EL582/BE620 --- Medical Imaging - I

Nuclide Imaging: Planar Scintigraphy, SPECT, PET

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Based on J. L. Prince and J. M. Links, Medical Imaging Signals and Systems, and lecture notes by Prince. Figures are from the textbook except otherwise noted.

Lecture Outline

- Nuclide Imaging Overview

- Review of Radioactive Decay

- Planar Scintigraphy

  - Scintillation camera

  - Imaging equation

- Single Photon Emission Computed Tomography (SPECT)

- Positron Emission Tomography (PET)

- Image Quality consideration

  - Resolution, noise, SNR, blurring

What is Nuclear Medicine
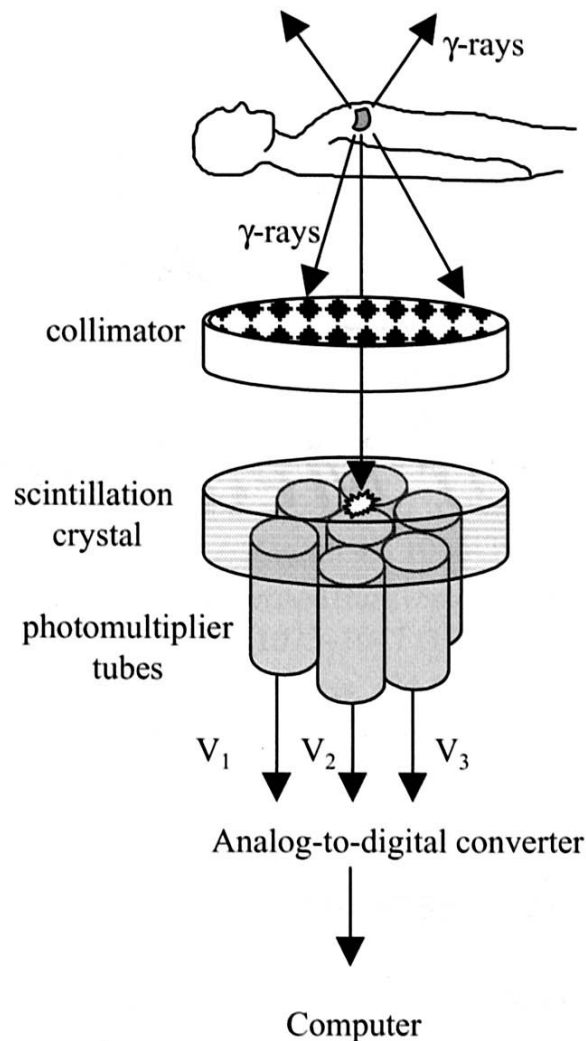
- Also known as nuclide imaging
- Introduce radioactive substance into body
- Allow for distribution and uptake/metabolism of compound $\Rightarrow$ *Functional Imaging*!
- Detect regional variations of radioactivity as indication of presence or absence of specific physiologic function
- Detection by "gamma camera" or detector array
- (Image reconstruction)

From H. Graber, Lecture Note for BMI1, F05

Examples: PET vs. CT

- X-ray projection and tomography:
  - X-ray transmitted through a body from a outside source to a detector (transmission imaging)
  - Measuring anatomic structure
- Nuclear medicine:
  - Gamma rays emitted from within a body (emission imaging)
  - Imaging of functional or metabolic contrasts (not anatomic)
    - Brain perfusion, function
    - Myocardial perfusion
    - Tumor detection (metastases)

PET

CT Attenuation

Inherent Registration
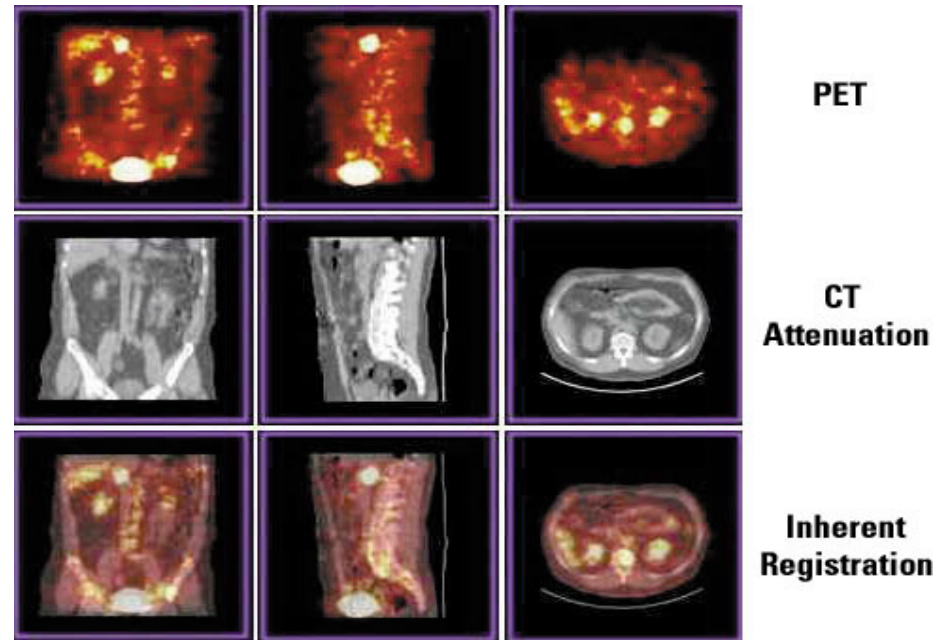
From H. Graber, Lecture Note, F05

What is Radioactivity?

- <u>Radioactive decay</u>: rearrangement of nucleii to
  <u>lower energy</u> states = greater mass defect
- <u>Parent</u> atom decays to <u>daughter</u> atom
- Daughter has higher binding energy/nucleon than parent
- A radioatom is said to <u>decay</u> when its nucleus is rearranged
- A <u>disintegration</u> is a radioatom undergoing radioactive decay.
- Energy is <u>released</u> with disintegration.

Positron Decay and Electron Capture

- Also known as Beta Plus decay
  - A proton changes to a neutron, a positron (positive electron), and a neutrino
  - Mass number A does not change, proton number Z reduces
- The positron may later annihilate a free electron, generate two gamma photons in opposite directions
  - These gamma rays are used for medical imaging (Positron Emission Tomography)

From: http://www.lbl.gov/abc/wallchart/chapters/03/2.html
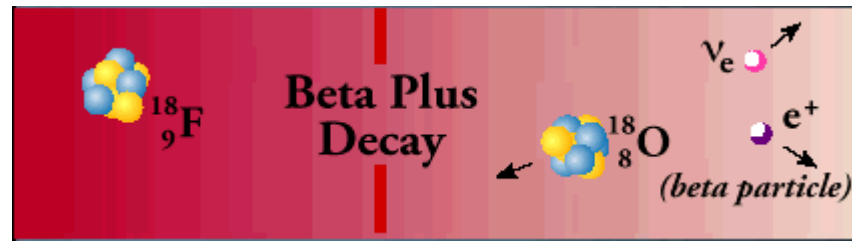
Gamma Decay (Isometric Transition)

- A nucleus (which is unstable) changes from a higher energy state to a lower energy state through the emission of electromagnetic radiation (photons) (called gamma rays). The daughter and parent atoms are isomers.
    - The gamma photon is used in Single photon emission computed tomography (SPECT)
- Gamma rays have the same property as X-rays, but are generated different:
    - X-ray through energetic electron interactions
    - Gamma-ray through isometric transition in nucleus

From: http://www.lbl.gov/abc/wallchart/chapters/03/3.html
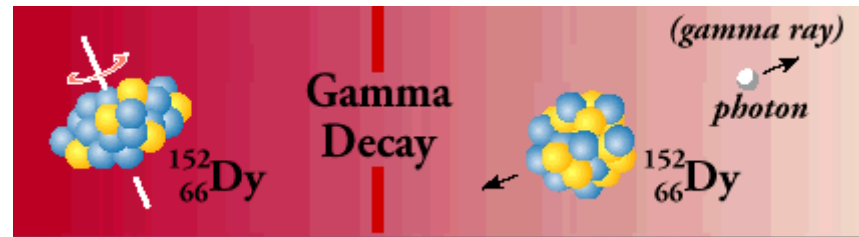
Measurement of Radioactivity

- <u>Radioactivity</u>, A, # disintegrations per second

$$1 \text{ Bq} = 1 \text{ dps}$$

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

Bq=Bequerel
Ci=Curie:

(orig.: activity of 1 g of 226Ra)

Naturally occurring radioisotopes discovered 1896 by Becquerel
First *artificial* radioisotopes produced by the Curies 1934 (32P)

The intensity of radiation incident on a detector at range r from a radioactive source is

$$I = \frac{AE}{4\pi r^2}$$

A: radioactivity of the material; E: energy of each photon

Radioactive Decay Law

- N(t): the number of radioactive atoms at a given time
- A(t): is proportional to N(t)

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

$$\lambda : \text{decay constant}$$

- From above, we can derive

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

$$A(t) = A_0 e^{-\lambda t} = \lambda N_0 e^{-\lambda t}$$

- The number of photons generated (=number of disintegrations) during time T is

-

$$\Delta N = \int_0^T A(t)dt = \int_0^T \lambda N_0 e^{-\lambda t} dt = N_0(1 - e^{-\lambda T})$$

Common Radiotracers

- Gamma Ray Emitters:
    - Iodine-123 (13.3 h, 159 keV)
    - Iodine-131 (8.04 d, 364 keV)
    - Iodine-125 (60 d, 35 keV) (Bad. Why?)
    - Thallium-201 (73 h, 135 keV)
    - Technetium-99m (6 h, 140 keV)
- Positron Emitters:
    - Fluorine-18 (110 min, 202 keV)
    - Oxygen-15 (2 min, 696 keV)

Thyroid function

Kidney function

Most commonly used

Oxygen metabolism

Overview of Imaging Modalities

- Planar Scintigraphy
  - Use radiotracers that generate gammay decay, which generates one photon in random direction at a time
  - Capture photons in one direction only, similar to X-ray, but uses emitted gamma rays from patient
  - Use an Anger scintillation camera
- SPECT (single photon emission computed tomography)
  - Use radiotracers that generate gammay decay
  - Capture photons in multiple directions, similar to X-ray CT
  - Uses a rotating Anger camera to obtain projection data from multiple angles
- PET (Positron emission tomography)
  - Uses radiotracers that generate positron decay
  - Positron decay produces two photons in two opposite directions at a time
  - Use special coincidence detection circuitry to detect two photons in opposite directions simultaneously
  - Capture projections on multiple directions

Planar Scintigraphy
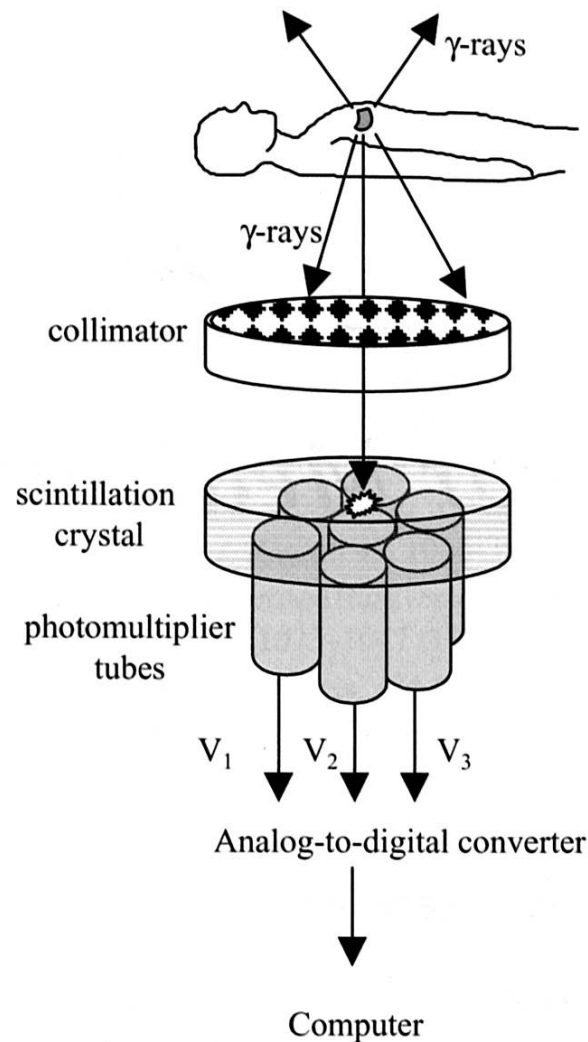
- Capture the emitted gamma photons (one at a time) in a single direction

- Imaging principle:
  - By capturing the emitted gamma photons in one particular direction, determine the radioactivity distribution within the body

