Radioactive decay

Process by which some atomic nuclei disintegrate.

- alpha decay
- beta decay
- gamma decay
- electron capture EC

Many radioactive isotopes, particularly heavy ones such as uranium, disintegrate by a series of radioactive decays (radioactive series) until they have been transformed into stable atoms.

Radioactive decay: **exponential** decay.

N_0 : initial number of radioactive isotopes
$N(t)$: the number remaining after a time t

$$N(t) = N_0 \exp(-\lambda t)$$

where λ is the radioactive decay constant.
The **half life** $t_{1/2}$ is defined as the time during which the number of radioactive nuclei decays to half its initial value:

$$1/2 = N\, t_{1/2} / N_0 = \exp(-\lambda\, t_{1/2}), \text{ hence}$$

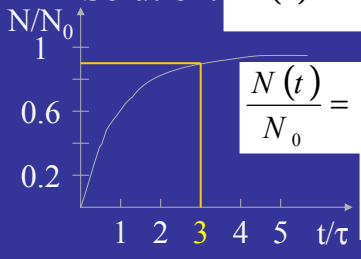
$$t_{1/2} = \lambda \ln 2$$

The half life of isotopes extends from the extremely short times observed only in experimental atomic reactions to times in the minute-to-hour range used in modern nuclear imaging to the extremely long half lives, encountered in isotopes such as uranium-238, which has a half life of several billion years. The way in which radioactive isotopes decay are usually represented in so called **decay schemes** or disintegration schemes.

Radioactivity

$$-\lambda B e^{-\lambda t} = R_0 - \lambda\left(A + B e^{-\lambda t}\right) \Rightarrow A = \frac{R_0}{\lambda}$$

- Initially: $N(0) = 0 = \frac{R_0}{\lambda} + B \Rightarrow B = -\frac{R_0}{\lambda}$
-
- Solution: $N(t) = \frac{R_0}{\lambda}\left(1 - e^{-\lambda t}\right) = N_0\left(1 - e^{-\lambda t}\right)$



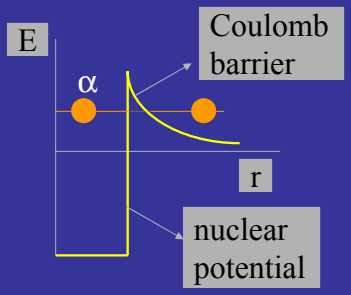
$$\frac{N(t)}{N_0} = \left(1 - e^{-t/\tau}\right), \tau = \frac{t_{1/2}}{\ln 2} = 3.5 \text{ min}$$

$$\frac{t}{\tau} = 3 \Rightarrow \frac{N(t)}{N_0} = 95\ \%$$

t≈10min

Radioactive Decay Types

- α-decay
  - Spontaneous emission of an α-particle (^{4}He nucleus) in the decay of heavy radioisotopes, with discrete energies of 4-8 MeV



QM Tunneling Effect: very long $t^{1/2}$

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

Z→Z-2, A →A-4

– large energy release

– very short range in tissue: no medical imaging application

– useful in radioisotope production

Radioactive Decay Types

- β^--decay

– Neutron in a neutron-rich nucleus (high N/Z ratio) converts to a proton and an electron (β^-) is emitted.

– Free neutron decay: $n \xrightarrow{t^{1/2}=11\ \text{min}} p + e^- + \bar{\nu}_e$

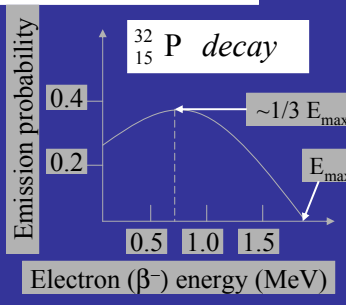
caused by weak force

electron antineutrino, $(\bar{\nu}_e)$,

nearly mass-less, spin=½ particle,

had to be introduced to explain energy-momentum conservation

(3-body decay energy distribution)



Radioactive Decay Types

- Example:

$$^{A}_{Z}X \rightarrow {}^{A}_{Z+1}Y + \beta^{-} + \bar{\nu}_e$$

$$^{99}_{42}Mo \rightarrow {}^{99}_{43}Tc + \beta^{-} + \bar{\nu}_e$$

$$\frac{N}{Z} = 1.33 \qquad \frac{N}{Z} = 1.30$$ → Increased stability

- β^+-decay
  - Proton-rich nuclei may decay by positron (β^+, e^+) emission

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

$$^{68}_{31}Ga \rightarrow {}^{68}_{30}Zn + \beta^{+} + \nu_e$$

$$\frac{N}{Z} = 1.19 \qquad \frac{N}{Z} = 1.26$$

Radioactive Decay Types

- Basic process: $p \rightarrow n + e^{+} + \nu_e$
  - possible only inside the nucleus. WHY ?
  - e^+: all quantum numbers of e^- except charge (+1/–1)
  - Positron lifetime ?
  - Range in tissue ~ 1mm: excitation, ionization, followed by annihilation (inverse of pair production):
  - $e^+ + e^- \rightarrow \gamma + \gamma$ (back-to-back, 511 keV photons)
- Electron Conversion/Capture (EC)
  - Absorption of an atomic (usually K-shell) electron in a proton-rich nucleus $p + e^{-} \rightarrow n + \nu_e$

