Handout 7. Radionuclide Imaging

7.1 What is Radionuclide Imaging?

Radiography: Transmission – measuring attenuation coefficients

Radionuclide imaging:

- ❖ Inject radiopharmaceuticals (radioactive material + pharmacologic agent);
- ❖ The radiopharmaceuticals is SELECTIVELY taken up in specific regions of the anatomy;
- ❖ Detect or image the Gamma rays emitted by the radioactive material.

Radionuclide imaging is NOT an attenuation based imaging.

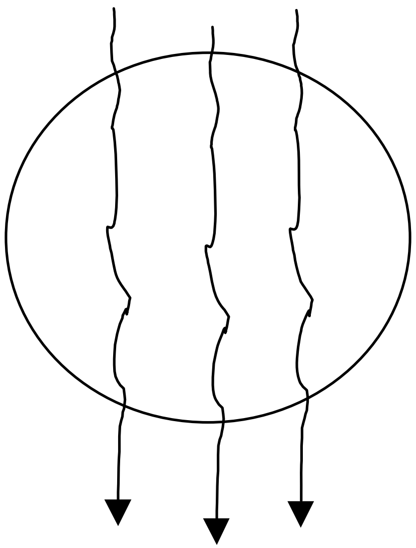
Energy range for radionuclide imaging

- To minimize patient dose – requires high energy
- Quantum efficiency considerations in detection – requires low energy
- A compromise: such as Gamma rays of 140KeV (by Technetium –99m)

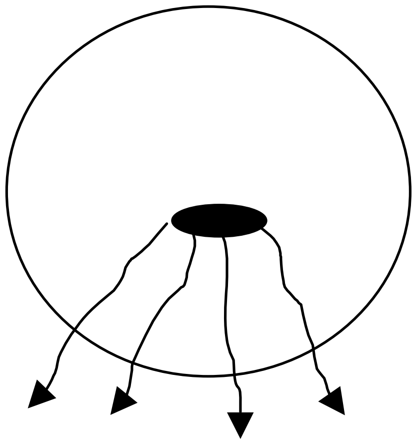
X-ray VS Gamma Ray: X-rays are generated by electron events and Gamma rays are generated by nuclear events.

Advantages of radionuclide imaging:

- It can provide information about the physiological functions of the patient that is difficult or impossible to obtain from other imaging modalities.



X-ray



Gamma ray

7.2 Fundamentals of Radioactivity:

- **Atom:** The electron cloud of an atom is 2 to 3×10^{-10}m in diameter. Its nucleus is a thousand times smaller and several thousand times more massive.
- **Nucleus:** A nucleus is made up of protons and neutrons.
- **Proton:** A proton bears a charge of the same magnitude as an electron but of opposite sign, and is 1800 times more massive.
- **Neutron:** A neutron is uncharged and slightly more massive than a proton.
- **Atomic number (Z):** The number of protons in a nucleus is called the atomic number and is commonly denoted Z.

- **Element type:** Virtually all the normal chemical, electrical and mechanical characteristics of an atom are determined solely by Z, that is, by its element type. These properties are independent of the number of neutrons.
- **Isotopes:** The isotopes of an element are those nuclear types with the same Z but different numbers of neutrons. The nuclear properties depend strongly on isotope type.
- **Radionuclide:** "**nuclide**" refers to a nuclear species with well-defined characteristics, including a particular value for Z, and for the total number of nucleons (protons plus neutrons). **"radio"** implies that the nuclide is unstable.
- **Radioactivity (radioactive decay):** Radioactivity is the process whereby an excited, unstable nucleus drops into a state of lower energy and greater (usually) stability. Radioactive decay results emission of radiation (nuclear particles, such as Alpha, Beta, Gamma rays).

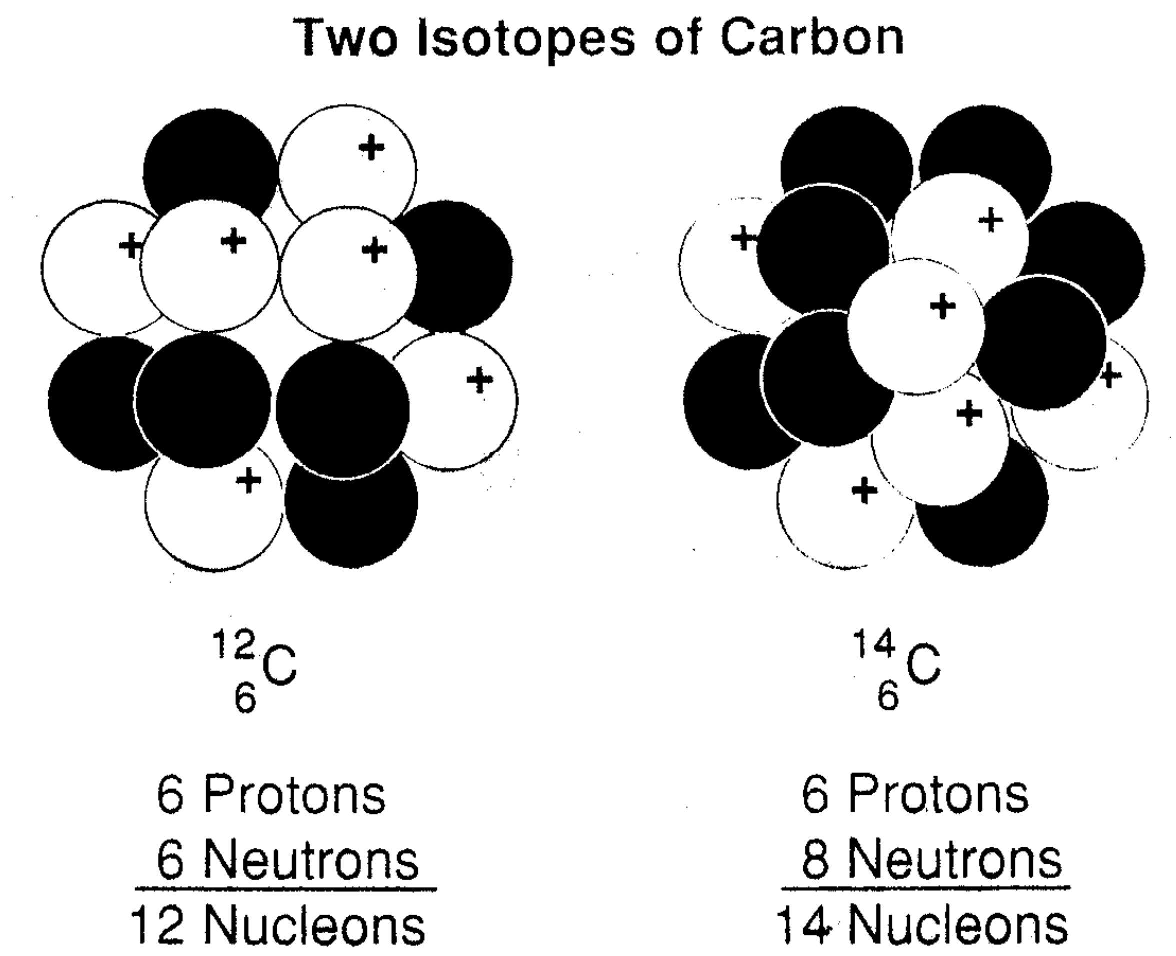


Figure: Nuclei of the isotopes ^{12}C and ^{14}C of the element carbon contain the same number of protons (6), but different numbers of neutrons.

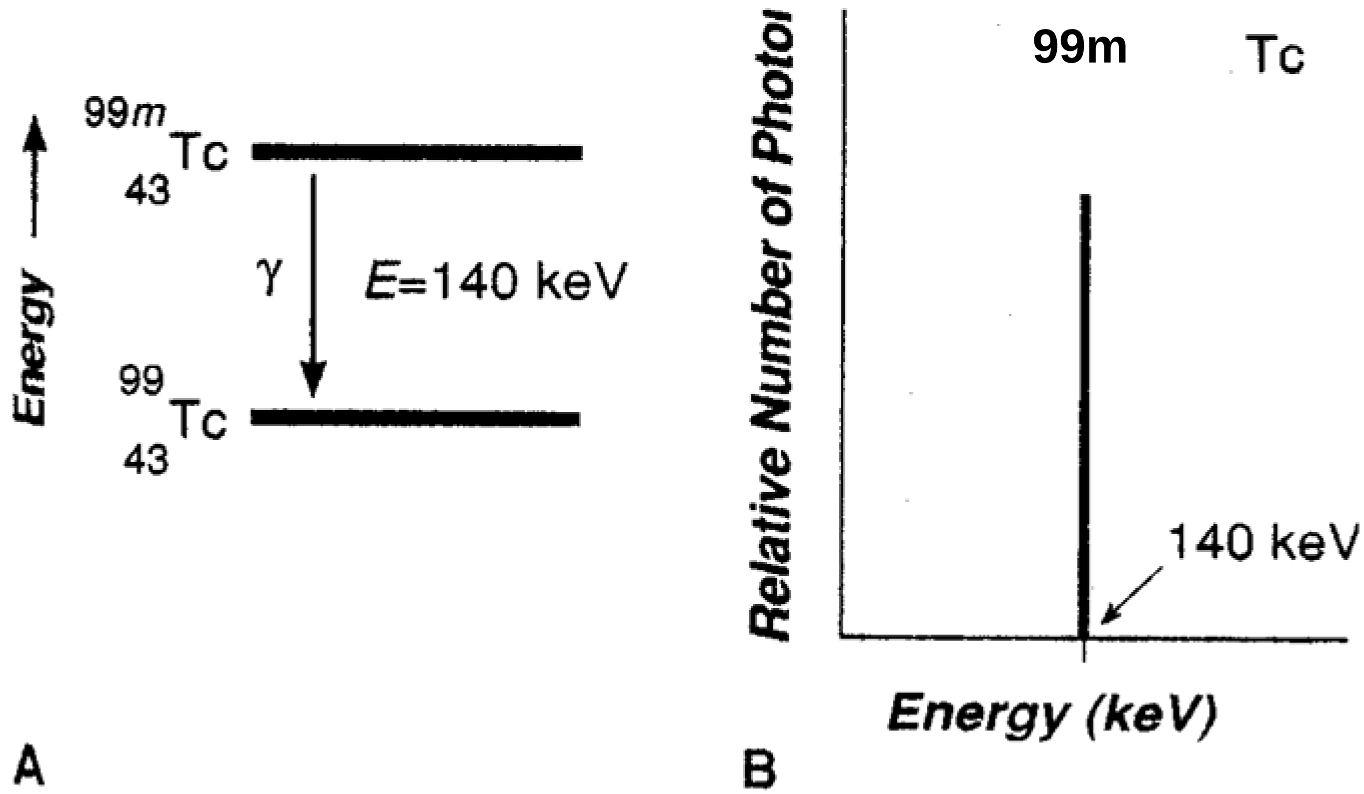


Figure: A metastable technetium-99 nucleus deexcites by emitting a 140keV gamma ray photon. A Gamma ray photon is identical to an x-ray photon of the same energy, but it is of nuclear (rather than electron orbital or bremsstrahlung) origin. (A) Energy level diagram for this Gamma emission process. (B) (Discrete) Gamma ray emission spectrum.

