



Fundamentals of Positron Emission Tomography (PET)

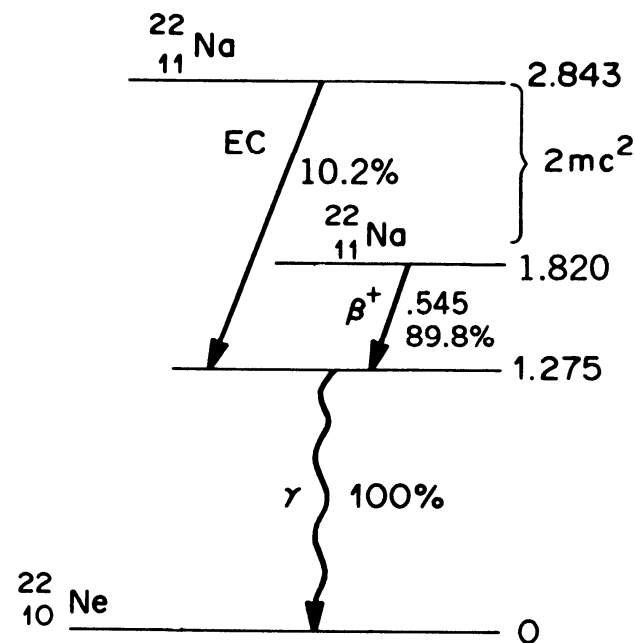
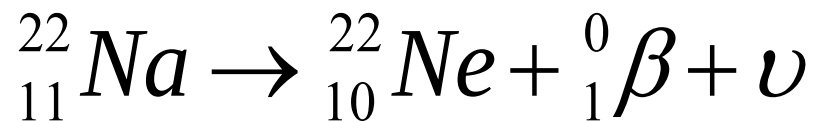


Content

- Fundamentals of PET
- Camera & Detector Design
- Real World Considerations
- Performance Evaluation
- Clinical Uses

Positron Emission

- A **positron** is the anti-particle of electrons, which carries the same mass as an electron but is positively charged.
- Positrons are normally generated by those nuclides having a **relatively low neutron-to-proton ratio**.
- An typical example of positron emitter is

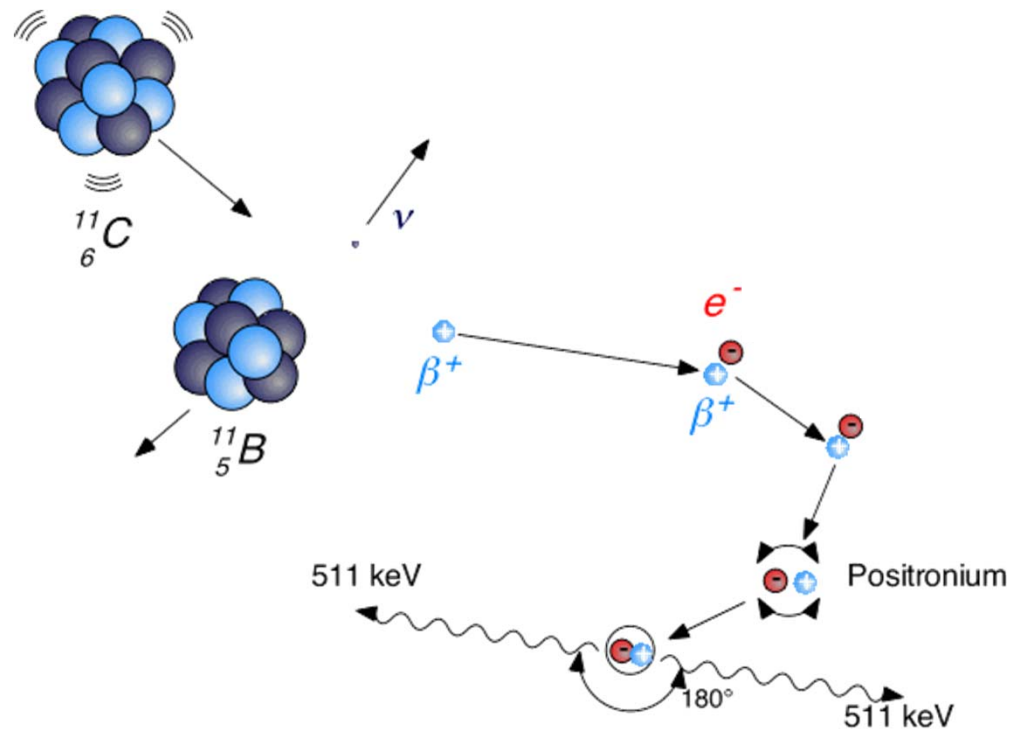
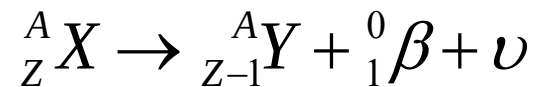


(c)

FIGURE 3.11. Decay scheme of ${}_{11}^{22}\text{Na}$.

