Medical Physics

Nuclear Medicine Principles and Applications

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Definitions

Radioactivity

The process of transmutation of an unstable element to another element by the emission of radiation.

Radioactive Decay

For every radioactive element a probability of decay exists. The relationship between this probability and the number of atoms in a large sample that will decay in a given time is called the "Radioactive Decay Law".

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

where

λ is a proportionality constant

N_0 is number of atoms undecayed at time $t = 0$

N is number of atoms undecayed at time t

Activity

The activity of a sample is defined as the number of disintegrations per second (dps) and is given by

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

$$= \lambda N_0 e^{-\lambda t}$$

Units of Activity

Curie (Ci)

Historical unit of activity, corresponding to the activity of 1 gram of pure 226Ra. 1 Ci = 3.7 x 10^{10} disintegrations per second

Commonly expressed as mCi or μCi.

Bequerel (Bq)

SI Unit of activity
1 Bq = 1 disintegration per second

Commonly expressed as MBq or GBq.

Half Life $(T_{1/2})$

The time taken for the number of undecayed radioactive atoms In a large sample to halve.

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

Some Types of Decay

Charged particle decay

Alpha Decay

$$^{A}_{Z}\mathrm{X} \rightarrow ^{A-4}_{Z-2}Y + \alpha$$

$$^{226}_{88}\mathrm{Ra} \rightarrow ^{222}_{86}\mathrm{Rn} + \alpha$$

In this example alpha particles of two different energies may be emitted – 4.78 MeV or 4.60 MeV.

Alpha emitters are of little use in nuclear medicine as they do not penetrate tissue, but they represent a severe health hazard if ingested or inhaled.

Beta (β^-) decay

$$n \rightarrow p^+ + e^- + \nu + energy$$

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

A neutron is transformed to a proton.
Continuous (non-discrete) energy of emission.

Decay by (β^-, λ) emission

Beta emission leaves the daughter nucleus in an excited state. The daughter nucleus then decays to a more stable state by emitting a γ-ray.

$$ {}^{A}_{Z}\mathrm{X} \rightarrow {}^{A}_{Z+1}Y^{*} + \beta^{-} $$

$$ {}^{A}_{Z+1}Y^{*} \rightarrow {}^{A}_{Z+1}Y + \gamma $$

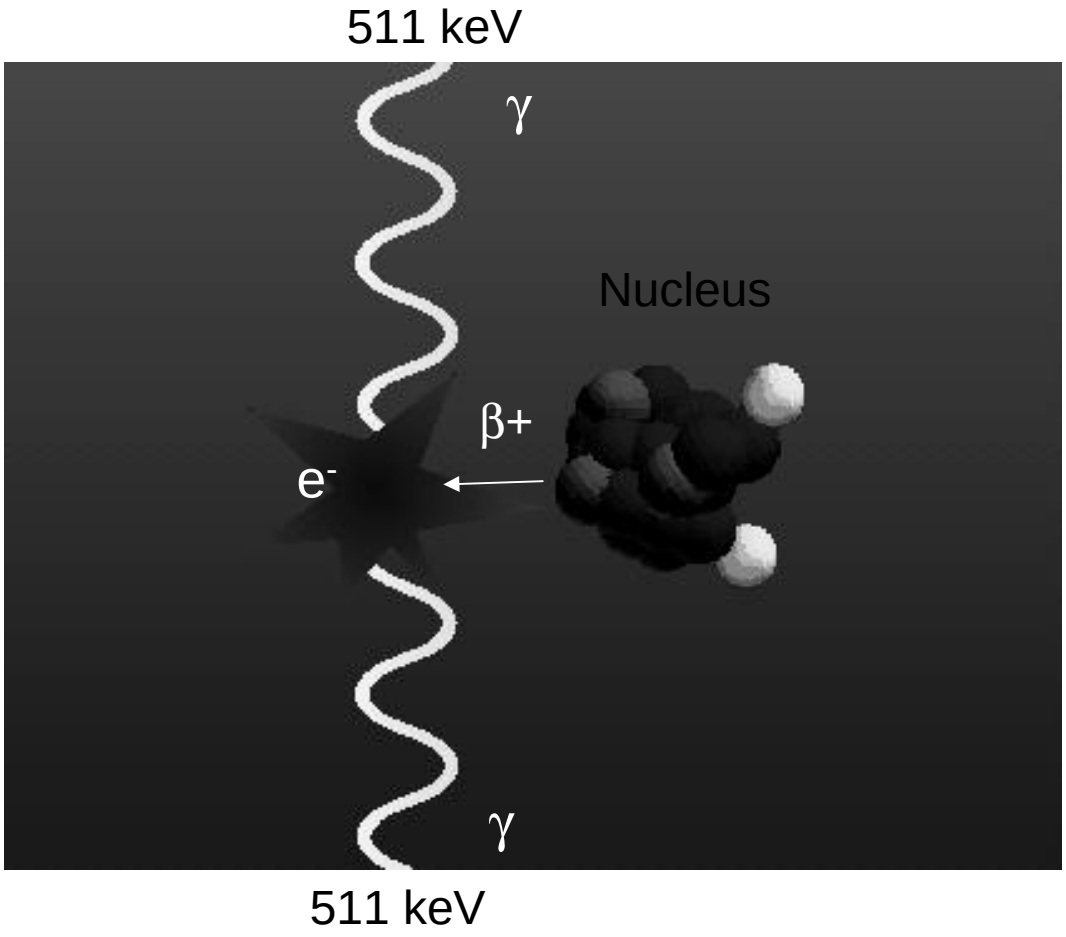
Positron Decay

$$p^+ \rightarrow n + \beta^+ + \nu + energy$$

$${}^{A}_{Z}\mathrm{X} \rightarrow {}^{A}_{Z-1}Y + \beta^+$$

The positron travels a short distance before it encounters an electron.

When the positron encounters an electron the two annihilate, converting their combined mass to energy in the form of two 511 keV photons in opposite directions.



Photons

- Gamma (γ) rays
- X-rays

Differ only in origin. Gamma rays are emitted from the nucleus, while X-rays are emitted from the atom, usually the orbital electrons. No charge.

More penetrating than charged particles.

Radiation Detectors

Types

1. Gas Filled Detectors

Ionization chambers – personal dosimeters, dose calibrators.

Geiger-Muller counters for measuring ambient radiation.

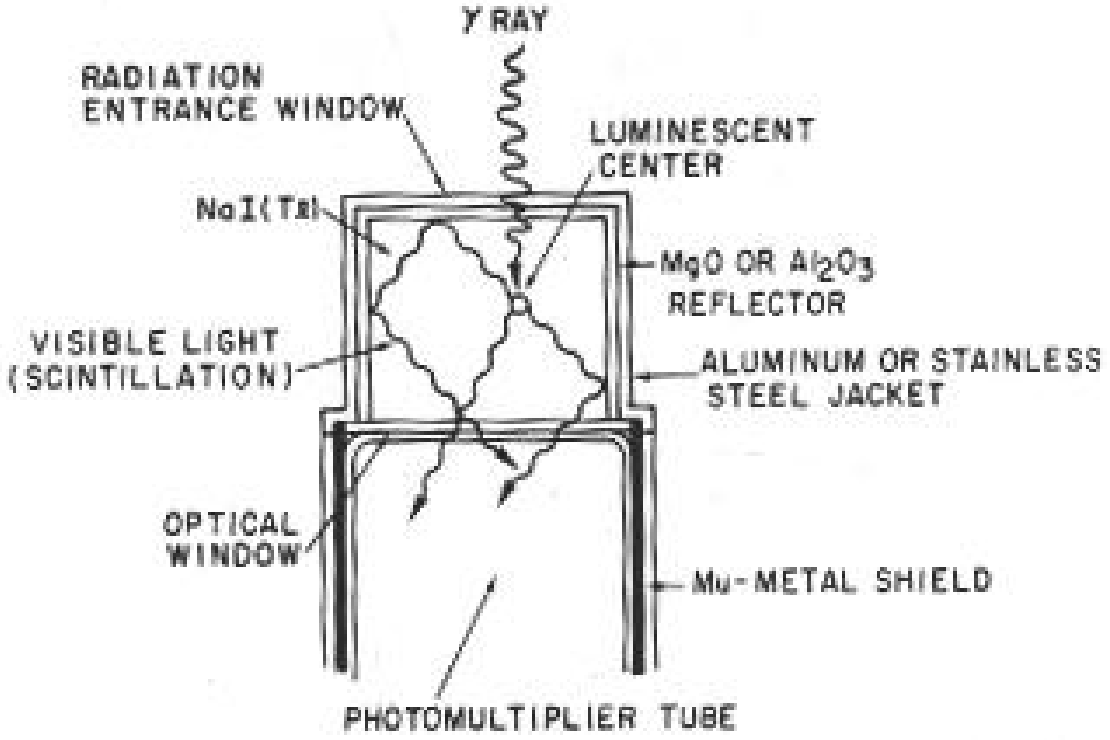
Principle – Incident radiation ionizes gas particles. The ionization of gas within an electrically charged enclosure alters the voltage potential between two electrodes.

2. Scintillation Detector

Ionizing radiation absorbed by the scintillator.

Energy converted to light photons.

Photons strike photocathode of PM tube.



Inorganic crystal scintillators

When the scintillator is struck by a gamma ray the photon energy is imparted to orbital electrons within the crystal lattice. The energy state of the electrons is increased from the valence band to the conduction band, which enables them to move from atom to atom. When one of these electrons encounters an electron hole it returns to the valence band and in doing so emits light photons. This process takes about 10^{-12} seconds.

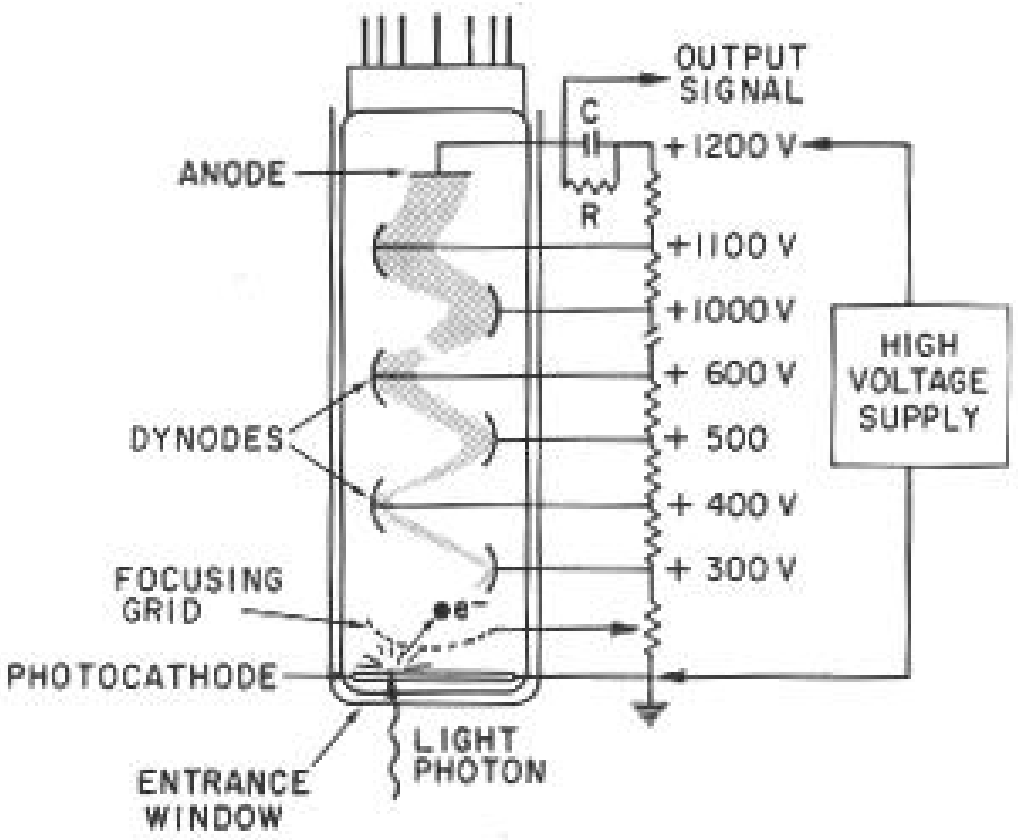
In sodium iodide (NaI) crystals (one of the most commonly used detector materials in nuclear medicine) this process is aided by the addition of a small amount of thallium (Tl) which provides electron holes.

A single photon will be converted into many light photons (about 1 photon per 30 to 50 eV of absorbed gamma energy).

Photomultiplier Tube (PMT)

Photons strike photocathode of PM tube.

Electrons ejected from photocathode and amplified by a series of dynodes to produce a voltage pulse at the output proportional to the energy of the incident photons.



Scintillator Materials

- Plastic and liquid phosphors
- Inorganic crystals e.g. NaI, CsI, CaF.

Desirable properties of scintillator

- High detection efficiency for the incident radiation, i.e. its atomic number and density should be high to enhance the probability of interaction.

- It should convert the energy of the radiation absorbed into detectable light with high efficiency, i.e. have a high light output.

- The light yield should be proportional to the deposited energy.

- The material should be transparent to the emitted light to allow light transmission and collection.

- The light should decay quickly to allow counts to be distinguished at high count rate.

Scintillator Materials

Many different materials produce fluorescence when struck by ionizing radiation. Each has its own characteristic density, emission wavelength, light output, and decay time.

Table 4-2
Properties of Some Scintillator Materials

Property	Material					
	NaI (Tl)	*CsF*	*BGO*[‡]	*Plastic*	*GSO*[§]	*BaF_2*
ρ (g/cm^3)	3.67	4.61	7.13	1.03	6.71	4.89
Atomic numbers	11,53	55,9	83,32,8	6,1	58,64,14,8	56,9
Effective atomic number	50	53	74		59	54
Scintillation decay time (nsec)*	230	2.5	300	2	60	0.8[‖] 620[#]
Photon yield[†] (per keV)	40	2.5	4.8	15	6.4	2.0 6.5
Index of refraction	1.85	1.48	2.15	1.58	1.9	1.56
Hygroscopic	Yes	Very	No	No	No	very little
Wavelength of maximum emission (Å)	4150	3900	4800	—	4300	2250[‖] 3100[#]

Reprinted from Eriksson L, Bohn C, Kesselberg M, Litton J-E, Bergstrom M, Blomquist G: A high resolution positron camera. In *The Metabolism of the Human Brain Studied with Positron Emission Tomography*. Greitz T, Ingvar DH, Widen L (eds.). Raven Press, New York, 1985. pp. 33–46. With permission.

*Time required for emission of ~67% of the light.