  - On the contrary, X-ray imaging tries to determine the attenuation coefficient to the x-ray

Anger Scintillation Camera
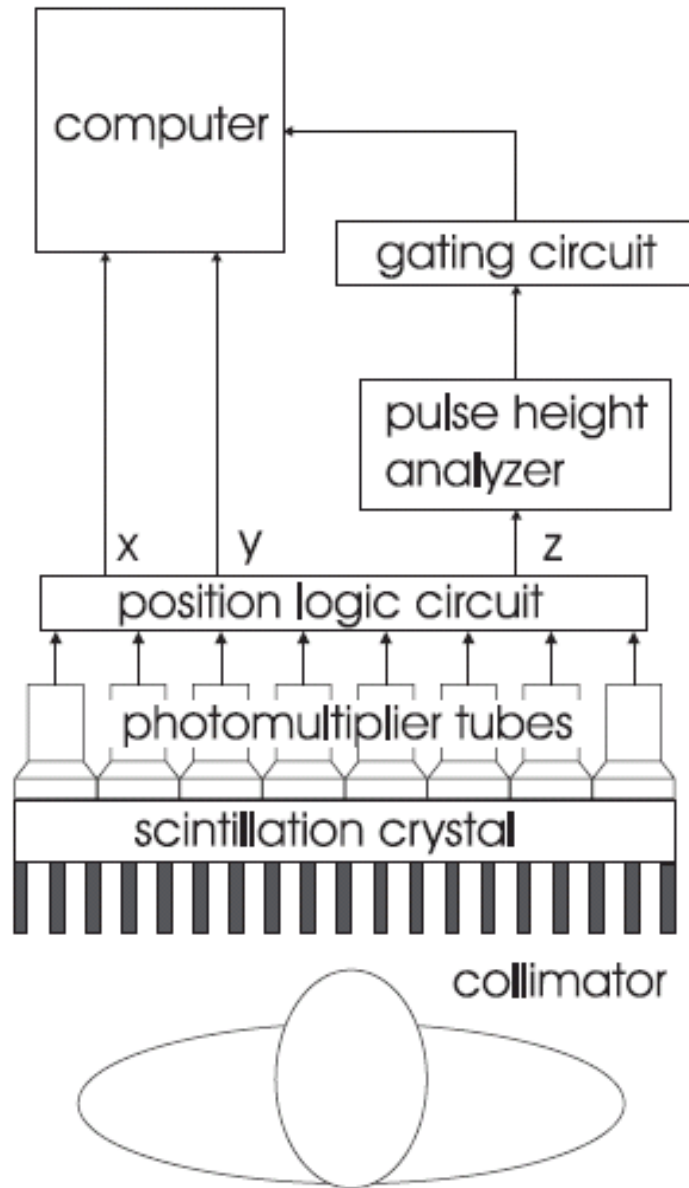
Compare the detected signal to a threshold
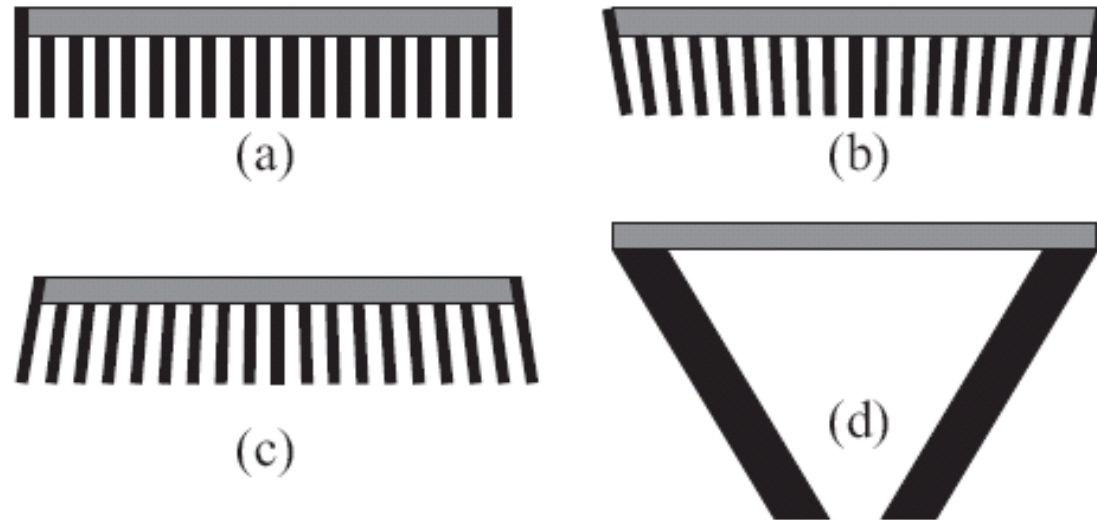
Compute the location with highest activity

Convert light to electrical currents

Convert detected photons to lights

Absorb scattered photons

Collimators

(a)

(b)

(c)

(d)

(a) Parallel hole

(b) Converging hole (magnifies)

(a) Diverging hole (minifies)

**(a)** Pin-hole (2–5 mm)

Scintillation Detector

- Scintillation crystal:
  - Emit light photons after deposition of energy in the crystal by ionizing radiation
  - Commonly used crystals: <u>NaI(Tl)</u>), BGO, CsF, BaF$_2$
  - Criteria: Stopping power, response time, efficiency, energy resolution

- Detectors used for planar scintigraphy

  - Single large-area NaI(Tl) crystal
  - Diameters:
    - 30–50 cm in diameter
    - Mobile units: 30 cm
    - Fixed scanners: 50 cm
  - Thickness:
    - High-E emitters: 1.25 cm thick
    - Low-E emitters: 6–8 mm thick
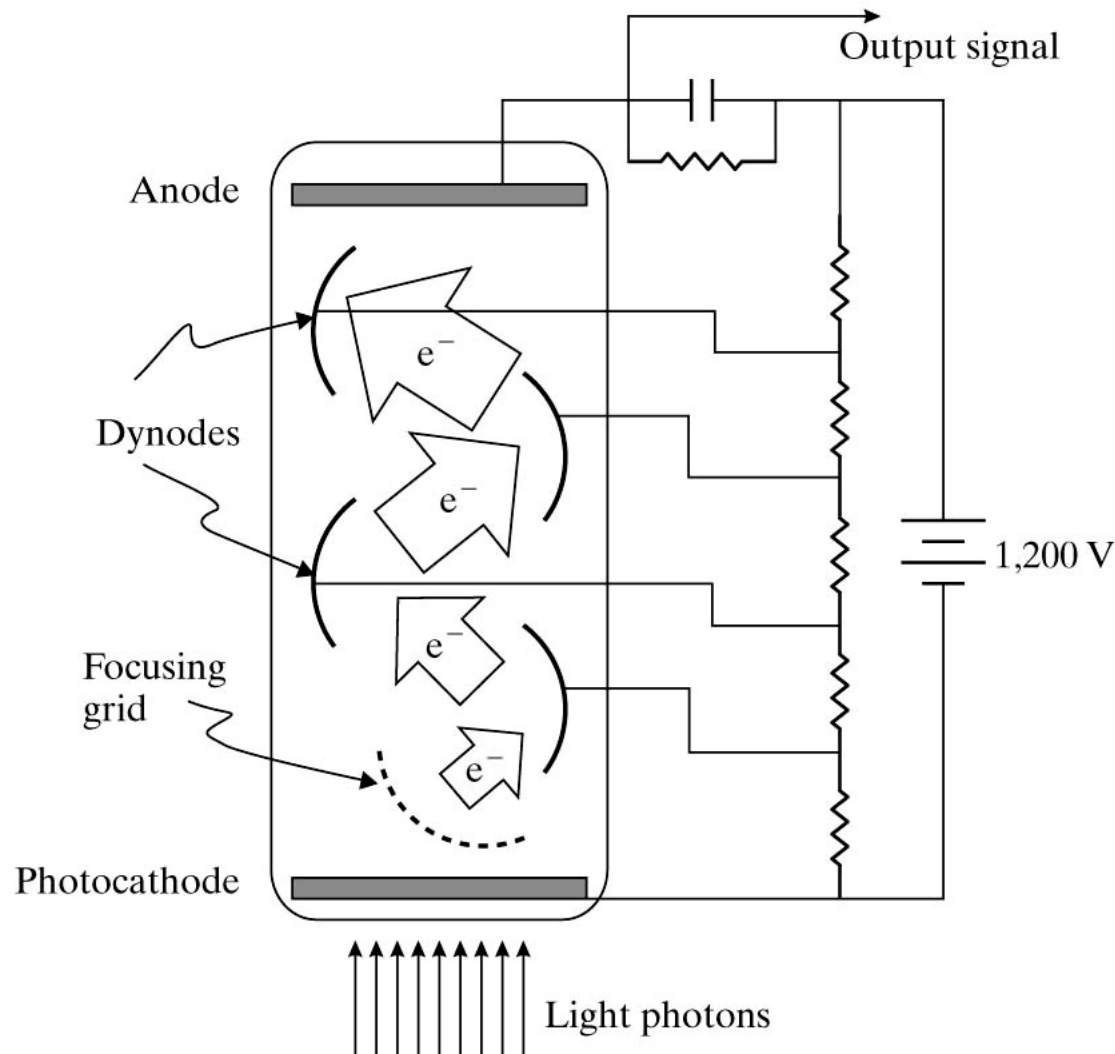
Photomultiplier Tubes

- Each tube converts a light signal to an electrical signal and amplifies the signal
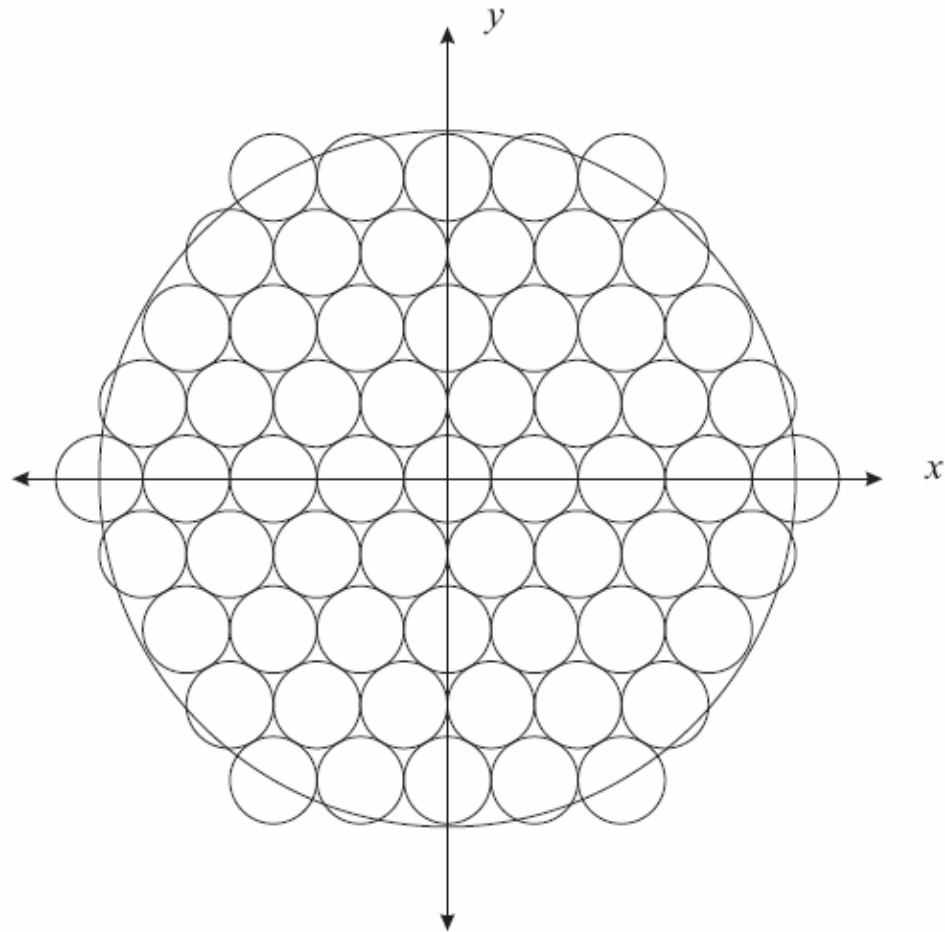
Inside a Photomultiplier Tube

Output signal

Anode

Dynodes

Focusing grid

Photocathode

Light photons

1,200 V

10^6-10^8 electrons reach anode for each electron liberated from the cathode

Increasing in voltage, Repeatedly generates more electrons, 10-14 steps

Dynode: positively charged
For each electron reaching a dynode, 3-4 electrons are released

For every 7-10 photons incident upon the photocathode, an electron is released

Outputs a current pulse each time a gamma photon hits the scintillation crystal.
This current pulse is then converted to a voltage pulse through a preamplifier circuit.