Annihilation Radiation following Positron Emission

Beta - plus decay or positron decay :



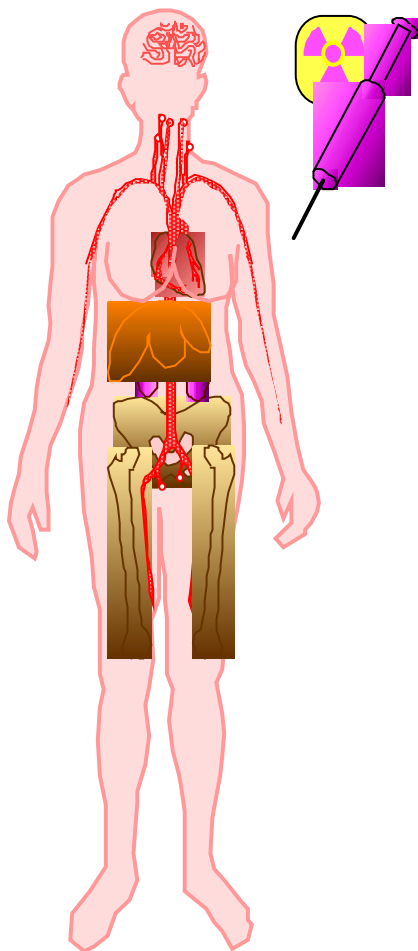


Commonly Used PET Isotopes

Isotope	half-life (min)	Maximum positron energy (MeV)	Positron range in water (FWHM in mm)	Production method
^{11}C	20.3	0.96	1.1	cyclotron
^{13}N	9.97	1.19	1.4	cyclotron
^{15}O	2.03	1.70	1.5	cyclotron
^{18}F	109.8	0.64	1.0	cyclotron
^{68}Ga	67.8	1.89	1.7	generator
^{82}Rb	1.26	3.15	1.7	generator

Table 2. Properties of commonly used positron emitting radio-isotopes

The Tracer Principle Again



- **Drug is labeled with positron (β^+ , anti-particle of an electron) 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).**



Why PET

- Interesting Chemistry
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 $\Rightarrow$ local production.

^{18}F	2 hour half-life
$^{15}\text{O}, ^{11}\text{C}, ^{13}\text{N}$	2–20 minute half-life

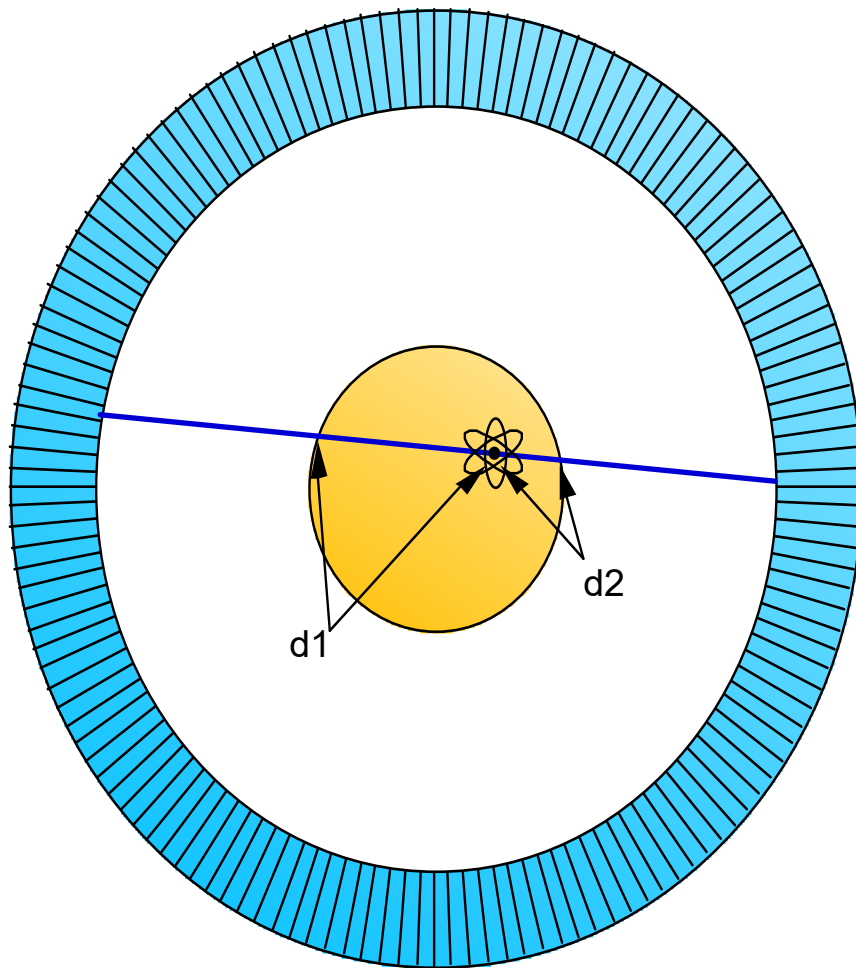


Ideal Tracer Isotope

- Tracers contain elements of life – perfect for providing the functional information such as metabolism rate.
- Electronic collimation – high sensitivity.
- Easier attenuation correction.