Radioactive Decay Types

- The probability for EC increases with the mass number, A, because average electron distance ("orbit") is closer to the nucleus. [remember simple Bohr's model dependence, $r_n = n^2 a_0/Z$]
- Example:

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

$$ {}^{201}_{81}Tl + e^{-} \rightarrow {}^{201}_{80}Hg + \nu_e $$

$$ \frac{N}{Z} = 1.48 \qquad \frac{N}{Z} = 1.51 $$

- Mercury-201 nucleus disposes of extra energy by emitting characteristic x-rays. These are used in cardiac perfusion imaging

Radioactive Decay Types

- Internal Conversion (IC)
  - Photon emitted by a nucleus knocks out one of atomic electrons (usually K-shell). Vacancies in the inner orbitals get filled, leading to emissions of characteristic x-rays or Auger electrons.
- Isomeric Transitions (IT)
  - A daughter nucleus is formed in an excited state. γ-rays are emitted as the daughter nucleus transitions to a lower energy state. Long-lived excited states of a nucleus ($t^{1/2}$: 10^{-12}s-600 yr) are called metastable or isomeric, and indicated by "m". Example: ^{99m}Tc

Weak Decay Summary

Q: 0=+1-1+0
B: 1=1+0+0

particle antiparticle

$$n \rightarrow p + e^- + \bar{\nu}_e \quad \beta^-\text{-decay}$$

$$n + \nu_e \rightarrow p + e^- \quad \nu\text{-scattering}$$

$$p + e^- \rightarrow n + \nu_e \quad \text{EC}$$

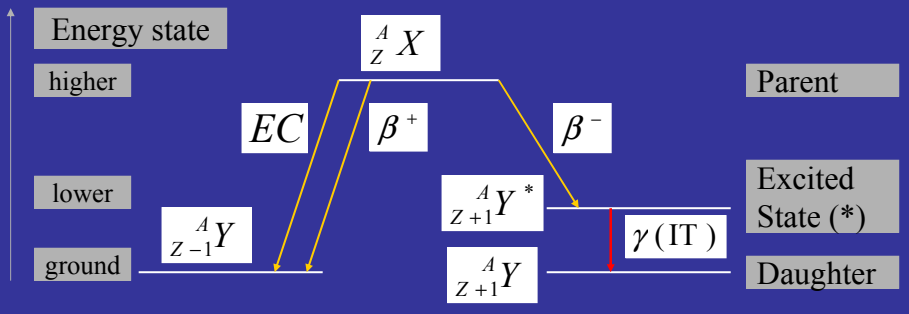
$$p \rightarrow n + e^+ + \nu_e \quad \beta^+\text{-decay}$$

inside nucleus

1st process sufficient, others easy to derive. Charge (Q) and barion (B) numbers must be conserved. Particle becomes an antiparticle if "carried over" to the other side of an equation.

Generalized Decay Scheme

– Decay process and emitted radiation can be summarized in a line diagram called *a decay scheme*

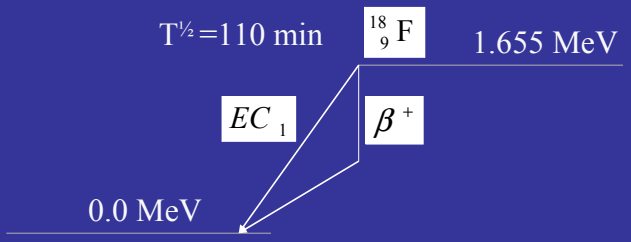


^{99m}Technetium Decay Scheme

Radiation		Mean Number per disintegration	Mean Energy (keV)
Gamma	1	0.0000	2.1
M IC e^-		0.9860	1.6
Gamma	2	0.8787	140.5
K IC e^-		0.0913	119.4
L IC e^-		0.0118	137.7
M IC e^-		0.0039	140.0
Gamma	3	0.0003	142.6

nuclear medicine

Fluorine-18 Decay Scheme



Most-widely used for PET

Radiation	Mean # per decay	Energy (keV)
β^+	0.970	249.6
Annihil. rad.	1.94	511.0

Radionuclide Production

1. Nuclear Reactor Production
2. Charged particle accelerators
   - Linear Accelerator (LINAC)
   - Cyclotron

– Radionuclides produced via the interaction of charged particles ($H^{\pm}$, D^{+}, $^{3}He^{++}$, $^{4}He^{++}$,…) with the stable nuclei

– Ions must have sufficient kinetic energy to overcome the repulsion of positively charged nuclei. Required energies per nucleon are **1-100 MeV**

– Big advantage: produced isotopes have different Z and can be chemically separated from the target material

Charged Particle Bombardment

– Examples:

