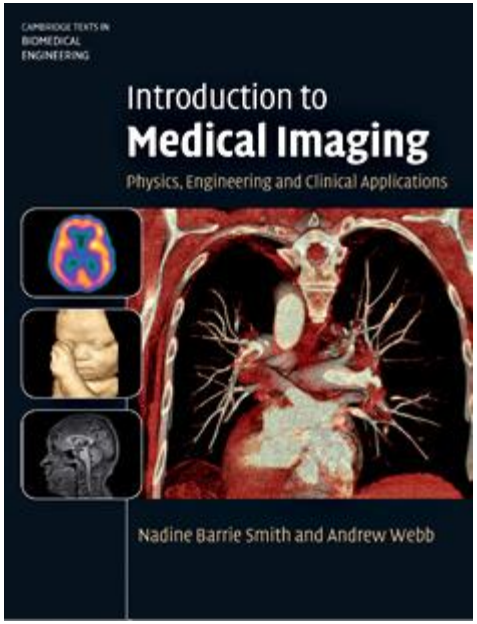
NUCLEAR MEDICINE

Recommended Textbook

- *Introduction to Medical Imaging: Physics, Engineering and Clinical Applications*, by Nadine Barrie Smith and Andrew Webb, Cambridge University Press, 2010.



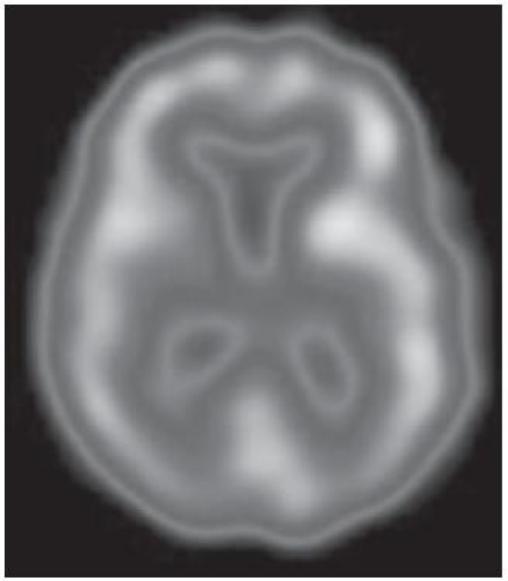
Nuclear Medicine Basics

- Nuclear medicine scans a very small amount (e.g., nanograms) of radioactive material called a radiotracer is injected intravenously into the patient
  - Agent then accumulates in specific organs in the body
  - How much, how rapidly and where this uptake occurs are factors which can determine whether tissue is healthy or diseased
- Three different modalities under the general umbrella of nuclear medicine
  - Plain scintigraphy
  - Single photon emission computed tomography (SPECT)
  - Positron emission tomography (PET)

Nuclear Medicine Basics

- Relative to most other imaging modalities, nuclear medicine scans (in particular planar scintigraphy and SPECT) are characterized as having:
  - Poor SNR
  - Low spatial resolution (~5–10 mm)
  - Slow image acquisition
  - Extremely high sensitivity
  - Very high specificity (no natural radioactivity from the body)
  - Intrinsic functional characteristics of the information content of the images

Operation of a Nuclear Medicine Gamma Camera



Radioactivity

- A radioactive isotope is one which undergoes a spontaneous change in composition of the nucleus, termed disintegration

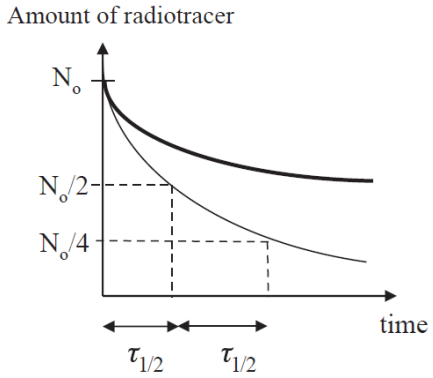
$$Q = -\frac{dN}{dt} = \lambda N \quad \Rightarrow \quad \boxed{N(t) = N(t=0)e^{-\lambda t}}$$

- Radioactivity is measured in units of curies (Ci), where one curie equals 3.73×10^{10} disintegrations per second

Half-Life Time

- Half-life ($\tau_{1/2}$): time required for the radioactivity to drop to one-half of its value

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



- Biological half-life of the radiotracer ($\tau_{1/2,bio}$) (how long the radiotracer remains in the body) must also be considered
- Effective half-life ($\tau_{1/2,eff}$) is a combination of the two half-lives

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

Radioactivity Example:

- *Two patients undergo nuclear medicine scans. One receives a dose of radiotracer A and the other radioatracer B. The half-life of A is 6 hours and of B is 24 hours. If the administered dose of radiotracer A is three times that of radiotracer B, and the biological half-lives of A and B are 6 and 12 hours respectively, at what time is the radioactivity in the body the same for the two patients?*

Solution:

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

→ Obtain values for decay constants λ_A, λ_B

$$3e^{-t\lambda_A} = e^{-t\lambda_B}$$

→ Obtain values for required time t

Properties of Ideal Radiotracers

- Radioactive half-life that is short enough to produce significant radioactivity without requiring a very large initial dose, but not so short that there is significant decay before the required post-injection delay to allow the radiotracer to clear the blood and distribute in the relevant organs
- Decay should be via emission of a mono-energetic γ-ray without emission of alpha- or beta-particles.
  - A mono-energetic γ-ray allows discrimination between Compton scattered and unscattered γ-rays, thereby improving image contrast. Alpha- or beta-particles are completely absorbed within tissue, therefore increasing the radioactive dose without giving any useful image information

Properties of Ideal Radiotracers

- The energy of the γ-ray should be greater than ~100 keV so that a reasonable proportion of γ-rays which are emitted deep within the tissue have sufficient energy to travel through the body and reach the detector
- The energy of the γ-ray should be less than ~200 keV so that the rays do not penetrate the thin lead septa in the collimator (which is analogous to the anti-scatter grid in X-ray imaging)
- The radiotracer should have a high uptake in the organ of interest and relatively low non-specific uptake in the rest of the body. These two factors lower the required dose for the patient and increase the image contrast, respectively

Example Radiotracers

- Most widely used radiotracer is ^{99m}Tc which is involved in over 90% of planar scintigraphy and SPECT studies
  - It exists in a metastable state (one with a reasonably long half-life)
  - Formed from ^{99}Mo
  - Energy of the emitted γ-ray is 140 keV

$$^{99}_{42}\mathrm{Mo} \xrightarrow{\tau_{1/2} = 66\,\text{hours}} {}^{0}_{1}\beta + {}^{99m}_{43}\mathrm{Tc} \xrightarrow{\tau_{1/2} = 6\,\text{hours}} {}^{99g}_{43}\mathrm{Tc} + \gamma.$$

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

Technetium Generator

- Tc generator is delivered to a nuclear medicine department at the beginning of the week, returned at the end of the week
  - Very convenient method for producing ^{99m}Tc

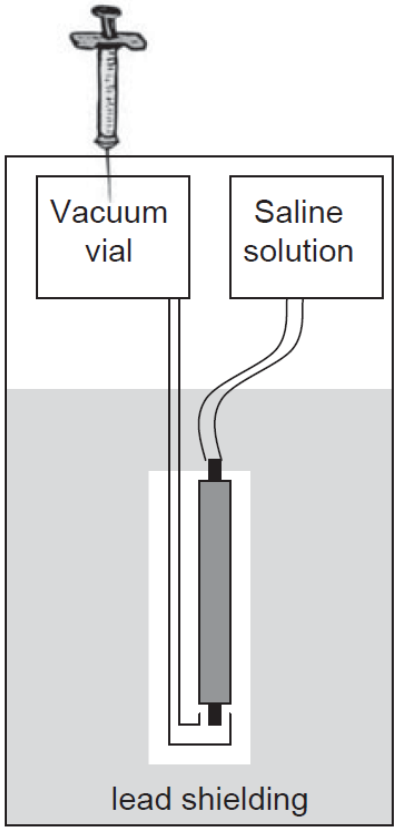
$$^{99}Mo \xrightarrow{\lambda_1} {}^{99m}Tc \xrightarrow{\lambda_2} {}^{99g}Tc$$