Positioning Logic

Each incident photon causes responses at all PMTs, but the amplitude of the response is proportional to its distance to the location where the photon originates. Positioning logic is used to estimate this location.

- Tube centers at (x_k, y_k) $k = 1, \ldots, K$
- Center of mass of pulse responses is

$$X = \frac{1}{Z} \sum_{k=1}^{K} x_k a_k$$

$$Y = \frac{1}{Z} \sum_{k=1}^{K} y_k a_k$$
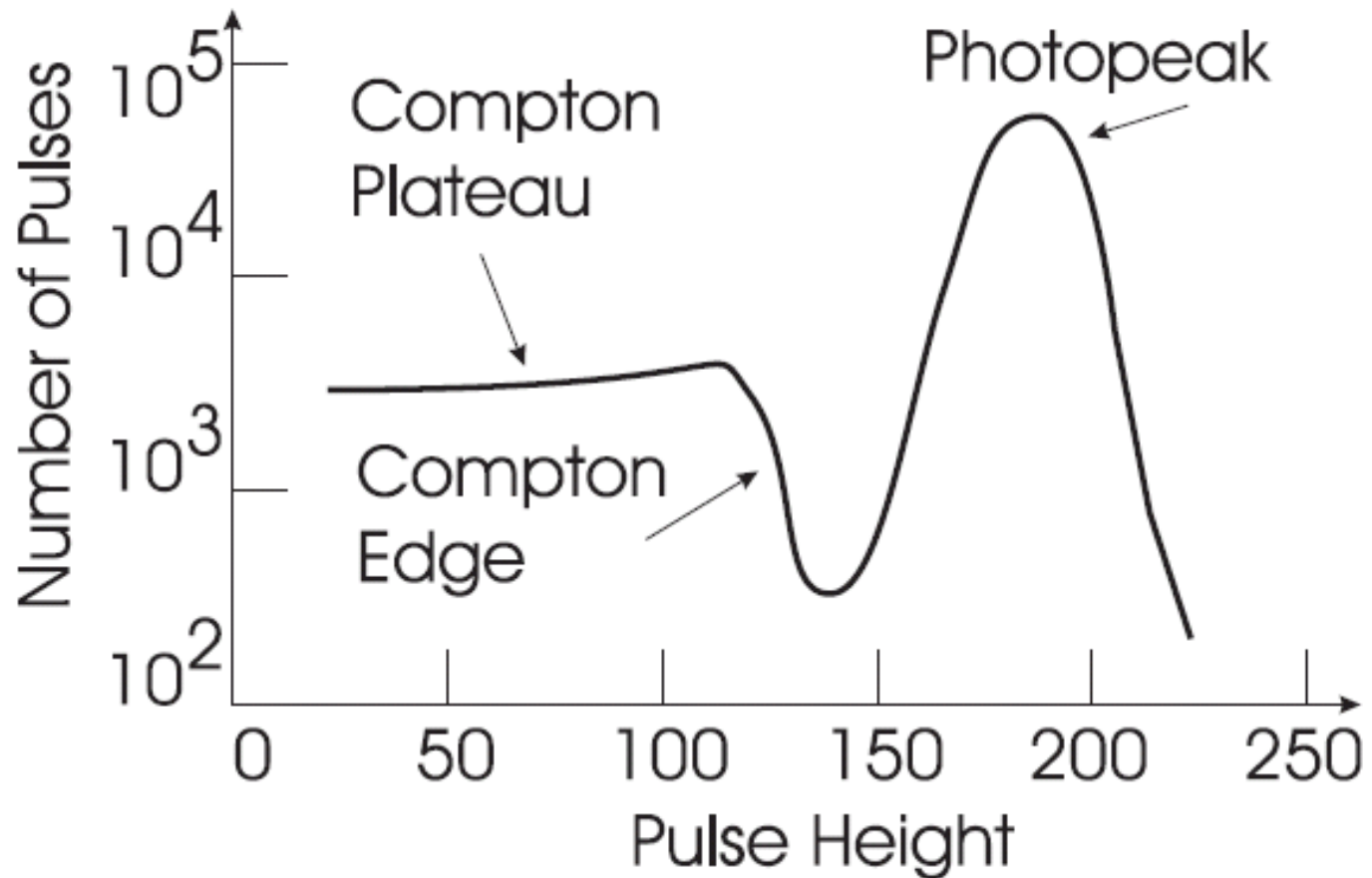
- This is pulse location

Pulse Height Calculation

- PMT responses, a_k, $k = 1, \ldots, K$
- Total response of cammera is Z-pulse

$$Z = \sum_{k=1}^{K} a_k$$

- Height of Z pulse is important
    - Can remove Compton photons
    - Can reject multiple hits

Pulse Height Analysis

- Discriminator circuit rejects non-photopeak events

Acquisition Modes

- How to use the camera to make images?
  - List mode
  - Static frame mode
  - Dynamic frame mode
  - Multiple-gated acquisition
  - Whole body mode

List Mode

$$(X_1, Y_1, Z_1, t_1)$$
$$(X_2, Y_2, Z_2, t_2)$$
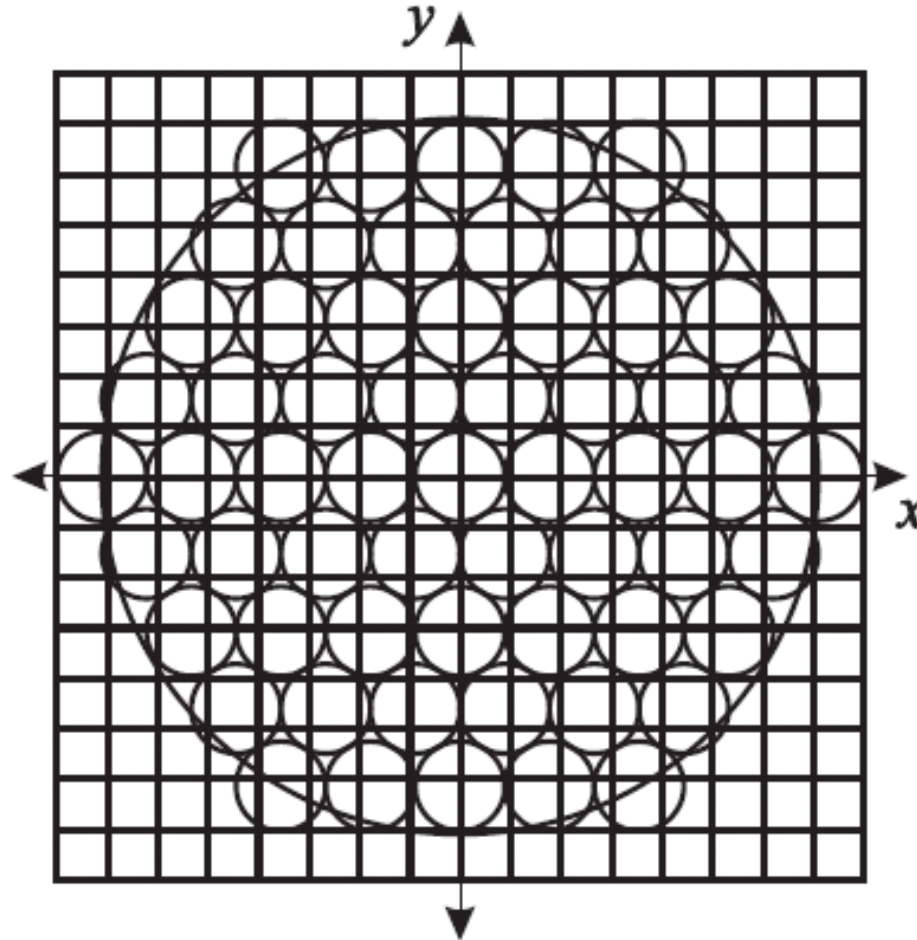$$(X_3, Y_3, Z_3, t_3)$$
$$\vdots$$
$$(X_n, Y_n, Z_n, t_n)$$
$$\vdots$$

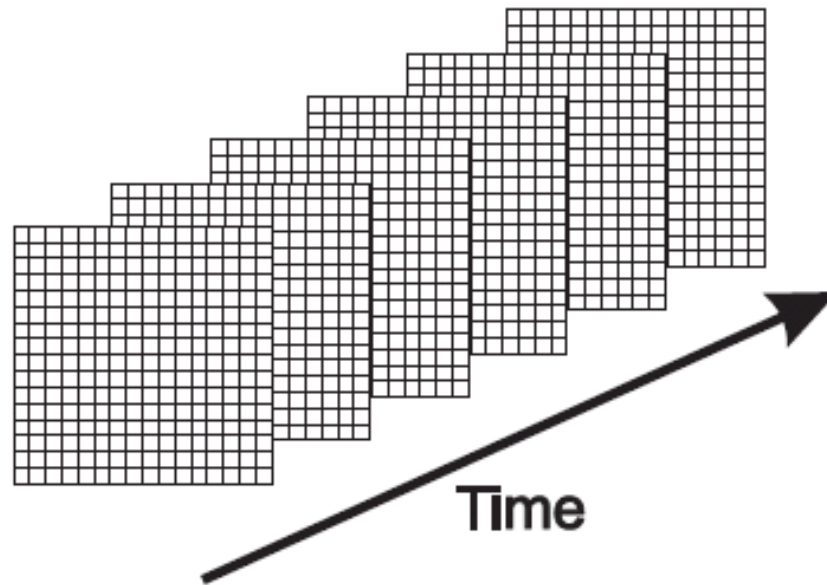Complete information, but memory hog

Single Frame Mode

The value in each pixel indicates the number of events happened in that location over the entire scan time