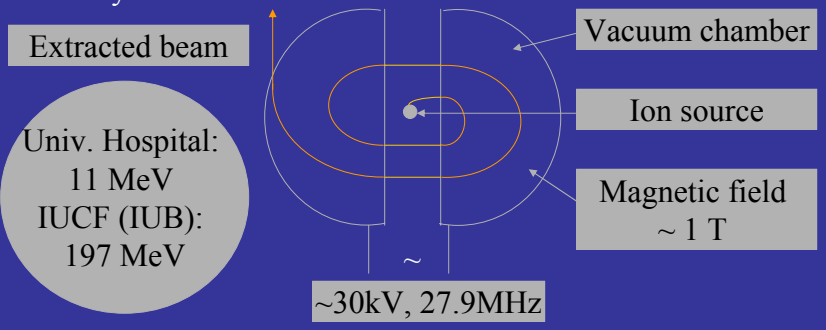
$$p + {}^{68}_{30}Zn \rightarrow {}^{67}_{31}Ga + 2n$$

$$\alpha + {}^{16}_{8}O \rightarrow {}^{18}_{9}F + p + n$$

–

–

– Cyclotron schematic:

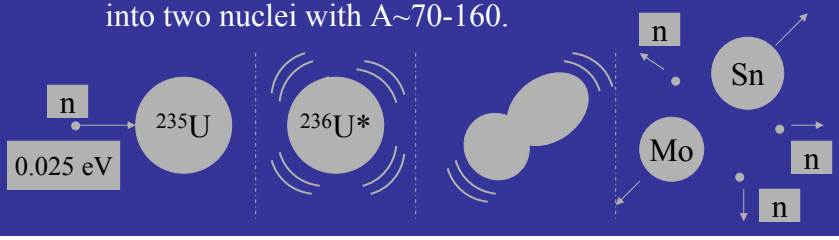


Cyclotron-produced Isotopes for PET

Isotope	γ-ray (keV)	$T^{1/2}$	Reaction
$^{11}_{6}C$	511 (β^+)	20.4 min	**^{14}N (p,α) ^{11}C** ^{10}B (d,n) ^{11}C
$^{13}_{7}N$	511 (β^+)	10 min	**^{13}C (p,n) ^{13}N** ^{12}C (d,n) ^{13}N
$^{15}_{8}O$	511 (β^+)	2 min	**^{15}N (p,n) ^{15}O** ^{14}N (d,n) ^{15}O
$^{18}_{9}F$	511 (β^+)	110 min	**^{18}O (p,n) ^{18}F**

Nuclear Reactor Isotope Production

- Nuclear Fission
  - Heavy "fissile" nucleus (^{235}U,^{239}Pu,^{237}U,^{232}Th) is excited by the capture of a thermal neutron and splits into two nuclei with A~70-160.



$$^{1}_{0}n + ^{235}_{92}U \rightarrow ^{236}_{92}U \rightarrow ^{99}_{42}Mo + ^{134}_{50}Sn + 3\,^{1}_{0}n + \gamma$$

Fission fragments

Q=+200 MeV

Nuclear Fission

- Fission products are neutron-rich and decay primarily via β^-–emission, useful for therapy but not imaging
- Radionuclides used in Nuclear Medicine: **^{99}Mo, ^{131}I, ^{133}Xe**
- Extensive purification is needed to extract a desired radionuclide from the mixture. However, almost no stable isotope ("carrier") is present so the concentration or specific activity (Bq/g) is very high → highly desired
- Neutron Activation Production
  - Thermal neutron bombardment of stable target nuclei may result in their capture and production of radioactive nuclei

Neutron Activation

- The most common neutron capture process: (n,γ)
- Other neutron capture processes: (n,p), (n,α) → low Z
- Examples: $^{31}_{15}P\,(n,\gamma)\,^{32}_{15}P$ $T_{½}$=14.3 days
-
- Problem: cannot be chemically separated, low efficiency (i.e., material mostly contains carrier rather than the desired radionuclide), lower specific activity (impurities produce other radionuclides)
- Exception: $^{124}_{54}Xe\,(n,\gamma)\,^{125}_{54}Xe \xrightarrow{\text{EC or } \beta^+} {}^{125}_{53}I$ $T_{½}$=17hr

Radionuclide Generator

- Principle: if a radioactive daughter has a different Z than its parent, the parent and daughter can be chemically separated.
  - Daughter is compatible with medical imaging, **$t_{½}$~ min-hr** (→ visible change in counting rate)
  - Parent $t_{½}$ long enough for production, processing, and shipping: **$t_{½}$~ hr-day**

$$P \xrightarrow[\lambda_1]{} D \xrightarrow[\lambda_2]{} GD$$

P = parent nuclide
D = daughter nuclide
GD = granddaughter

$$N_1(0) = N_1^0 \;\&\; N_2(0) = 0$$

Initial condition: only N_1 (parent), no N_2 (daughter)

Radionuclide Generator

$$\frac{dN_2}{dt} = \lambda_1 N_1 - \lambda_2 N_2 = \lambda_1 N_1^0 e^{-\lambda_1 t} - \lambda_2 N_2$$