$$(N_1) \qquad (N_2) \qquad (N_3)$$

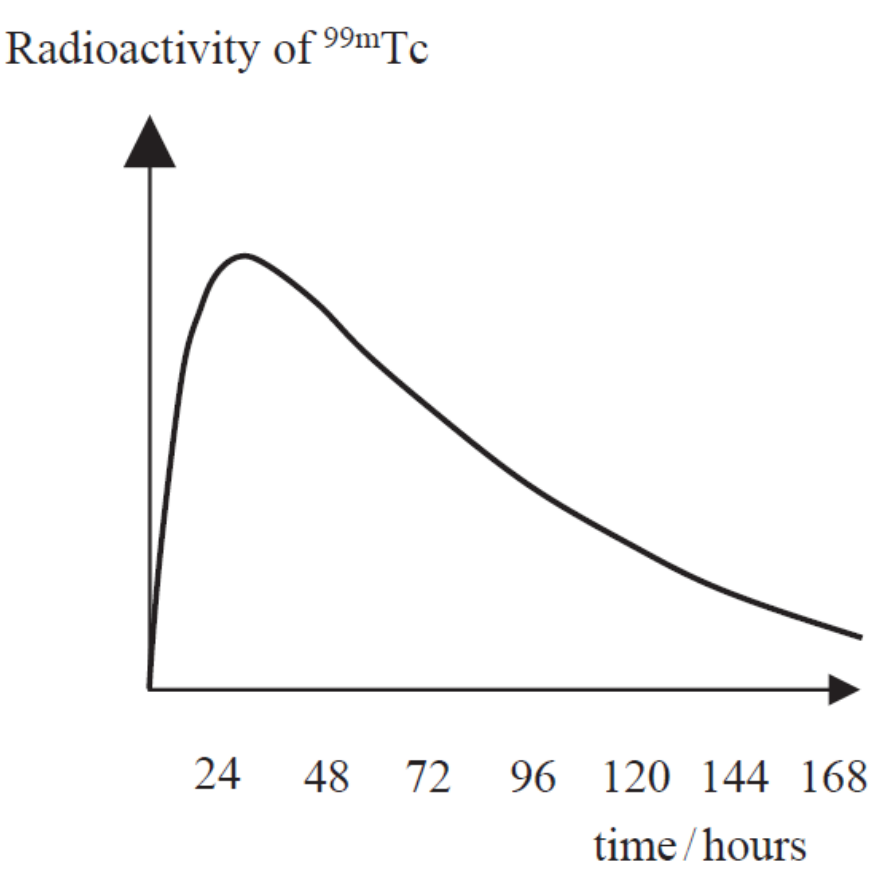
$$N_1 = N_o e^{-\lambda_1 t}$$

$$\frac{dN_2}{dt} = \lambda_1 N_1 - \lambda_2 N_2 \Rightarrow \frac{dN_2}{dt} + \lambda_2 N_2 = \lambda_1 N_1 .$$

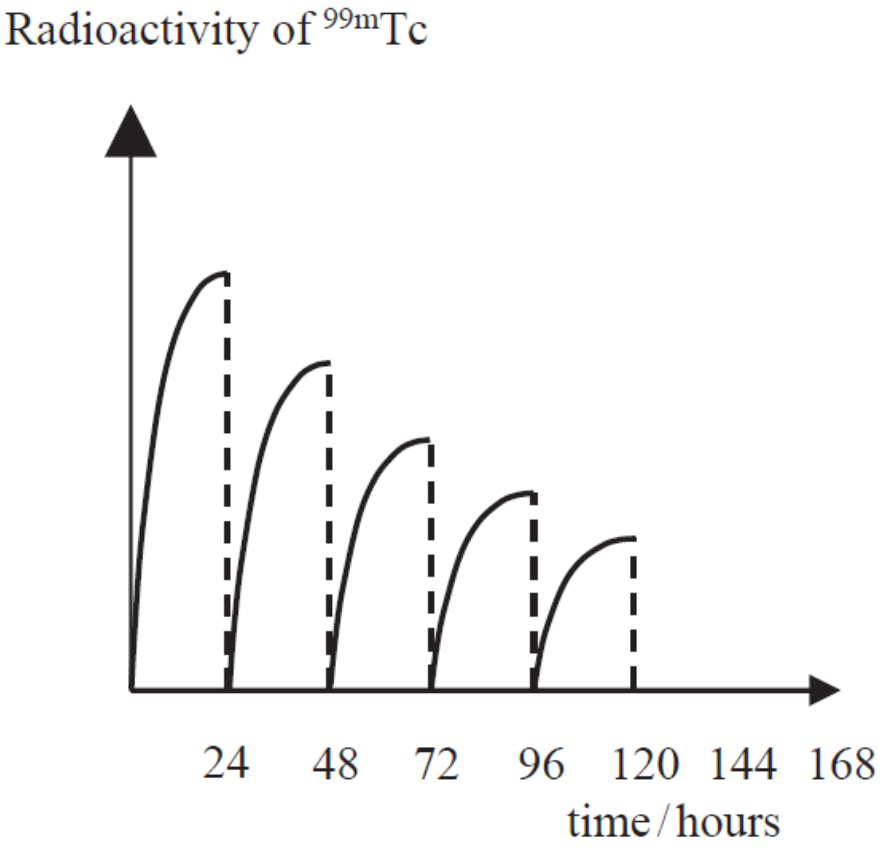
$$N_2 = -\frac{\lambda_1 N_0}{\lambda_2 - \lambda_1} e^{-\lambda_2 t} + \frac{\lambda_1 N_0}{\lambda_2 - \lambda_1} e^{-\lambda_1 t}$$