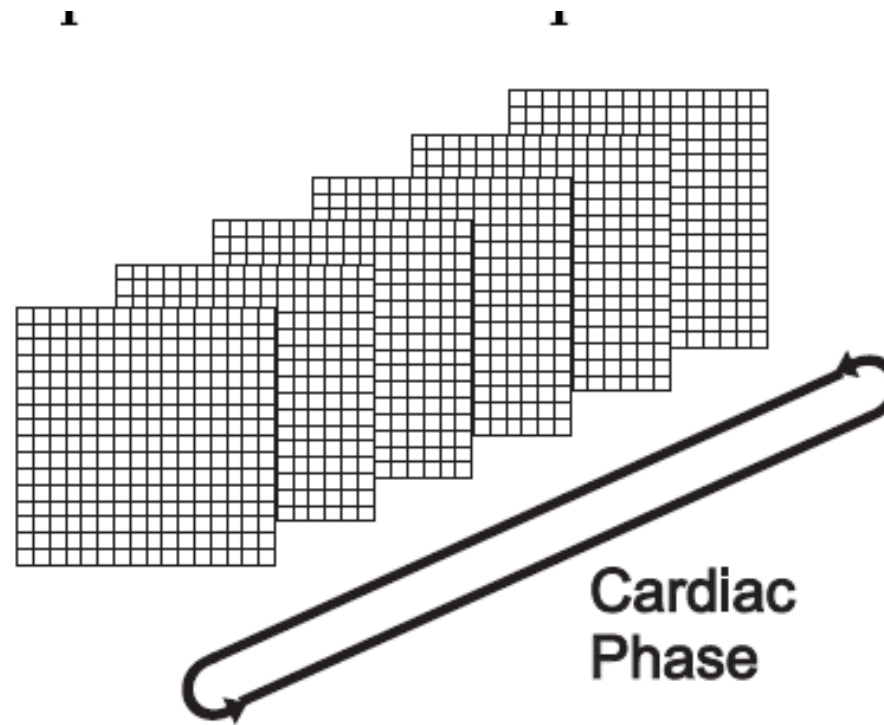Matrix sizes: 64×64, 128×128, 256×256

Dynamic Frame Mode

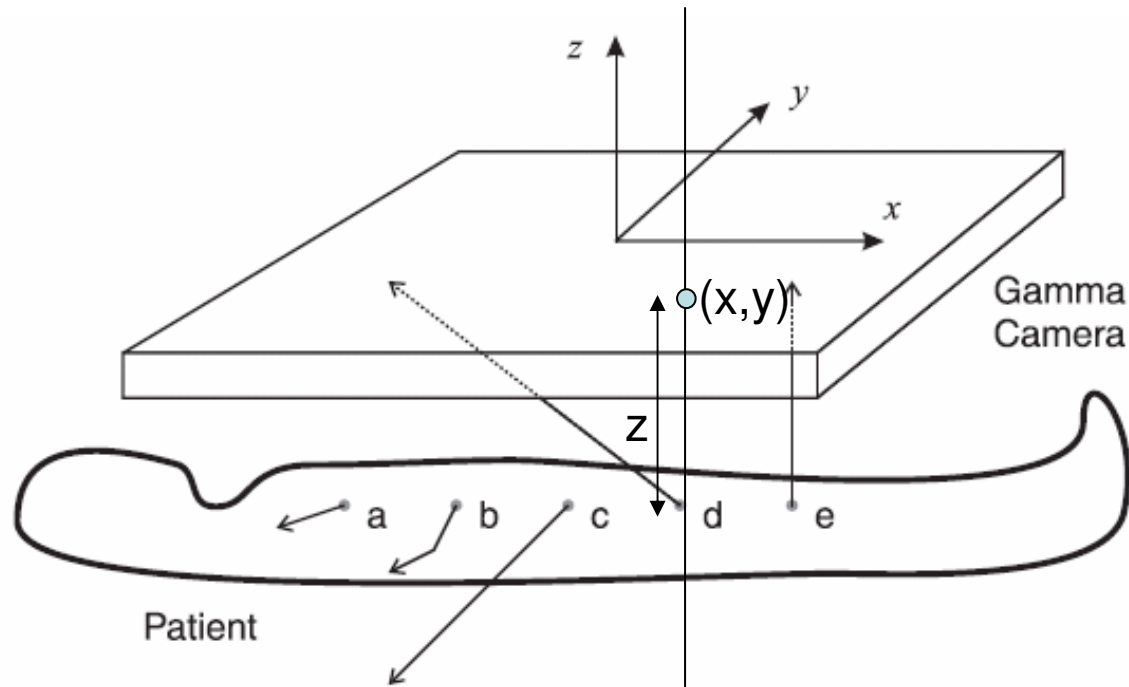
Time

Useful for imaging transient physiological processes

Multiple Gated Acquisition

Cardiac Phase

Cardiac (ECG) gated. Data resorted using ECG

Imaging Geometry and Assumption

- Lines defined by (parallel) collimator holes
- Ignore Compton scattering
- Radioactivity is $A(x, y, z)$
- Monoenergetic photons, energy E

Imaging Equation

- Photon fluence on detector is

$$\phi(x, y) =$$

$$\int_{-\infty}^{0} \frac{A(x, y, z)}{4\pi z^2} e^{-\int_{z}^{0} \mu(x, y, z'; E)dz'} dz$$

- Depth-dependent effects from:
  - inverse square law, and
  - object-dependent attenuation
- Consequences:
  - Near activity brighter
  - Front and back are different

Planar Source

- $A_{z_0}(x, y)$ has radioactivity on $z = z_0$

$$A(x, y, z) = A_{z_0}(x, y)\delta(z - z_0)$$

- Detected photon fluence rate

$$\phi(x, y) = A_{z_0}(x, y)\frac{1}{4\pi z_0^2} \exp\left\{-\int_{z_0}^0 \mu(x, y, z'; E)\right.$$

- Two terms attenuate desired result
  - inverse square law: constant for (x, y)
  - μ: not constant for (x, y)

Examples

- Example 1: Imaging of a slab
- Example 2: Imaging of a two-layer slab

- Go through on the board

SPECT

- Instrumentation
- Imaging Principle

SPECT Instrumentation

- Similar to CT, uses a rotating Anger camera to detect photons traversing paths with different directions

- Recent advances uses multiple Anger cameras (multiple heads), reducing scanning time (below 30 minutes)

- Anger cameras in SPECT must have significantly better performances than for planar scintigraphy to avoid reconstruction artifacts
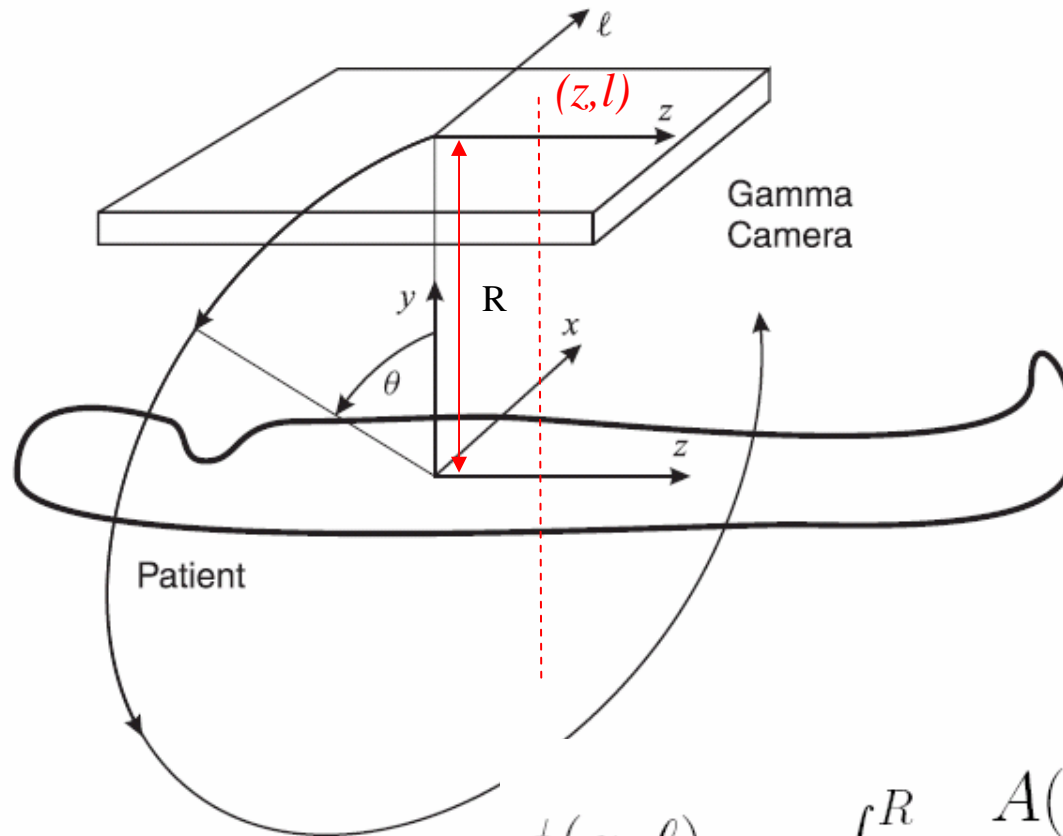
A typical SPECT system
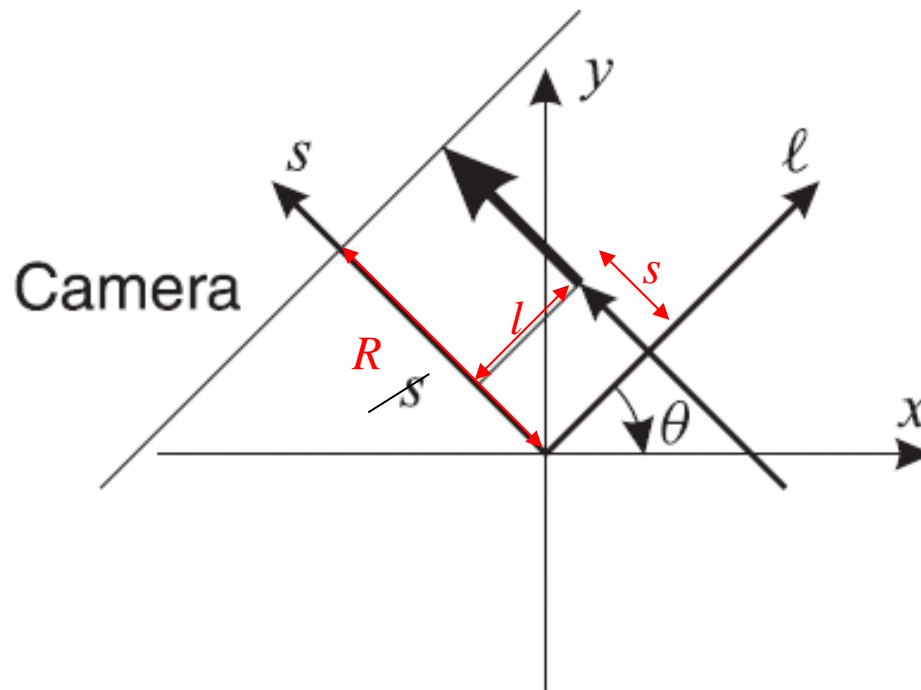

Fig. 9.1 A dual head system

Imaging Equation: θ=0

Replace *x* by *l*

$$\phi(z, \ell) = \int_{-\infty}^{R} \frac{A(x, y, z)}{4\pi(y - R)^2} \exp\left\{-\int_{y}^{R} \mu(x, y', z; E)\,dy'\right\}\,dy$$

General Case: Imaging Geometry

$$x(s) = \ell \cos \theta - s \sin \theta$$
$$y(s) = \ell \sin \theta + s \cos \theta$$

General Case: Imaging Equation

$$\phi(\ell, \theta) = \int_{-\infty}^{R} \frac{A(x(s), y(s))}{4\pi(s-R)^2}$$

$$\exp\left\{-\int_{s}^{R} \mu(x(s'), y(s'); E)ds'\right\} ds$$

- Two unknowns:
  - $A(x, y)$
  - $\mu(x, y)$
- Generally intractable $\Rightarrow$
  - ignore attenuation (often done)
  - assume constant
  - measure and apply atten correction

Approximation

- Bold approximations: ignore attenuation, inverse square law, and scale factors:

$$\phi(\ell, \theta) = \int_{-\infty}^{\infty} A(x(s), y(s)) ds$$

- Using line impulse:

$$\phi(\ell, \theta) = \int_{-\infty}^{\infty}\int_{-\infty}^{\infty} A(x, y)\delta(x\cos\theta + y\sin\theta - \ell)\, dx\, dy$$

Under this assumption, A can be reconstructed using the filtered backprojection approach
The reconstructed signal needs to be corrected!

Correction for Attenuation Factor

- Use co-registered anatomical image (*e.g.*, MRI, x-ray CT) to generate an estimate of the tissue μ at each location

- Use known-strength γ-emitting standards (*e.g.*, [153]Gd (Webb, *§*2.9.2, p. 79) or [68]Ge (*§* 2.11.4.1, p. 95)) in conjunction with image data collection, to estimate μ at each tissue location

- Iterative image reconstruction algorithms

  – In "odd-numbered" iterations, treat $\mu(x,y)$ as known and fixed, and solve for $A(x,y)$

  – In "even-numbered" iterations, treat $A(x,y)$ as known and fixed, and solve for $\mu(x,y)$

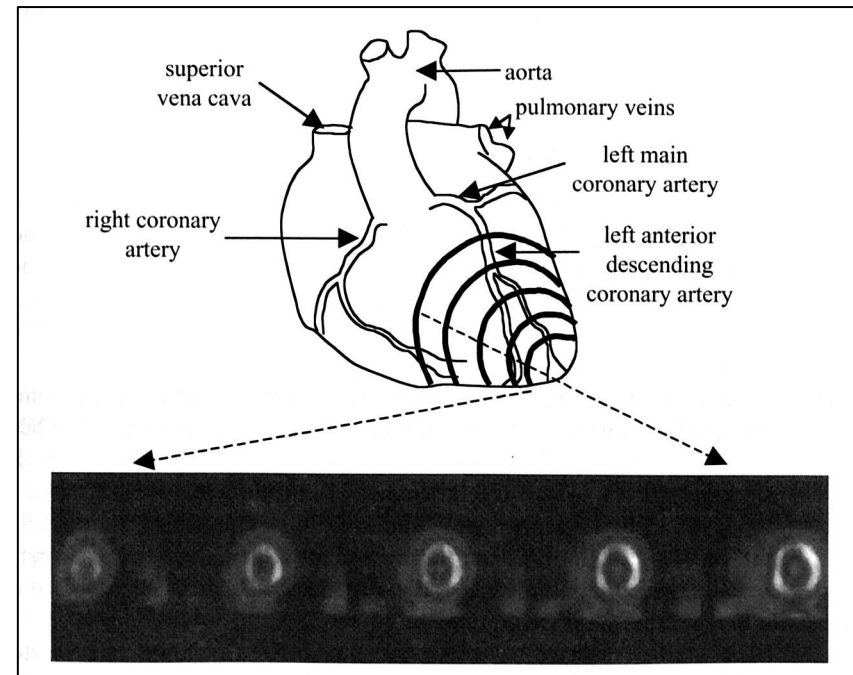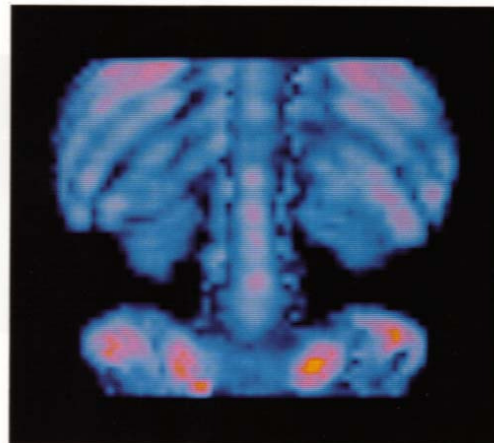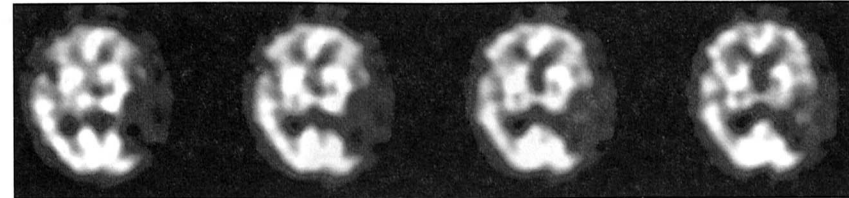- From Graber, Lecture Slides for BMI1,F05

