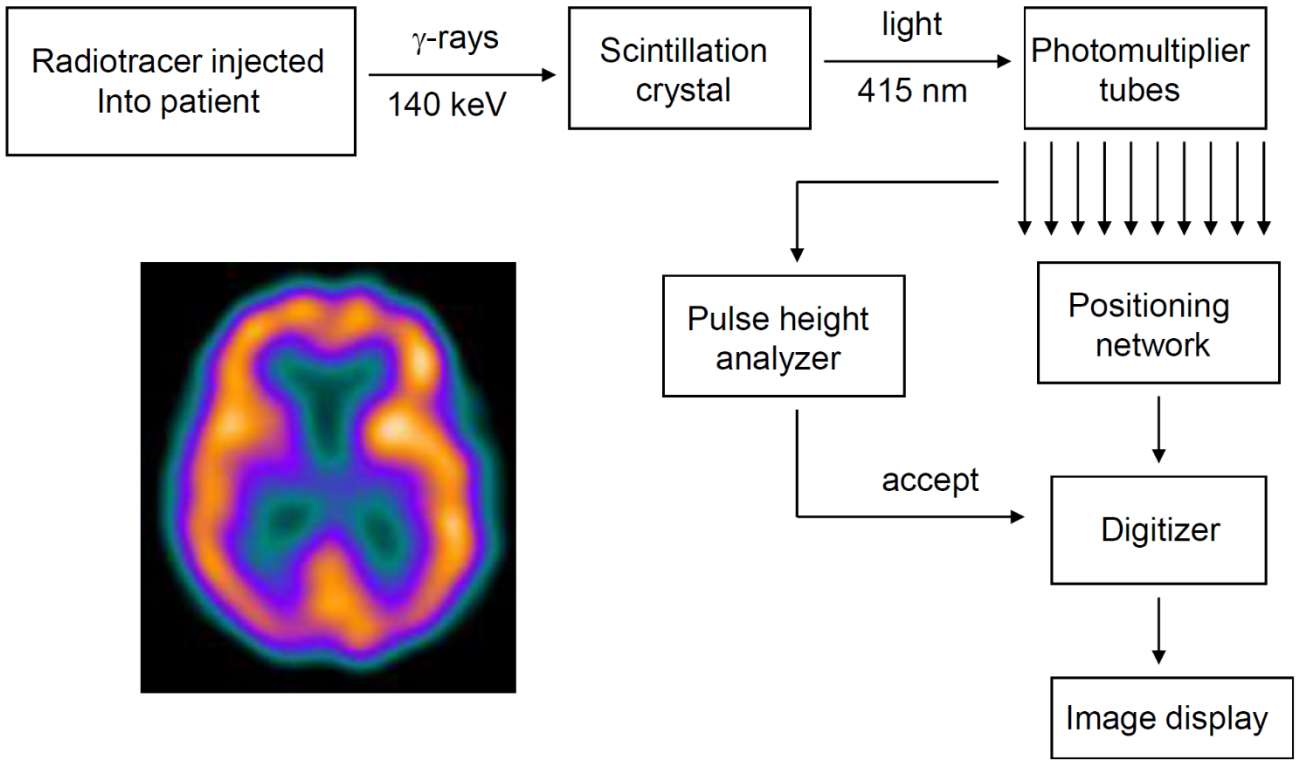

Fig. The operation of a nuclear medicine gamma camera. The inset shows a SPECT brain scan using ^{99m}Tc.

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Radioactive decay

- A radionuclide loses energy by emitting radiation in form of particles (α- or β- particles) and EM rays (Photons, γ rays)
- Photon energy: ~60-600KeV for nuclear medicine
- The radioactive decay modes
  - Nucleon emission or capture: usually α-decay
  - Electron emission or capture
    - ✓ Electron (β^-) emission (电子发射)
    - ✓ Electron capture (EC，电子捕获)
    - ✓ Positron emission (β^+ decay) (正电子发射)

Nucleon emission or capture

- Mainly α- decay: ${}^{A}_{Z}X \rightarrow {}^{A-4}_{Z-2}Y + {}^{4}_{2}\mathrm{He}^{2+}$
- heavy damage to tissue due to high kinetic energy (3-7MeV), therefore used for radiotherapy not imaging
- Shore range of an α-particle : 0.01-0.1mm in water and soft tissue
- To reach deep located tumor, neutron capture can be applied, where the neutron penetrate into the tissue until captured by an injected chemical component

$$ {}^{A}_{Z}X + \mathrm{n} \rightarrow {}^{A+1}_{Z}X + \gamma \rightarrow {}^{A-3}_{Z-2}Y + {}^{4}_{2}\mathrm{He}^{2+} $$