Radioactivity of ^{99m}Tc vs Time

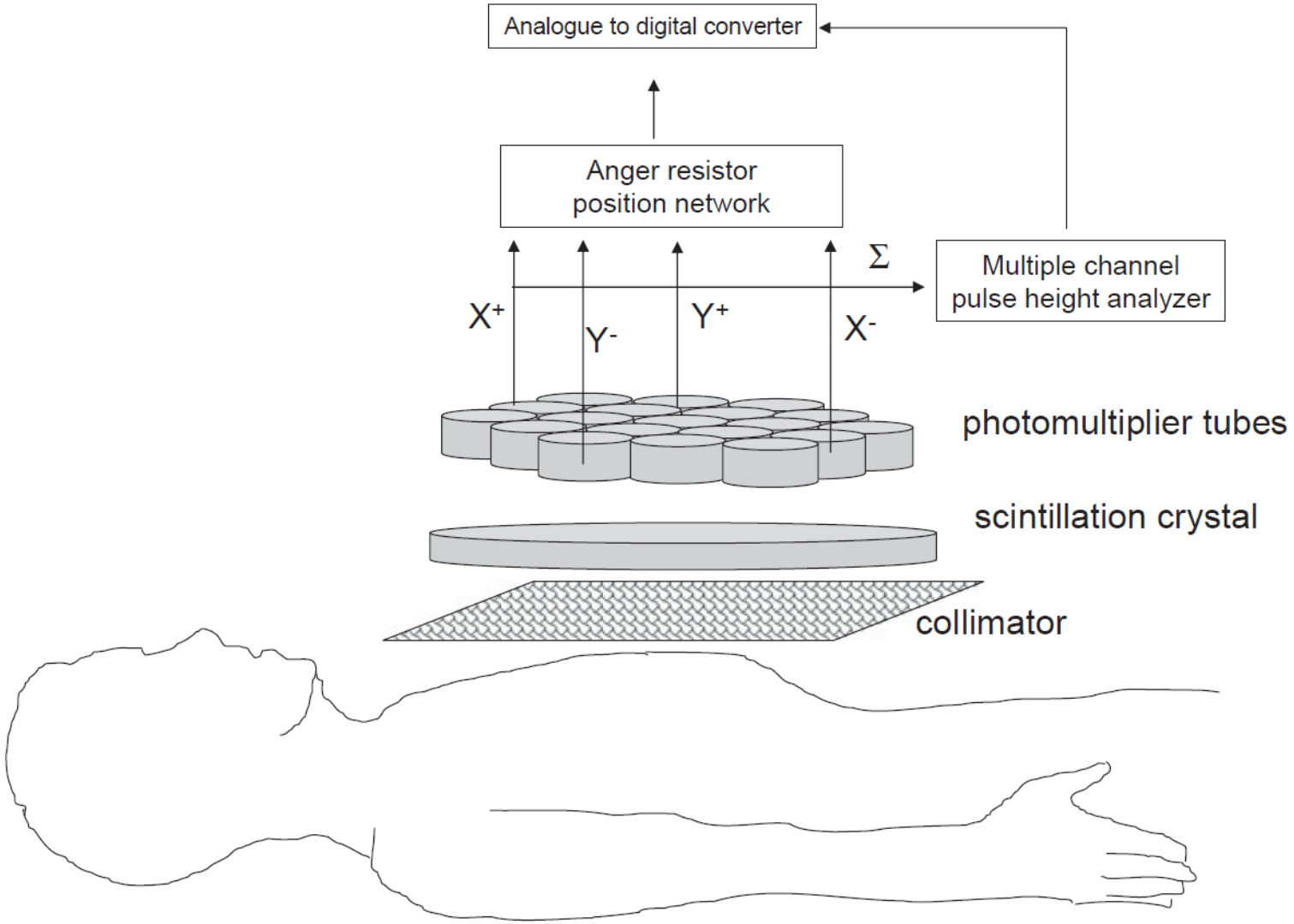


Generator that is not milked



Generator that is milked every 24 hours

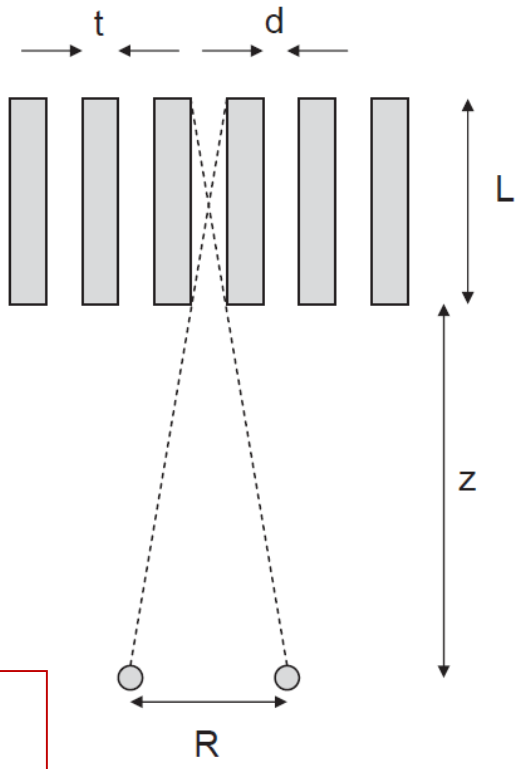
Gamma Camera

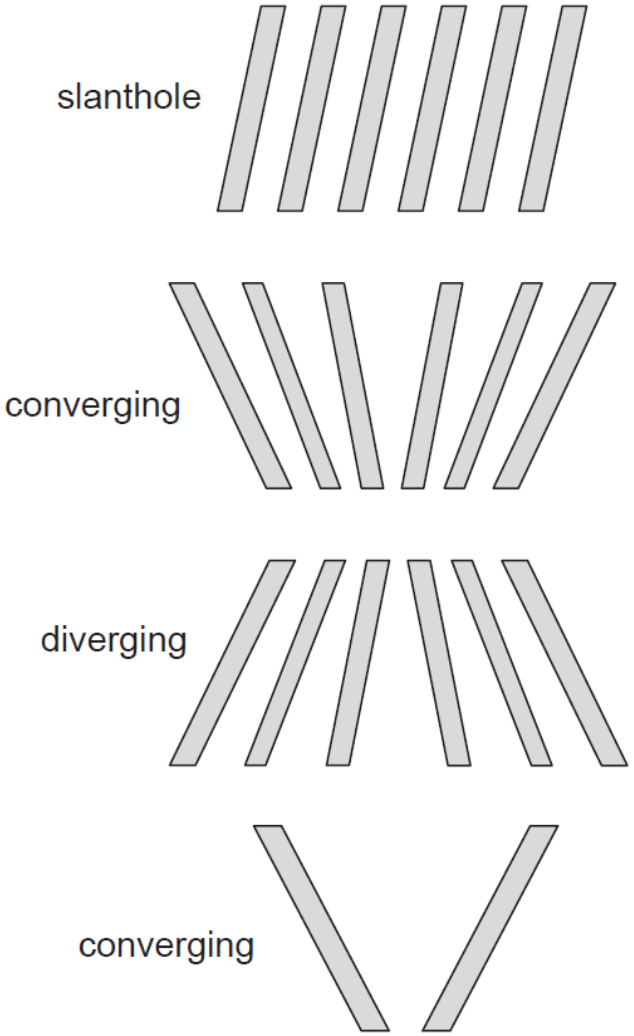


Collimator

Parallel Collimator

$$L_{eff} = L - \frac{2}{\mu_{septa}}.$$





Spatial Resolution (R)

$$R = \frac{d(L_{eff} + z)}{L_{eff}}$$

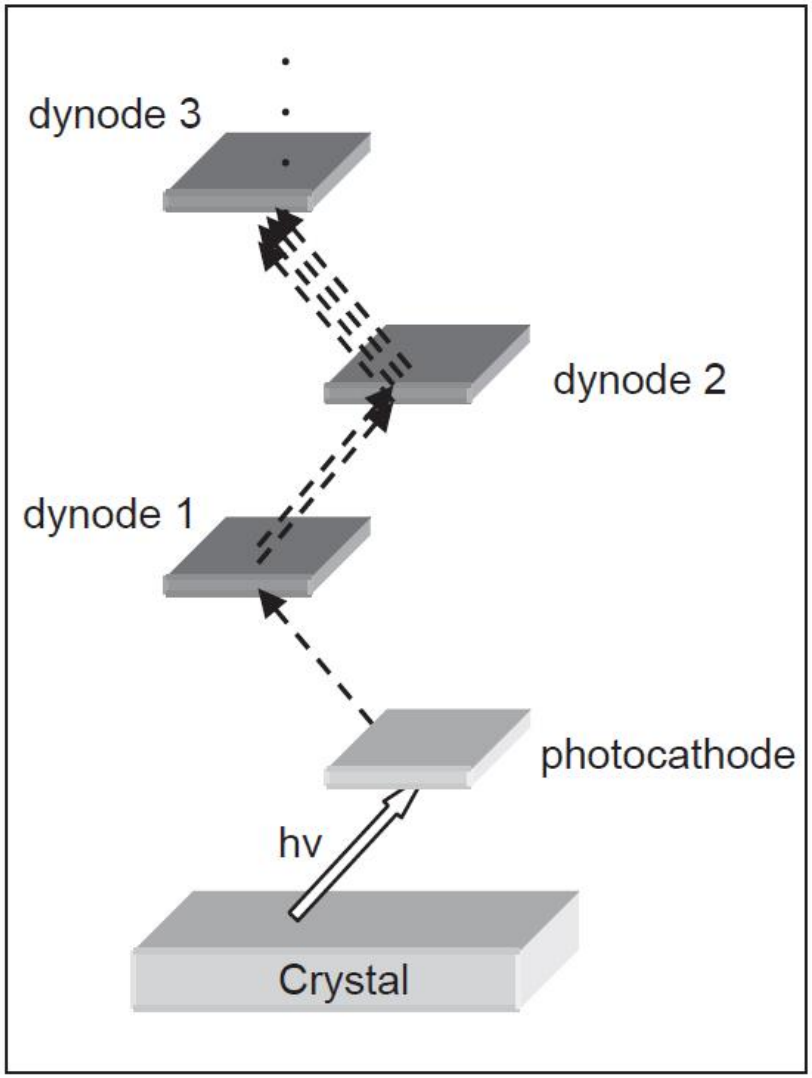
Efficiency (g)

$$g \approx K^2 \frac{d^2}{L_{eff}^2} \frac{d^2}{(d + t)^2}$$

Detector Scintillation Crystal

- In the gamma camera, the detector is a large single crystal of thallium-activated sodium iodide, NaI(Tl), 40–50 cm diameter
- When a γ-ray strikes the crystal, it loses energy through photoelectric and Compton interactions which result in a population of excited electronic states within the crystal
- De-excitation of these states occurs ~230 nanoseconds later via emission of photons with a wavelength of 415 nm (visible blue light), corresponding to a photon energy of ~4 eV
- A very important characteristic of scintillators such as NaI(Tl) is that the amount of light (the number of photons) produced is directly proportional to the energy of the incident γ-ray

Photomultiplier Tube (PMT)



Photomultiplier Tube (PMT)

- Produces between 10^5 and 10^6 electrons for each initial photoelectron, creating an amplified current at PMT output
- Since each PMT has a diameter of 2–3 cm, and the NaI(Tl) crystal is much larger in size, a number of PMTs are closely coupled to the scintillation crystal.
  - Most efficient packing geometry is hexagonally-close-packed
  - Arrays of 61, 75 or 91 PMTs are typically used, with a thin optical coupling layer used to interface the surface of each PMT with the scintillation crystal
  - Each PMT should ideally have an identical energy response. If this is not the case, then artifacts are produced in the image. For planar nuclear medicine scans, a variation in uniformity of up to **10%** can be tolerated whereas only values less than **1%** can be tolerated in SPECT