Example

- Imaging of a rectangular region, with the following structure. Derive detector readings in 4 positions (A,B,C,D)
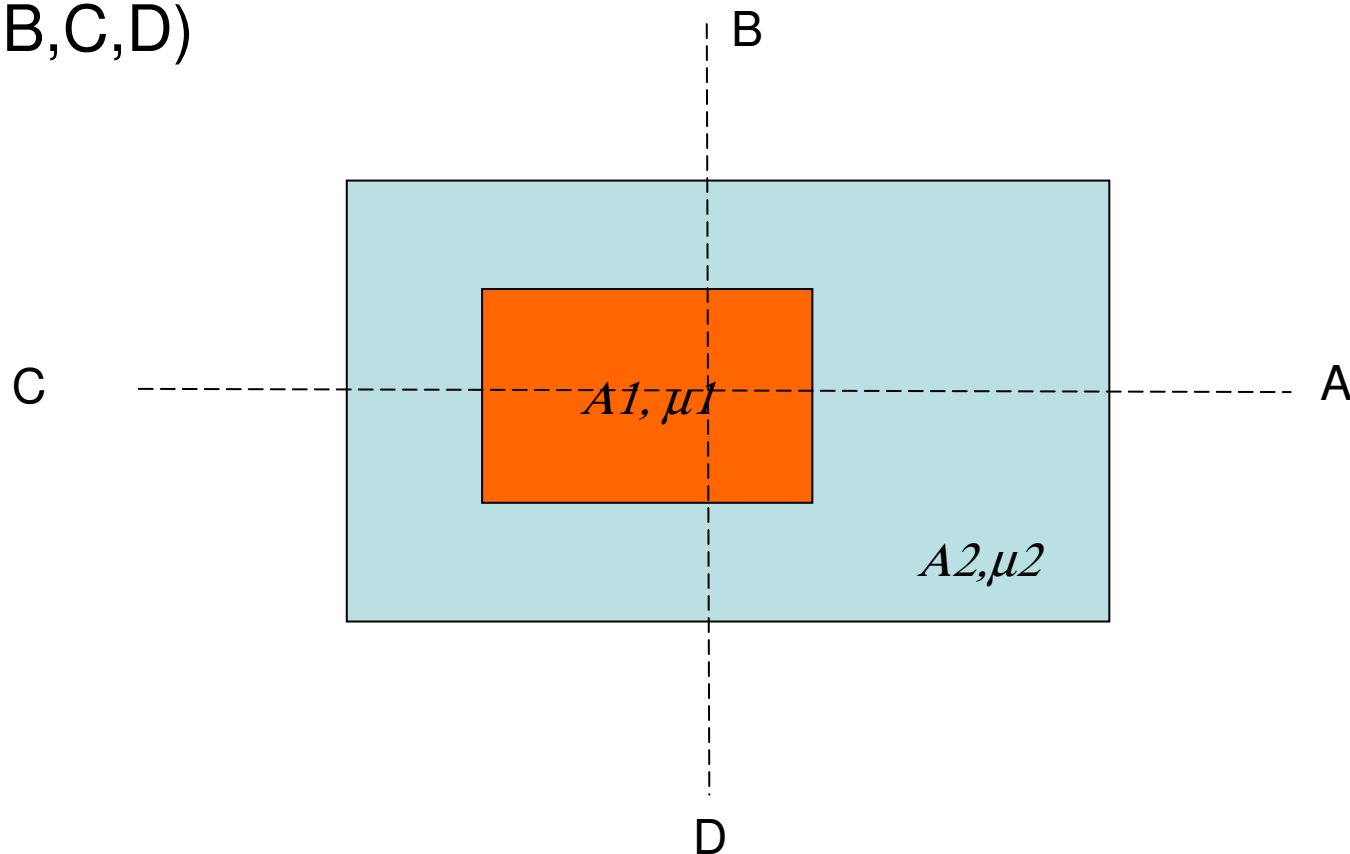
Do you expect the reading at B and D be the same? What about at A and C?

SPECT applications

- Brain:
  - Perfusion (stroke, epilepsy, schizophrenia, dementia [Alzheimer])
  - Tumors
- Heart:
  - Coronary artery disease
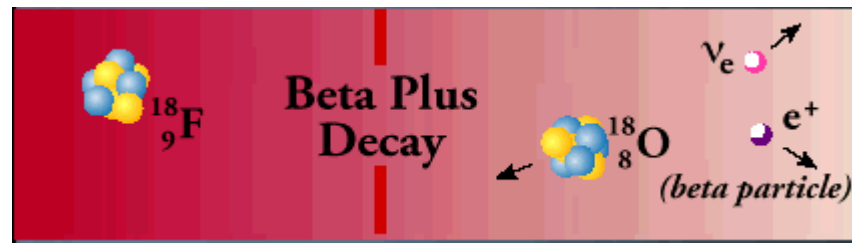 - Myocardial infarcts
- Respiratory
- Liver
- Kidney

- From Graber, Lecture Slides for BMI1,F05
- See Webb Sec. 2.10

PET Principle

- Positron emitters
- Positron annihilation:
    - short distance from emission
    - produces two 511 keV gamma rays
    - gamma rays 180° opposite directions
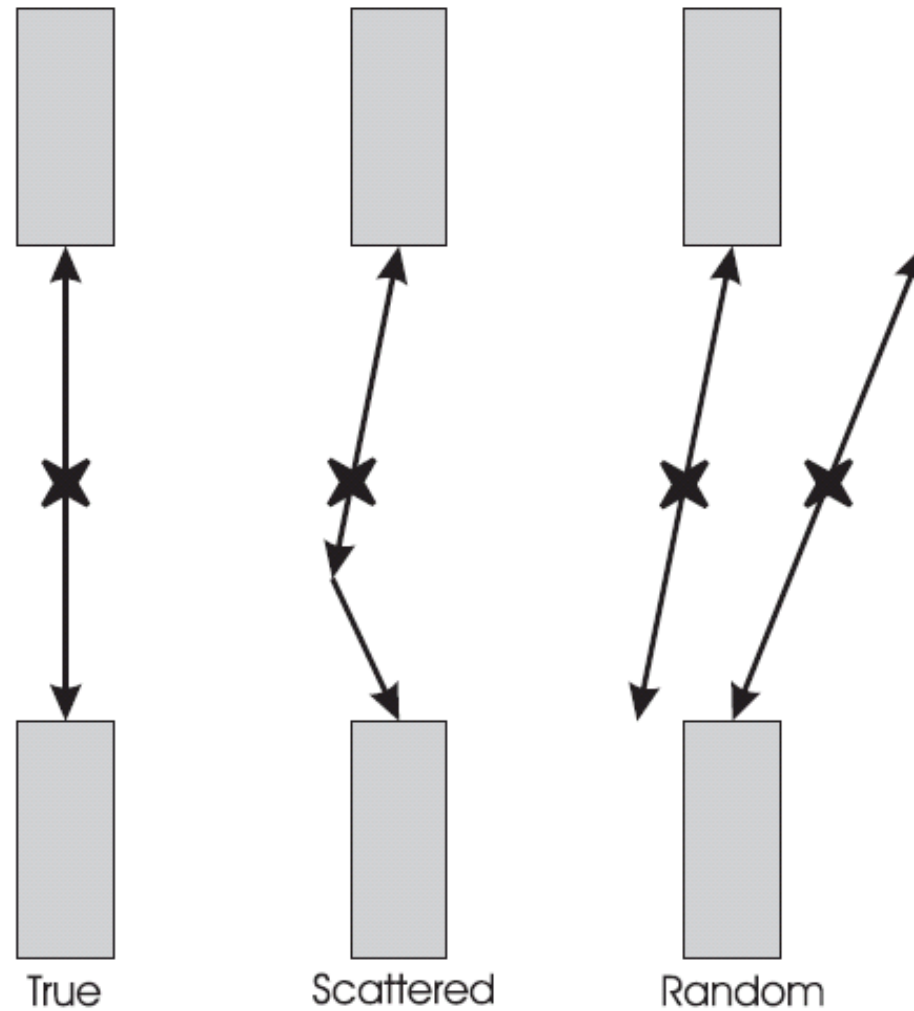- Principle: detect <u>coincident</u> gamma rays

Annihilation Coincidence Detection

- Detect two events in opposite directions occurring "simultaneously"
- Time window is 2-20 ns, typically 12 ns
- No detector collimation is required
  - Higher sensitivity
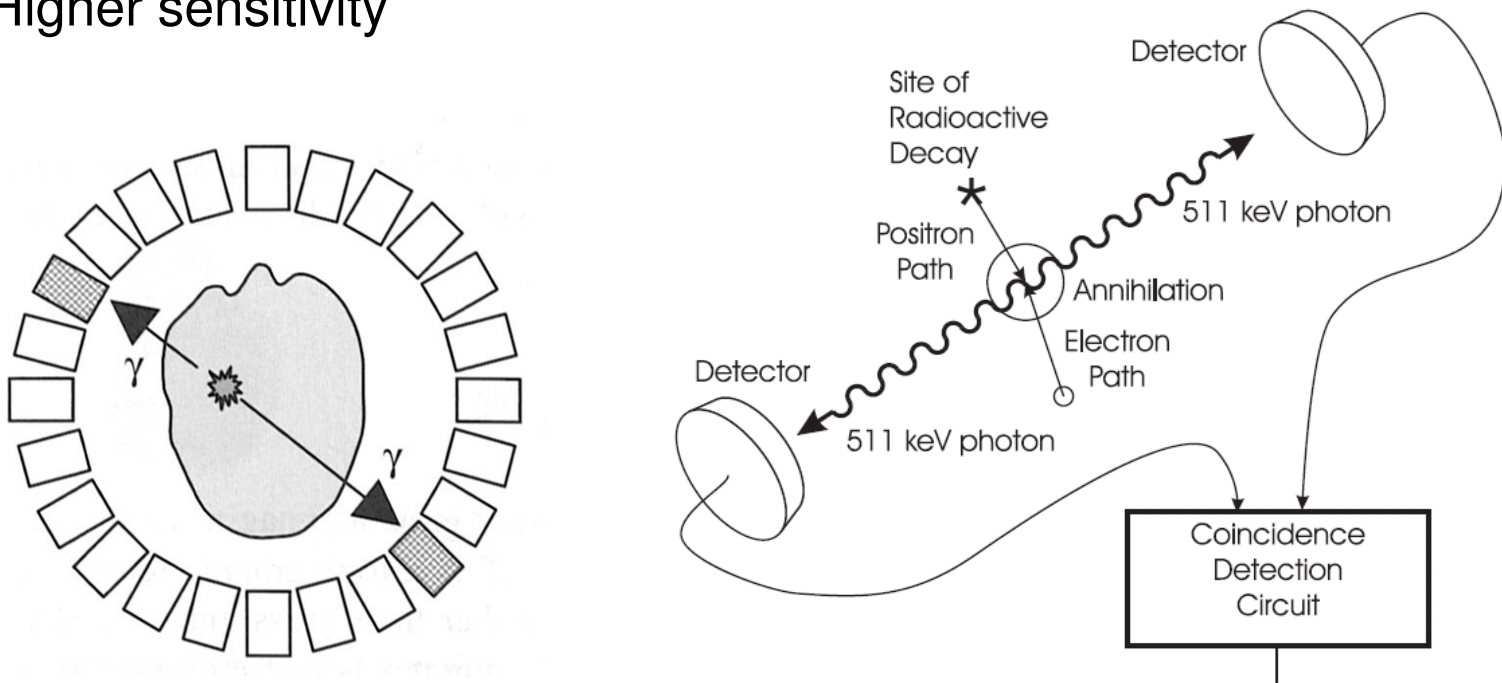
Detected PET Events