^{18}F	2 hour half-life
$^{15}\text{O}, ^{11}\text{C}, ^{13}\text{N}$	2–20 minute half-life

Attenuation of Internal Source



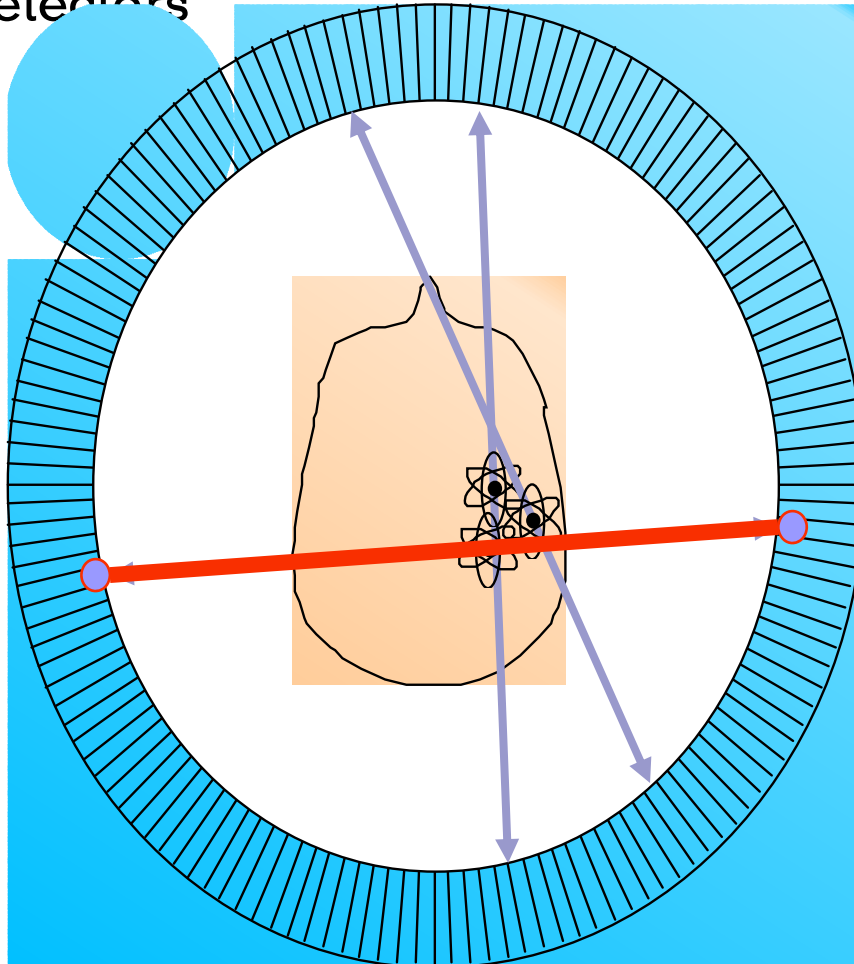
$$P_1 = e^{-\mu \cdot d_1} \quad P_2 = e^{-\mu \cdot d_2}$$

$$P = e^{-\mu \cdot (d_1 + d_2)}$$

Event detection probability is product of individual photon detection probabilities.