†Average number of scintillation photons emitted per keV of ionizing radiation energy absorbed.

‡$Bi_3Ge_4O_{12}$.

§Ge_2SiO_5 (Ce).

‖Fast component.

#Slow component.

Scintillation Detectors

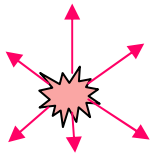
Dead Time

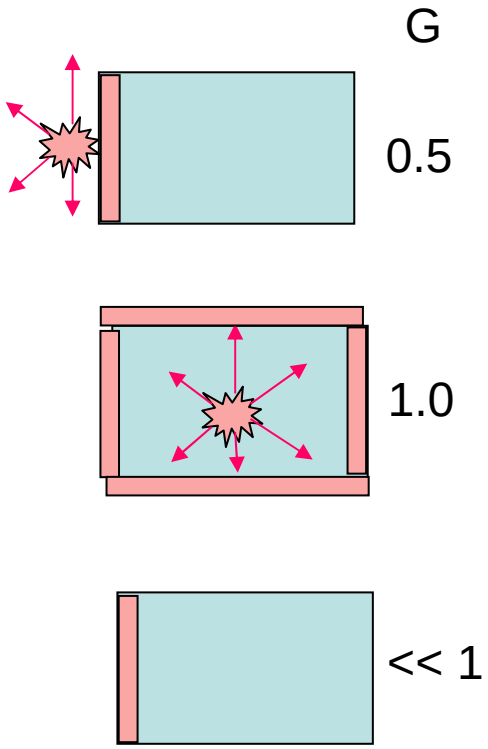
All radiation detection systems have a characteristic dead time that is related to the time required to process an individual detected event. An event gives rise to a voltage pulse in the detection system. If a second pulse occurs before the first one has disappeared the two pulses will overlap and form a single, distorted pulse. The distorted pulse may give the appearance of a single high-energy event and thus be rejected by the energy discrimination circuit. In some detectors the second event will not have any effect on the first but will be lost. In either case it will not be apparent that two separate events occurred.

Such counting losses are called deadtime losses.
The shorter the dead time the smaller the deadtime losses.

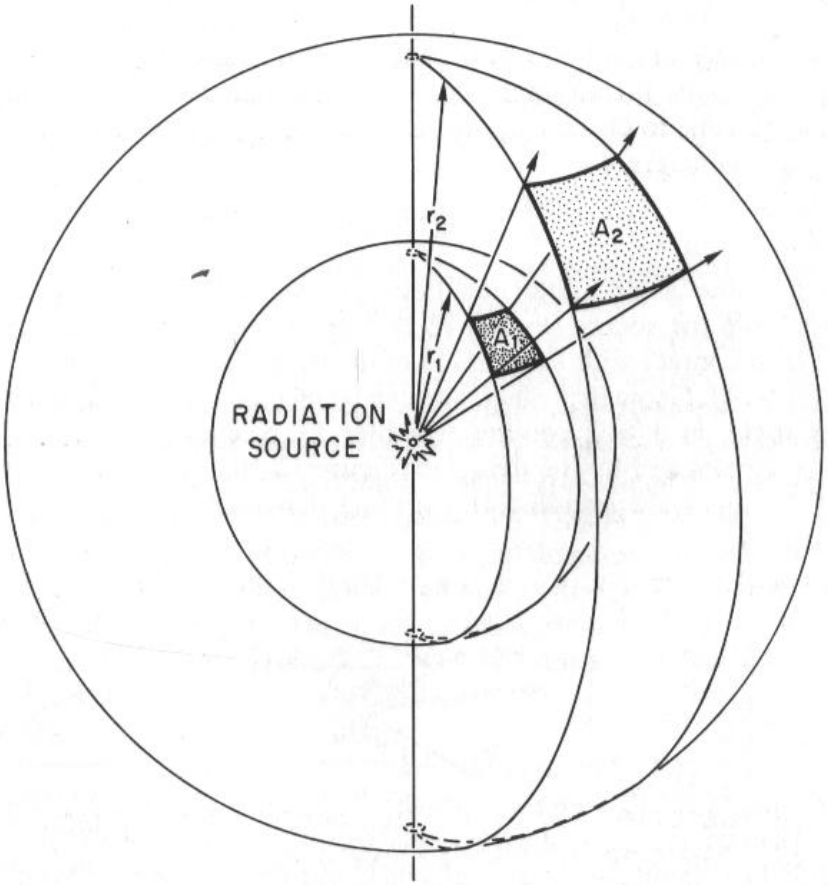
Counting Efficiency

Geometric Efficiency, G





The Inverse Square Law



Flux I per unit surface area at distance r is

$$I = \xi / 4\pi r^2$$

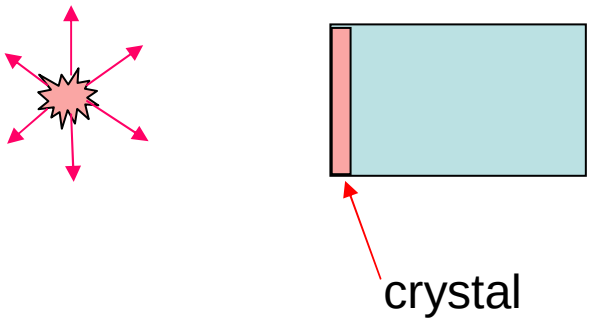
where ξ is the emission rate of the source

Intrinsic Efficiency, $(0 \le \varepsilon \le 1)$

The fraction of radiation striking the detector that interacts with it.

$$\varepsilon = \frac{\text{number of radiations interacting with detector}}{\text{number of radiations striking the detector}}$$

Depends on type and energy of radiation and attenuation coefficient and thickness of detector



Attenuation

The removal of γ-rays from the radiation beam due to absorption or scattering.

For mono-energetic rays

$$I = I_0 e^{-\mu x}$$

where

$I_0 =$ incident intensity with no absorber present

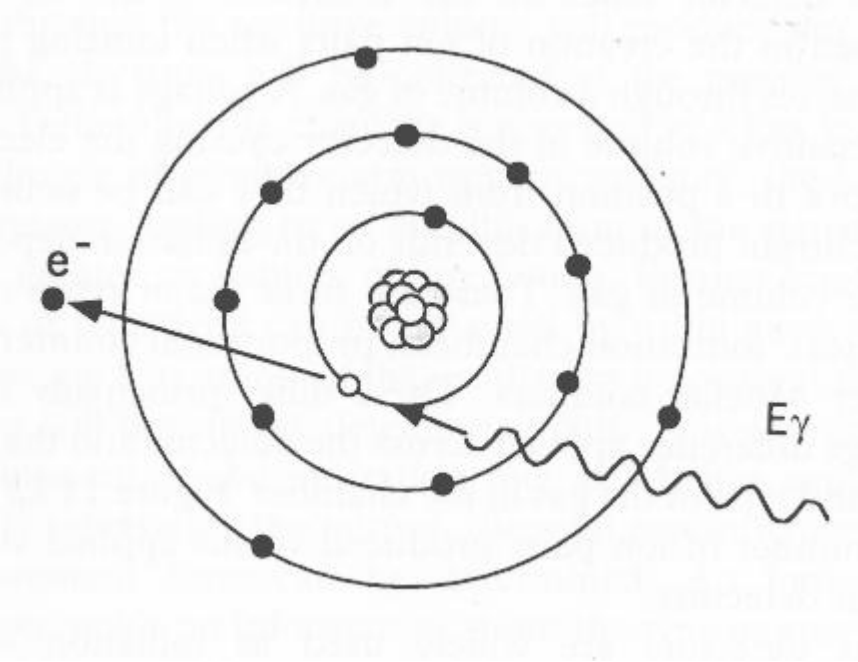
$I =$ intensity measured with absorber present

$\mu =$ linear attenuation coefficient

$x =$ thickness of absorber

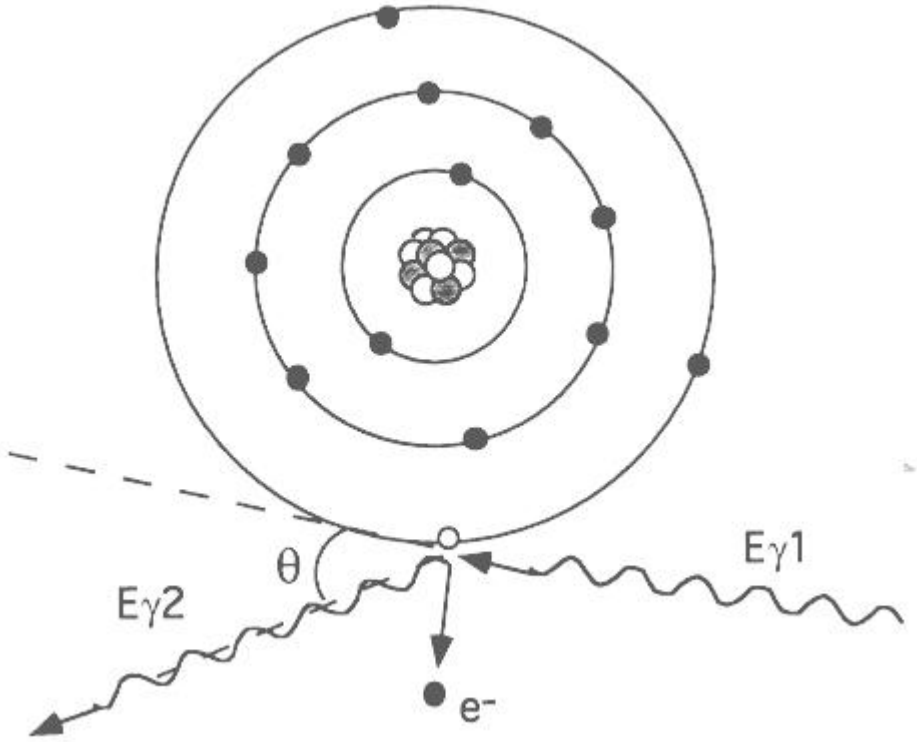
Photoelectric Effect

The atom absorbs all of the energy of the incoming γ–ray.
The electron, from an inner shell and called a photoelectron, has an energy equal to the γ-ray energy minus the binding energy of the electron shell.



Compton Scattering

Compton scattering is a collision between a photon and a loosely bound outer shell orbital electron of an atom. The photon does not disappear but is deflected through a scattering angle θ. Part of its energy is transferred to the recoil electron.
The photon loses energy and changes direction in the process.



Nuclear Medicine

Tracer Principle

Attributed to George de Hevesy (1920s), the first to use radioactive elements as tracers to study the pathway of stable elements in biological systems.
A tiny amount of a radioactive element – much less than can be detected by chemical analysis - can be easily followed.

The Idea

- Inject a tiny quantity of a compound that is “labelled” with a radioactive atom.
- Ascertain the distribution of the tracer within the system by external detection of the emitted gamma rays.
- The distribution after some time reflects the physiological behaviour of the compound, revealing blood flow, metabolism, cellular transport, receptor binding, excretion, etc.
- Uses in medical research, diagnosis and therapy.

The Radioactive Tracer
(also called radiotracer, or radiopharmaceutical).

The amount introduced should be small enough that it does not perturb the system being studied (typically inject of the order of 10^{-9} g in 10 – 20 mCi)

The tracer should mimic the behaviour of the endogenous compound of interest, e.g. ^{18}F-deoxyglucose ⇔ glucose.

Radiopharmaceutical Production

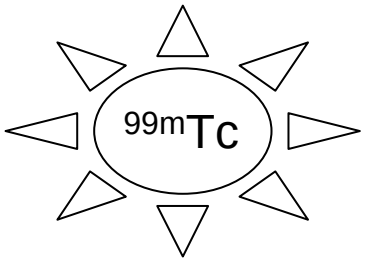
1. Produce the radionuclide (in reactor or cyclotron)
2. Chemically synthesize molecules of the desired compound, incorporating radioactive atoms.

Molecule

e.g. ^{11}C (O, O)

or

Chelate



Production of Radionuclides

Naturally occurring radionuclides are usually very long-lived (eg. ^{40}K half life is 10^9 y), or are very heavy elements that are unimportant in physiological processes.

All radionuclides used in nuclear medicine are “man made”. They are produced by bombarding nuclei of stable atoms with subnuclear particles (neutrons, protons, etc) so as to cause nuclear reactions that convert a stable nucleus into an unstable (radioactive) one. The bombardment occurs in either a nuclear reactor or a cyclotron.

Reactor Production of Radionuclides for Nuclear Medicine

The core of a nuclear reactor has a very high flux of neutrons that are produced in a self-sustaining nuclear chain reaction.

When neutrons strike a target, some of the neutrons are captured by the nuclei of the target atoms. If the nucleus of the target atom becomes radioactive as a result, neutron activation is said to have occurred.

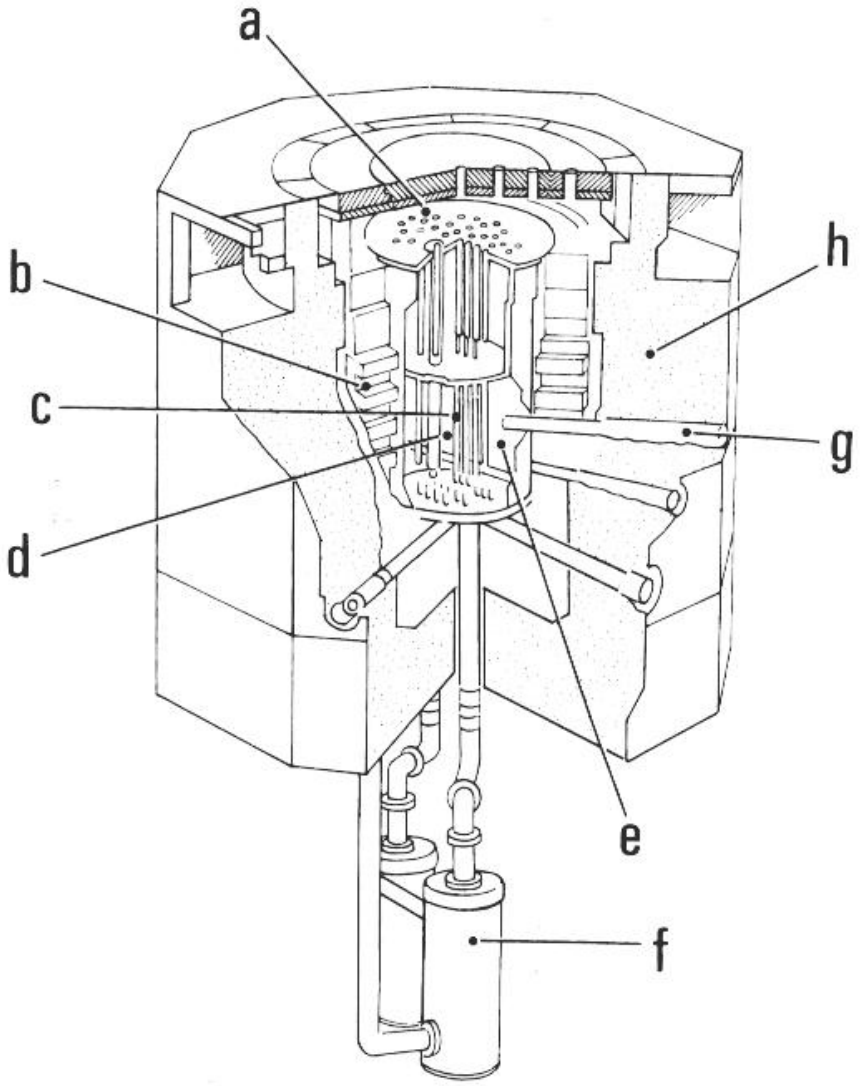


Fig. 118.2 A nuclear reactor for the production of radioisotopes. Identified features are: (a) vertical irradiation facility, (b) graphite neutron reflector, (c) assembly of uranium fuel elements, (d) intense flux of neutrons, (e) heavy water, neutron moderator and primary heat exchanger fluid, (f) bank of heat exchangers, (g) horizontal irradiation facility, (h) concrete biological shield.