7.3 Mathematical Expression of Radioactivity Decay

❖ The **quantity** of radioactive material, expressed as the number of radioactive atoms decaying per unit time, is called **activity**, and expressed as

$$A = -\frac{dN}{dt}$$

where N is the numbers of radioactive atoms.

❖ The SI unit of activity (A) is the **becquerel (Bq)**

$$1 \text{ Bq} = 1 \text{ decay event / second}$$

❖ The US unit of activity (A) is **curie (Ci)**

$$1 \text{ Ci} = 3.7 \times 10^{10} \text{ Bq}$$

❖ The number of radioactive atoms decaying per unit time is proportional to the number of unstable atoms present at any given time (Nuclear decay is a random process).

$$A \propto N$$

$$A = \lambda N$$

where λ is defined as **decay constant** (Unit: hour $^{-1}$)

Fundamental decay equation

❖ The above two equations lead to the following:

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

which on integration gives: $\ln N = -\lambda t + k$

❖ If t = 0 corresponds to $N = N_{0,}$ then, $k = \ln N_0$ and so:

$$\ln N = -\lambda t + \ln N_0 \Rightarrow \ln N - \ln N_0 = -\lambda t$$

$$\Rightarrow \ln \frac{N}{N_0} = -\lambda t \Rightarrow \frac{N}{N_0} = e^{-\lambda t}$$

Therefore: $$N_t = N_0 e^{-\lambda t}$$

or $$A_t = A_0 e^{-\lambda t}$$

❖ **Physical half-life of radionuclide**: time required for half of radioactive atoms in a sample to decay

$$N_t = N_o\, e^{-\lambda t} \quad \rightarrow \quad N_t / N_o = e^{-\lambda t}$$

$$1/2 = e^{-\lambda t}$$

$$\ln(1/2) = \ln(e^{-\lambda t})$$

$$-0.693 = -\lambda t$$

$$T_{p1/2} = 0.693 / \lambda$$

❖ The physical half-life (and decay constant) is **unique** for each radionuclide

❖ **Biological half-life:** time required for half of radionuclides to be removed from body by biological process

$$T_{b1/2} = 0.693 / \lambda_b$$

❖ **Effective half-life:**

$$1 / T_{eff} = 1 / T_{p1/2} + 1 / T_{b1/2}$$

Exercise

A nuclear medicine technologist injects a patient with 500μCi of In-111 ($T_{p\ 1/2}$=2.82 days) labeled autologous platelets. Two days later the patient is imaged. Assuming none of the activity was biologically excreted, how much activity remains at the time of imaging?

Solution:

Given:

$A = A_o\, e^{-\lambda t}$; A_o =500 μCi ; t =48 hr;

$\lambda = 0.693/(2.82 \text{ days})\times(24 \text{ hrs/day})=1.02\times10^{-2}\ /\text{hr} = 0.0102\ /\text{hr}$

Therefore:

$$A_t = 500\ \mu\text{Ci}\ e^{-(0.0102\ /\ \text{hr})\times(48\ \text{hr})}$$

$$= 500\ \mu\text{Ci}\ e^{-0.49} = (500\mu\text{Ci})\times(0.612)$$

$$A_t = 306\ \mu\text{Ci}$$

- **Production of radionuclide:** Various radionuclides can be produced by different means, such as: nuclear reactors, cyclotrons, Radionuclide generator.

- **^{99m}Tc**, which can be attached to various organ-specific agents, is almost the ideal radionuclide for nuclear medicine imaging.

Radionuclide property	
Gamma ray emission	140 keV, monochromatic
Half-life	6 hours
Toxicity	Nontoxic
Radionuclide production	
Source	On-site, molybdenum-99 generator
Source replacement	Weekly
Cost	Low
Agents	
Availability	In kits
Specificity	Specific to variety of organs
Preparation	In minutes
Binding to technetium	Stable

7.4 Detection of Nuclear Emission

Nuclear radiation detectors: Ion collection detector, semiconductor detector, scintillation detector

(1) Ion collection detector:

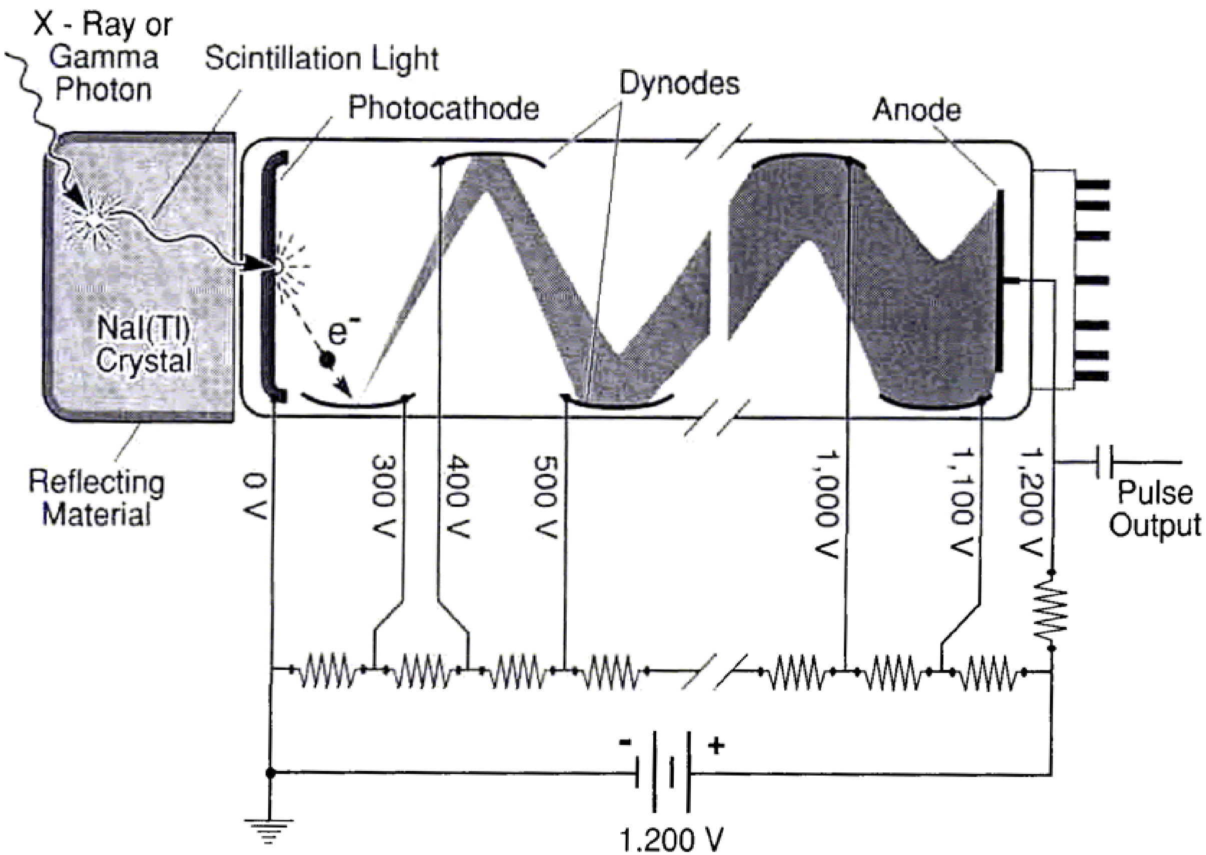
- **Principle**: Produced current is linearly proportional to the intensity of radiation at a certain voltage
- **Limitation**:
  - (a) Poor detection efficiency for high energy
  - (b) The response time of such detector is long compared with other type of radiation detectors.

(2) Solid-state detectors

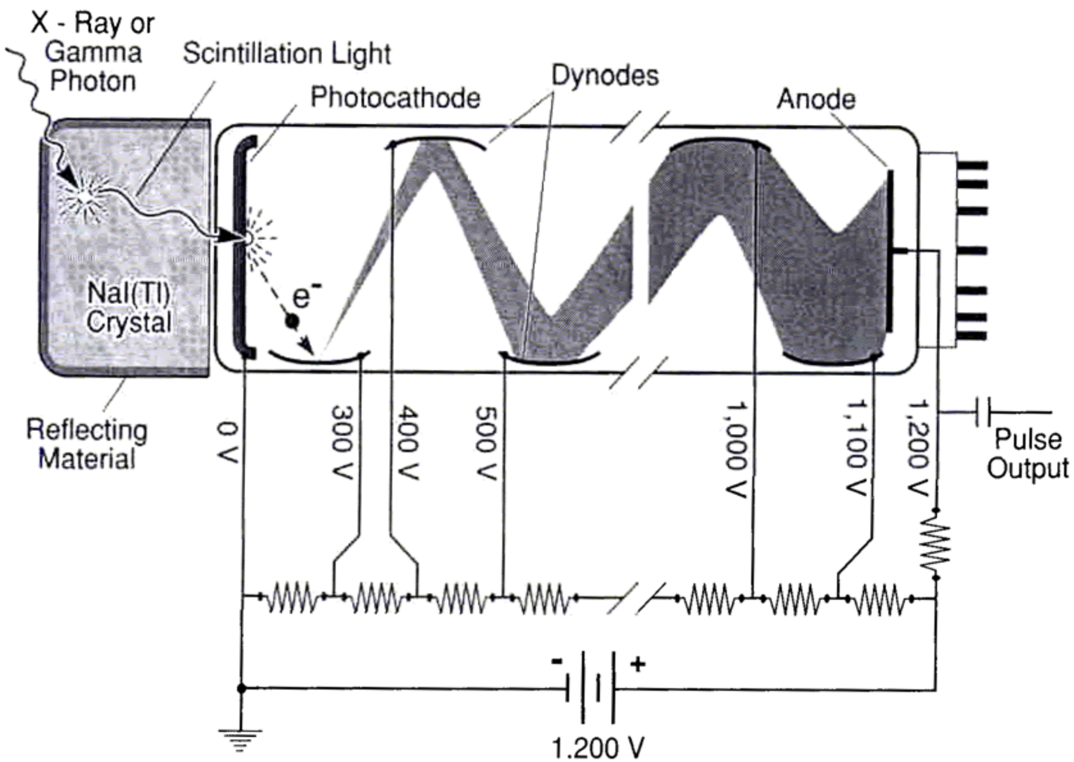
- **Principle:** A Gamma ray photon or energized particle can interact with the semiconductor material to form electron/hole pairs. The magnitude of reverse current I_r is proportional to the absorbed radiation energy.
- **Limitation:** small size, high cost

(3) Scintillation detector

- A **scintillating detector** consists of a scintillating crystal such as thallium-doped sodium iodide NaI(TI), attached to a photomultiplier tube (PMT).
- The scintillation crystal produces a burst of light of intensity proportional to the energy of the initiating x-ray photon.