Solution guess: $N_2(t) = Ae^{-\lambda_1 t} + Be^{-\lambda_2 t}$

Solution: $N_2(t) = \frac{\lambda_1 N_1^0}{\lambda_2 - \lambda_1}\left(e^{-\lambda_1 t} - e^{-\lambda_2 t}\right)$ $*\lambda_2$

Daughter activity: $A_2(t) = \frac{\lambda_2 A_1^0}{\lambda_2 - \lambda_1}\left(e^{-\lambda_1 t} - e^{-\lambda_2 t}\right)$

$t_1^{1/2} >> t_2^{1/2} \Rightarrow \lambda_1 << \lambda_2$

"secular equilibrium"

Parent lives much longer than the daughter nuclide

Radionuclide Production Summary

- Method: cyclotron, nuclear fission, neutron activation, radionuclide generator
- Bombarding particle: charged (p,d,t,α), n, none (parent decay)
- Product: neutron poor or neutron excess
- Decay types: β^+, β^-, EC,…$\rightarrow \gamma$
- Carrier free or not carrier free
- High or low specific activity
- High or low relative cost

Radiopharmaceuticals

- Characteristics
  - Short half-life compatible with the duration and objective of the study (evaluation of function)
  - Scintillation cameras optimized ~ 100-300 keV: patient attenuation, spatial resolution and detection efficiencies.
  - High target/Non-target activity: increased or decreased concentration in localized areas (“hot spots” – “cold spots”)
  - Low toxicity, stable compounded form, high specific activity, minimal particulate radiation, localization in the organ and tissue of interest, cost,…

Radiopharmaceuticals

- Localization mechanisms: compartmental localization and leakage (^{133}Xe, ^{99m}Tc), passive diffusion (blood-brain barrier: ^{99m}Tc), metabolism (FDG), active transport (thyroid:^{201}Tl), capillary blockade (^{99m}Tc), perfusion, receptor binding(^{111}In),… → Appendix D in the textbook

- Nuclear Medicine:
  - Dominant radionuclide: ^{99m}Tc
  - also used diagnostically: ^{123}I,^{67}Ga,^{111}In, ^{133}Xe, ^{203}Tl
- PET:
  - ^{18}F in fluorodeoxyglucose (FDG) ~85% clinical cases
  - Used, currently evaluated: ^{11}C,^{13}N,^{15}O, ^{68}Ga, ^{82}Rb

TOMOGRAPHY IN NUCLEAR MEDICINE IMAGING

- **firstly let us consider what might be called the 'dilemma' of NM imaging with a conventional gamma-camera**
- **that the resolution and sensitivity become worse with depth of the source in tissue**

- the NM image therefore provides a better representation of the activity distribution in superficial tissues (ie those closest to the camera face) rather than in deep tissues
- indeed even quite large lesions at depth in tissue can be 'missed'
- this, in part, is due to the fact that the gamma-camera image is a 2D image of a 3D activity distribution

- this is not a major problem in NM imaging of most organs
- however, for some

  eg the liver and

  the myocardium

  it is a significant problem

- in such cases TOMOGRAPHIC IMAGING offers the potential for improved diagnosis

- there have been many tomographic NM imaging devices developed
- however only two (three?) are in common use

1) The ROTATING CAMERA which is a SPECT DEVICE

2) PET DEVICES, and

3) COINCIDENCE SPECT devices which are a bit of SPECT and a bit of PET

abbreviations

- ECAT Emission Computer Assisted Tomography (or simply ECT)

which includes

- SPECT Single Photon Emission Computed Tomography
- PET Positron Emission Tomography

- tomography in most medical imaging modalities relies upon getting information or images of the same structures from different angles eg in CT or linear x-ray tomography

- SPECT in NM imaging is similar in principle to x-ray CT in that tomographic image slices are reconstructed from views obtained at various angles as a camera is rotated around the subject

tomography in NM imaging is however more difficult than x-ray CT because

- in x-ray CT there is only one unknown

  ----- the attenuation

- in NM tomography

  the unknown is the activity distribution and the

  attenuation is a complicating factor

- in addition the photon flux is much smaller in NM tomography than in x-ray CT because of limitations imposed by patient dose.
- Therefore the NM image suffers somewhat from poorer statistics of counting

THE ROTATING CAMERA

- a conventional gamma camera is mounted on a rotating gantry
- a parallel hole collimator is generally used

- data are obtained as the camera is rotated about the patient.
- the camera acts as multiple rings of detectors and hence
- multiple slices (up to 64) may be obtained simultaneously

PERFORMANCE PARAMETERS

- up to 64 transverse slices obtained simultaneously
- full rotation 1-20 min
- slice thickness 4-16 mm
- resolution (within slice) 10 mm