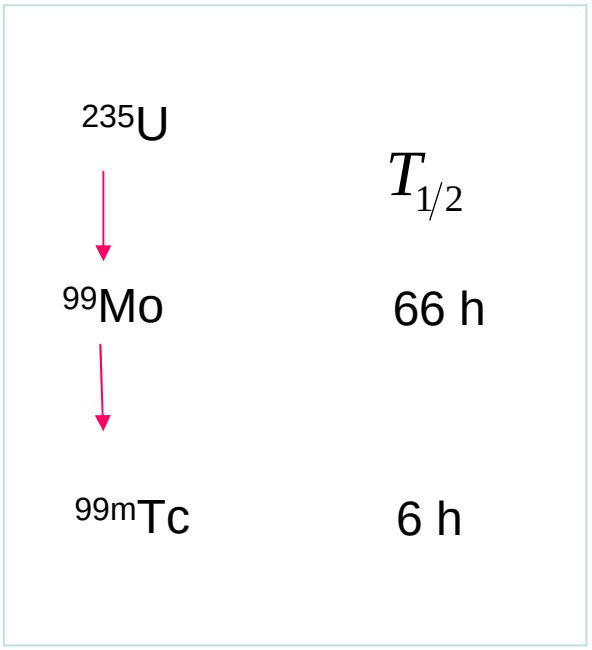
(n, γ) reaction – the target nucleus immediately undergoes deexcitation by emitting a γ-ray. The target and product nuclei represent different isotopes of the same element.

(n, p) reaction – the target nucleus promptly ejects a proton. The target and product nuclei do not represent the same element.

Radioisotope	Reactor Produced $t_{1/2}$	Production reaction
^{32}P	14.3 d	$^{32}S(n.p)$
^{51}Cr	27.7 d	$^{50}Cr(n,\gamma)$
^{64}Cu	12.7 h	$^{63}Cu(n,\gamma)$
^{90}Y	2.7 d	$^{89}Y(n,\gamma)$
^{99m}Tc	6 h	$^{235}U(n,f)^{99}Mo \rightarrow {}^{99m}Tc$
^{131}I	8 d	$^{130}Te(n,\gamma)$
^{153}Sm	46.3 h	$^{152}Sm(n,\gamma)$
^{166}Ho	26.8 h	$^{164}Dy(n,\gamma)^{165}Dy(n,\gamma)\ ^{166}Dy \rightarrow {}^{166}Ho$
^{186}Re	3.7 d	$^{185}Re(n,\gamma)$
^{188}Re	17 h	$^{186}W(n,\gamma)^{187}W(n,\gamma)\ ^{188}W \rightarrow {}^{188}Re$
^{198}Au	2.7 d	$^{197}Au(n,\gamma)$

Technetium ^{99m}Tc Emits IC electrons and140 keV γ-rays

Most commonly used radionuclide in nuclear medicine.
Can be incorporated in hundreds of different radiopharmaceuticals.

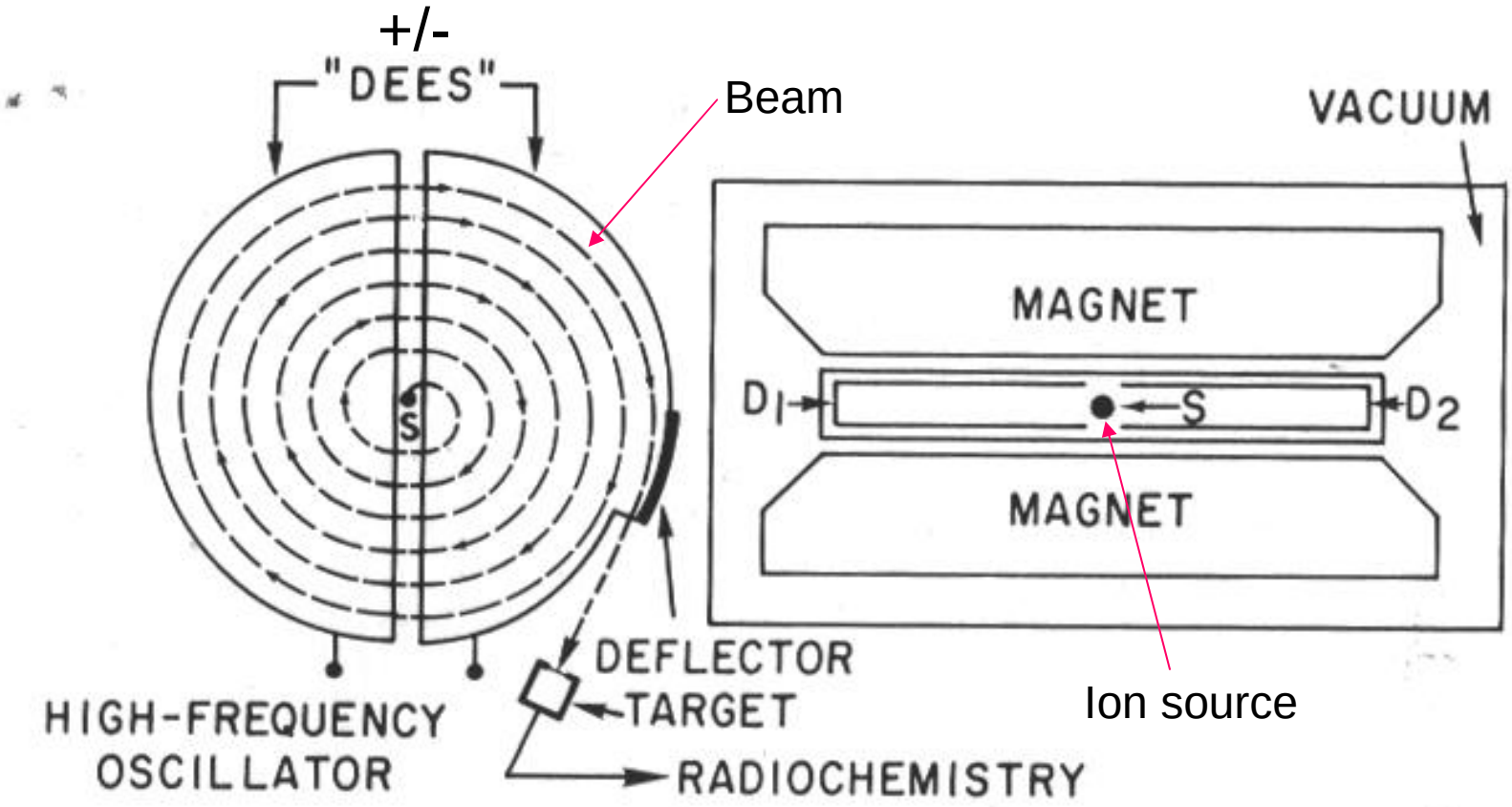


Some common ^{99m}Tc-labelled radiopharmaceuticals:

- Sulphur colloid for liver, spleen, bone marrow imaging.
- Albumin for lung imaging
- Red cells for blood pool visualisation
- Pertechnetate for thyroid imaging
- HMPAO for brain blood flow
- MDP for bone
- HIDA for liver function
- DTPA for renal function
- Technegas for lung ventilation

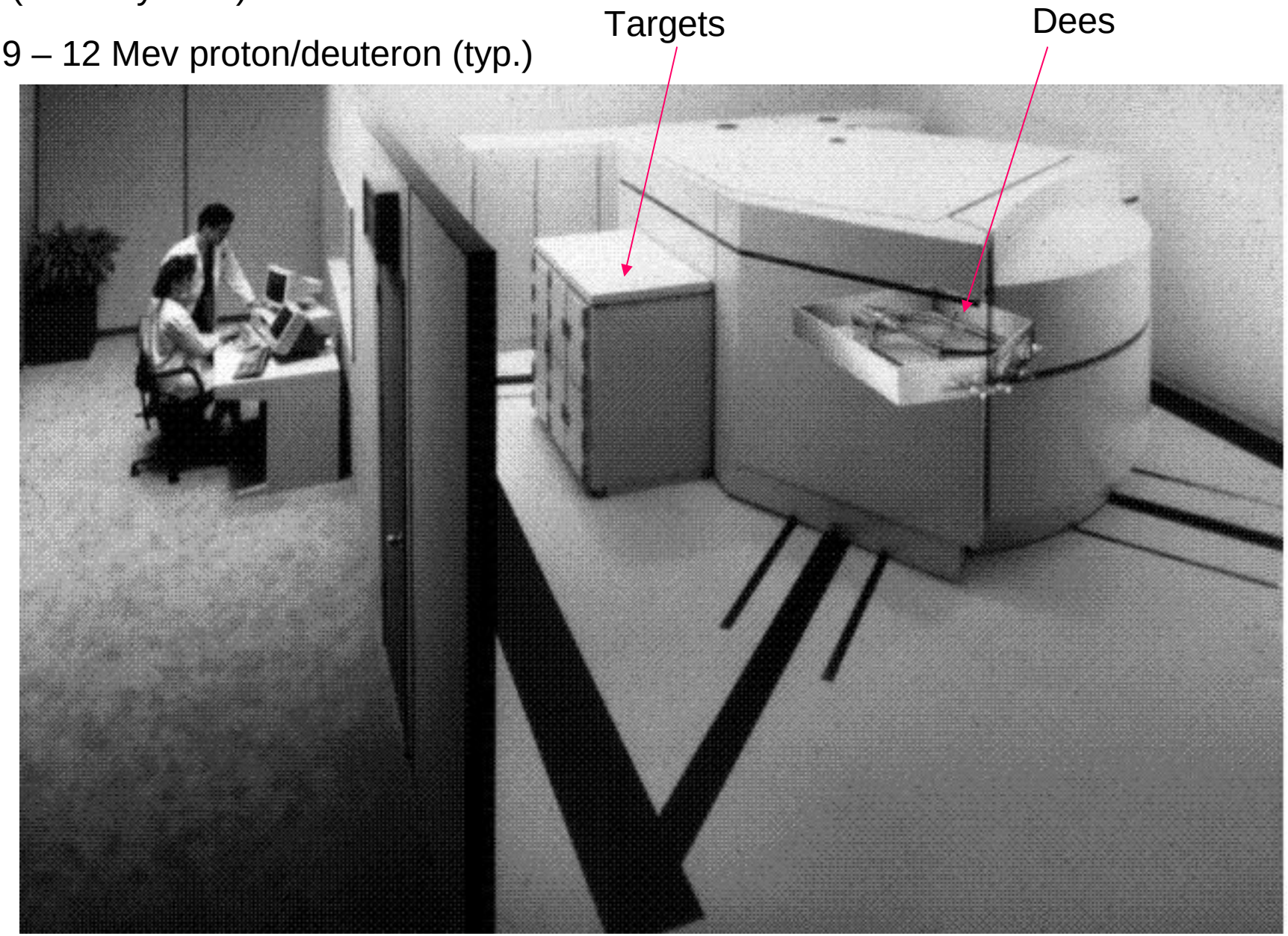
Cyclotron production of Radionuclides
for Nuclear Medicine

A cyclotron consists of hollow metal electrodes called “dees” between the poles of a large electromagnet.