- ❖ The light ejects from the photocathode of the PMT a number of electrons proportional to the intensity of the light burst.
- ❖ Every photoelectron is accelerated to the first dynode, where it ejects several secondary electrons. Each of these, in turn, heads for the second dynode, where the process repeats itself.
- ❖ The end result is the arrival of a bunch of electrons at the anode and an output voltage pulse of size proportional to the original x-ray photon energy.



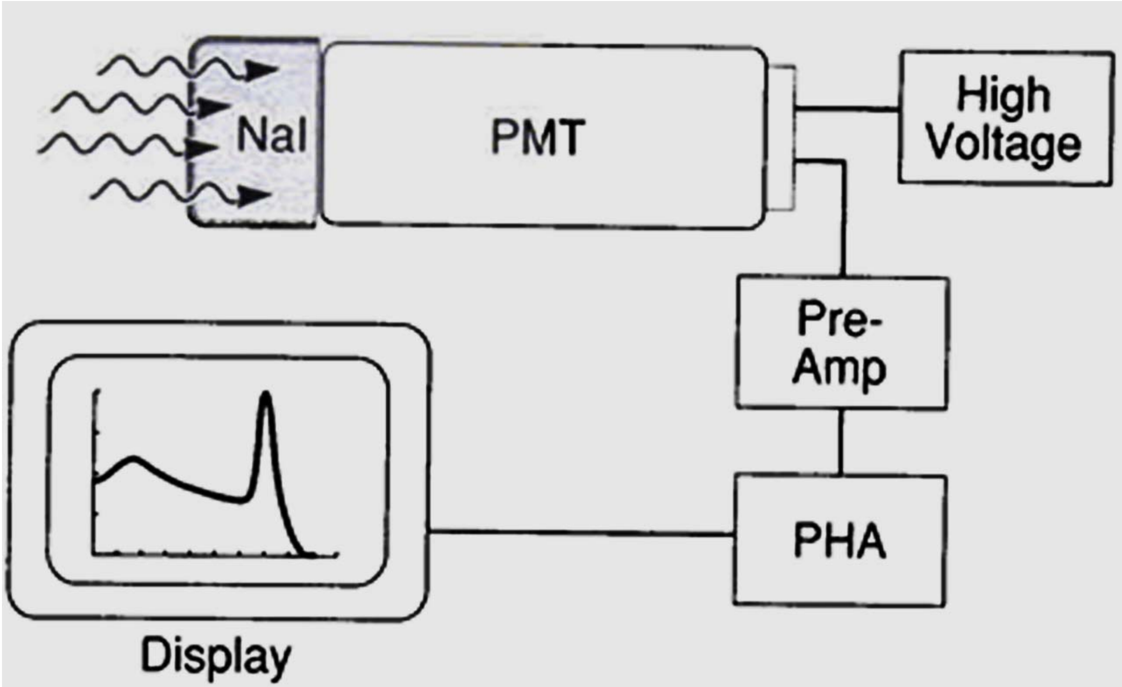
As explained above:

- **Scintillation crystal:** converting high-energy x-ray or Gamma ray photons into visible light photons. Sodium iodide activated with thallium [NaI(TI)] is used for most of the nuclear medicine applications.

- **Photomultiplier tube (PMT):** Convert visible light photons into an electrical signal and amply the signal.

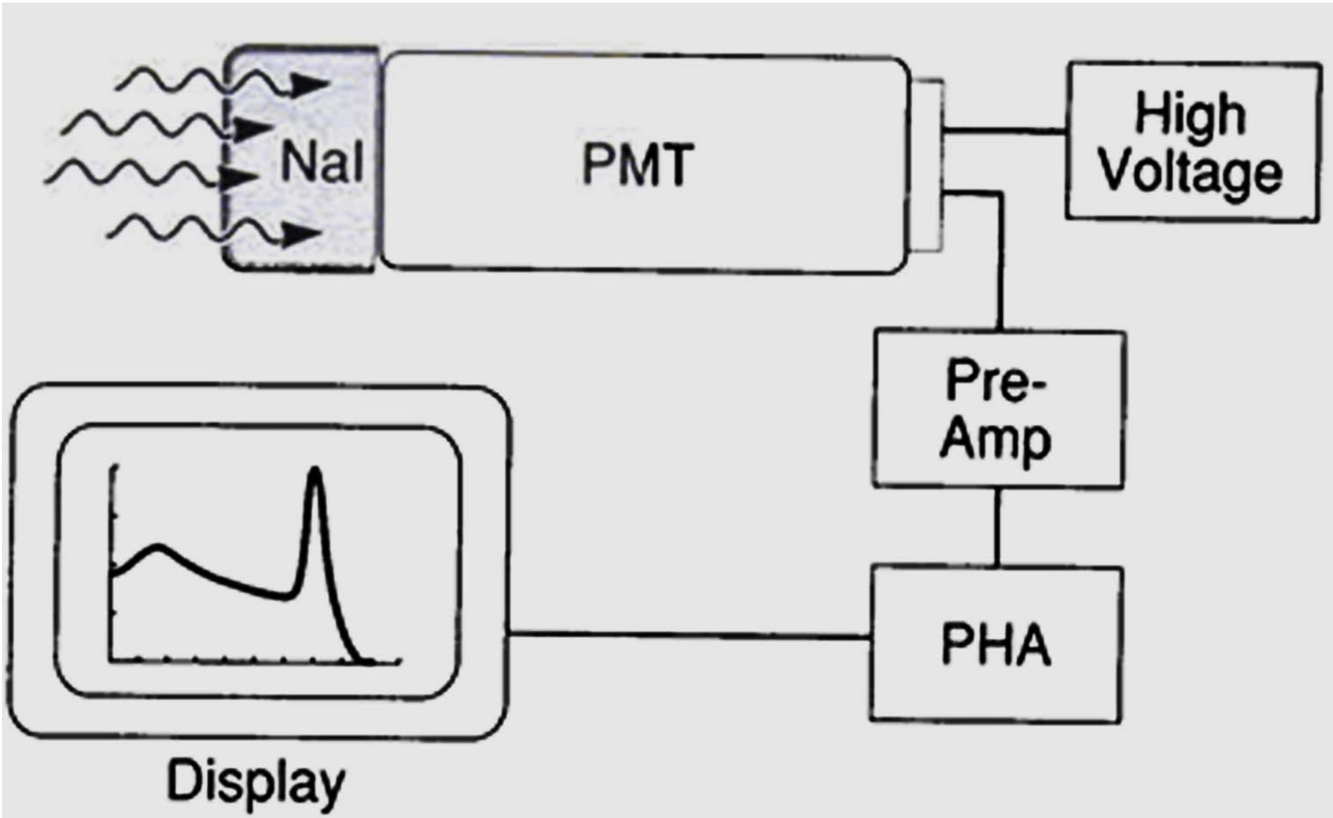
Working principle of scintillation detector

- The detector **counts the number of Gamma ray photons, and also determine the energy of the photon detected.**
- The intensity of light scintillations or the number of visible light photon emissions generated is proportional to the energy of the absorbed photon.



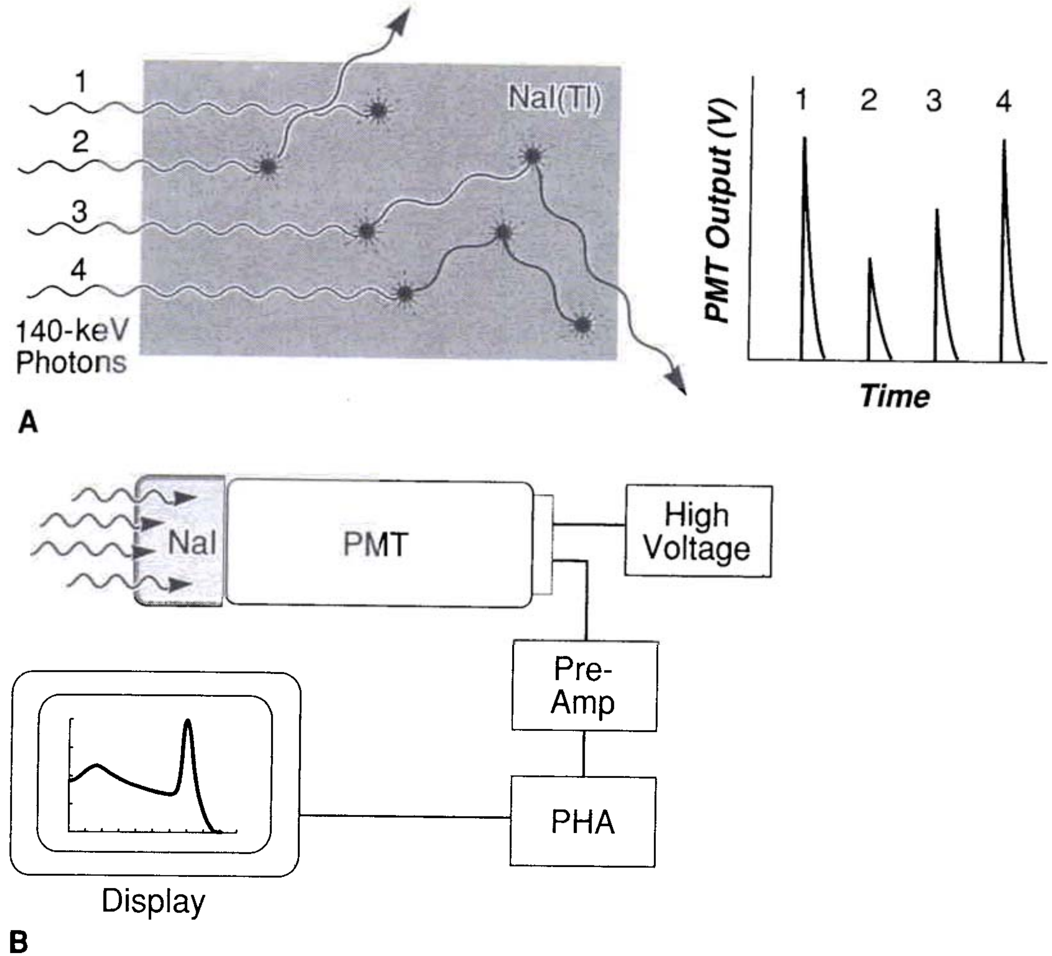
- The amplitude of the voltage pulse from the PMT (photomultiplier tube) is proportional to the number of light photons incident on the PMT.
- Therefore, **the pulse height is proportional to the energy of the absorbed photons**.