DISADVANTAGES

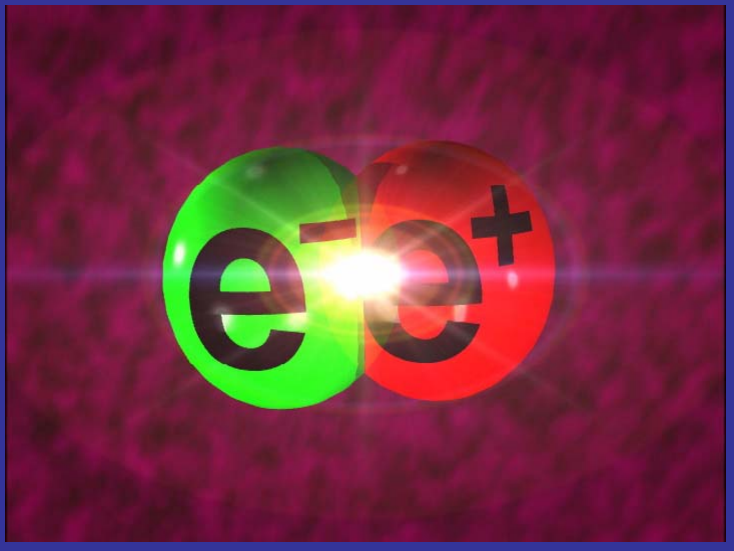
- relatively slow.
- efficiency and sensitivity vary with depth in the slice. (ie same problem as conventional camera)

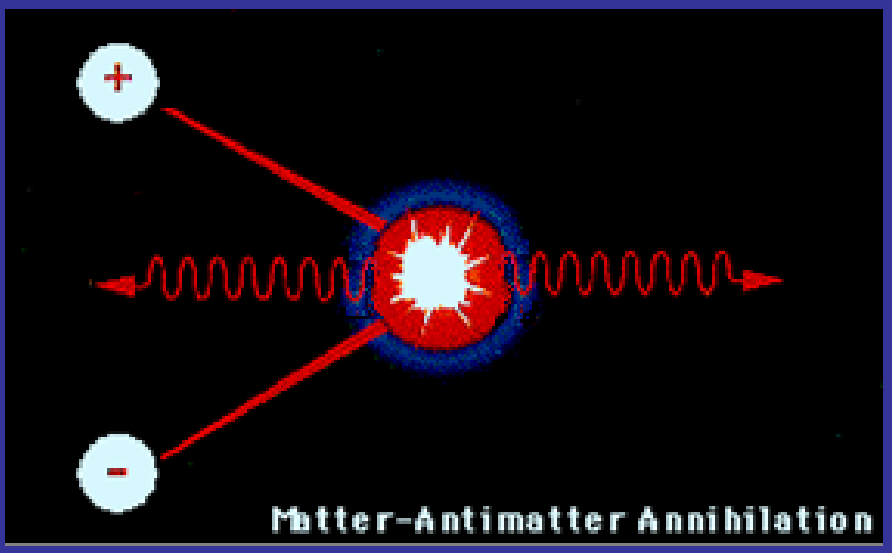
ADVANTAGES

- simultaneous multiple slices
- is a conventional camera so has dual application

PET (sometimes called dual photon ECAT) and Coincidence SPECT

- These devices form images by detection of positron annihilation
- this requires the simultaneous (coincident) detection of the two photons emitted when a positron annihilates.





- important physical principle:
- when a β^+ (positron) annihilates two photons are emitted these are:

  in time coincidence

  each of 0.511 MeV

  at 180^0 to one another ie back to back

principle of image formation

- obviously the isotope used must be a positron (β^+) emitting isotope
- the β^+ is stopped and annihilates less than 1 mm from its site of origin
- counts are used for image formation only when

  two 0.511 MeV photons are detected in time coincidence by two opposed detectors

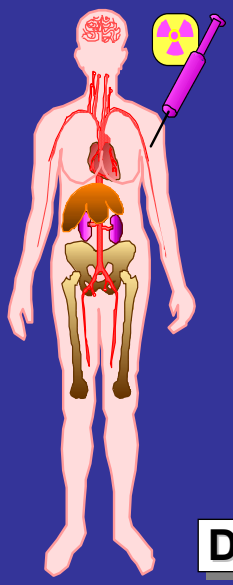
- time coincidence means within approx 10 ns ie 10^{-8} s
- opposed detectors means at 180° to one another

In a PET scanner

- the detector system consists of an array (circular or hexagonal).
- the patient is placed in the centre of this detector array
- information is recorded only when two opposed detectors simultaneously detect a 511 keV photon.

- the two detectors define a line of sight this is called electronic collimation

Step 1: Inject Patient with Radioactive Drug



- **Drug is labeled with positron (β^+) emitting radionuclide.**
- **Drug localizes in patient according to metabolic properties of that drug.**
- **Trace (pico-molar) quantities of drug are sufficient.**
- **Radiation dose fairly small (<1 rem).**

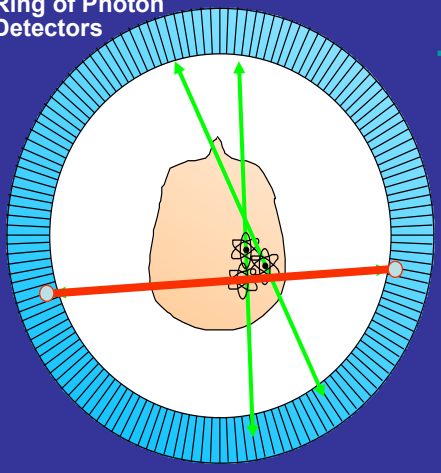
Drug Distributes in Body

Ideal Tracer Isotope

- Interesting Biochemistry
  Easily incorporated into biologically active drugs.
- 1 Hour Half-Life
  Maximum study duration is 2 hours.
  Gives enough time to do the chemistry.
- Easily Produced
  Short half life ⇒ local production.