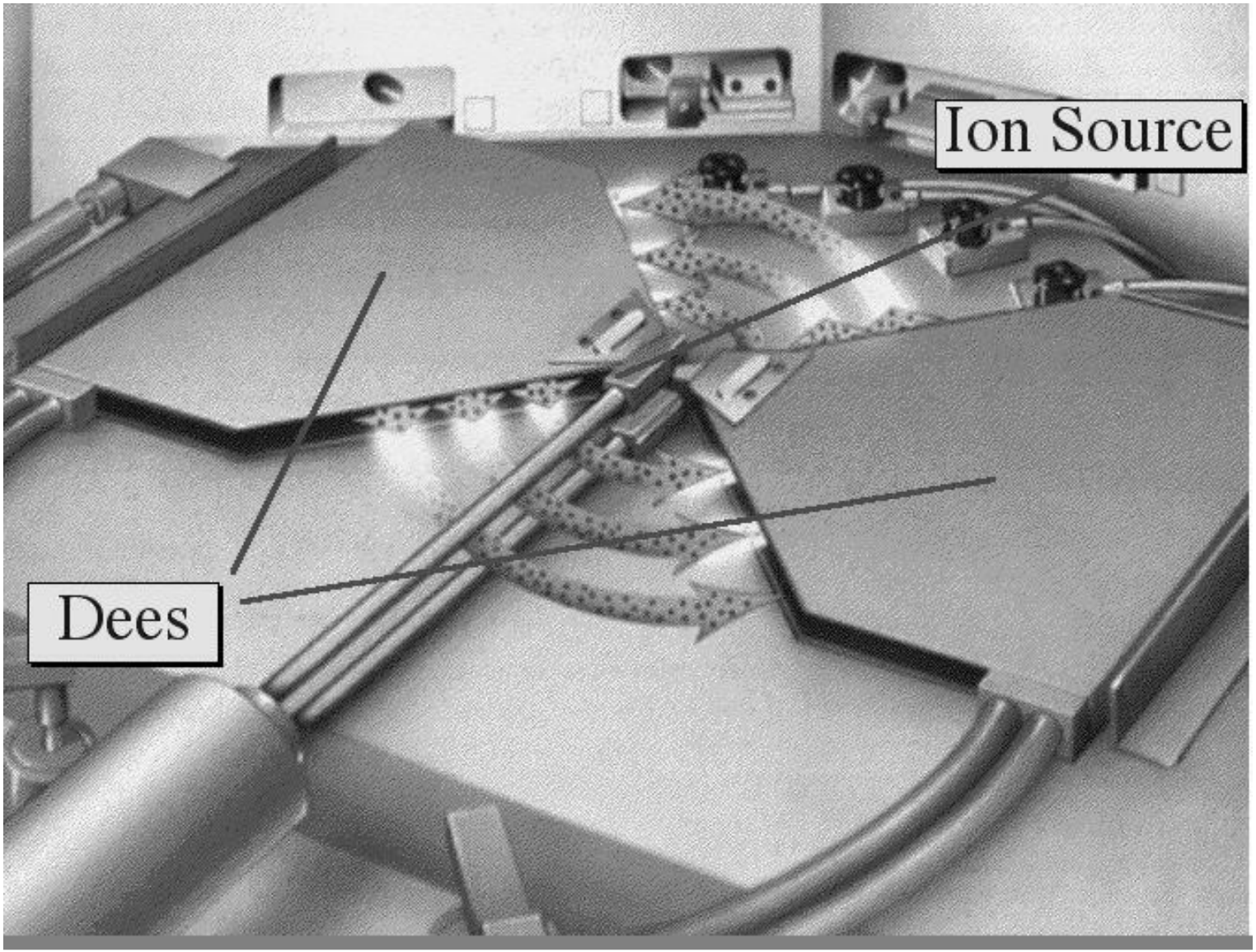


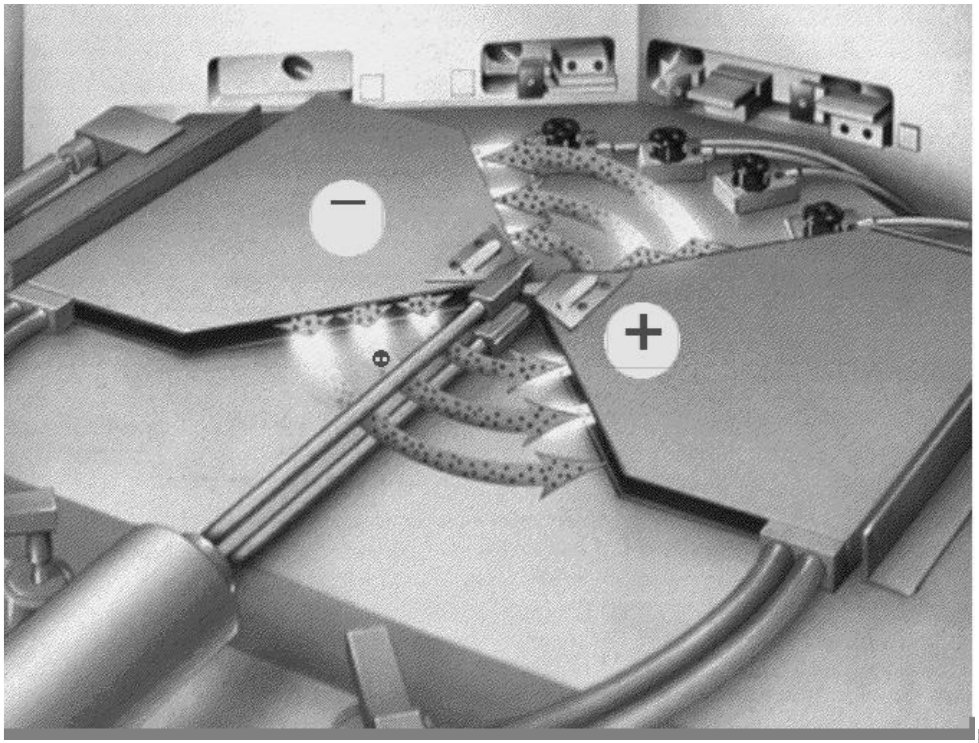
Self-shielded medical cyclotron
(cutaway view)

9 – 12 Mev proton/deuteron (typ.)