- ❖ Energy discrimination is achieved by rejection of pulses above or below an energy window set by operator.
- ❖ Pulse height analyzer (PHA) keep track of the number of pulses that arrive with various voltages, and display his information as histogram.



A scintillating detector can be used to determine the energies of high-energy photons. But even a monochromatic source produces a complex (rather than a single peak) spectrum.

Considering the following example:

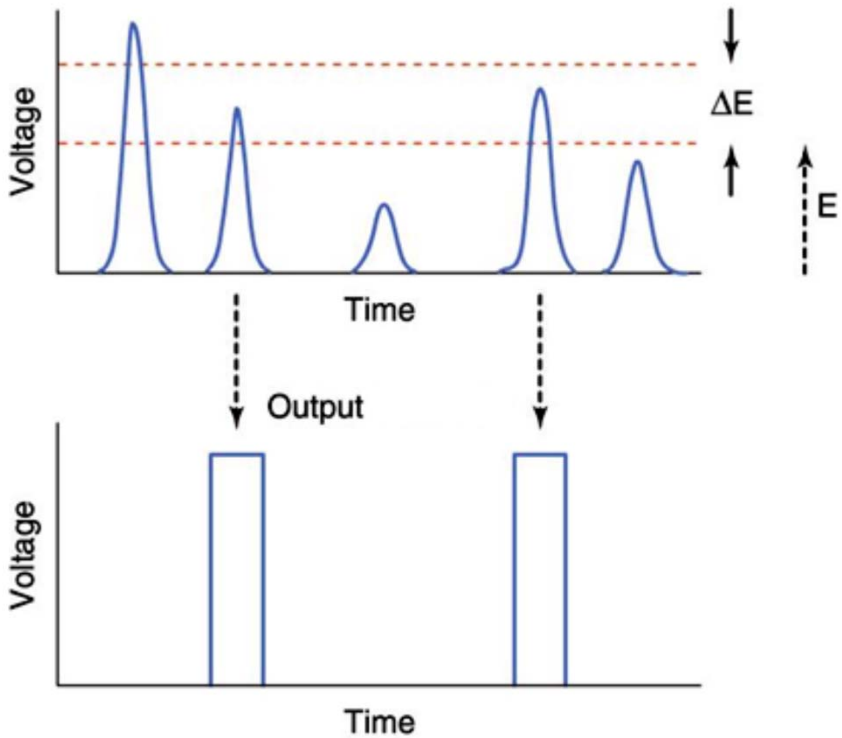


- ❖ Four 140 keV photons strike a scintillating detector in sequence. Photons 1 and 4 deposit all their energy within the NaI(TI) crystal. Some of the energy of photon 2 and 3 escapes as Compton scatter, however, and the PMT output pulses are of correspondingly lower voltage.

(4) Pulse height analyzer

- ❖ The amplitudes of the voltage pulses are assessed by a pulse height analyzer (PHA). The PHA keeps track of the number of pulses that arrive with the various voltages, and displays this information as a histogram.
- ❖ Pulse height analyzers (PHAs) are electronic systems that may be used to perform pulse height spectroscopy and energy-selective counting.
- ❖ In energy-selective counting, only interactions that deposit energies within a certain energy range are counted.

- Energy-selective counting can be used to reduce the effects of background radiation, to reduce the effects of scatter, or to separate events caused by different radionuclides in a sample containing multiple radionuclides.



- Above figure illustration of the function of a PHA. Energy discrimination occurs by rejection of pulses above or below the energy window set by the operator.

- The pulse height spectrum for technetium-99m is not a single sharp peak at the voltage corresponding to 140 keV. The full width at half-maximum (FWHM) of the 140 keV photopeak is 15 to 20 keV, rather, and there is lower-energy structure in the spectrum attributable to Compton scatter in the NaI(TI) crystal and to other causes.
- **Energy resolution:** the spread or broadening of the energy peak.
- It affects the ability of a radiation detector to distinguish Gamma-ray photons with similar energies.

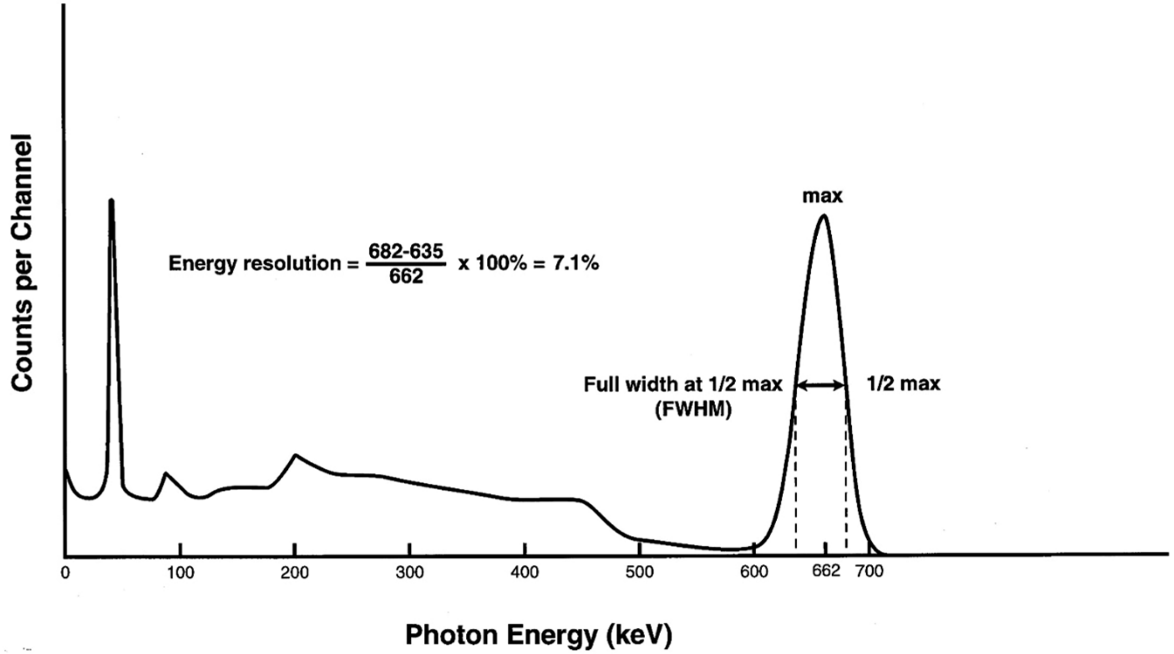


Figure: Energy resolution. The spectrum shown above is that of Cs-137, obtained by using a NaI (TI) scintillator.

7.5 Radionuclide Imaging Systems

❖ **Rectilinear scanner**

Collimator has major effect on the spatial resolution and detection efficiency of a rectilinear scanner, spatial resolution is low.

❖ **Has largely been replaced by the Gamma camera**

Gamma camera, (also called Anger camera)

❖ It is the most commonly used radionuclide imaging device.