Particle Therapy

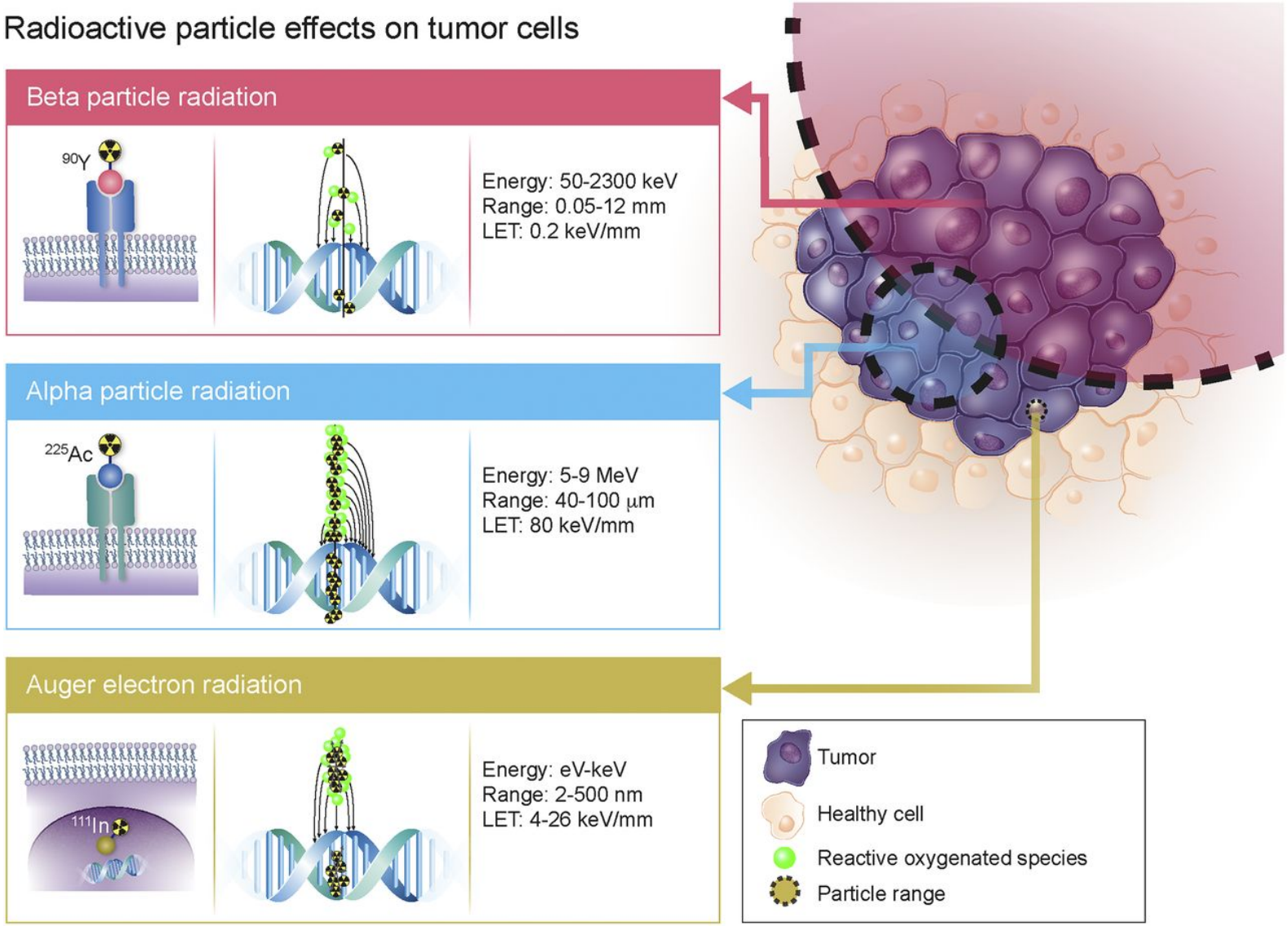


Fig. Comparison of therapeutic particle energies, particle ranges, LET(linear energy transfer), and DNA damage potencies.
Sophie Poty et al. J Nucl Med 2018;59:878-884