True   Scattered   Random

Coincidence Timing

- Three classes of events
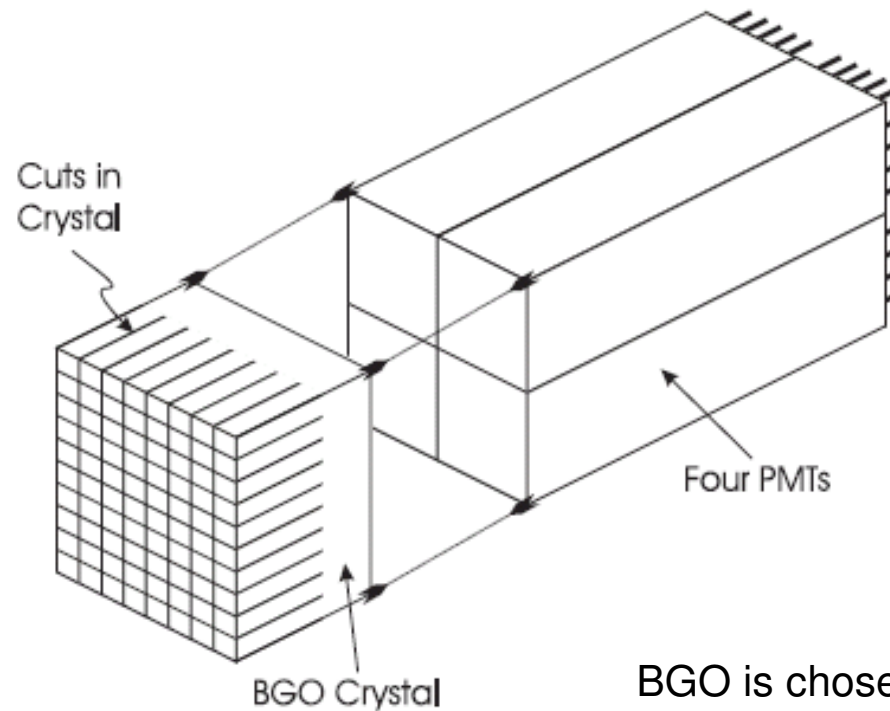 - true coincidence
  - scattered coincidence
  - random coincidence
- Sensitivity in PET
  - measures capability of system to detect "trues" and reject "randoms"

PET Detector Block

Cuts in
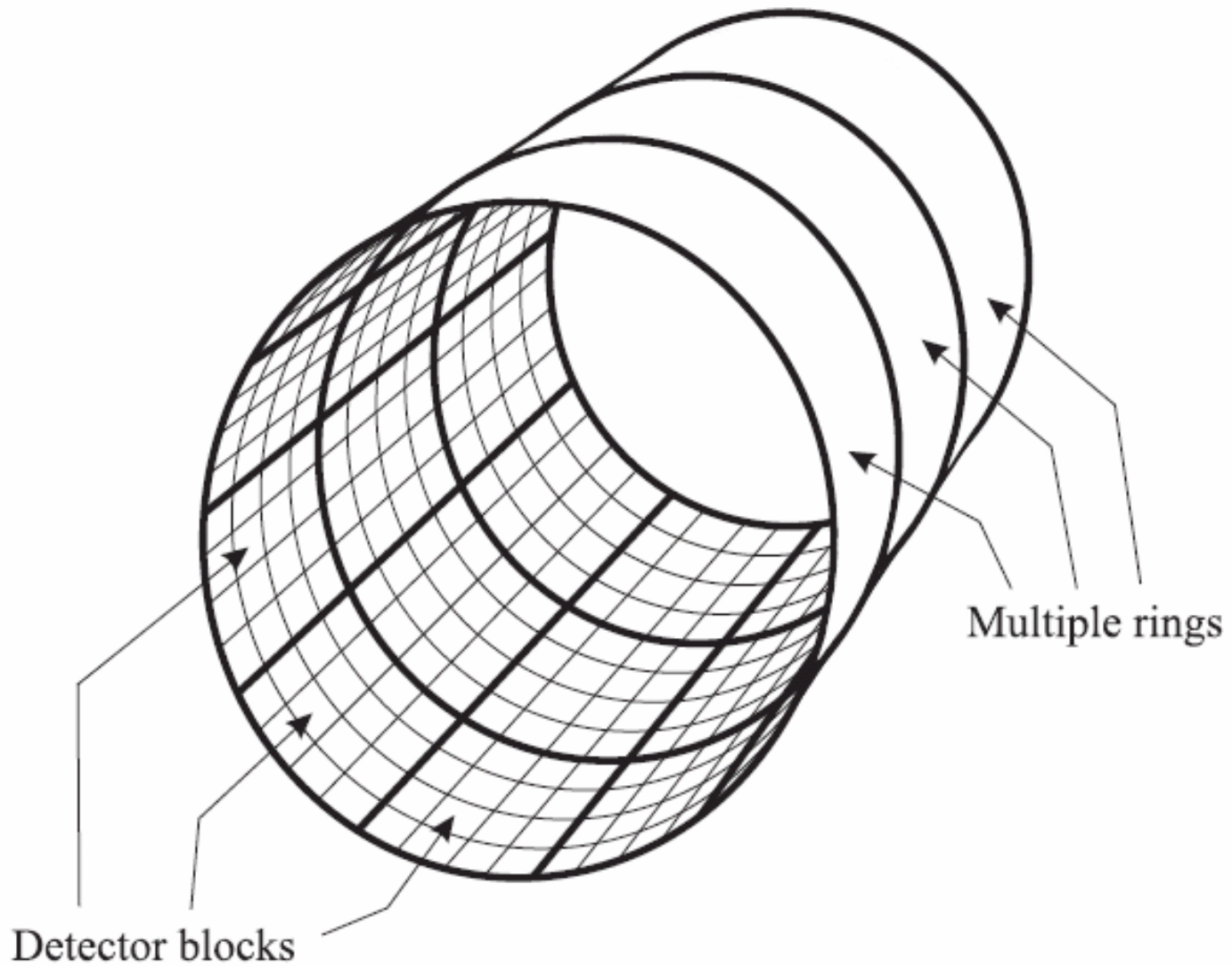Crystal

Four PMTs

BGO Crystal

BGO is chosen because of the higher
energy (511KeV) of the photons

- Crystals plus PMTs
- BGO = Bismuth Germanate
- BGO has 3x stopping power than NaI(Tl)

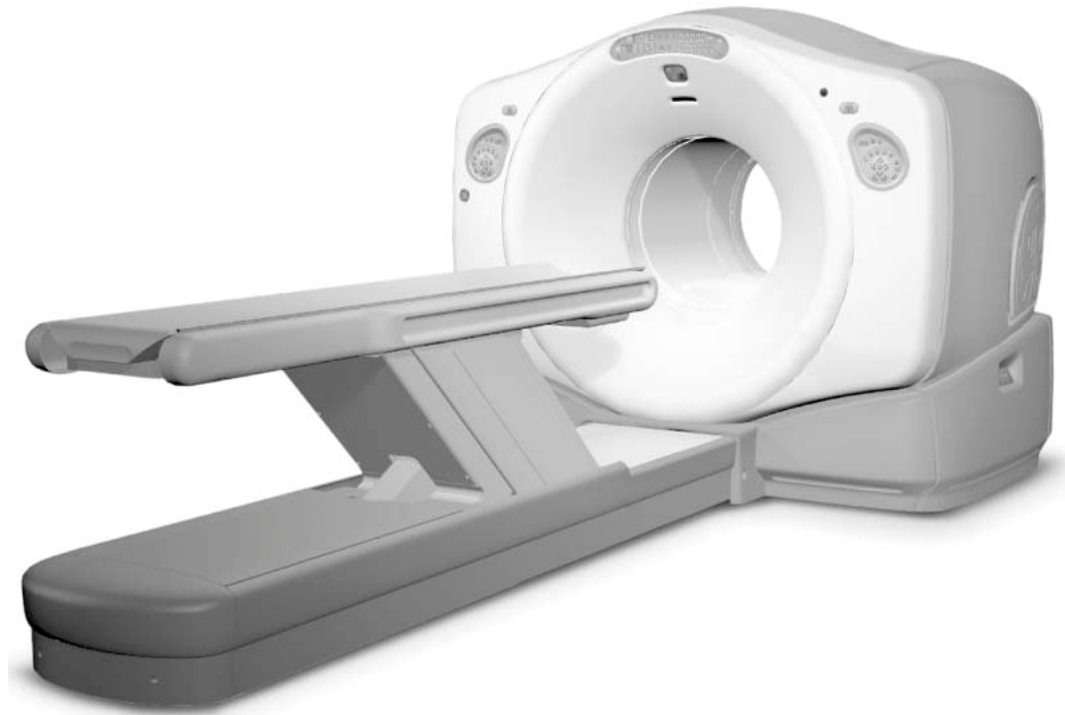# Multiple Ring Detector

Multiple rings

Detector blocks

PET Detector Configuration

- Typical numbers:
  - 8 by 8 blocks; 2 mm $\times$ 2 mm element
  - 2 by 2 PMTs per block
  - 3 major rings
  - $\Rightarrow$ 24 detector rings
  - 48 detector blocks per major ring
  - $\Rightarrow$ 384 detectors per ring
  - $\Rightarrow$ 8216 crystals total

A Typical PET Scanner

Combined PET/CT Systems

- CT: provides high resolution anatomical information
- PET: Low resolution functional imaging
- Traditional approach:
  - Obtain CT and PET images separately
  - Registration of CT and PET images, to help interpretation of PET images
- Combined PET/CT: Performing PET and CT measurements within the same system without moving the patient relative to the table
  - Make the registration problem easier
  - But measurement are still taken separately with quite long time lag

Imaging Equation
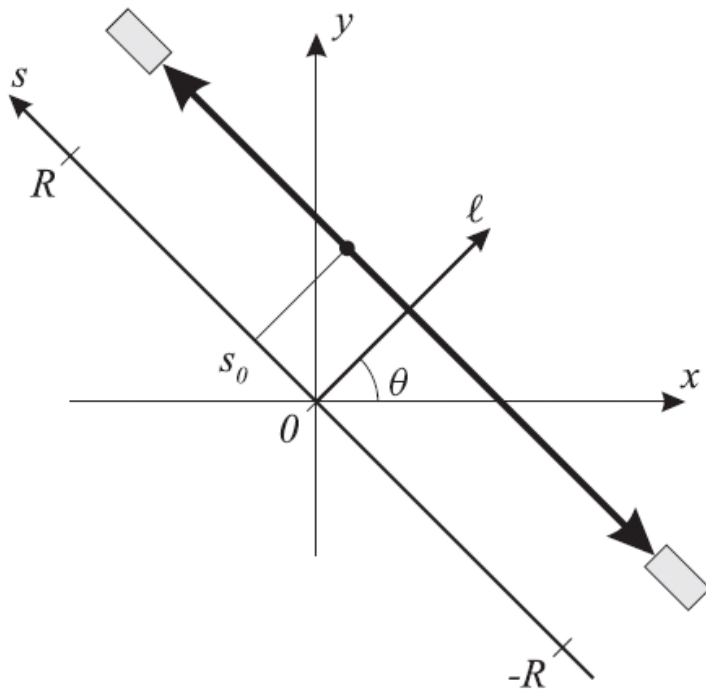
$$N^+(s_0) = N_0 \exp\left\{-\int_{s_0}^{R} \mu(x(s'), y(s')); E)ds'\right\}$$

$$N^-(s_0) = N_0 \exp\left\{-\int_{-R}^{s_0} \mu(x(s'), y(s')); E)ds'\right\}$$

$$N_c(s_0) = N_0 \exp\left\{-\int_{s_0}^{R} \mu(x(s'), y(s')); E)ds'\right\}$$

$$\bullet \exp\left\{-\int_{-R}^{s_0} \mu(x(s'), y(s')); E)ds'\right\}$$

$$= N_0 \exp\left\{-\int_{-R}^{R} \mu(x(s'), y(s')); E)ds'\right\}$$

$$\varphi(l,\theta) = K\int_{-R}^{R} A(x(s), y(s)) \exp\left\{-\int_{-R}^{R} \mu(x(s'), y(s'))ds'\right\}ds = K\int_{-R}^{R} A(x(s), y(s))ds \bullet \exp\left\{-\int_{-R}^{R} \mu(x(s'), y(s'))ds'\right\}$$

$A(x, y)$ and $\mu(x,y)$ can be separated!