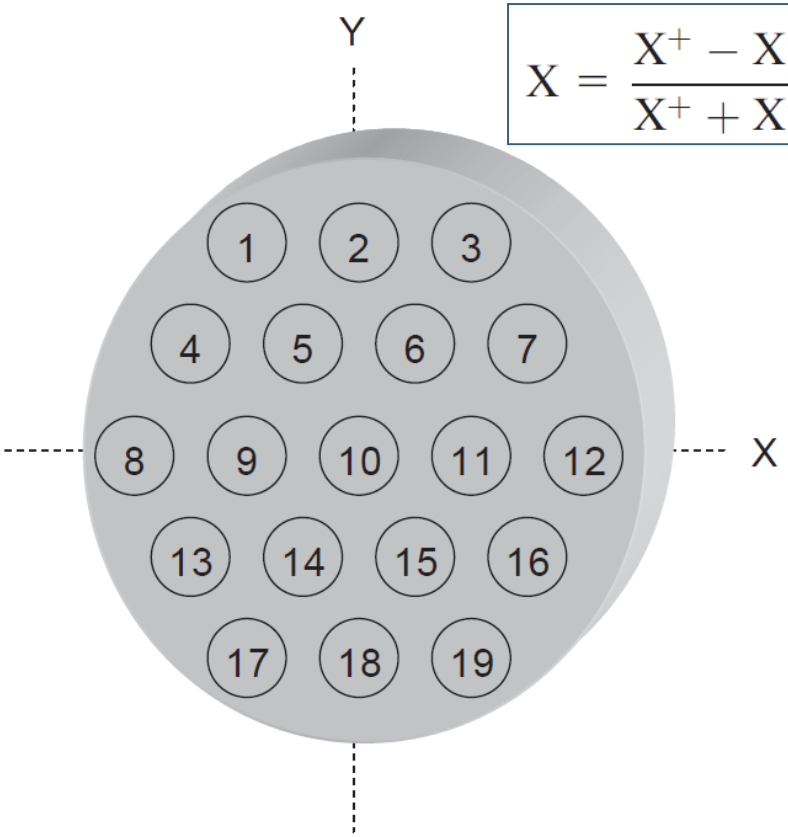
Anger Position Network

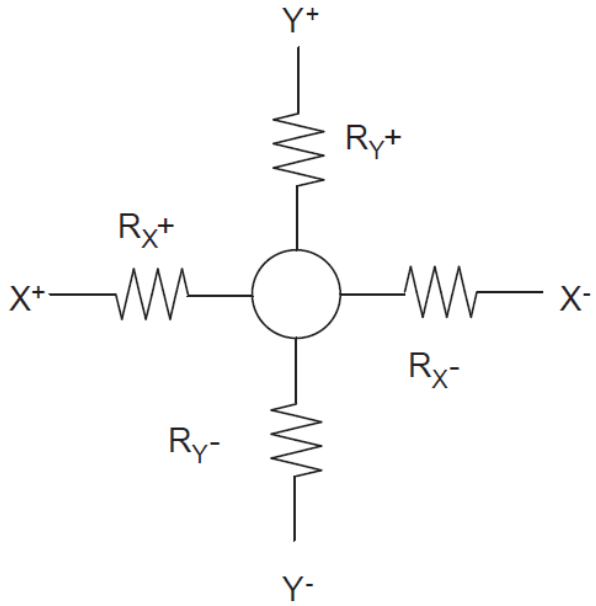
- Whenever a scintillation event occurs in a NaI(Tl) crystal the PMT closest to the scintillation event produces the largest output current.
  - If this were only method of signal localization, then the spatial resolution would be no finer than dimensions of the PMT, i.e., several cm
- Adjacent PMTs produce smaller output currents, with the amount of light detected being approximately inversely proportional to the distance between the scintillation events and the particular PMT
  - By comparing the magnitudes of the currents from all the PMTs, the location of the scintillation within the crystal can be much better estimated

Anger Position Network

- In older analog gamma cameras this process was carried out using an Anger logic circuit, which consists of four resistors connected to the output of each PMT

$$X = \frac{X^+ - X^-}{X^+ + X^-}, Y = \frac{Y^+ - Y^-}{Y^+ + Y^-}$$





Pulse Height Analyzer (PHA)