Electron emission or capture

- **Electron (β^-) emission (电子发射)**

$$ {}^{A}_{Z}X \rightarrow {}^{A}_{Z+1}Y + \mathrm{e}^- \quad , \quad \mathrm{n} \rightarrow \mathrm{p}^+ + \mathrm{e}^- $$

$$ {}^{Am}_{Z+1}Y = {}^{A}_{Z+1}Y + \gamma $$

- **Electron capture (EC，电子捕获)**

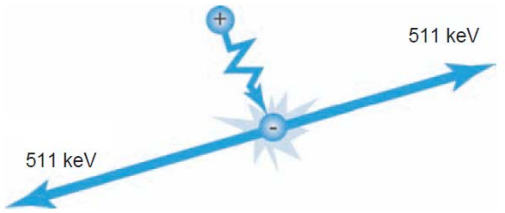
$$ {}^{A}_{Z}X + \mathrm{e}^- \rightarrow {}^{A}_{Z-1}Y \quad , \mathrm{p}^+ + \mathrm{e}^- \rightarrow \mathrm{n} $$

$$ {}^{Am}_{Z-1}Y = {}^{A}_{Z-1}Y + \gamma $$

- **Positron emission (β^+ decay) (正电子发射)**

$$ {}^{A}_{Z}X \rightarrow {}^{A}_{Z-1}Y + \mathrm{e}^+ \quad , \mathrm{p}^+ \rightarrow \mathrm{n} + \mathrm{e}^+ $$

$$ \mathrm{e}^+ + \mathrm{e}^- = 2\gamma \text{ (annihilation, 湮灭)} $$



Disintegration (衰变)

- **Radioactivity (放射性活度)**: $Q = -dN/dt = \lambda N$ (unit: Bq 贝克勒尔, 1Ci(居里)=3.7*10^{10}Bq)
- **Decay constant (衰变常数)**: $\lambda = Q/N$,

  and the number of radioactive isotopes at time t: $N(t) = N(t_0)e^{-\lambda(t-t_0)}$

- **Half life (半衰期)**: the time required for radioactivity to drop to one half of its value.

$$\tau_{1/2} = \frac{\ln 2}{\lambda} = 0.693/\lambda$$

the effective half life: $\tau_{1/2,\mathrm{eff}} = \frac{\tau_{1/2}\tau_{1/2,\mathrm{bio}}}{\tau_{1/2}+\tau_{1/2,\mathrm{bio}}}$

Where $\tau_{1/2}$: the half life of the isotope

$\tau_{1/2,\mathrm{bio}}$: the biological half life related to excretion

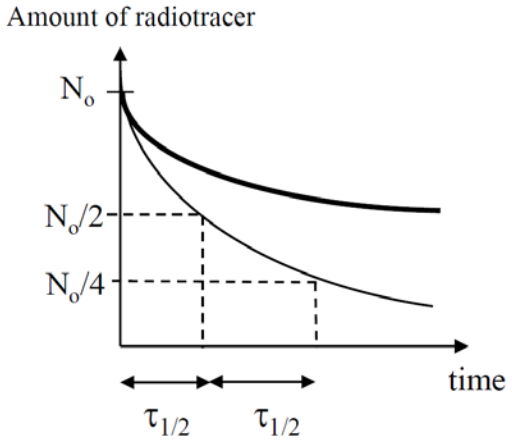


Fig. A plot of the amount of two different radiotracers as a function of time. The thin line corresponds to a radiotracer with a shorter half-life than the one indicated by the thick line. The $\tau_{1/2}$ refers to the radiotracer with the shorter half-life.