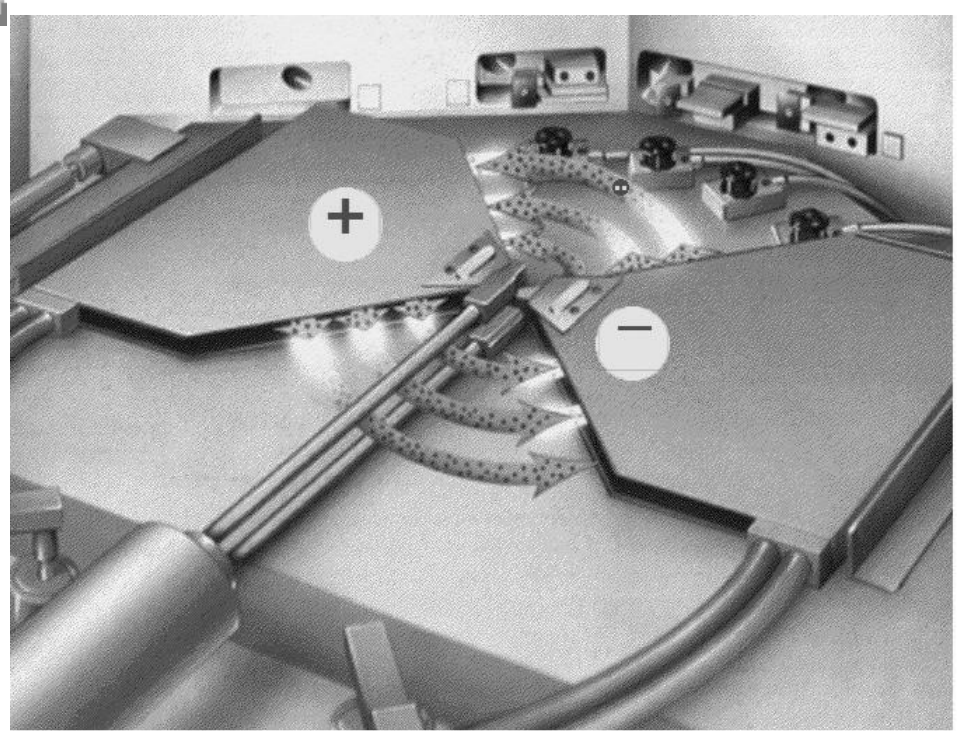


Cyclotron Dees

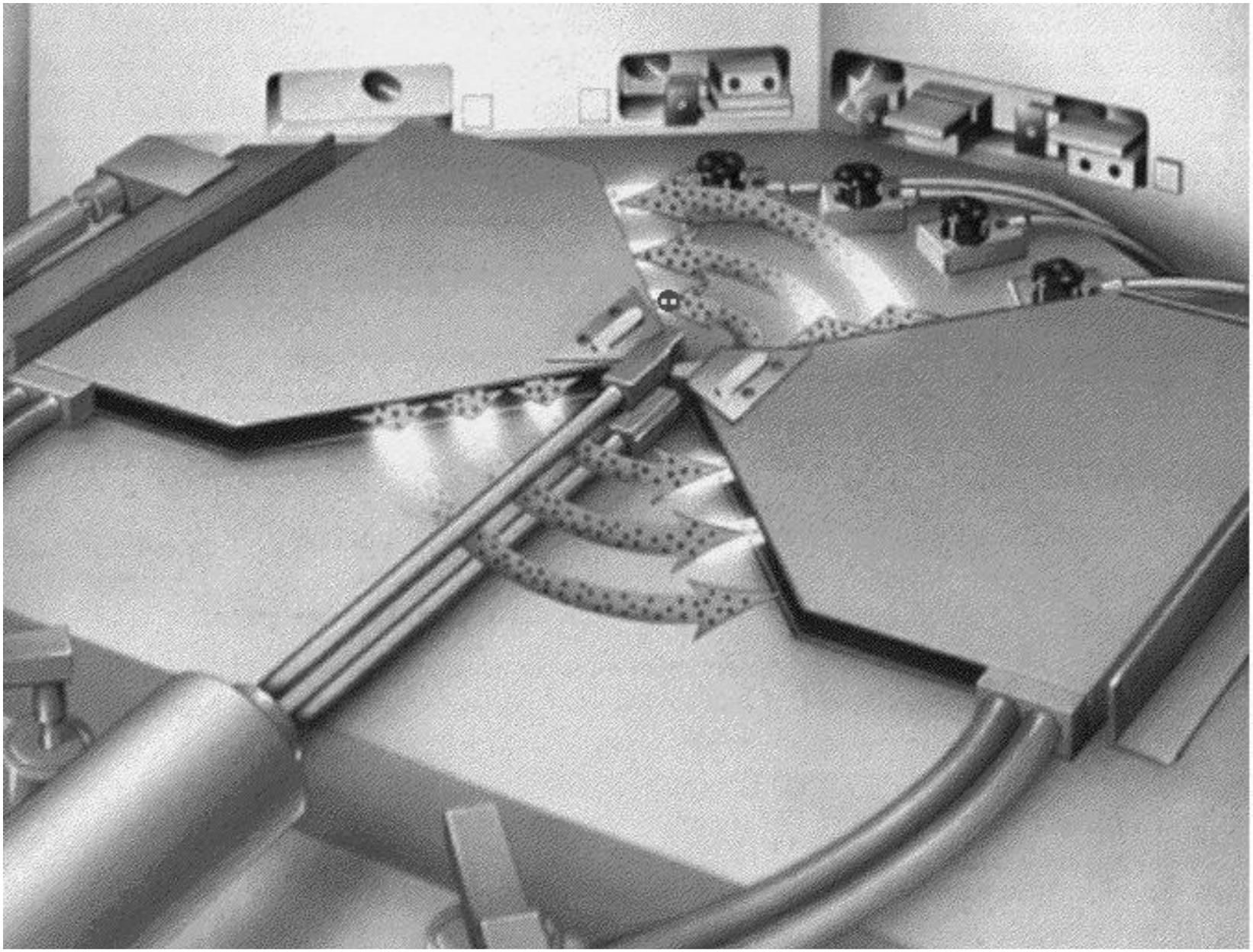




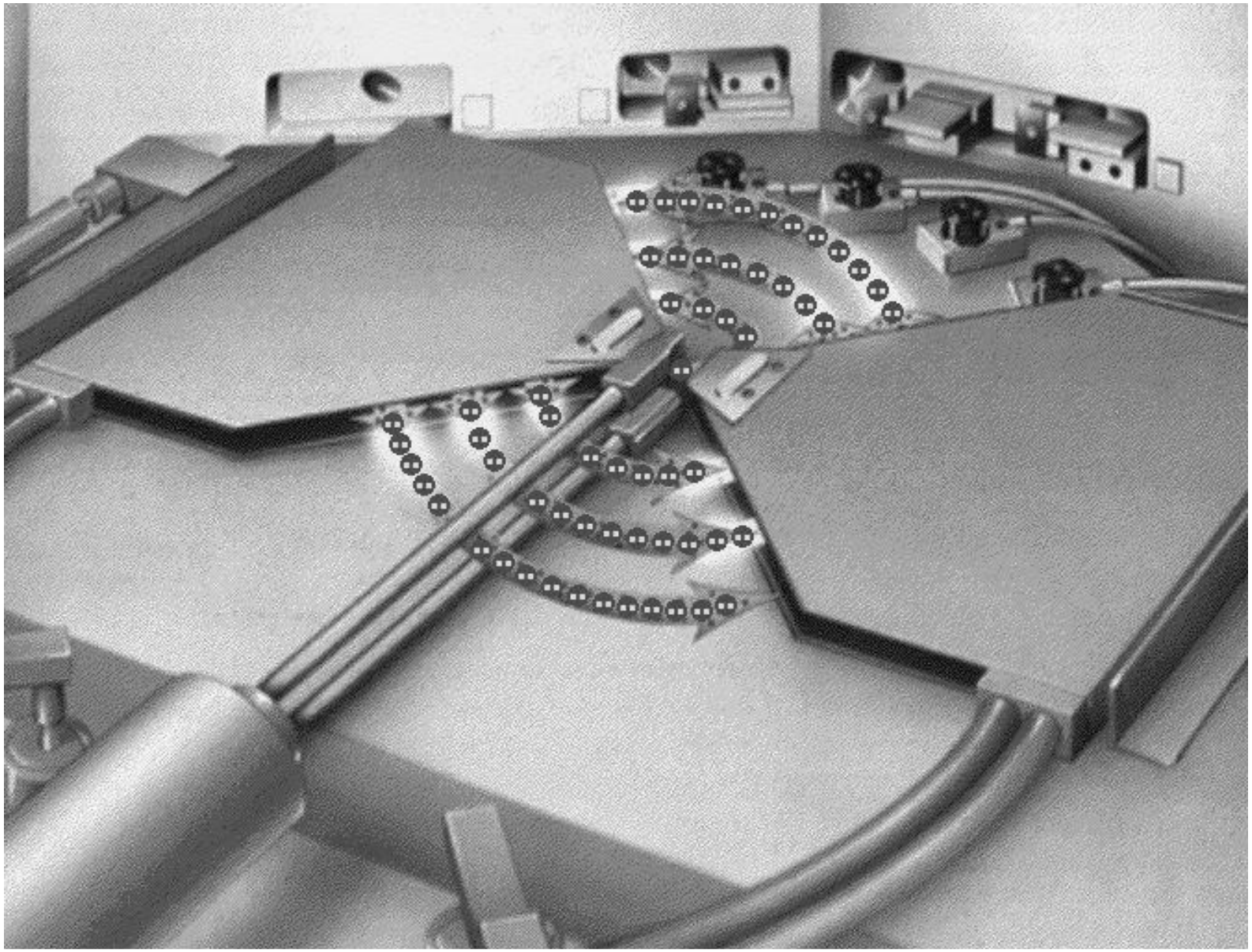
The applied potential alternates



Introduction of a negatively charged ion



Path of beam



Energy of accelerated particles

$$E \cong 4.8\text{x}10^{-3} \frac{(HRZ)^2}{A} \text{ MeV}$$

where

E is the energy of the particles

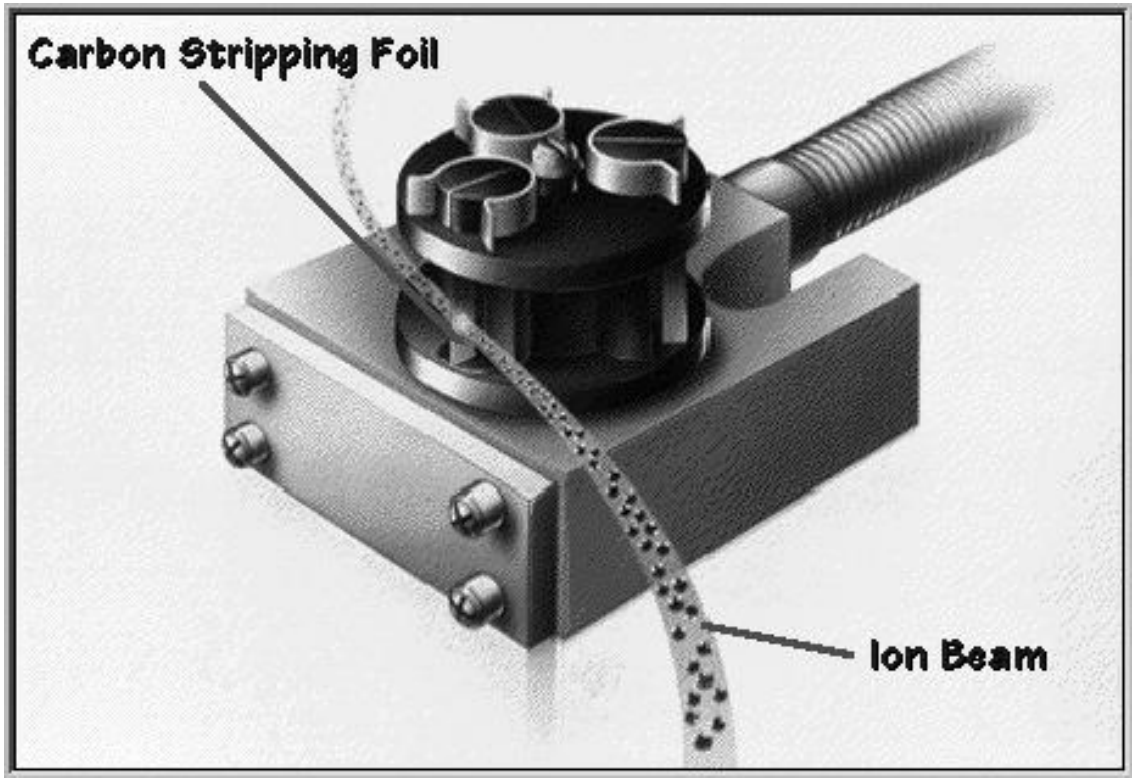
H is the magnetic field strength in Tesla

R is the radius of the orbit in cm, and

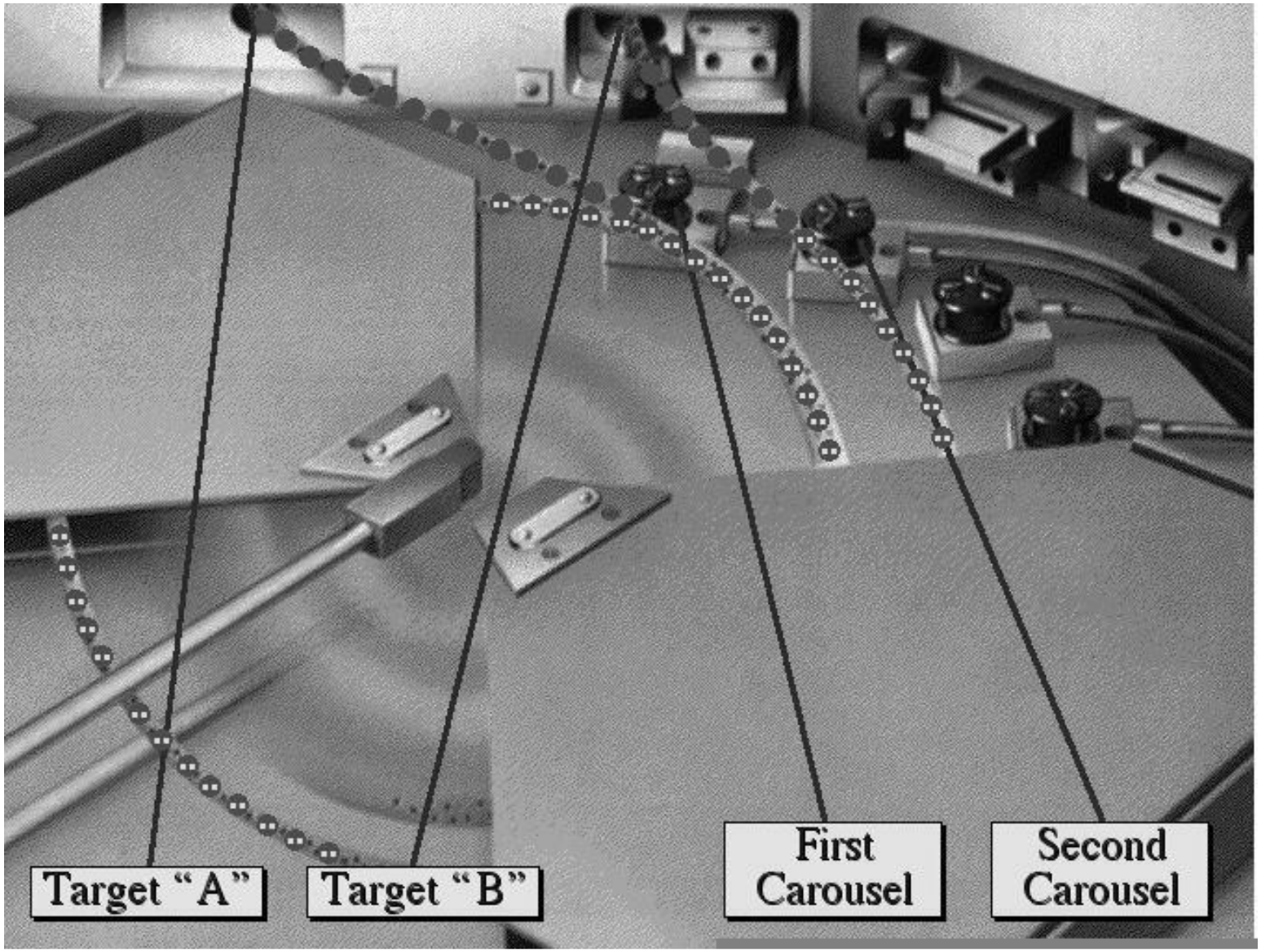
Z and A are the atomic number (charge) and mass number of the particle, respectively.

e.g. H=1.5T, R=38cm
Proton (Z=1, A=1)
E = 15.5 MeV

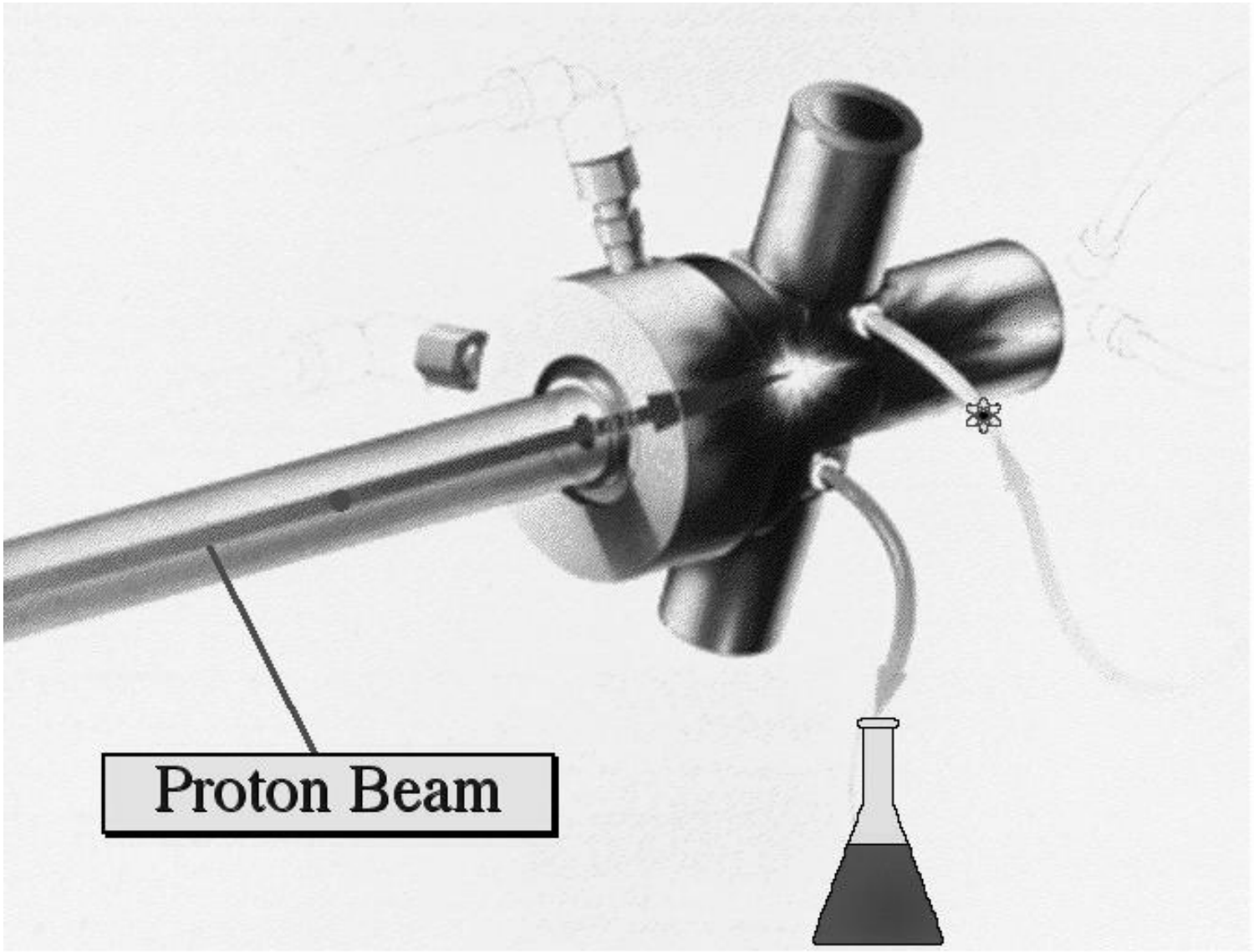
Stripping Foil



Beam Extraction



Target



Radioisotope	Cyclotron Produced $t_{1/2}$	Production rea
^{11}C	20 m	$^{14}N(p,\alpha)$
^{13}N	10 m	$^{16}O(p,\alpha)$
^{15}O	2 m	$^{16}O(p,pn)$
^{18}F	110 m	$^{18}O(p,n)$
^{52}Fe	8.3 h	$^{55}Mn(p,4n)$
^{57}Co	271 d	$^{58}Ni(p,2p)$
^{67}Cu	2.6 d	$^{68}Zn(p,2p)$
^{67}Ga	78.2 h	$^{68}Zn(p,2n)$
^{111}In	67.3 h	$^{112}Cd(p,2n)$
^{123}I	13.2 h	$^{124}Xe(p,2n)$
^{201}Tl	72.9 h	$^{203}Tl(p,3n)$

Of special interest since constituents of all biologic substances.

Fluorine can often be substituted for hydrogen.

All 4 are positron emitters and produce annihilation photons.

Most cyclotron activation processes add positive charge to the nucleus.
Many of the products therefore decay by β^+ emission.

Imaging in Nuclear Medicine

Planar Techniques (2-D)

- Rectilinear scanner (obsolete)
- Gamma camera

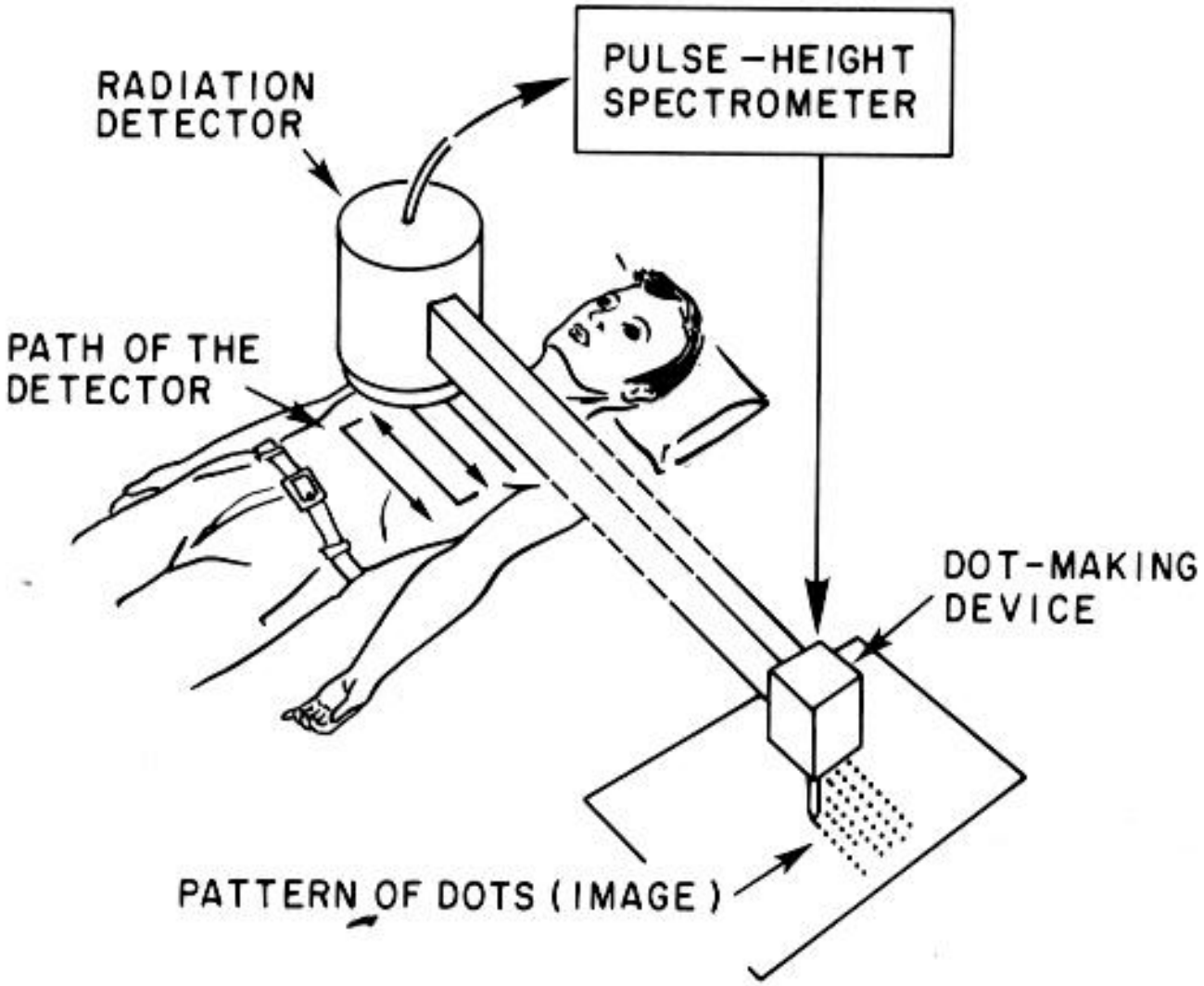
Tomographic Techniques (3-D)