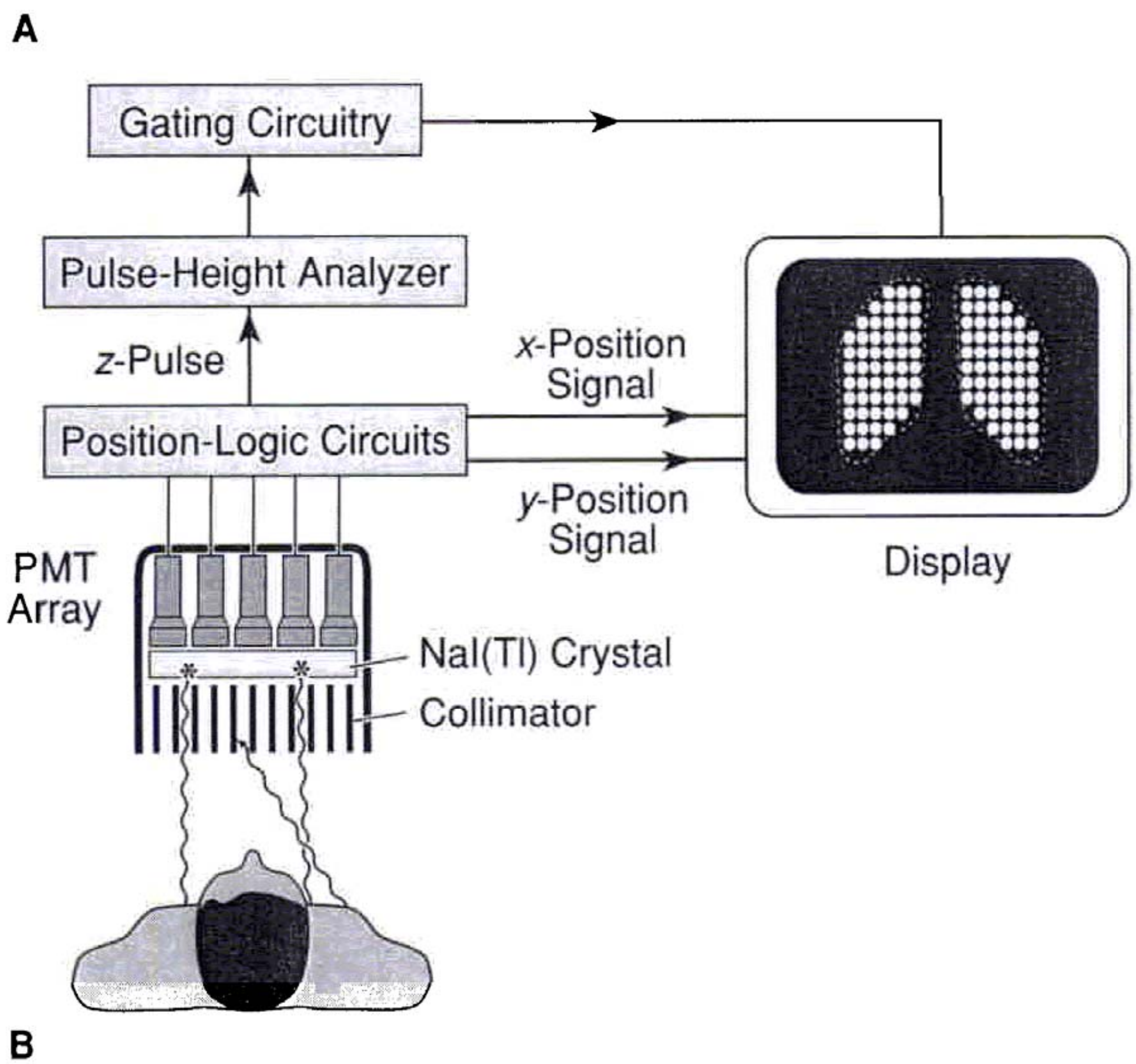
❖ **Principle:** Estimate the position of a single event by measuring its contribution to a number of detectors. Therefore, the system is capable of achieving "high resolution" with a limited number of detectors.

(1) Configuration:

❖ Main components:

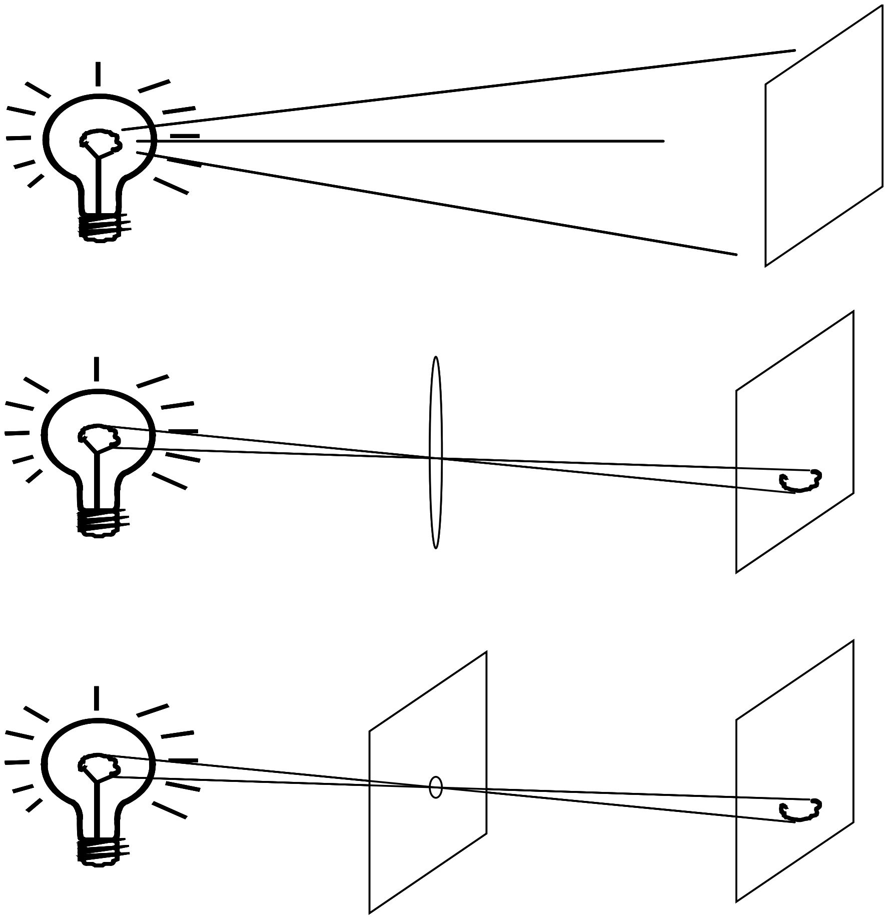
(a) Camera head: collimator, a single scintillation crystal (0.6-1cm thick, 25-60cm in diameter), and a close-packed hexagonal array of 37 PMTs (FOV: 41cm in diameter, PMT diameter: 7.6cm), or 75, or 91 PMTs (PMT diameter: 5.1cm)

(b) Electronic processing unit

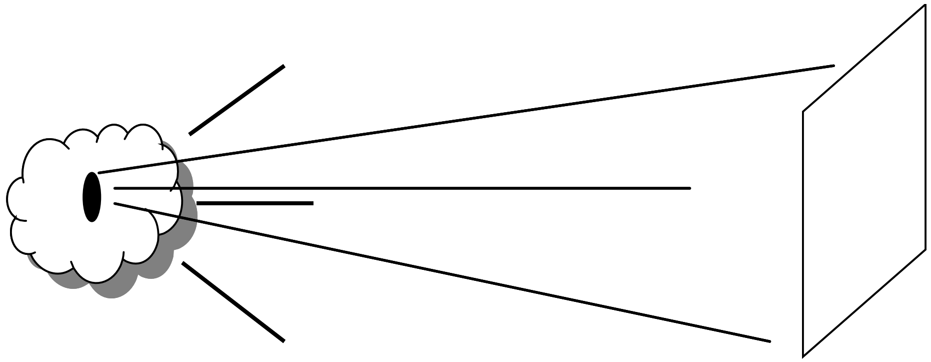


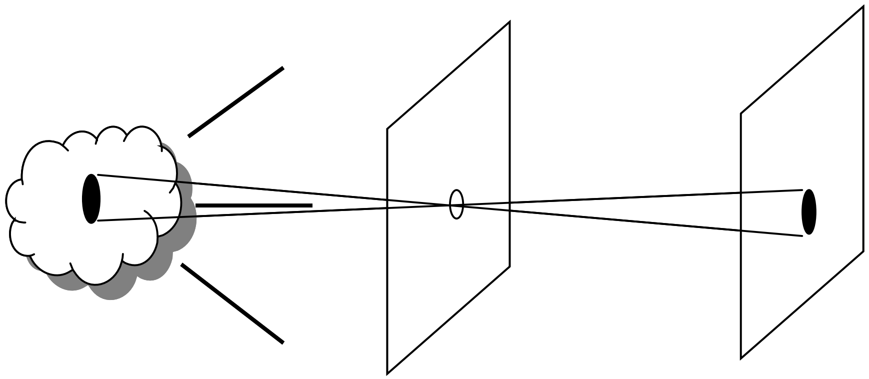
(2) Collimator

In optical imaging, lenses are used to focus the image onto the photosensitive surface of the detector.



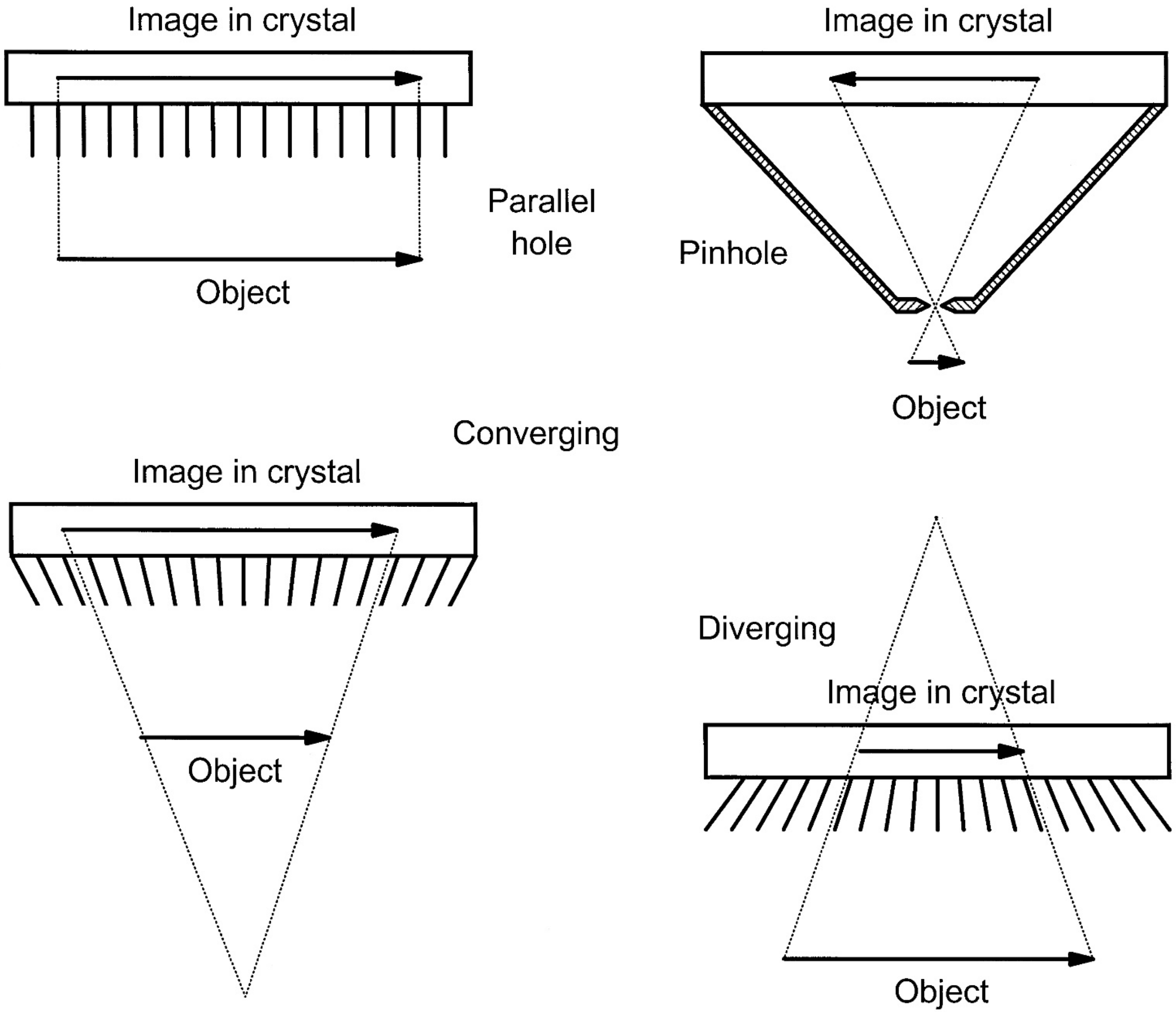
- Gamma ray can not be focused by optical lens, so the role of the lenses is played by collimators.