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Properties of Radiotracer (放射示踪剂)

- **The adequate radioactive half-life**
  - Short enough to produce significant radioactivity without requiring a large initial dose
  - Not so short that causes significant decay before the required post-injection delay
- **Mono-energetic γ-ray without emission of α- or β- particles**
  - Differentiated from Compton scattered γ-ray to improve image contrast
  - α- or β- particles increasing radiation without any image information
- **Energy of γ-ray greater than ~100KeV for enough γ-rays from deeply located issues to reach detectors.**
- **Energy of γ-ray less than ~200KeV so that the rays do not penetrate the thin lead septa in the collimator.**
- **High uptake in the organ of interest and low non-specific uptake in the rest of the body.**

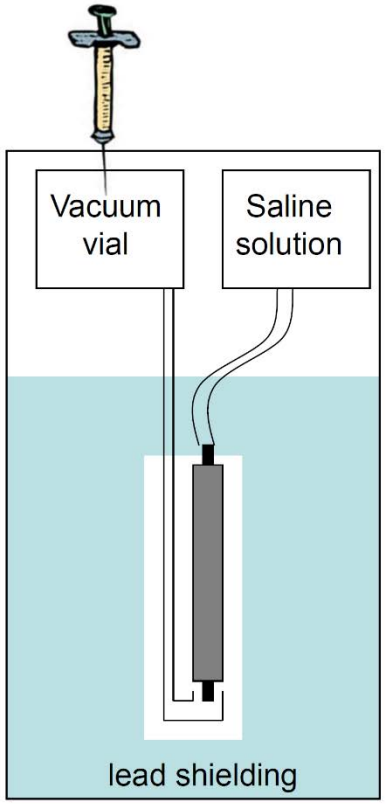
Commonly used radiotracer

Properties of common radiotracers used in planar scintigraphy and SPECT

Radiotracer	Half-life (hours)	γ-ray energy (keV)	Clinical application
^{99m}Tc	6.0	140	various
^{67}Ga	76.8	93, 185, 300, 394	tumour detection
^{201}Tl	72	167, 68–82 (X-rays)	myocardial viability
^{133}Xe	127.2	81	lung ventilation
^{111}In	67.2	171, 245	inflammation

^{99m}Tc Generator

- To produce ^{99m}Tc on-site
- ^{99}Mo (parent or mother nucleus, 母体) → ^{99m}Tc (daughter nucleus, 子体) → ^{99g}Tc
- ^{99}Mo absorbed on the surface of alumina ceramic column
- ^{99m}Tc is eluted from the column in the form of sodium pertechnetate (高锝酸钠)
- A mixture of ^{99}Mo , ^{99m}Tc and ^{99g}Tc



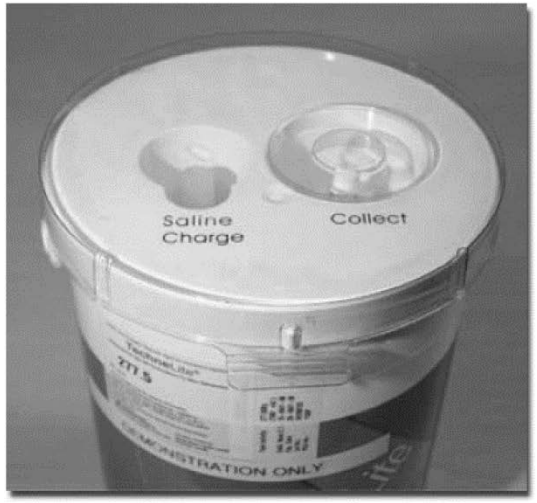


Fig. (left) A technetium generator. (right) A commercial technetium generator.

Time-dependent radioactivity

Radioactive decay: $^{99}_{42}\mathrm{Mo} \xrightarrow{\tau_{1/2}=66\mathrm{hrs}} {}^{99m}_{43}\mathrm{Tc} + {}^{0}_{1}\beta \xrightarrow{\tau_{1/2}=6\mathrm{hrs}} {}^{99g}_{43}\mathrm{Tc} + \gamma$

(N_1) (N_2) (N_3)

Where the radioactivity of $^{99m}_{43}\mathrm{Tc}$: $\frac{d\mathrm{N}_2}{dt} = \lambda_1\mathrm{N}_1 - \lambda_2\mathrm{N}_2 \Rightarrow \frac{d\mathrm{N}_2}{dt} + \lambda_2\mathrm{N}_2 = \lambda_1\mathrm{N}_1$

Solving the 1st-order differential equation:

homogenous: $\mathrm{N}_2 = \mathrm{C}e^{-\lambda_2 t}$ particular: $\mathrm{N}_2 = \mathrm{D}e^{-\lambda_1 t}$