- Perfomed with rotating detectors or complete ring of detectors.
- Single photon emission computed tomography (SPECT)
- Positron emission tomography (PET)

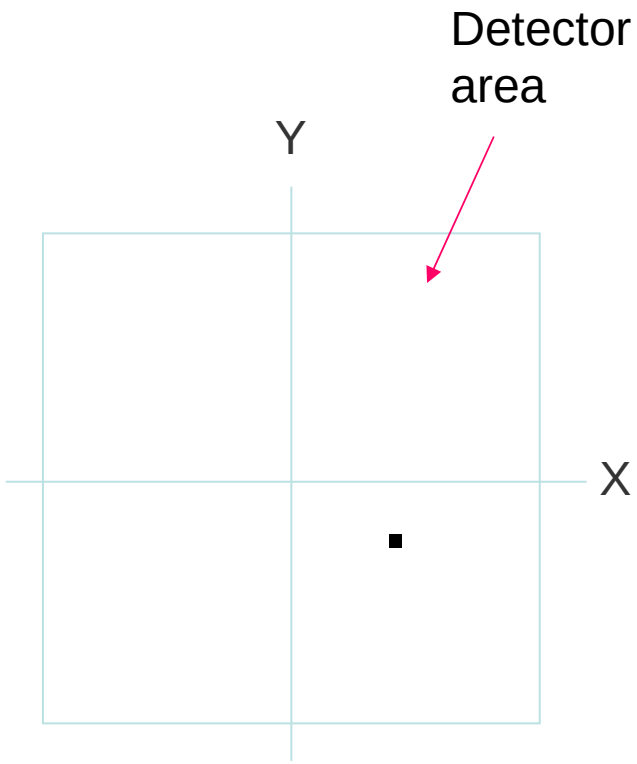
All the above imaging techniques can be performed with the added dimension of time by acquiring a series of images. This is termed dynamic imaging.

Dynamic imaging can provide functional information that is not obtainable from a static image.

Rectilinear scanner



Gamma Camera (Anger Camera)



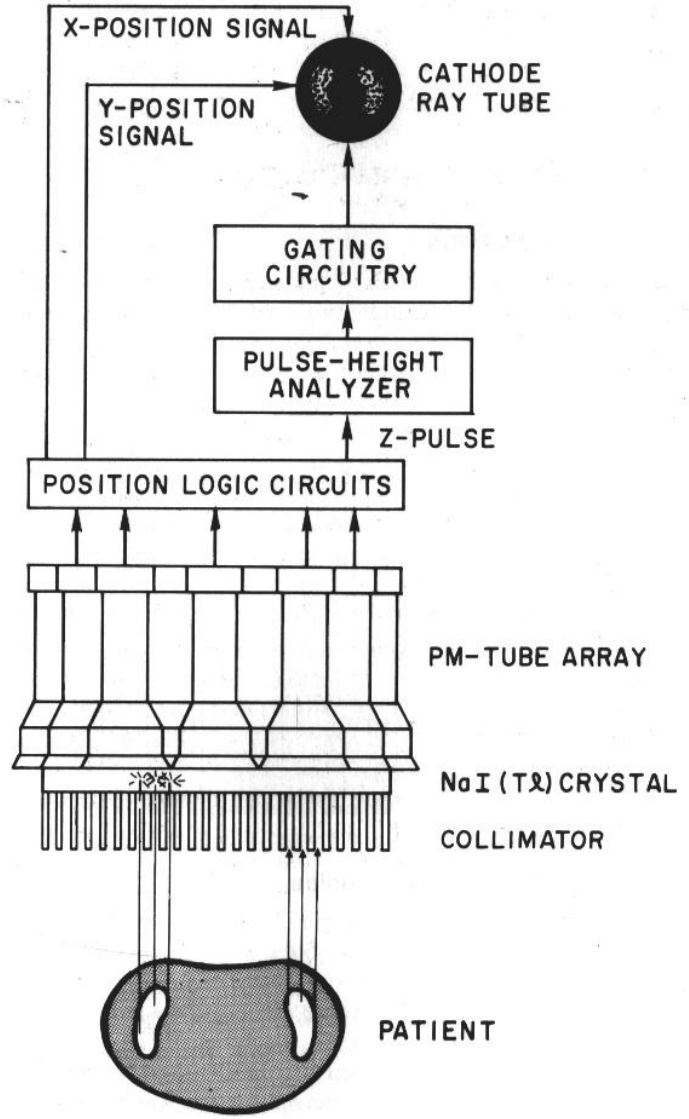
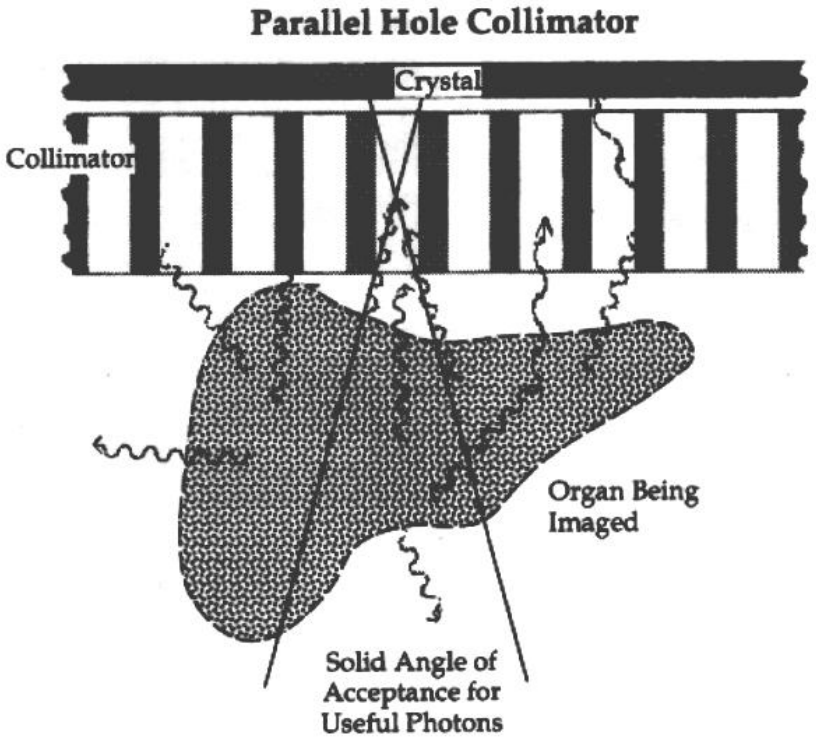


Fig. 15-1. Basic principles and components of the Anger camera.

The Collimator

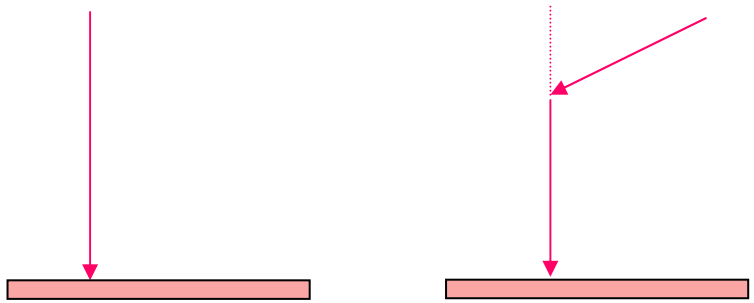
γ-rays have no charge and therefore cannot be deflected using electric or magnetic fields. Their energy is too high to be reflected or focussed like visible light. They can however be attenuated and this is the principle of the collimator. The collimator consists of channels through which γ-rays can pass, separated by lead or tungsten septa. Only photons travelling within the narrow solid angle of acceptance of the collimator holes can pass unhindered to the detector. The collimator thus restricts the γ-rays that reach the detector to those which form a planar projection of object being imaged.



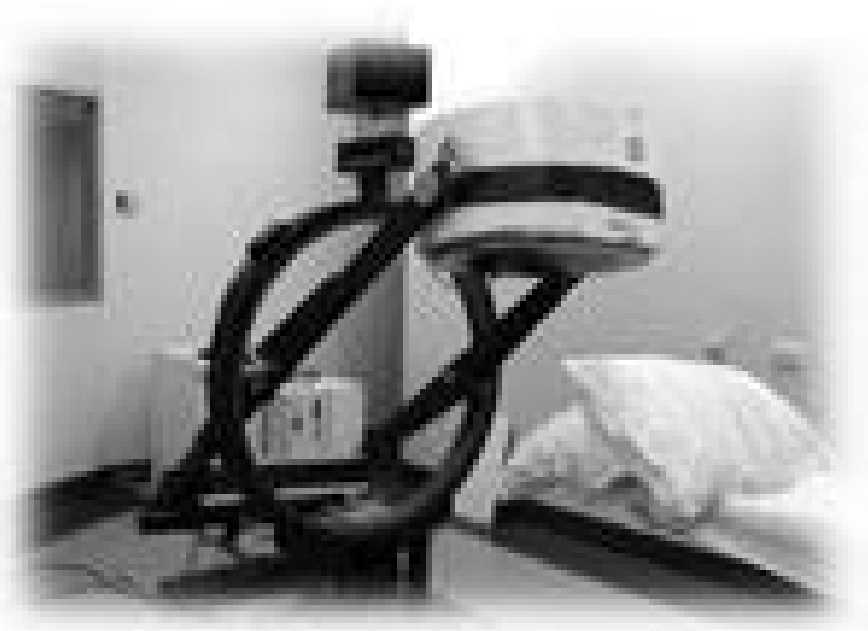
Collimator Types
Parallel hole
Converging
Diverging
Pin hole

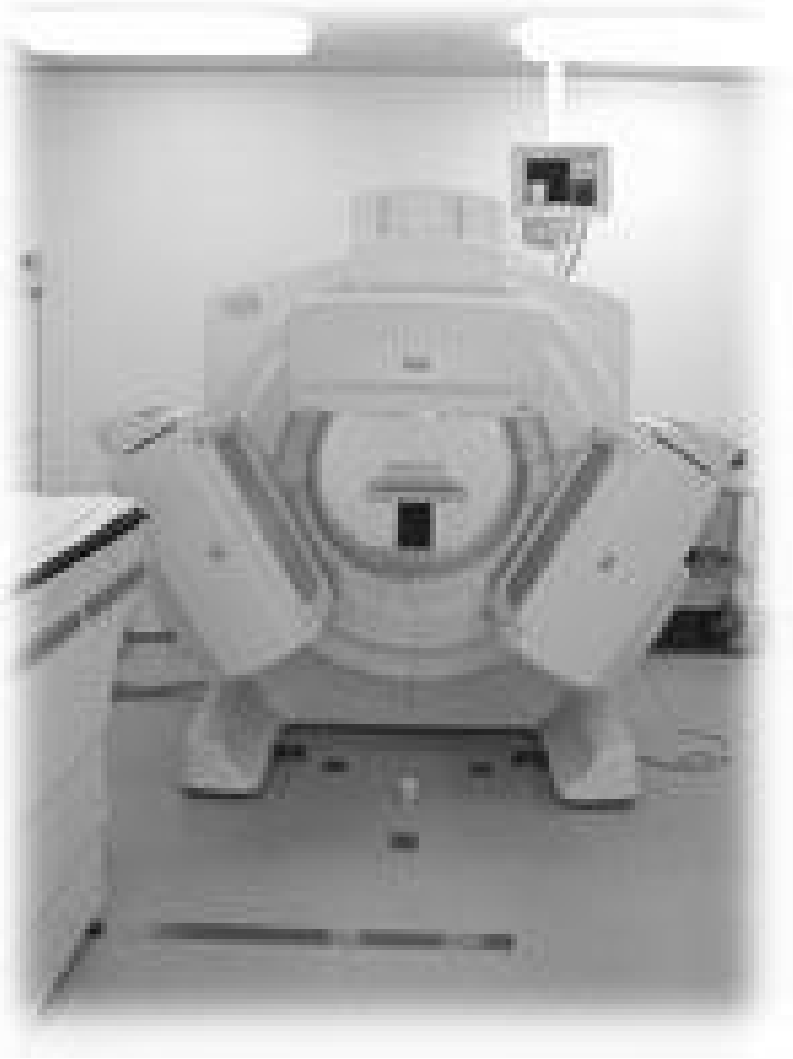
The Pulse Height Analyzer (PHA)

When a photon reaches the detector, it is assumed that it originated from a radioactive atom that lay on a straight line path parallel to the collimator holes. If however the photon underwent Compton scattering before reaching the detector, this assumption is most probably incorrect because Compton scattering causes the photon to change direction. The acceptance of these scattered photons causes a loss of resolution in the image and it is desirable to reject them.
Scattered photons can be identified by means of their lower energy relative to unscattered photons. The function of the pulse height analyzer is to reject photons whose energy does not lie within an assigned energy range and thus may have been scattered.



Gamma Camera





Collimator Performance

$$\text{Sensitivity} = \frac{CD^4}{(L_e(D+T))^2}$$

$$\text{Resolution} = \frac{D(L_e + H)}{L_e}$$

where

C is a constant determined by the hole shape, (C = 0.069 for hexagonal holes and 0.057 for round holes), D and L_e are the hole diameter and length, respectively, T is the thickness of the lead septa, and H is the distance from the hole to the source.