Detect Radioactive Decays

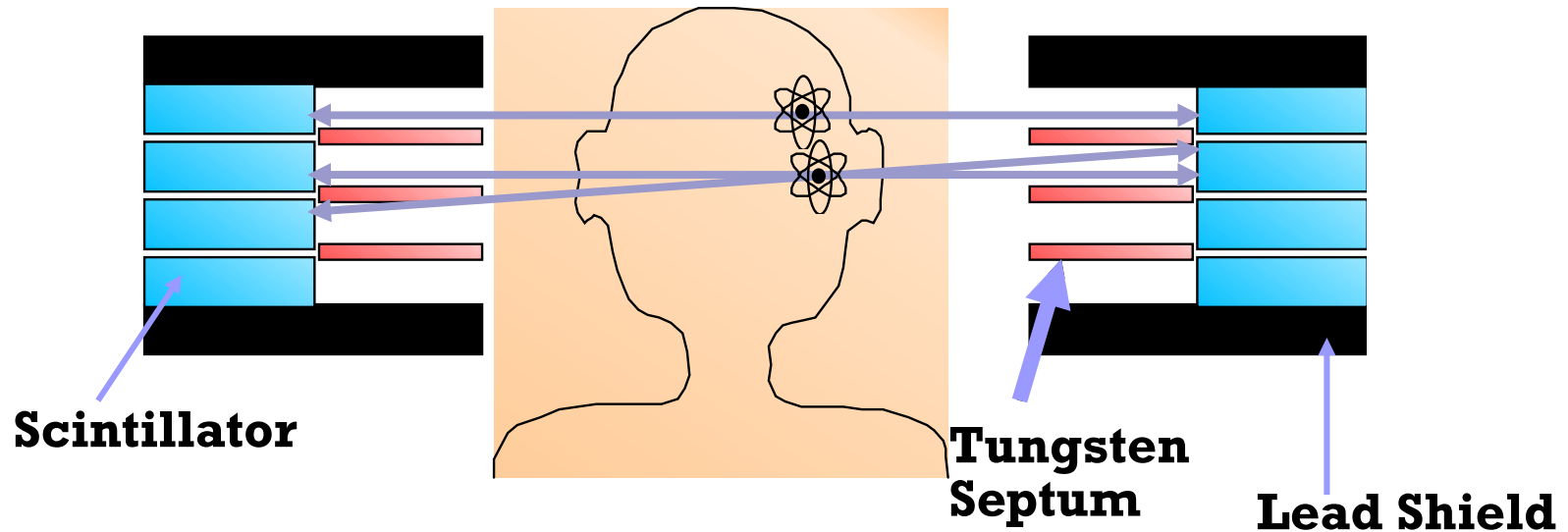
Ring of Photon
Detectors



- **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 Pair of Back-to Back 511 keV Photons