Attenuation Correction

- Corrected sinogram

$$\phi_c(\ell, \theta) = \frac{\phi(\ell, \theta)}{K \exp\left\{ -\int_{-R}^{R} \mu(x(s), y(s); E) \, ds \right\}}$$

- $\mu(x, y)$ found from CT (transmission PET)

- One can apply filtered backprojection algorithm to reconstruct A(x,y) from the corrected sinogram

Reconstruction from Corrected Sinogram
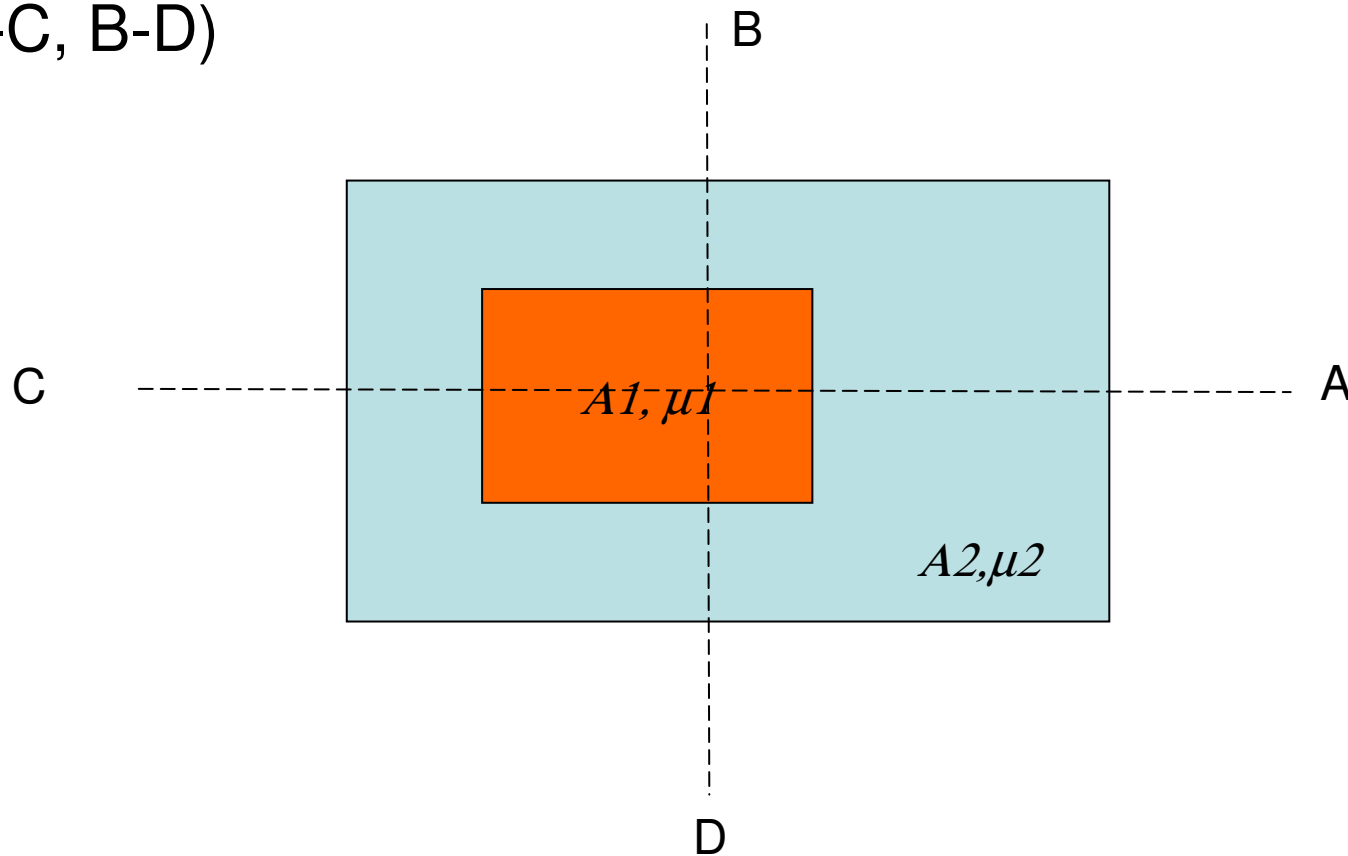
- Convolution backprojection yields $A(x, y)$

$$A_c(x, y) =$$
$$\int_0^\pi \int_{-\infty}^\infty \phi_c(\ell, \theta) \tilde{c}(x \cos\theta + y \sin\theta - \ell) \, d\ell \, d\theta$$

Example

- Imaging of a rectangular region, with the following structure. Derive detector readings in 2 paired positions (A-C, B-D)

How does the approach and results differ from SPECT?

PET resolution compared to MRI

PET

MRI
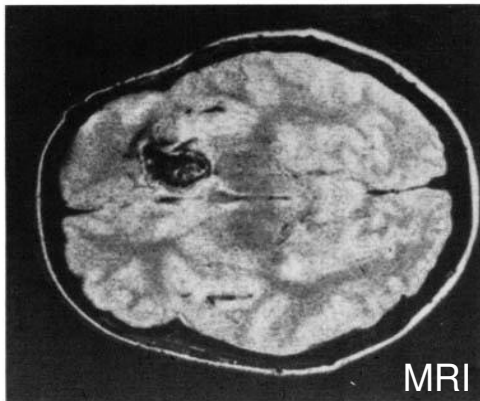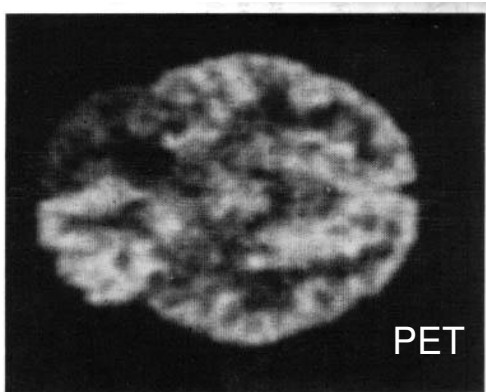
- Modern PET ~ 2-3 mm resolution (1.3 mm)

The evolution of resolution.
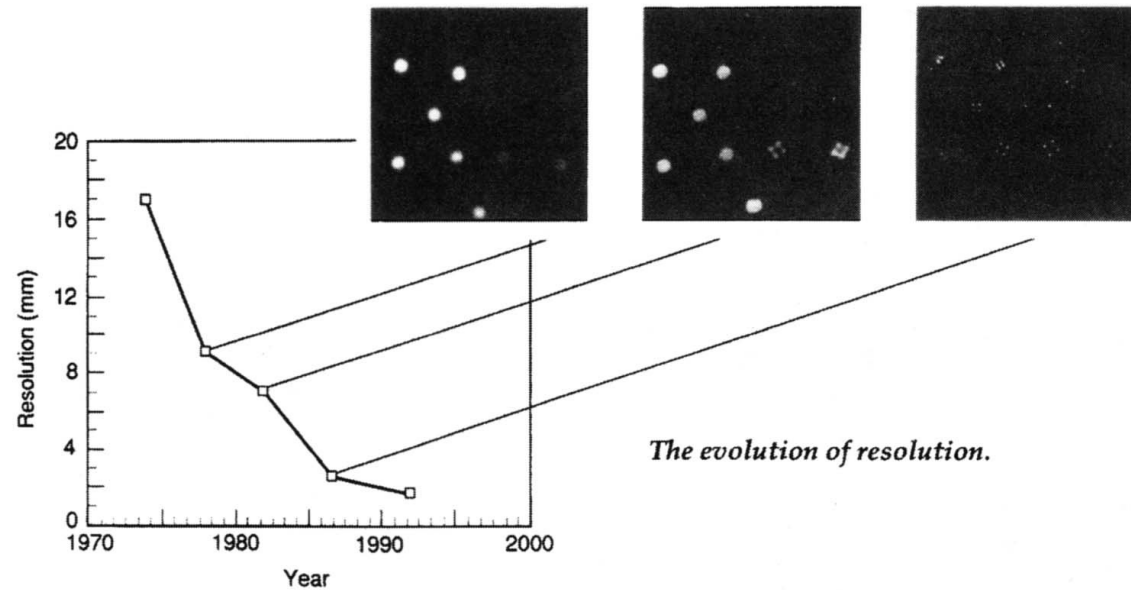
From H. Graber, lecture slides for BMI1,F05

PET evolution

NaI
- PET III 1975
- ECAT II 1977

BGO
- NeuroECAT 1978
- ECAT 931 1985
- EXACT HR+ 1995

LSO
- HRRT (pending 510k approval)
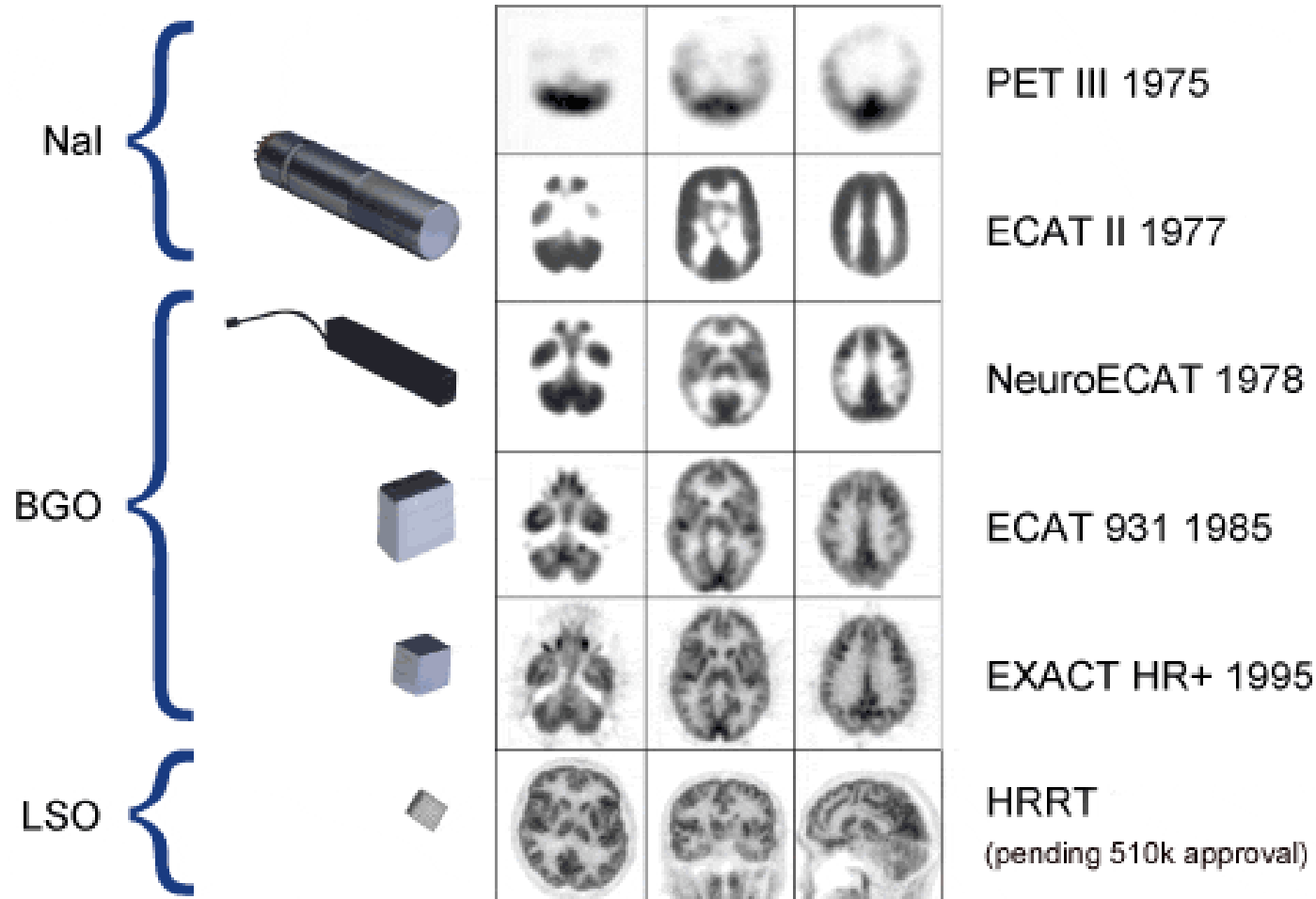
From H. Graber, lecture slides for BMI1,F05

PET applications

- Brain:
  - Tumor detection
  - Neurological function (pathologic, neuroscience app.)
  - Perfusion

- Cardiac
  - Blood flow
  - Metabolism

- Tumor detection (metastatic cancer)