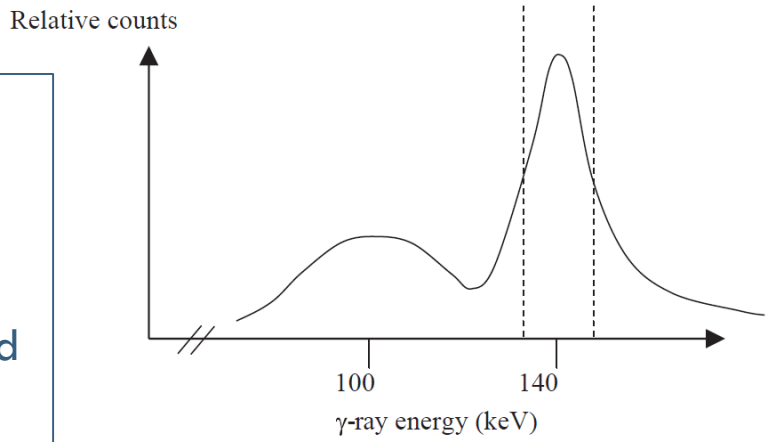
- In addition to recording the individual components X^+, X^-, Y^+ and Y^-, summed signal $R(X^+ + X^- + Y^+ + Y^-)$, termed the 'z-signal', is sent to PHA
- Role of the PHA is to determine which of the recorded events correspond to γ-rays that have not been scattered within tissue (primary radiation) and should be retained, and which have been Compton scattered in the patient, do not contain any useful spatial information, and so should be rejected.
- Since the amplitude of the voltage pulse from PMT is proportional to the energy of the detected γ-ray, discriminating on the basis of the magnitude of the output of the PMT is equivalent to discriminating on the basis of γ-ray energy

Pulse Height Analyzer (PHA)

- A multiplechannel analyzer (MCA), in which the term 'channel' refers to a specific energy range, uses an ADC to digitize signal, then produce a pulse-height spectrum
  - The number of channels in an MCA can be more than a thousand, allowing essentially a complete energy spectrum to be produced
  - After digitization, the upper and lower threshold values for accepting the γ-rays are applied

Energy resolution of the system is defined as the full-width-half-maximum (FWHM) of the photopeak

- Typically is about 14 keV (or 10%) for most gamma cameras without a patient present
- In a clinical scan with the patient in place, the threshold level for accepting the 'photopeak' is set to a slightly larger value, typically 20%



Instrument Dead Time

- If an injected dose of radiotracer is very large, the total number of γ-rays striking the scintillation crystal can exceed the recording capabilities of the system
  - Particularly true at the beginning of a clinical scan when radioactivity is at its highest level
  - Limitation is due to the finite recovery and reset times required for various electronic circuits in the gamma camera
- Two types of behaviour exhibited by the system components, termed **paralysable** and **nonparalysable**

Instrument Dead Time

- Paralysable behaviour is a phenomenon in which a component of the system cannot respond to a new event until a fixed time after the previous one, irrespective of whether that component is already in a non-responsive state.
  - Each time a γ-ray strikes the scintillation crystal it produces an excited electronic state, which decays in 230 ns to release a number of photons.
  - If another γ-ray strikes same spot in the crystal before the excited state decays, then it will take a further 230 ns to decay, and only one set of photons will be produced even though two γ-rays have struck the crystal
  - Very high rate of γ-rays striking detector can result in a considerably elongated dead-time and so the number of recorded events can actually decrease.

Instrument Dead Time

- Non-paralysable component cannot respond for a set time, irrespective of the level of radioactivity
  - For example, Anger logic circuit and PHA take a certain time to process a given electrical input signal, and during this time any further events are simply not recorded: this time is fixed, and is not elongated if further scintillation events occur
- Overall dead-time τ is determined by non-paralysable part

$$\tau = \frac{N - n}{nN}$$

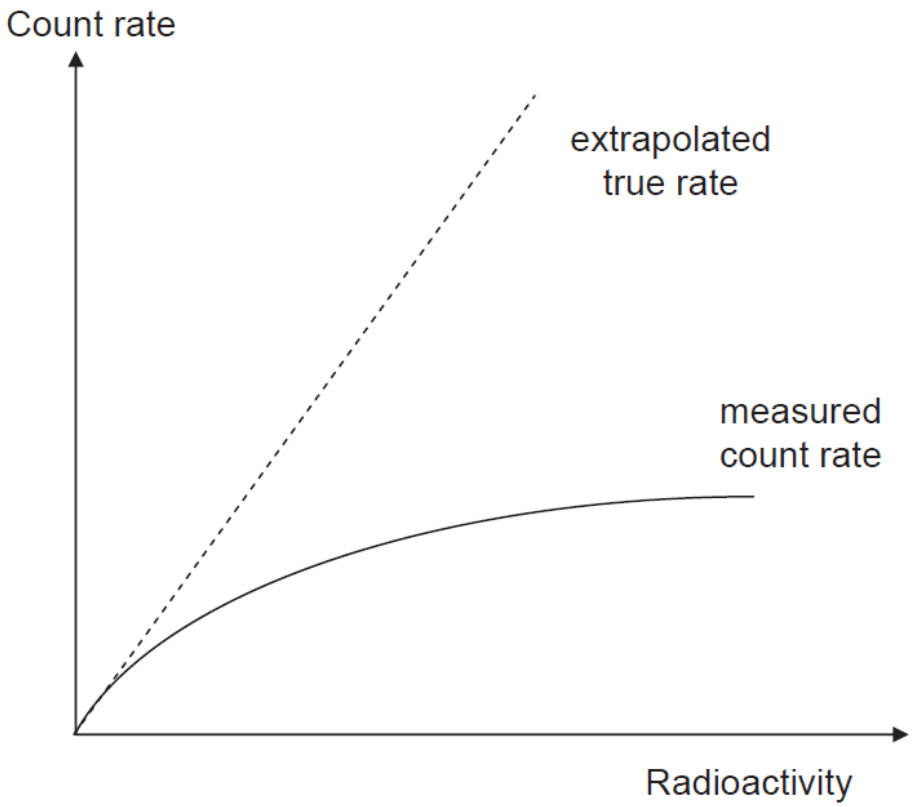
N: true count rate (number of scintillations per second), n: measured count rate, maximum measurable count rate is given by $1/\tau$