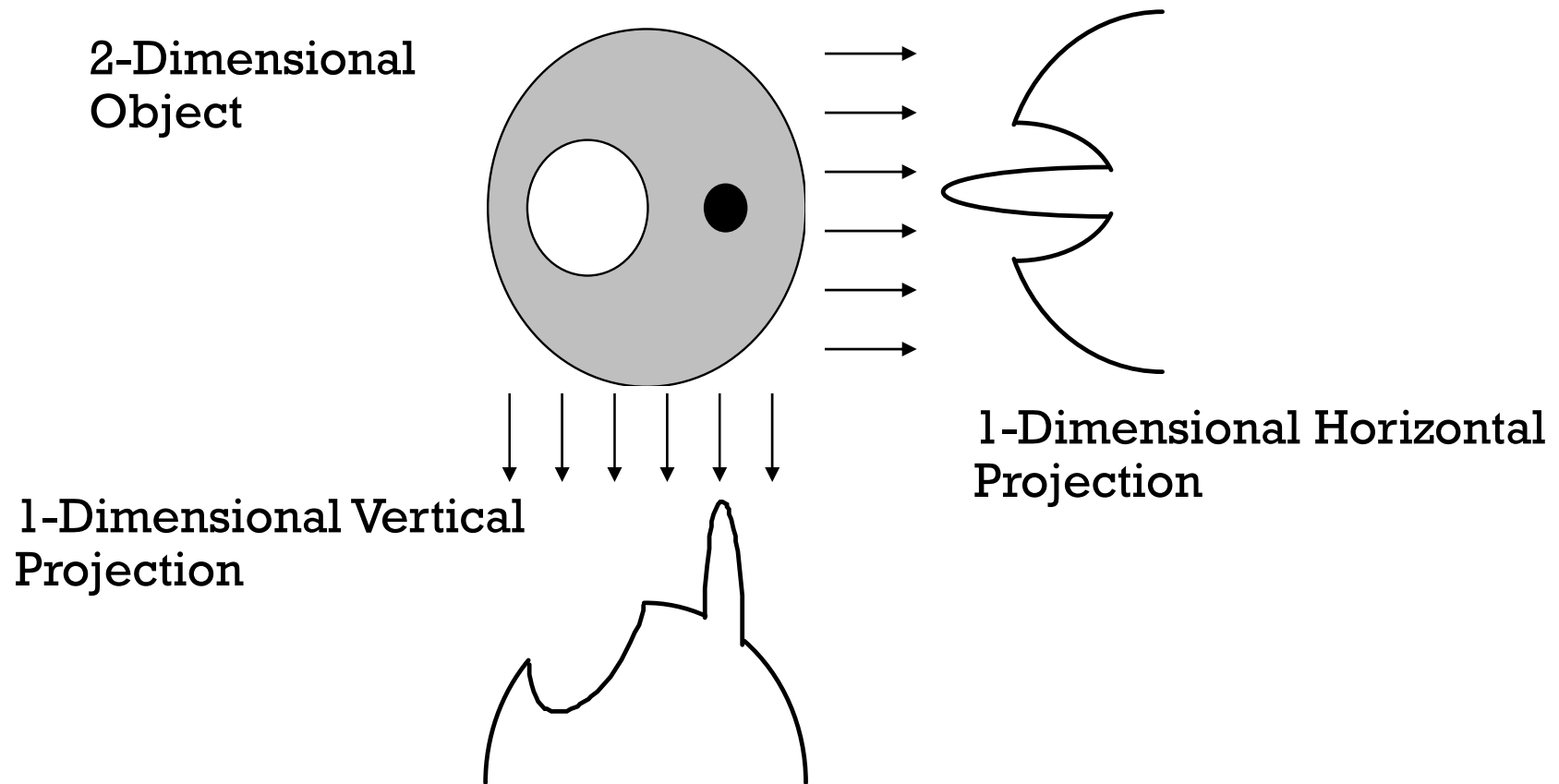
Multi-Layer PET Cameras



- 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

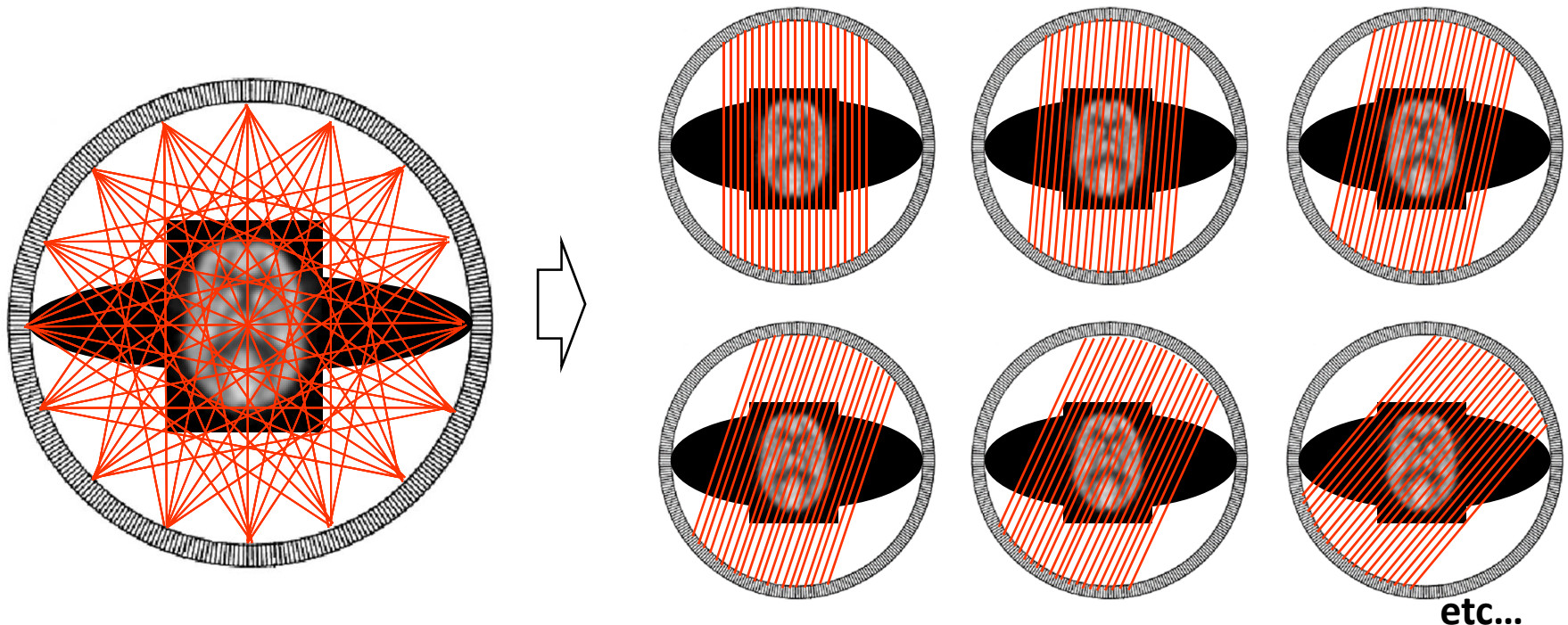
Principle of Computed Tomography



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

PET data acquisition

- Organization of data
 - True counts in LORs are accumulated
 - In some cases, groups of nearby LORs are grouped into one average LOR (“mashing”)
 - LORs are organized into projections