System Resolution

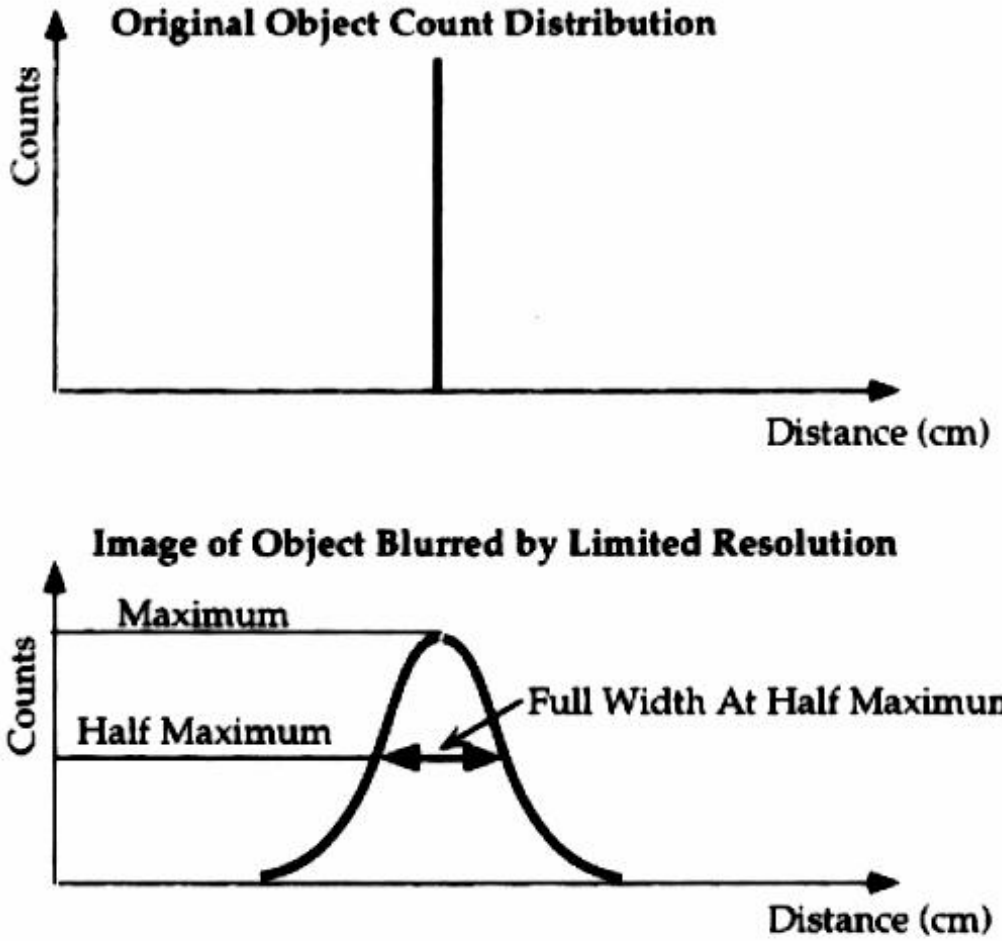
System resolution is a combination of the collimator resolution and the intrinsic detector resolution, i.e.

$$R_s = \sqrt{\frac{R_i^2}{M^2} + R_c^2}$$

where

R_s, R_i and R_c are the system, intrinsic, and collimator resolution, respectively, and M is the magnification factor.

System Spatial Resolution



Variation of system resolution with distance from a parallel hole collimator

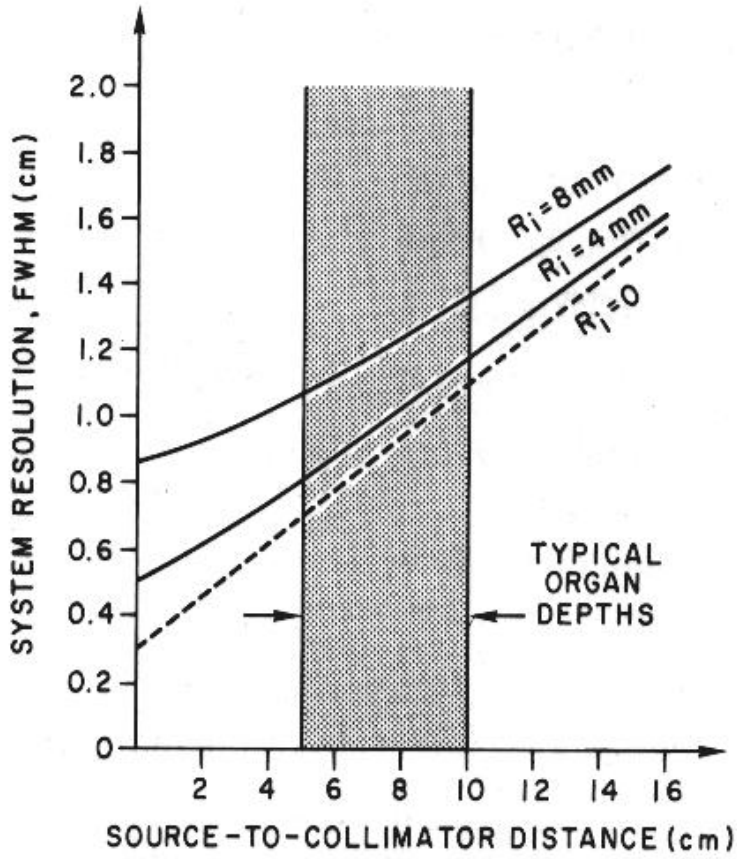
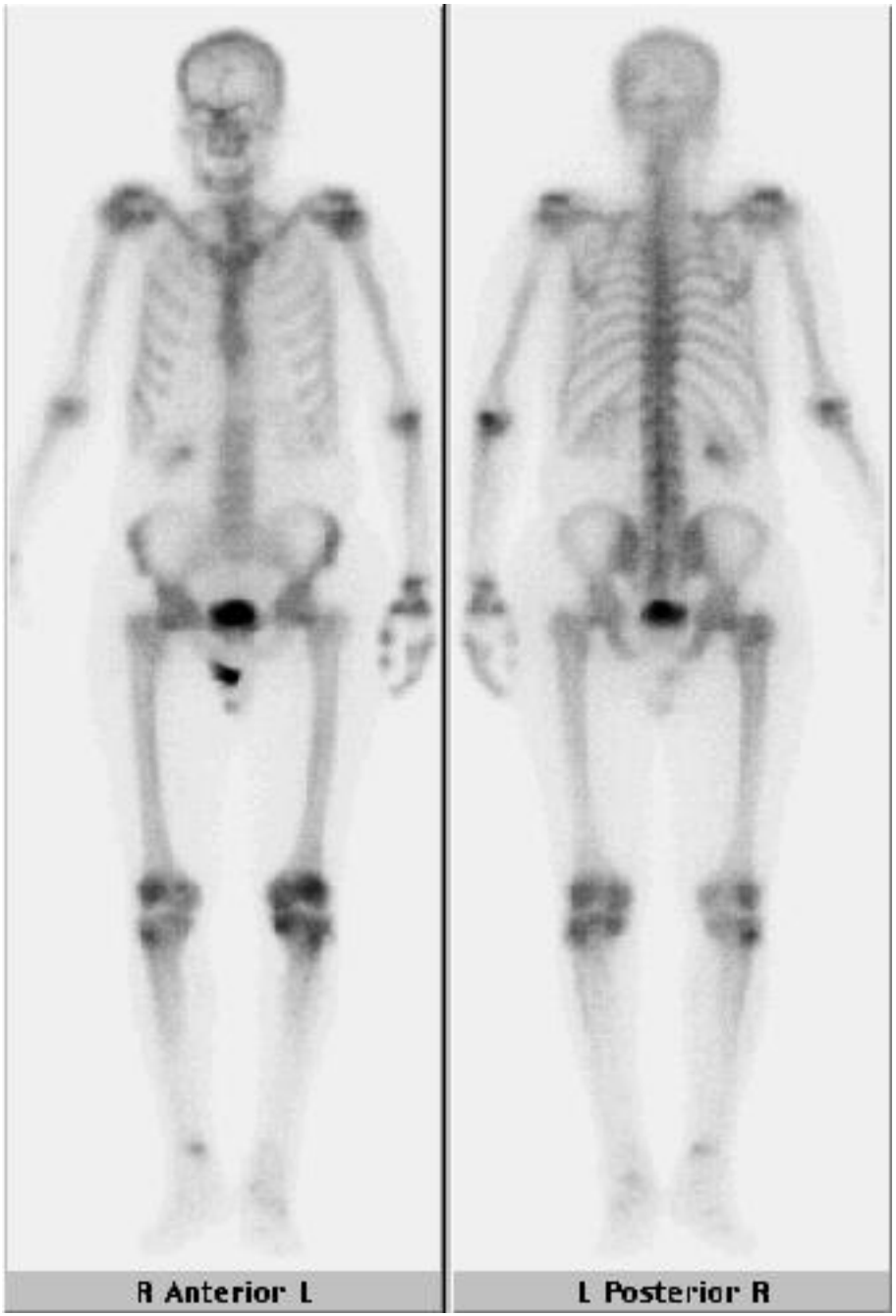


Fig. 16-16. System resolution versus source-to-collimator distance for a typical parallel-hole collimator and for different values of intrinsic resolution. At most typical organ depths, system resolution is determined primarily by collimator resolution.