- From H. Graber, lecture slides for BMI1,F05
- See Webb Sec. 2.11.7

PET Application: See and Hear

SEEING WORDS

HEARING WORDS
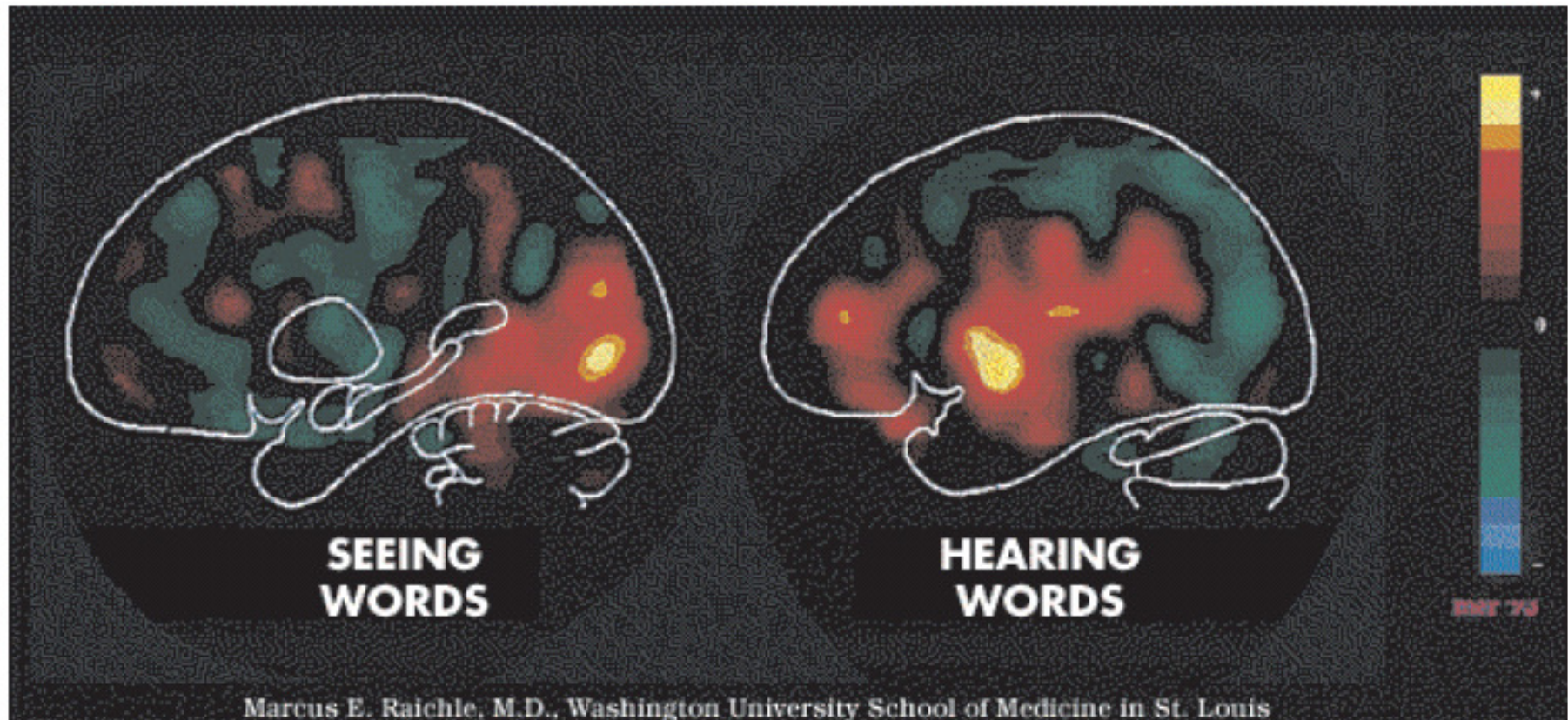
Marcus E. Raichle, M.D., Washington University School of Medicine in St. Louis

The PET scan on the left shows two areas of the brain (red and yellow) that become particularly active when volunteers read words on a video screen: the primary visual cortex and an additional part of the visual system, both in the back of the left hemisphere. Other brain regions become especially active when subjects hear words through ear-phones, as seen in the PET scan on the right.

Image Quality Consideration

- We will consider the following for scintigraphy, SPECT, and PET together

  – Resolution: collimator, detector intrinsic

  – Noise

  – SNR

- Ref: Sec. 8.4 in Textbook

Relation between True Image and Reconstructed Image in SPECT/PET

- Approximation:

$$\hat{f}(x, y) = f(x, y) * h(r)$$

- In SPECT, $h(r)$ includes:
  - collimator and intrinsic resolutions
  - ramp filter window effect
- In PET, $h(r)$ includes:
  - the positron range function
  - detector width effects
  - ramp filter window effect

Collimator Resolution

Scintillation Crystal $Rc(z)$

b

Collimator

d h l

r

z

Point Source

$$R_C(|z|) = \frac{d}{l}(l + b + |z|)$$
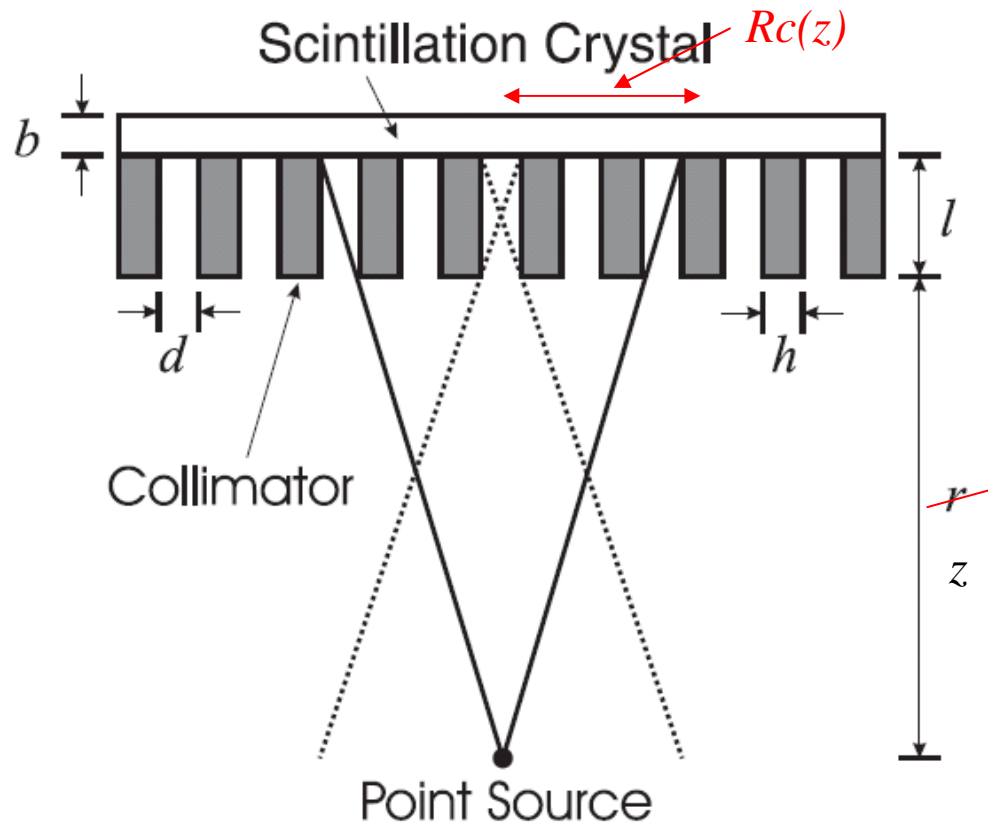
2* Rc(z) is the maximum width that a point source at distance z can reach w/o being absorbed by the collimator.
A single photon at distance z produces a circle with radius= *Rc(z)* in the detector plane

Rc(z) equal to FWHM of the PSF of the detector

Note that this resolution is dependent on *z:* targets farther away are blurred more.

Increase *l* can reduce *Rc* and hence increase the resolution, but also reduces sensitivity

Equivalent Blurring Function

- Gaussian approximation

$$h_c(x, y; |z|) = \exp\left\{-4r^2 \ln 2 / R_C^2(|z|)\right\}$$

- Planar source is blurred

$$\phi(x, y) = A_{z_0}(x, y)\frac{1}{4\pi z_0^2} \times$$

$$\exp\left\{-\int_{z_0}^{0} \mu(x, y, z'; E)dz'\right\} * h_c(x, y; |z_0|)$$

Intrinsic Resolution

- Where did the x-ray photon hit?
    - Compton in crystal spreads out light
    - Crystal thickness
    - Noise in light, PMTs, and electronics
- Gaussian approximation

$$h_I(x, y) = \exp\left\{-4r^2 \ln 2 / R_I^2\right\}$$

- Planar source is further blurred

$$\phi(x, y) = A_{z_0}(x, y)\frac{1}{4\pi z_0^2} \exp\left\{-\int_{z_0}^0 \mu(x, y, z'; E)\, dz'\right\}$$
$$* h_C(x, y; |z_0|) * h_I(x, y)$$

Collimator Sensitivity

- Collimator Efficiency $=$ Sensistivity $=$

$$\epsilon = \left(\frac{Kd^2}{l(d+h)}\right)^2$$

where $K \approx 0.25$.

- ϵ is the fraction of photons (on average) that pass through the collimator for each emitted photon directed at the camera

Detector Efficiency

- Depends on crystal thickness
  - thicker $\Rightarrow$ more efficient
  - 100% at 100keV; 10-20% at 511keV
- Tradeoff:
  - If E_γ low $\Rightarrow$ use thinner crystal
    * better intrinsic resolution
  - If E_γ high $\Rightarrow$ use thicker crystal
    * poorer intrinsic resolution
  - Higher E_γ, less abosorption in body

Signal to Noise

- Similar to X-ray imaging
- Model the number of detected photons as a random variable following the Poisson distribution

  Mean of detected photons $\eta = N$

- For a single detector:

  Variance of detected photons $: \sigma^2 = \eta = N$

  Intrinsic SNR $= \eta / \sigma = \sqrt{N} = \sqrt{\eta}$

- Frame mode detector with JxJ pixels

  Mean of detected photons over all pixels $\eta = N$

  Mean of detected photons per pixel $: \eta_p = N / J^2$

  Intrinsic SNR per pixel $= \sqrt{\eta_p} = \sqrt{N} / J$

- Contrast SNR

  Mean of detected photons over target region $\eta_t = \overline{N}_t$

  Mean of detected photons over background $: \eta_b = \overline{N}_b$

  Contrast $: C = (\overline{N}_t - \overline{N}_b) / \overline{N}_b$

  Noise Variance $: \sigma^2 = \overline{N}_b$

  Contrast SNR $= (\overline{N}_t - \overline{N}_b) / \sigma = (\overline{N}_t - \overline{N}_b) / \sqrt{N_b} = C \sqrt{N_b}$

Summary

- Three major imaging modalities:
  - Planar scintigraphy
  - SPECT
  - PET
- Principle of Anger camera: collimator, scintillation crystal, photomultiplier
- Imaging principles of planar scintigraphy and SPECT
  - Both based on gamma decay
  - Very similar to X-ray projection and CT, except for the attenuation factor
  - Practical systems mostly ignore the attenuation factor
- Imaging principle of PET:
  - Coincidence detection: detect two photons reaching two opposite detectors simultaneously (within a short time window)
  - Detected signal is the product of two terms, depending on the radioactivity A and attenuation μ separately
  - Can reconstruct radioactivity more accurately if μ can be measured simultaneously
- Image Quality

Reference

- Prince and Links, Medical Imaging Signals and Systems, Chap 8,9.

- A. Webb, Introduction to Biomedical Imaging, Chap. 2

- Handouts from Webb: Sec. 2.5 for Technetium generation; Sec. 2.10, Sec. 2.11.7 for Clinical applications of nuclear medicine.

- Recommended readings:

  – K. Miles, P. Dawson, and M. Blomley (Eds.), *Functional Computed Tomography* (Isis Medical Media, Oxford, 1997).

  – R. J. English, *SPECT: Single Photon Emission Computed Tomography: A Primer* (Society of Nuclear Medicine, Reston, VA, 1995).

  – M. Reivich and A. Alavi (Eds.), *Positron Emission Tomography* (A. R. Liss, NY, 1985).

Homework

- Reading:
  - Prince and Links, Medical Imaging Signals and Systems, Ch. 8,9.
  - Handouts

- Note down all the corrections for Ch. 8,9 on your copy of the textbook based on the provided errata.

- Problems for Chap 8,9 of the text book
  - P8.2
  - P8.7
  - P8.8
  - P9.2 (part a only)
  - P9.4