- The collimator plays an important role in the spatial resolution and detection efficiency of a scintillation camera.

❖ Types of collimators



(3) Centroid calculation: determines the position of a single event on the scintillation crystal.

❖ **Basic principle**: When a Gamma ray photon excites the scintillation crystal, the amplitude of the voltage pulse produced by any of the PMT tube depends on its distance from the light burst. The position logic circuit (using centroid calculation formula) weighs the output of the PMTs and estimates the most likely position, within the crystal, of the Gamma ray interaction

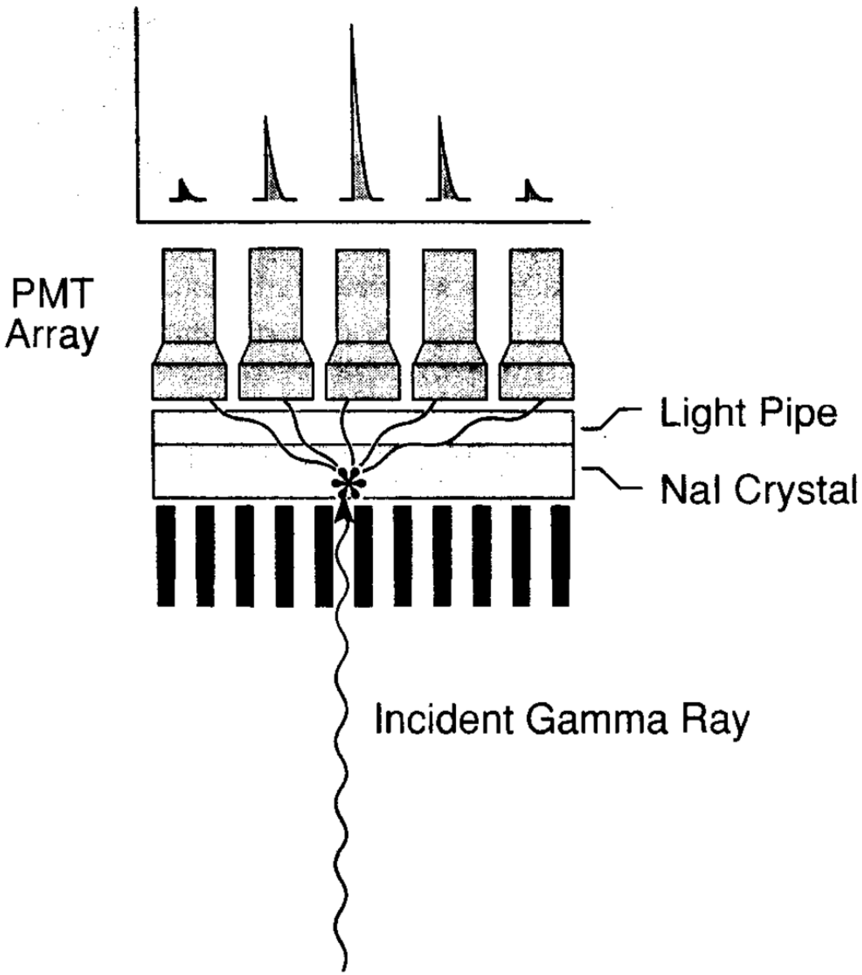
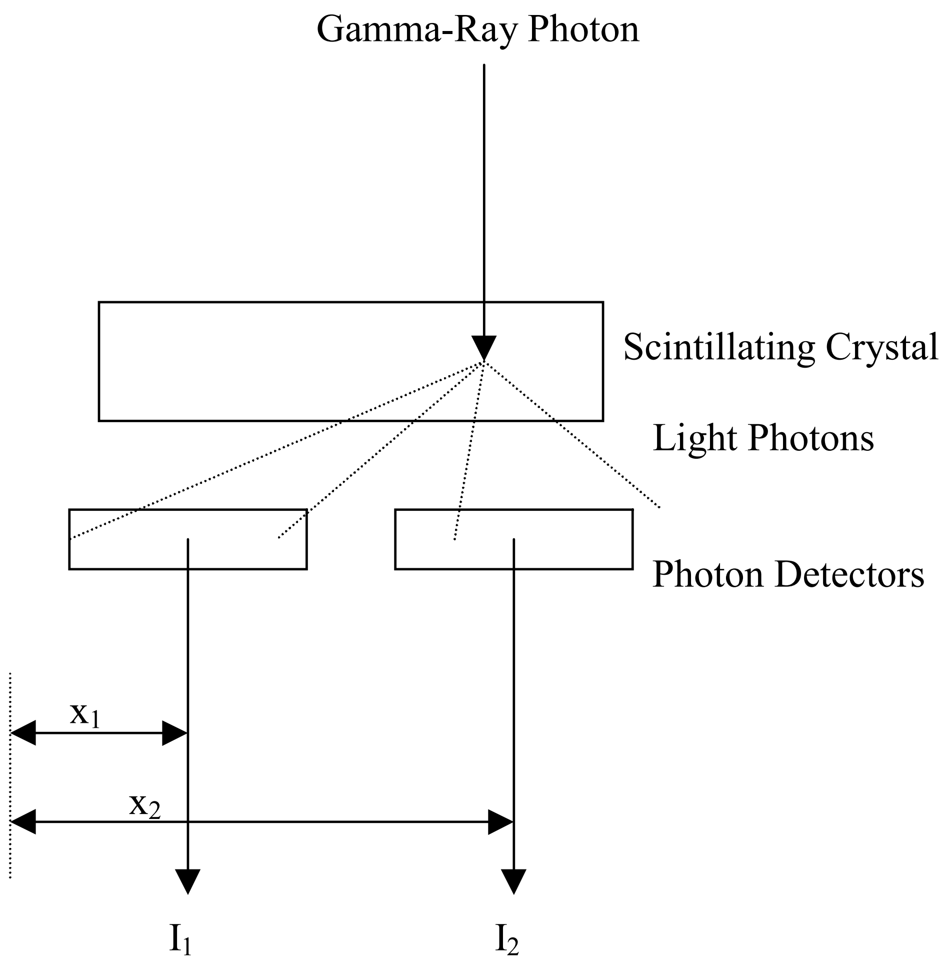


Illustration of centroid calculation

$$X = (I_1 x_1 + I_2 x_2) / (I_1 + I_2)$$

where the sum, $I_1 + I_2$, can be used to determine the energy of the **Gamma ray photon**



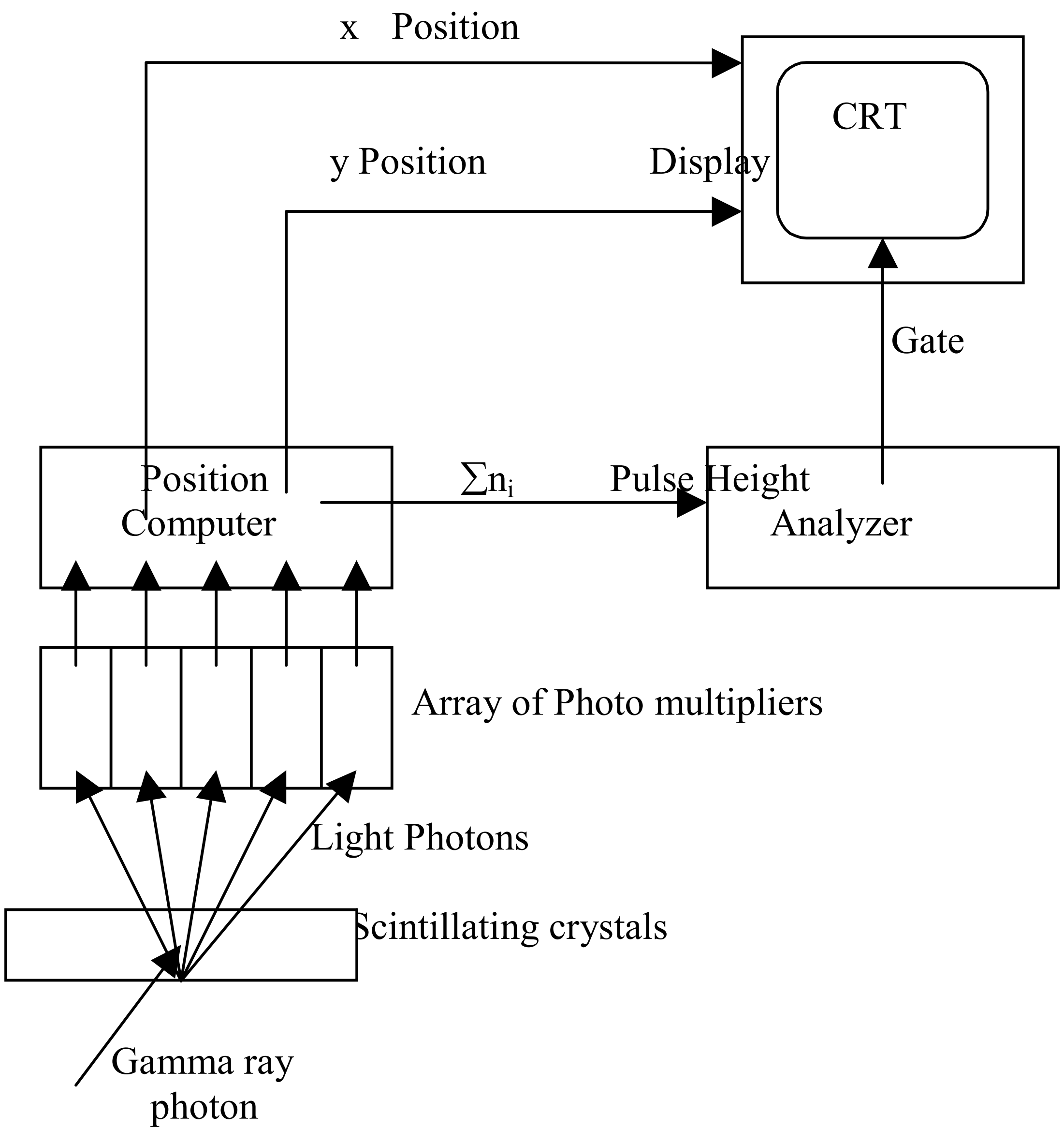
Anger Camera Principle

A common equation:

$$X = \sum x_i n_i / \sum n_i$$

$$Y = \sum y_j n_j / \sum n_j$$

where x_i *and* y_j are the *x* and *y* coordinates of the PMT; n_i and n_j are the output (the number of light photons, or pulse amplitudes) in each PMT