2-D Imaging with Gamma Camera

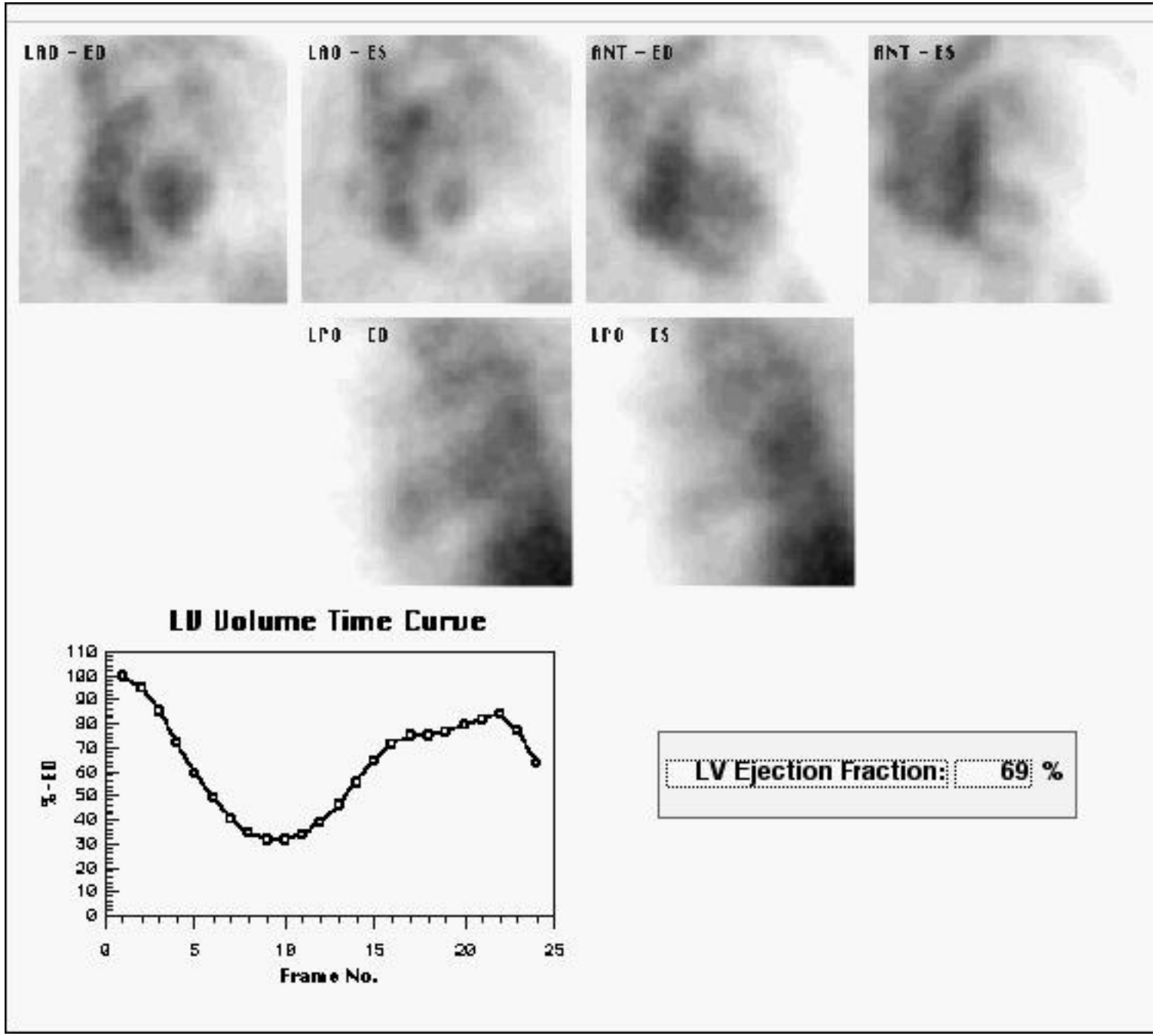
Whole body bone scan

^{99m}Tc-MDP



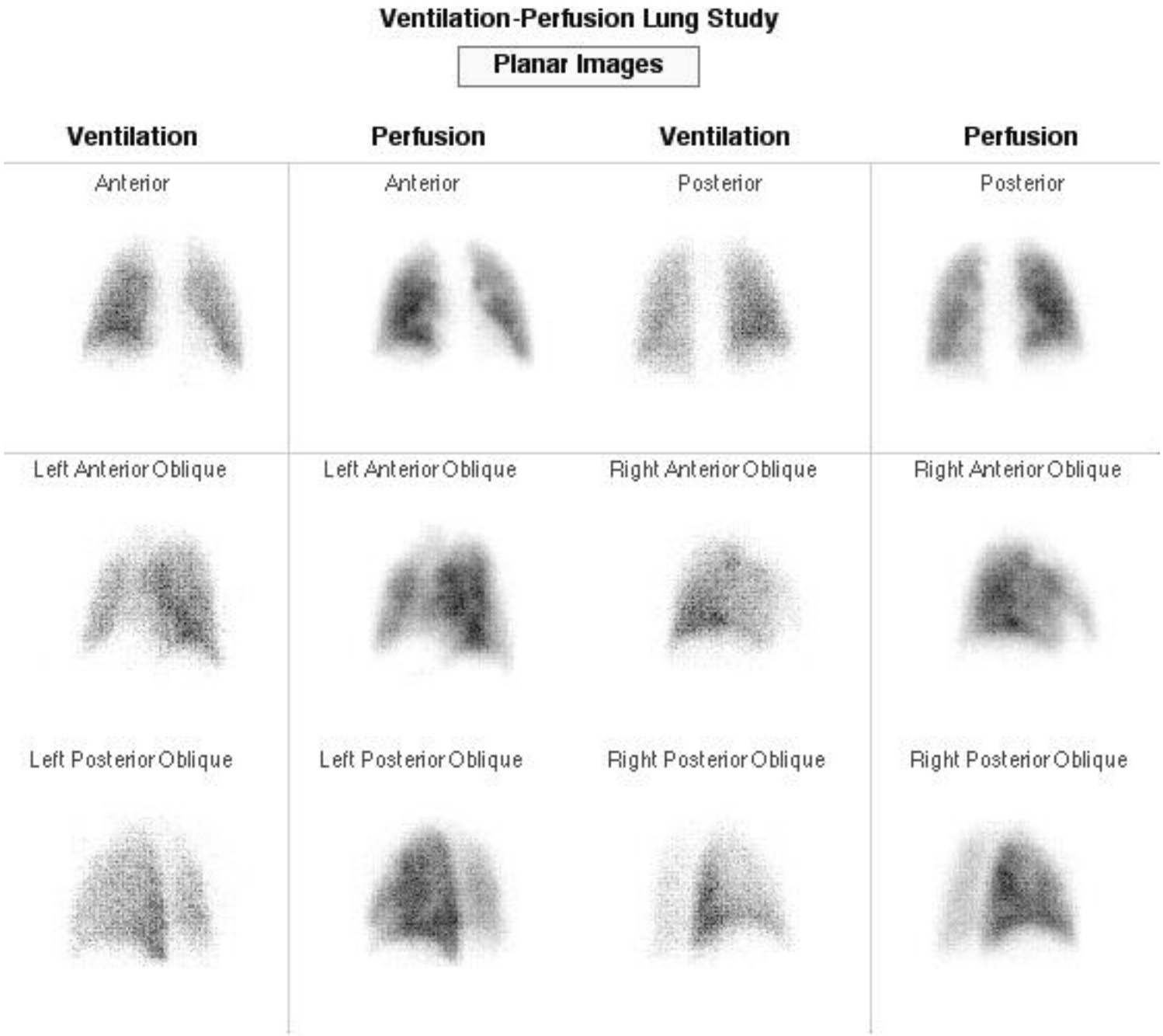
Gated Heart Pool Scan

^{99m}Tc-RBC



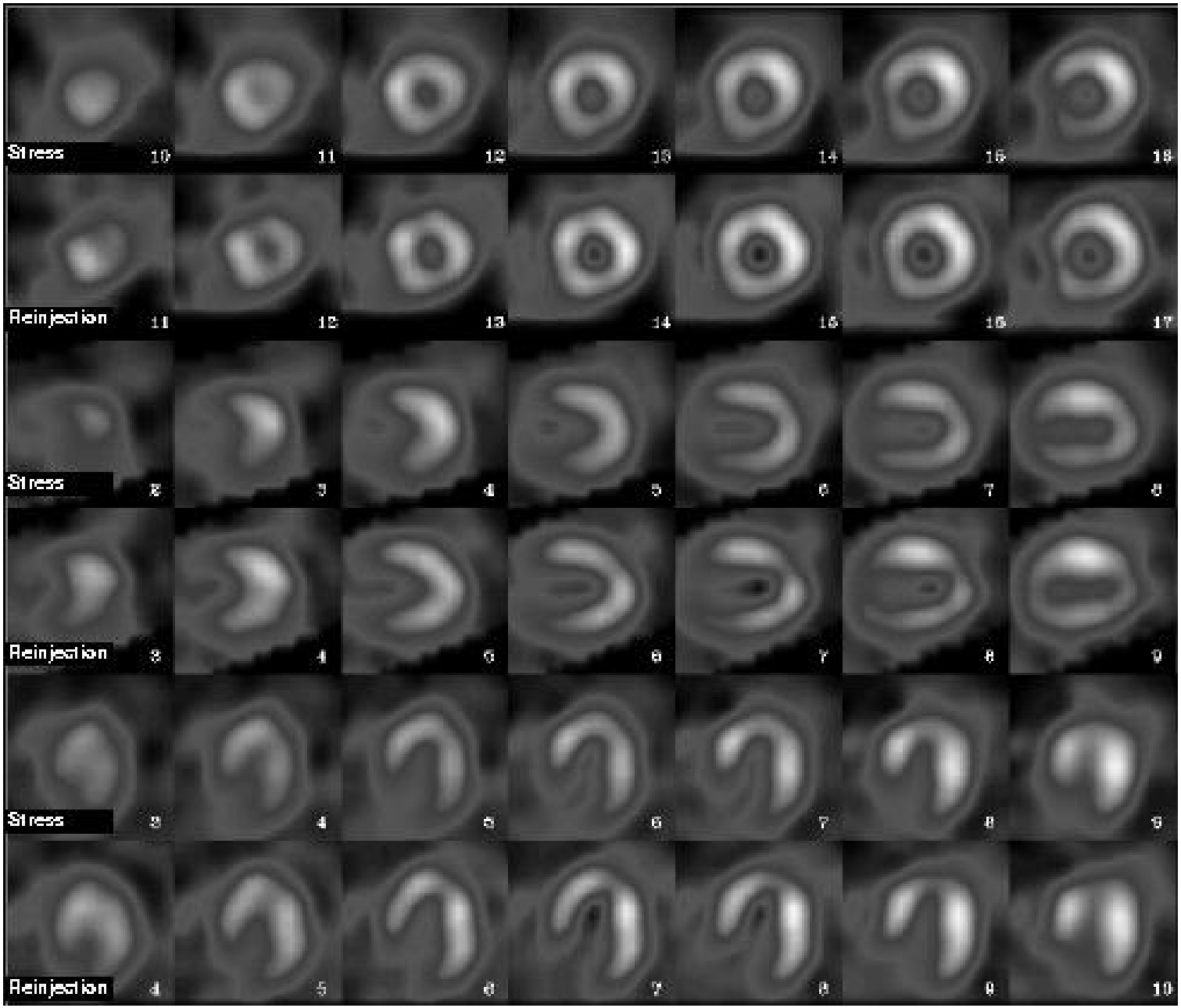
Lung Scan

^{99m}Tc-Technegas
^{99m}Tc-MAA



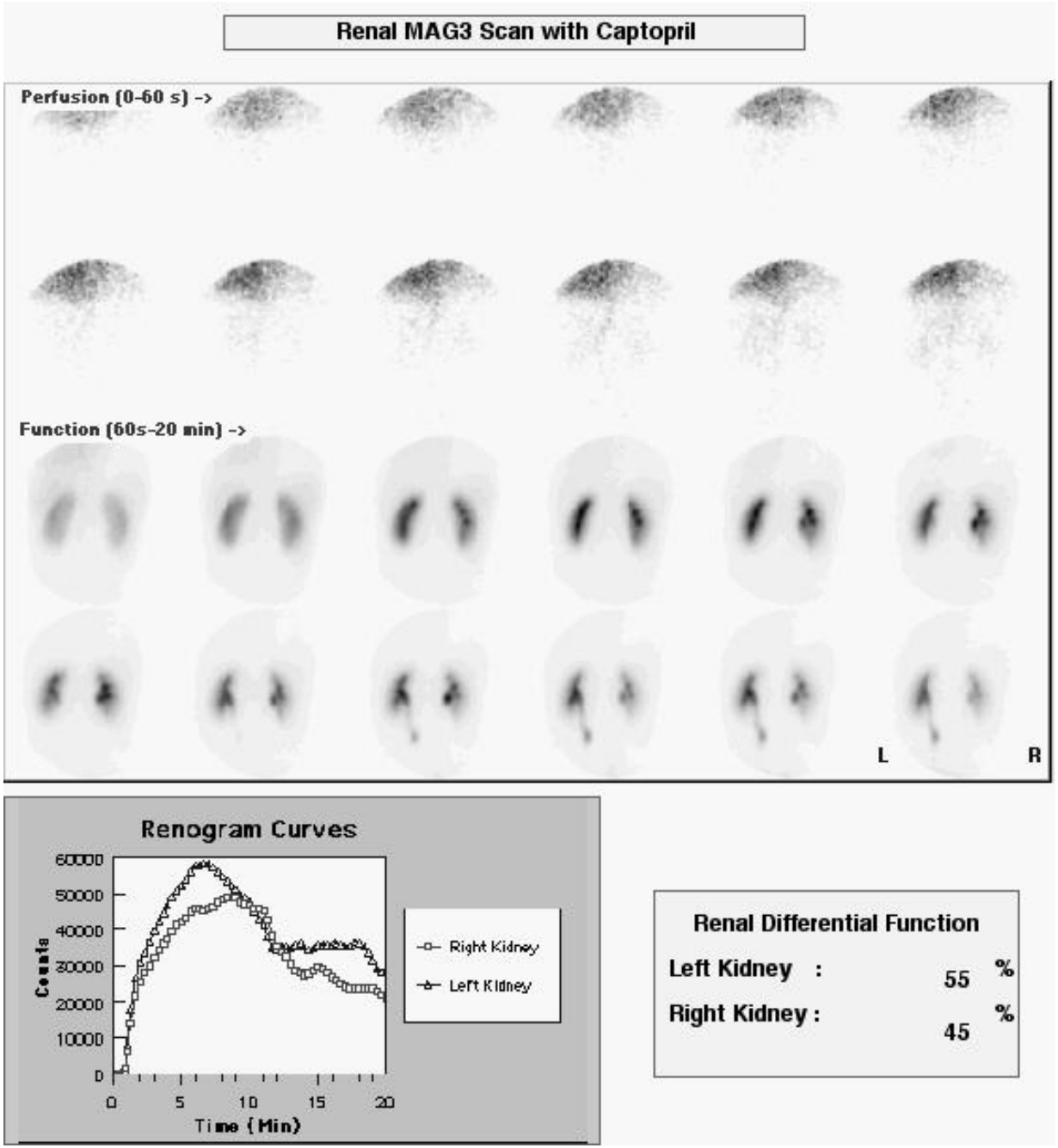
Myocardial Scan

99mTc-MIBI

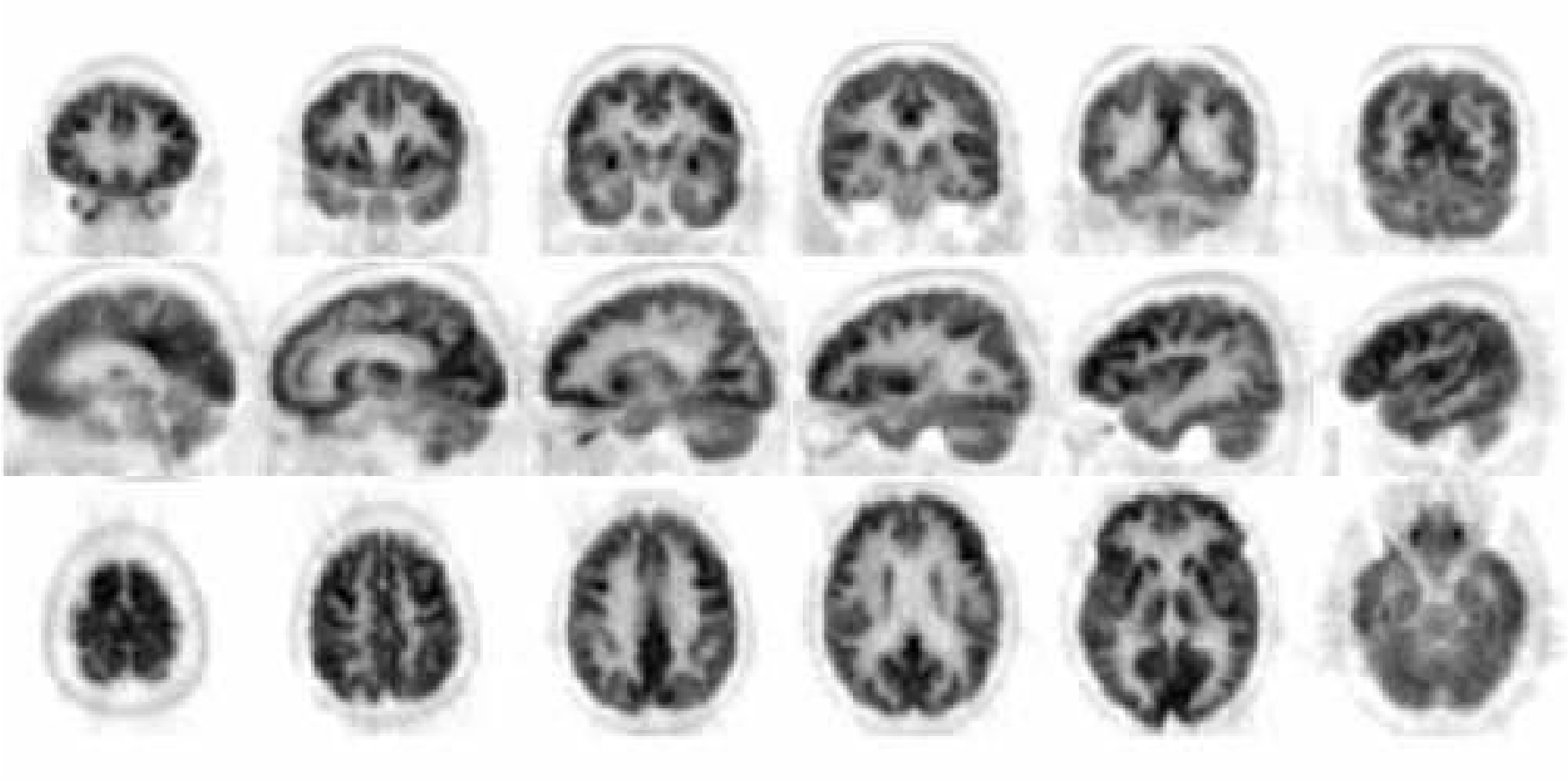


Renal Scan

^{99m}Tc-MAG3



PET ^{18}F-deoxyglucose (FDG) brain scan



Further reading:

Sorenson JA, Phelps ME, “Physics in Nuclear Medicine”, Grune and Stratton, Orlando, 1987.

Henkin RE, “Nuclear Medicine”, Mosby, St Louis, 1996.

Sarper RM, “Nuclear Medicine Instrumentation”, CC Thomas, Springfield, 1984.

Murray IPC, Ell P (ed.), “Nuclear Medicine in Clinical Diagnosis and Treatment”, Churchill Livingstone, Edinburgh, 1998.

Let’s Play PET
http://www.crump.ucla.edu/software/lpp/lpphome.html

Exploring the Table of the Isotopes
http://ie.lbl.gov/education/isotopes.htm

Uniserve
http://science.uniserve.edu.au/school/curric/stage6/phys/fromqtoq.html#radioactivity

Next Lecture

Principles of Tomography -

Single Photon Emission Computed Tomography (SPECT)
Positron Emission Tomography (PET)
Reconstruction Algorithms