Where $\mathrm{D} = \frac{\lambda_1\mathrm{N}_0}{\lambda_2-\lambda_1}$ and $\mathrm{C} = -\frac{\lambda_1\mathrm{N}_0}{\lambda_2-\lambda_1}$ with the boundary condition $\mathrm{N}_2 = 0|_{\mathrm{t}=0}$ and $\mathrm{N}_1 = \mathrm{N}_0 e^{-\lambda_1 t}$

Therefore the final solution: $\mathrm{N}_2 = \frac{\lambda_1\mathrm{N}_0}{\lambda_2-\lambda_1}(e^{-\lambda_1 t} - e^{-\lambda_2 t})$

and radioactivity of $^{99m}_{43}\mathrm{Tc}$: $\mathrm{Q}_2 = \lambda_2\mathrm{N}_2 = \frac{\lambda_1\lambda_2\mathrm{N}_0}{\lambda_2-\lambda_1}(e^{-\lambda_1 t} - e^{-\lambda_2 t})$

Where $\lambda_1 = 2.92*10^{-6}$/sec $\lambda_2 = 3.21*10^{-5}$/sec

Time-dependent radioactivity

The decay of ^{99} and increase of M o^{99m}Tc

Time (hr)	Radioactivity of ^{99}Mo (GBq)	Radioactivity of ^{99m}Tc (GBq)
0	100	0
1	99	10.8
2	97.9	20.6
3	96.9	29.1
6	93.9	47.9
12	88.2	69.7
18	82.5	77
24	77.8	78.8
48	59.7	59.5

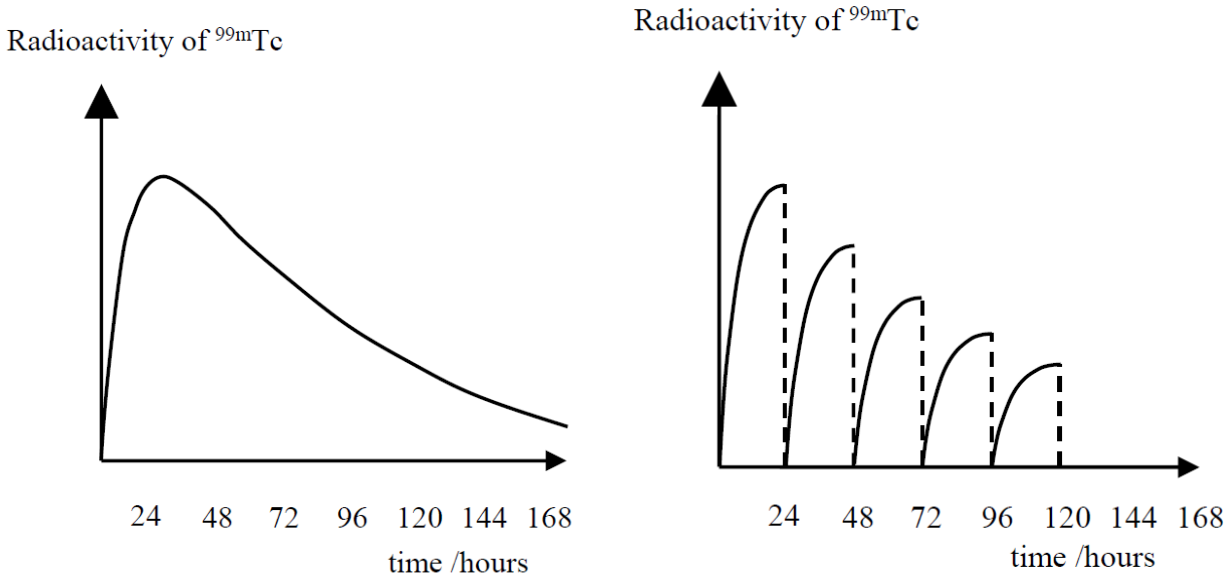


Fig. (left) Theoretical plot of the radioactivity of ^{99m}Tc vs time for a generator that is not milked. (right) Practical radioactivity curve in which the generator is milked every 24 hours, as shown by the dashed lines.

Distribution of radiotracer

The distribution of technetium-based radiotracer within the body

- Sodium pertechnetate is not widely used for nuclear medicine scans, and chemical modification is needed.
- For chemical ligand used for modification:
  - Strong chemical bond between chemical ligand and Tc ion
  - High selectivity for the organ of interest
- Factors affecting biodistribution
  - The strength of the binding to blood protein
  - The lipophilicity and ionization of the chemical ligand
  - The mean of excretion from the body