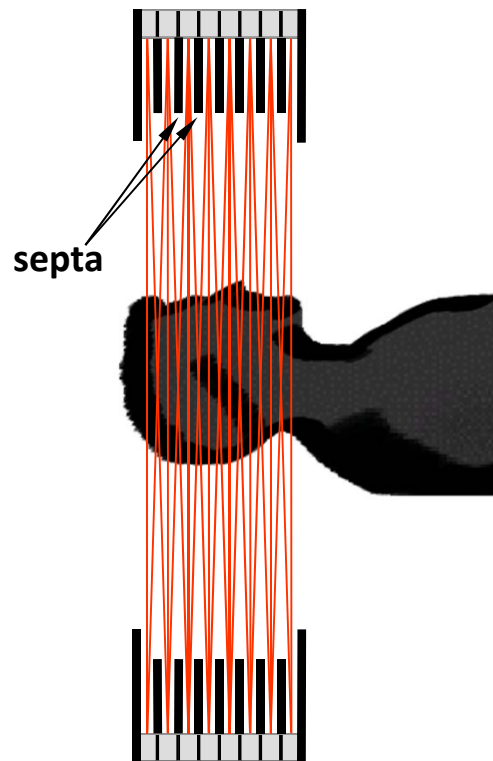


PET data acquisition

■ 2D and 3D acquisition modes

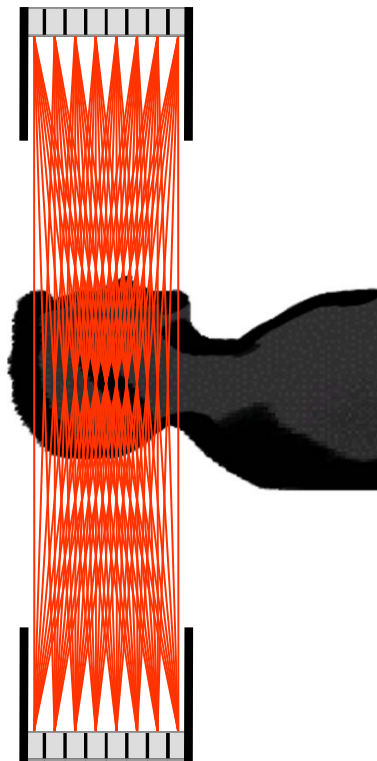
2D mode

(= with septa)



3D mode

(= no septa)



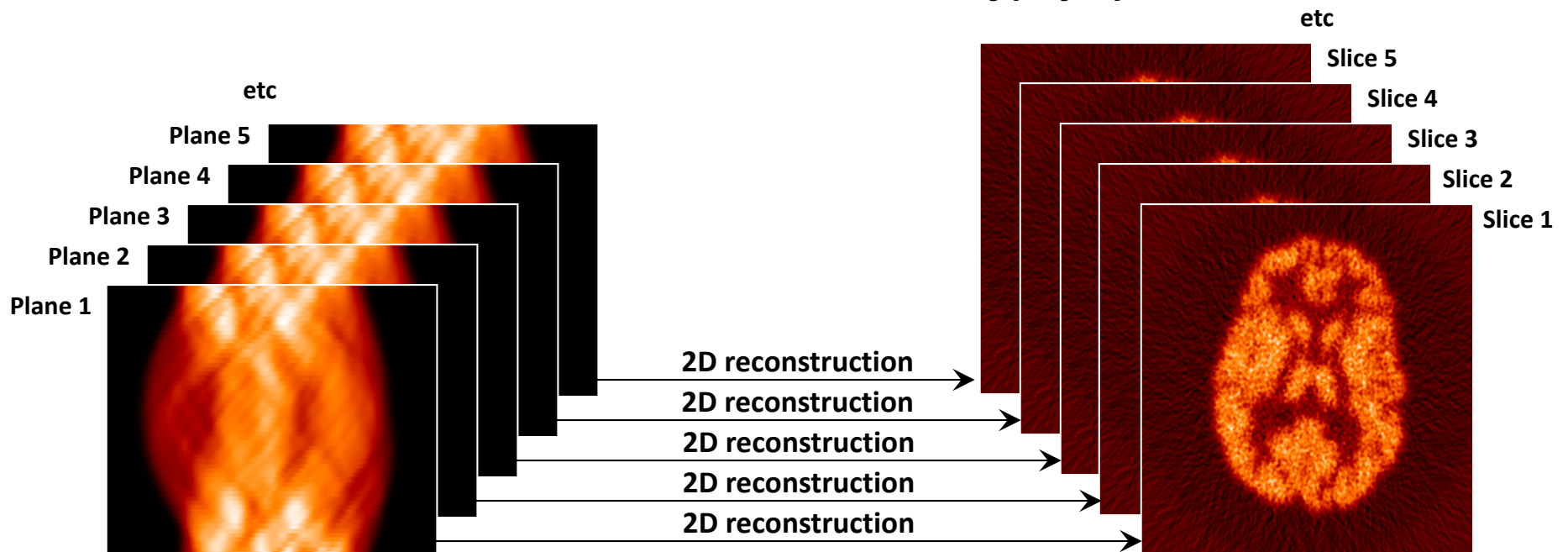
In the 3D mode there are no septa: photons from a larger number of incident angles are accepted, increasing the sensitivity.