^{18}F	**2 hour half-life**
^{15}O, ^{11}C, ^{13}N	**2, 20, & 10 minute half-lives**

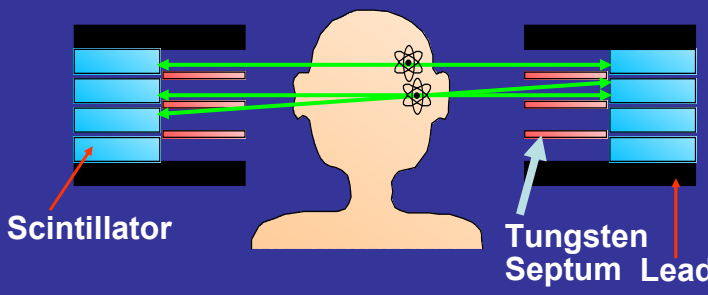
Step 2: Detect Radioactive Decays



- Radionuclide decays, emitting β^{+}.
- β^{+} annihilates with e^{-} from tissue, forming back-to-back 511 keV photon pair.
- 511 keV photon pairs detected via time coincidence.
- Positron lies on line defined by detector pair (known as a *chord* or a *line of response* or a *LOR*).

Detect Pairs of Back-to-Back 511 keV Photons

Multi-Layer PET Cameras

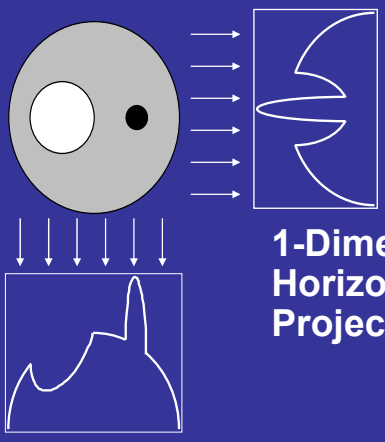


- Can image several slices simultaneously
- Can image cross-plane slices
- Can remove septa to increase efficiency ("3-D PET")

Planar Images "Stacked" to Form 3-D Image

Step 3: Reconstruct with Computed Tomography

2-Dimensional Object



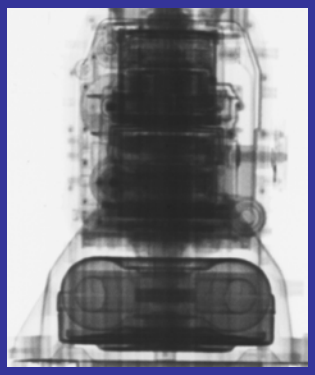
1-Dimensional Horizontal Projection

1-Dimensional Vertical Projection

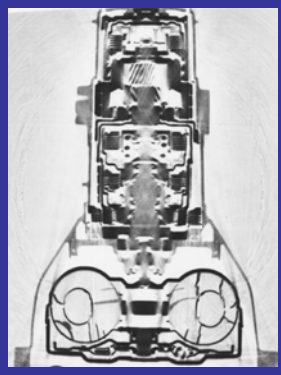
By measuring all 1-dimensional projections of a 2-dimensional object, you can reconstruct the object

Why Do Computed Tomography?

Planar X-Ray

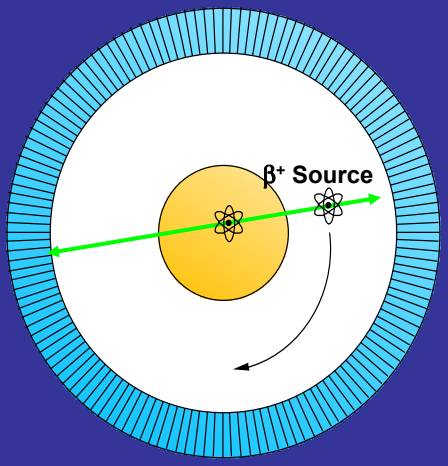


Computed Tomography



Separates Objects on Different Planes

Attenuation Correction



- Use external β^+ source to measure attenuation.
- Attenuation (for that chord) same as for internal source.
- Source orbits around patient to measure *all* chords.