Instrument Dead Time Correction

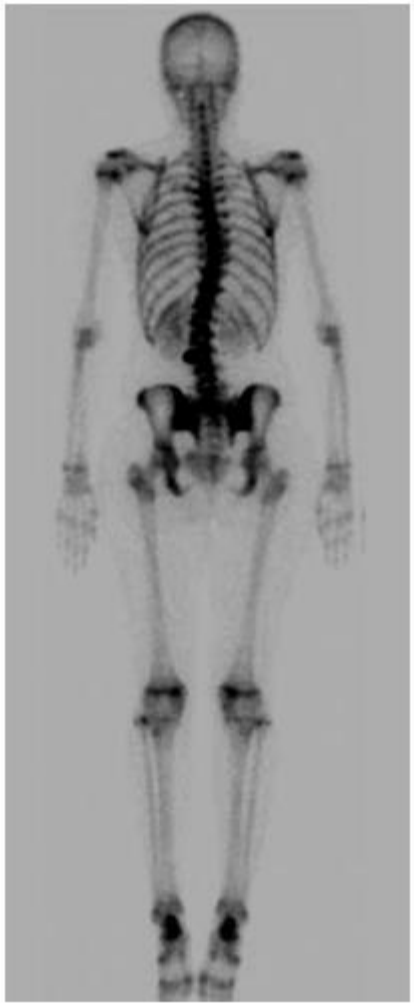
- Corrections for the dead-time are based upon calibrations using phantoms of known radioactivity, and also independent electronic measurements of the dead time of individual components of the system

Example: Suppose that the true count rate in a gamma camera is N=10,000 per second, but the measured rate is only n=8,000 per second. What is the dead time of the system?

Solution: $$\tau = \frac{N - n}{nN}$$

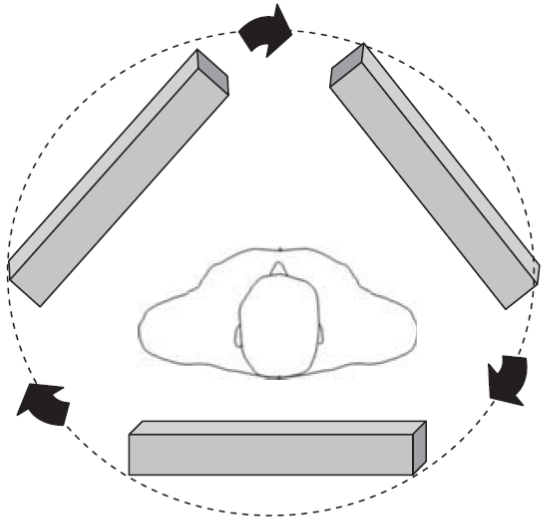


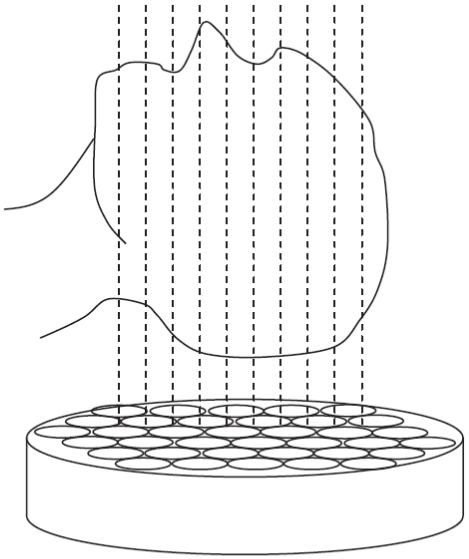
Practical Planar Scintigraphy

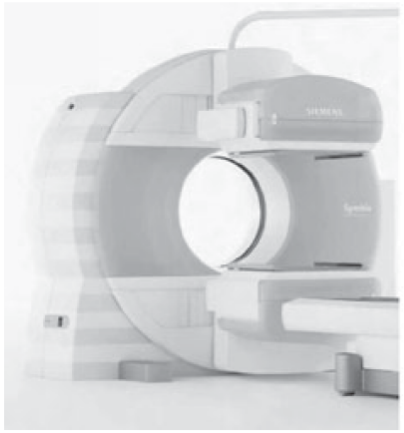


Single Photon Emission Computed Tomography (SPECT)

- Injected radioactive tracer
- Moving Gamma Camera
- Tomographic scans can be used to reconstruct image







Covered Material and Exercises

- Parts of chapter 3 of the Smith and Webb text book
- Solve problems: 3.1, 3.2, 3.3, 3.10