Note that despite the name, the 2D mode provides three-dimensional reconstructed images (a collection of transaxial, sagittal and transaxial slices), just like the 3D mode!

PET image reconstruction

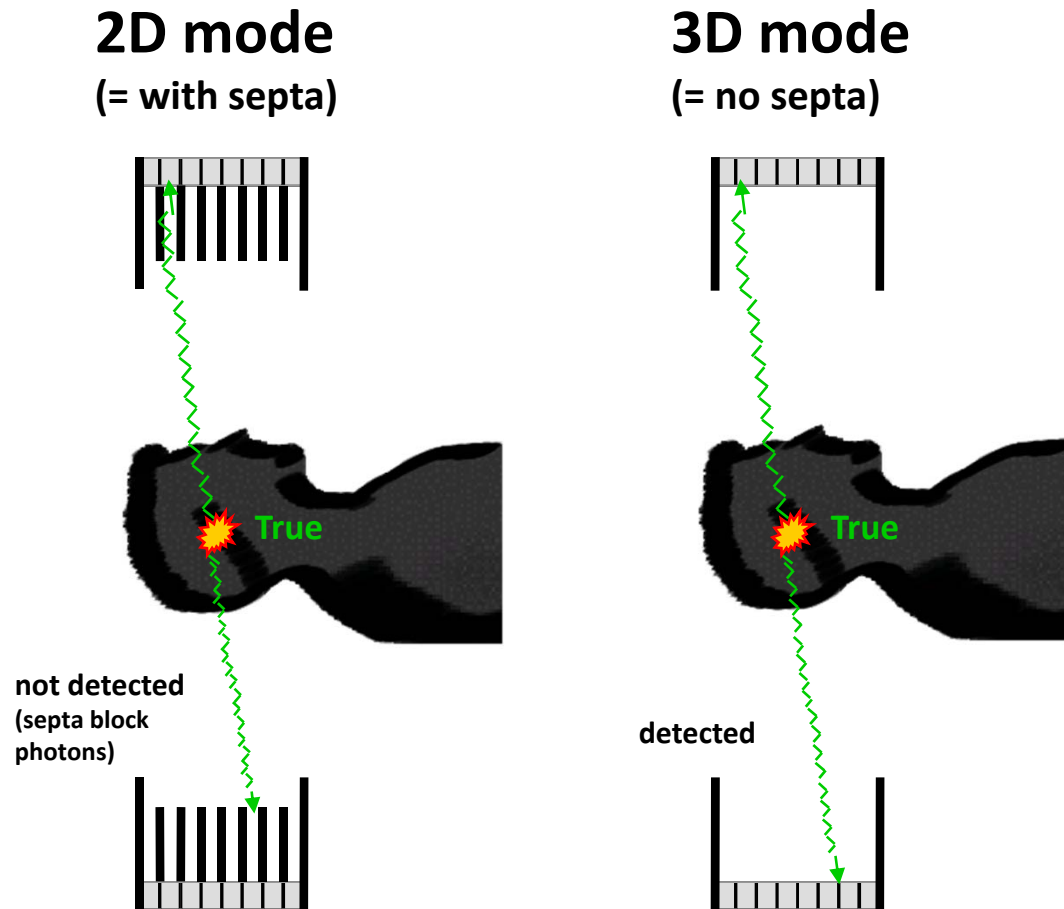
■ 2D Reconstruction

- Each parallel slice is reconstructed independently (a 2D sinogram originates a 2D slice)
- Slices are stacked to form a 3D volume $f(x,y,z)$