- Measure Attenuation Coefficient for Each Chord
- Obtain *Quantitative* Images

performance characteristics

- transverse slices
- slice thickness approx 1 mm
- resolution approx 6 mm

  and importantly this does not change significantly with depth since the 0.511 MeV photons are fairly penetrating
- scan time 5 s to 1 min

- One significant disadvantage of PET devices is that they are special and expensive.
- Hence they are mainly used for research or in practices with sufficient patient throughput to warrant the expense

Coincidence SPECT

- The performance of coincidence SPECT devices is somewhat worse than PET devices however
- coincidence SPECT is becoming more common because it is a relatively cheap addition to a (dual head) gamma camera.
- In coincidence SPECT the two opposed detectors are in fact the dual heads of a conventional gamma camera
- only requires the addition of coincidence electronics and reconstruction software

Advantages of PET or Coincidence SPECT

- attenuation in tissue is not a major problem because the 0.511 MeV photons used are relatively penetrating
- the spatial resolution is relatively independent of depth

Most inportantly

- the β^+emitting isotopes ^{11}C, ^{13}N, and ^{15}O are biologically important as eg CO, CO_2, O_2
- ^{18}F, another β^+ emitter can replace hydrogen in many important biological molecules without changing their function significantly
- for example ^{18}F labelled FDG can be used to measure glucose metabolism in tissues such as the brain

disadvantages

- positron emitting isotopes are not readily available
- most useful positron emitting isotopes have short half-lives

eg ^{13}N	$T_{1/2}$ =	10 min
^{11}C		20 min
^{15}O		2.5 min
^{18}F		100 min

- they are cyclotron produced and hence, except for ^{18}F, the application of PET needs a cyclotron on site
- and this is VERY expensive

TOFPET
(time of flight PET)

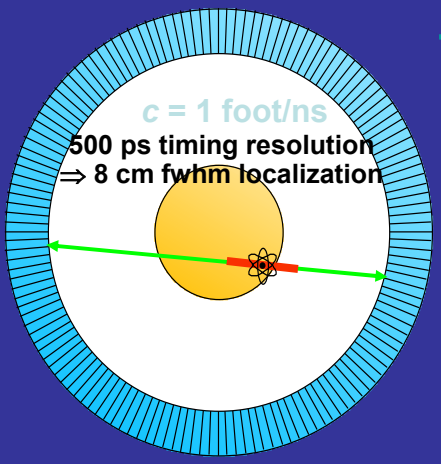
- the electronic collimation used in PET imaging defines a line of sight
- ie when coincident photons are detected it indicates that a positron has annihilated somewhere along the line joining the detectors
- but does not locate the position along that line at which the β^+ annihilated

- multiple projections (views) and reconstruction must be used to obtain the image ie the distribution of activity
- TOFPET attempts to provide the additional position info by measuring the time difference in the arrival of the two photons at the opposed detectors

- since the two photons are produced in exact time coincidence any difference in arrival time ie Δt is due to differences in distant travelled.
- this info may be used to locate where along the line of sight the positron annihilated
- present technology only allows Δt to be measured to within about 300 ps which locates the position to about 4 cm

- this is inadequate to permit direct imaging by TOFPET but the info may be used to 'assist" the reconstruction of PET images

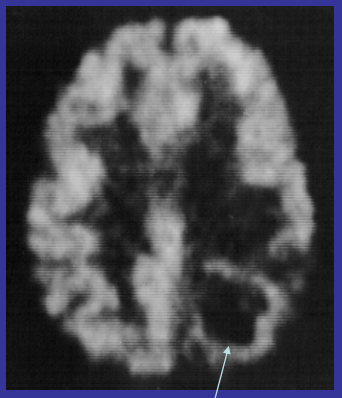
Time-of-Flight Tomograph



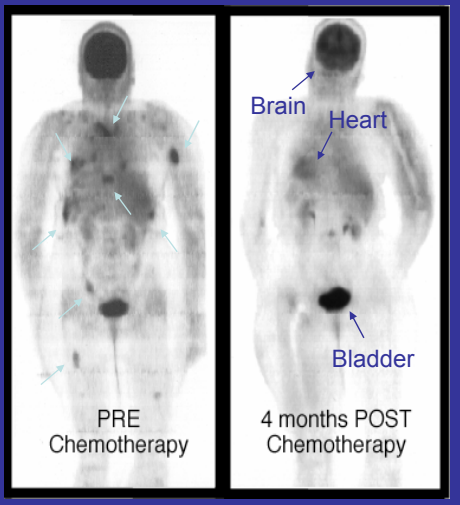
- Can localize source along line of flight.
- Time of flight information reduces noise in images.
- Time of flight tomographs have been built with BaF_2 and CsF.
- These scintillators force other tradeoffs that reduce performance.

Not Compelling with Present Technology...