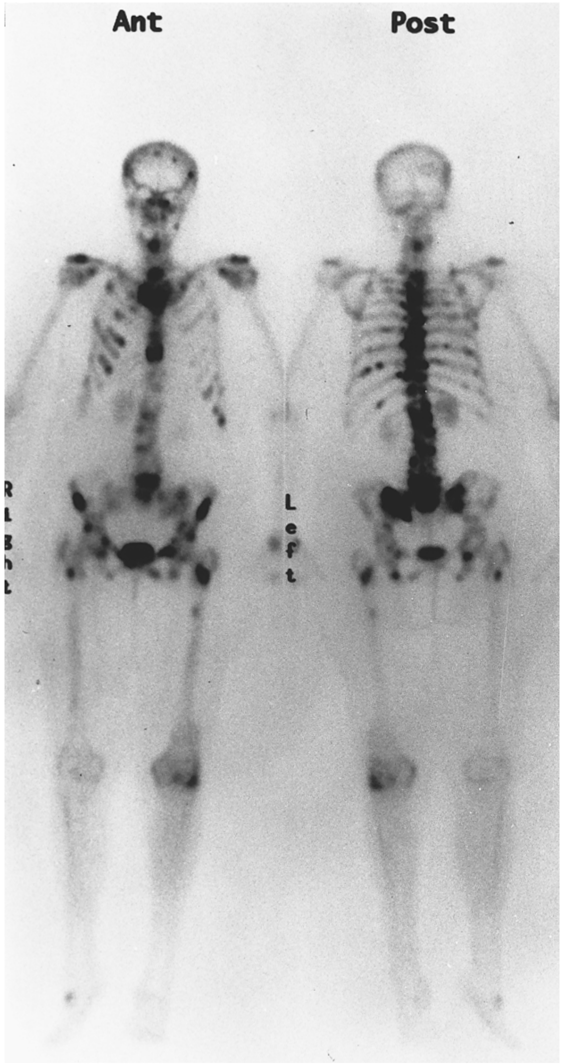


Block diagram of an Anger camera

The **resolution** of the system is determined by the accuracy of the formula and more important, the statistics of each measurement rather than by the size or number of detector elements.

As an example, a system consisting 19 PMTs may provide a resolution of over 1000 resolvable elements. This is made possible by analyzing single event. However, even with 1000 elements, the lateral resolution of the system is about 1cm, considerably less than that in radiography.

A radionuclide image



- ❖Anterior and posterior whole-body bone scan of a 74-year-old woman with a history of right breast cancer. This patient was injected with 925 MBq (25 mCi) of technetium (Tc) 99m methylenediphosphonate (MDP) and was imaged 3 hours later with a dual-headed whole-body scintillation camera.
- ❖The scan demonstrates multiple areas of osteoblastic metastases in the axial and proximal skeleton. Incidental findings include an arthritis pattern in the shoulders and left knee.

J.T. Bushberg, J.A. Seibert, E.M. Leidholdt, Jr., J.M. Boone, *The Essential Physics of Medical Imaging*

7.6 Advanced Radionuclide Imaging Methods

Similar to x-ray, conventional radionuclide imaging using projection imaging techniques suffers from low image contrast due to overlapping structures.

(1) Single-photon emission computed tomography (SPECT)

- **Configuration:** One or multiple standard Gamma camera heads mounted on a supporting gantry, are rotated slowly around the patient.
- SPECT is a three-dimensional imaging technology.
- Main advantage of SPECT: higher image contrast over other nuclear imaging.

Modern dual rectangular head scintillation camera. The two heads are in a 90 degree orientation for cardiac SPECT imaging. (Courtesy of Siemens Medical Solutions.)

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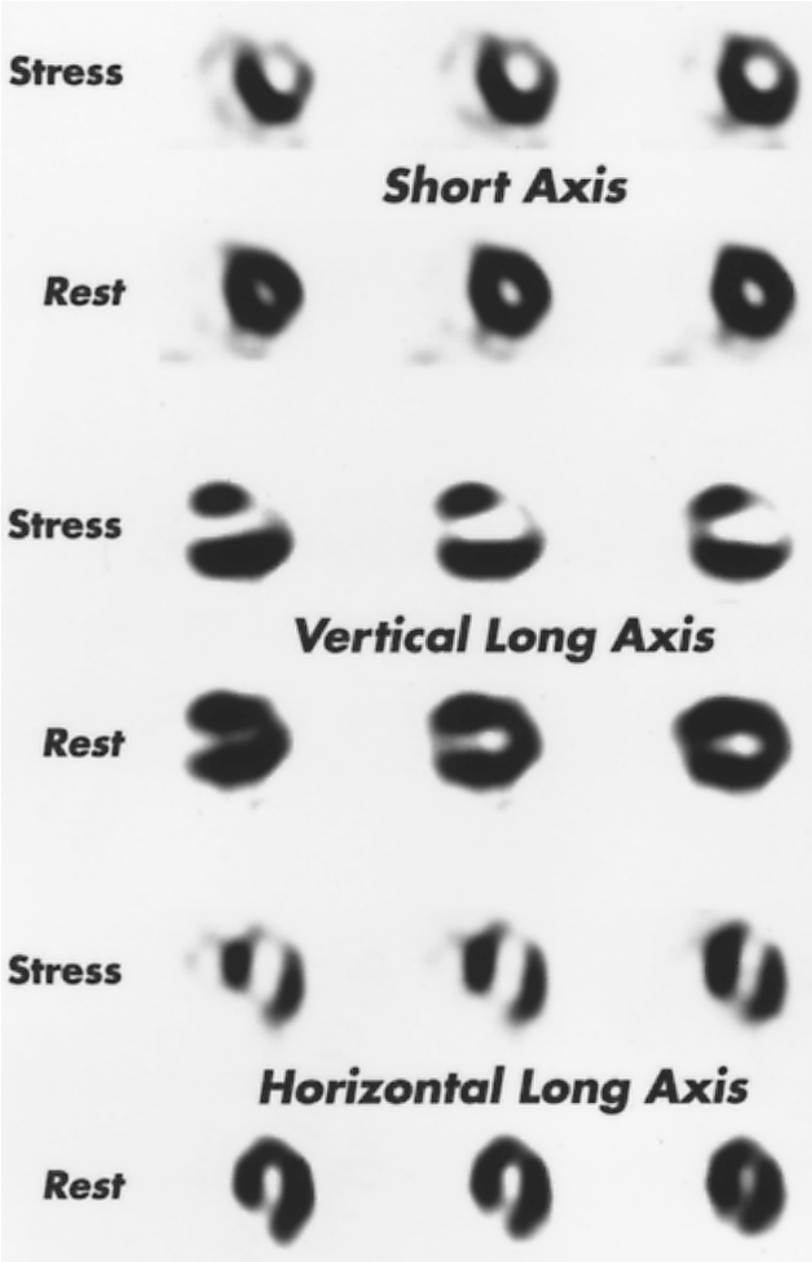

A sample of SPECT imaging

- A myocardial perfusion stress test utilizing thallium 201 (TI 201) and single photon emission computed tomography (SPECT) imaging was performed on a 79-year-old woman with chest pain. This patient had pharmacologic stress with dipyridamole and was injected with 111 MBq (3 mCi) of TI 201 at peak stress. Stress imaging followed immediately on a variable-angle two-headed SPECT camera.
- The rest/redistribution was done 3 hours later with a 37-MBq (1-mCi) booster injection of TI 201. Findings indicated coronary stenosis in the left anterior descending (LAD) coronary artery distribution.

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SPECT/CT system with two scintillation camera heads in a fixed 180-degree orientation and a non-diagnostic x-ray CT system for attenuation correction and anatomic correlation. The x-ray source is on the right side of the gantry and a fat-panel x-ray image receptor is on the left.

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(2) Positron emission tomography (PET)

- **Positron:** The positron is the "antipartical" to the electron -- identical to every respect except that it bears a positive charge

- A nucleus is held together by means of strong **nuclear force** acting among its protons and neutrons. But the protons also repel each another electrically because of their charge. For a nucleus with a relatively high proton-to-neutron ratio, this electrical repulsion, together with the weak nuclear force, may lead to nuclear instability. Such a nucleus will attempt to attain stability by reducing its net positive charge. And one way to do that is to emit a positron.

❖ **Positron decay:** When a positron collides with an electron, both particles annihilate to form 511-keV photons moving in opposite directions. It is the basic principles of PET.