PET Images of Cancer



Treated Tumor Growing Again on Periphery



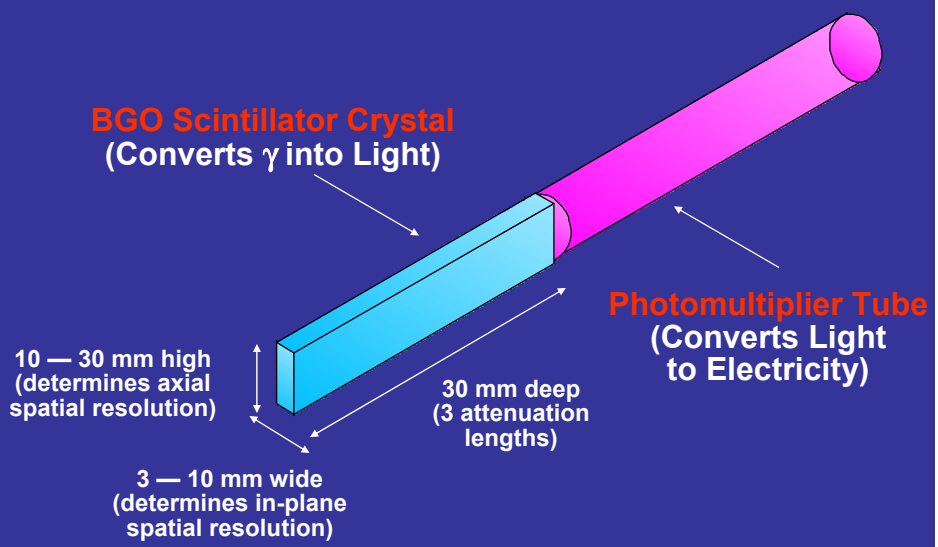
Metastases Shown with Red Arrows

Normal Uptake in Other Organs Shown in Blue

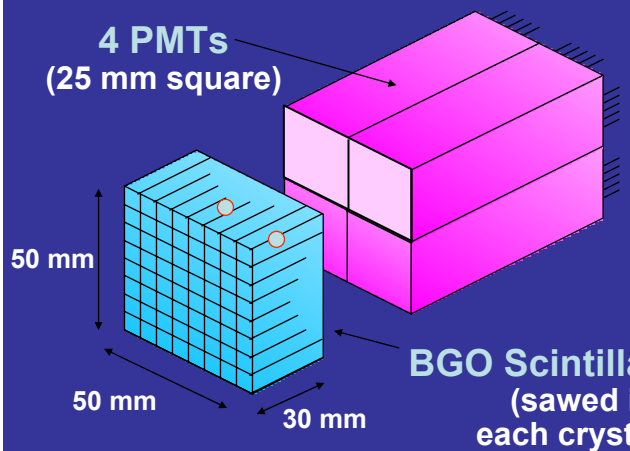
PET Cameras

- Patient port ~60 cm diameter.
- 24 to 48 layers, covering 15 cm axially.
- 4–5 mm fwhm spatial resolution.
- ~2% solid angle coverage.
- $1 – $2 million dollars.

Early PET Detector Element



Modern PET Detector Module

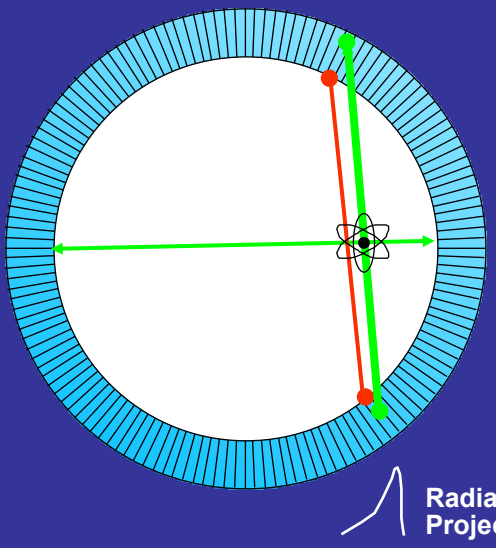


- Saw cuts direct light toward PMTs.
- Depth of cut determines light spread at PMTs.
- Crystal of interaction found with Anger logic (*i.e.* PMT light ratio).

BGO Scintillator Crystal Block
(sawed into 8x8 array,
each crystal 6 mm square)

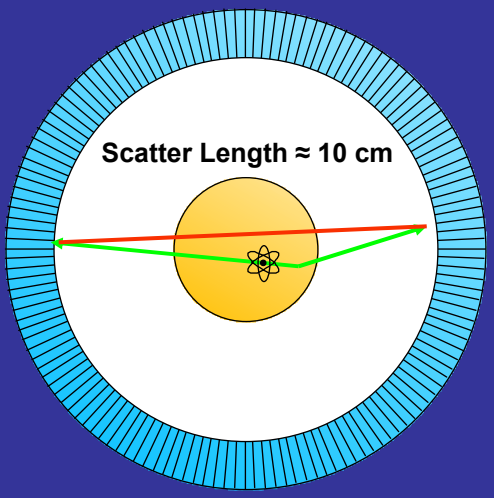
Good Performance, Inexpensive, Easy to Pack

Radial Elongation



- Penetration of 511 keV photons into crystal ring blurs measured position.
- Effect variously known as Radial Elongation, Parallax Error, or Radial Astigmatism.
- Can be removed by measuring depth of interaction.

No Pair Production / EM Showers



- Compton scatter in patient produces erroneous coincidence events.
- ~15% of detected events are scattered in 2-D PET (*i.e.* if tungsten septa used).
- ~50% of events are scattered in 3-D Whole Body PET.

- **Compton Scatter is Important Background**
  - **Use Energy to Reject Scatter in Patient**