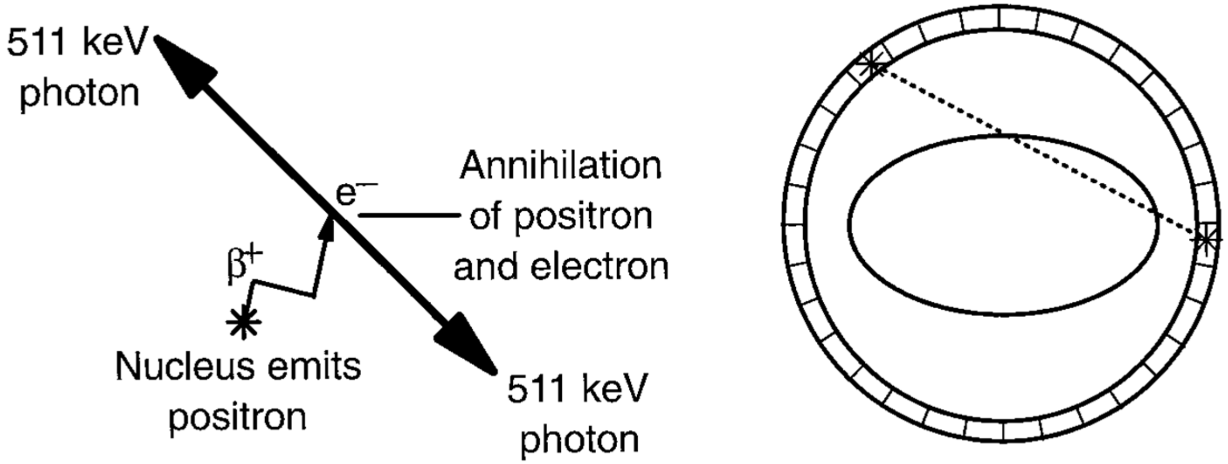

Figure Annihilation coincidence detection (ACD). When a positron emitted by a nuclear transformation loses most of its energy, it annihilates with an electron, resulting in two 511 keV photons that are emitted in early opposite directions (left). When two interations are simultaneously detected within a ring of detectors surrounding the patient (right), it is presumed that an annihilation occurred on the line connecting the interactions. This, ACD, by determining the path of the detected photons, performs the same function for the PET scanner as does the collimator of a scintillation camera.

- **Principle:** Coincidence detection
- The coincidence circuitry establishes the trajectories of detected photons, a function performed by collimation in SPECT (and in Gamma camera). However, this method is much less wasteful of photons than collimation.
- The typical detection efficiency of a PET scanner is about 10 to 20 times that of a single-head SPECT camera.

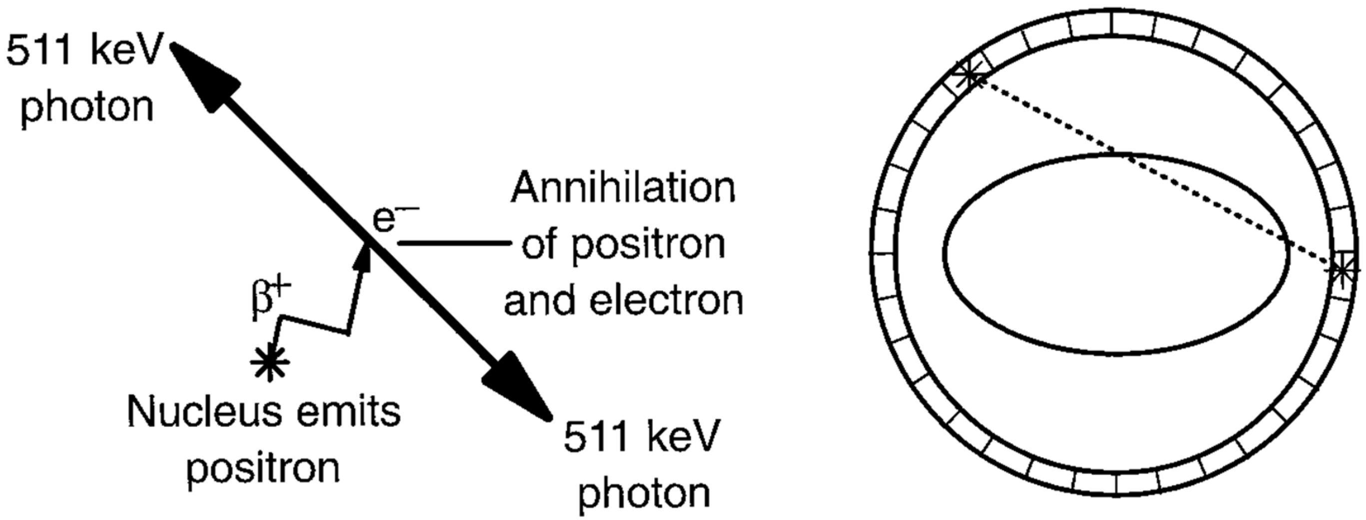

Figure Annihilation coincidence detection (ACD).

A commercial PET/CT scanner. (Photograph courtesy Siemens Medical Solutions, Nuclear Medicine Group.)

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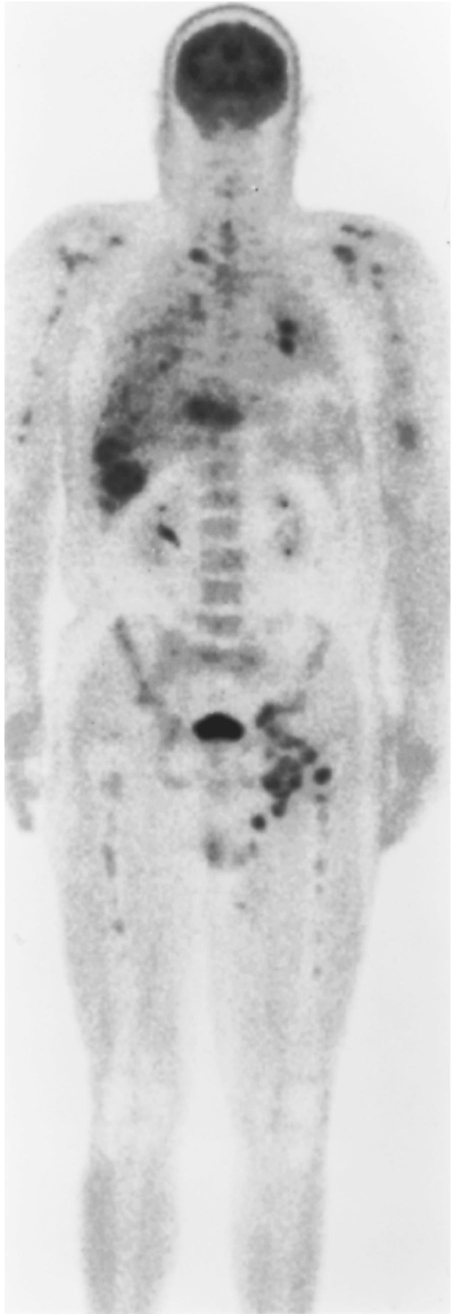
Advantages and disadvantages of PET:

- More sensitive than SPECT.
- Half-lives of positron emitters are short, the additional cost of cyclotron is high.

(3) Comparison of SPECT and PET

	SPECT	**PET**
Principle of projection data collection	Collimation	Annihilation coincidence detection
Image reconstruction	Filtered Back Projection	Filtered Back Projection
Radionucldes	Tc-99m, et al	Carbon-11, Iodine-122, et al
Cost	\$0.5M	\$2M and additional cost



A PET image

- Whole-body positron emission tomography (PET) scan of a 54-year-old man with malignant melanoma. Patient was injected intravenously with 600 MBq (16 mCi) of ^{18}F-deoxyglucose.
- The image demonstrates extensive metastatic disease with abnormalities throughout the axial and proximal appendicular skeleton, right and left lungs, liver, and left inguinal and femoral lymph nodes.

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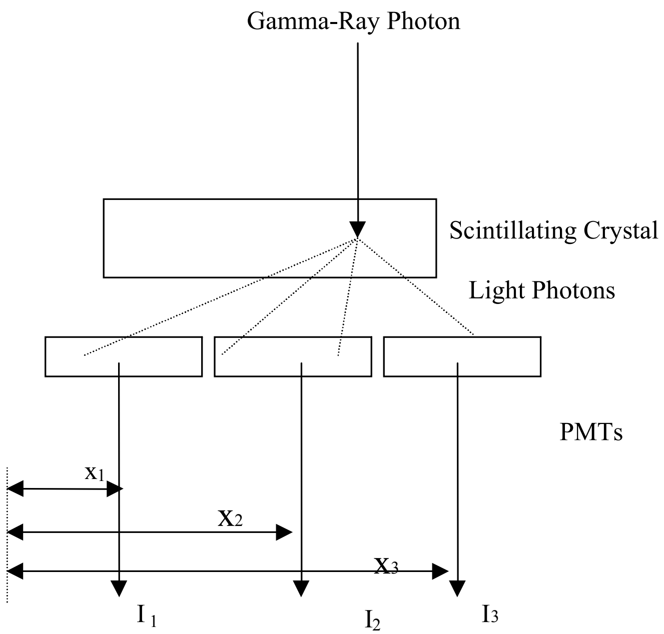
7.7 Summary

1) Gamma camera: counts number of photons and the energy of the photon detected
2) Concepts of energy discrimination, centroid calculation
3) SPECT and PET
4) Two kinds of imaging:
   - ❖ **anatomic imaging:** displaying configuration or structure of objects. (the most commonly used method)
   - ❖ **functional imaging:** providing information about function of objects or interest including fluid flow, perfusion and diffusion (PET, SPECT, fMRI and Doppler US).

PET: Positron emission tomography
SPECT: Single photon emission computed tomography
fMRI: Functional magnetic resonance imaging

Homework #6

1. The effective half-life of a radiopharmaceutical in the organ of interest is 2 hours. If the biological half-life is 3 hours, then what is the physical half-life of the radionuclide used to label the pharmaceutical?
2. In nuclear medicine imaging, (a) What advantage do higher energy isotopes have? (b) What disadvantage do they have ?
3. A Gamma camera is built with a scintillation crystal and three PMTs, as shown in the following diagram. When a Gamma ray photon excites the scintillation crystal, the amplitude of the voltage pulse produced by any of the PMT tube is given in the following table. Please using centroid calculation formula to estimates the most likely position, within the crystal, of the Gamma ray interaction.



Location of PMTs	PMT output
X_1 = 1cm	100 mV
X_2 = 5cm	1000 mV
X_3 = 10cm	500 mV