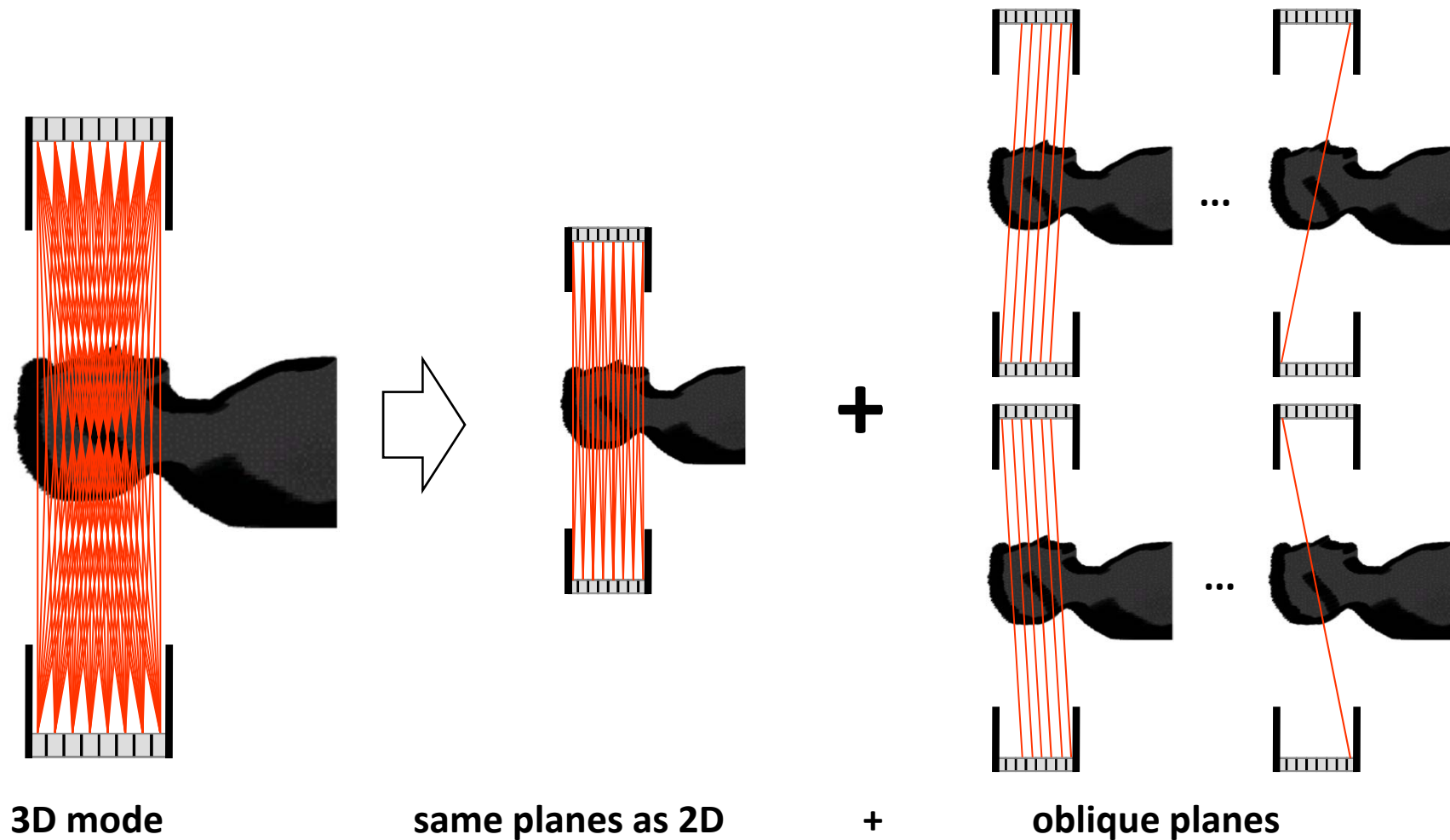
PET data acquisition

■ 2D mode vs. 3D mode



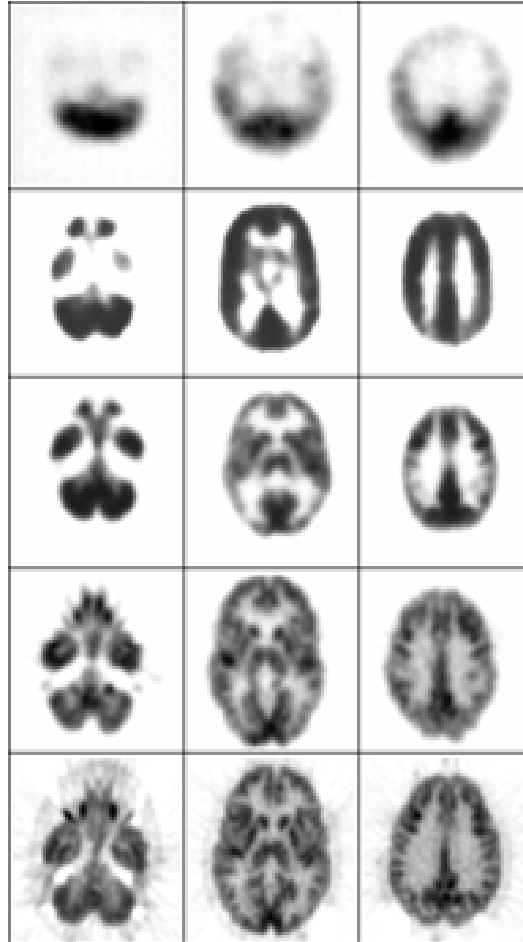
PET data acquisition

- Organization of data
 - In 3D, there are extra LORs relative to 2D



PET evolution: spatial resolution

Human brain



PET III
1975

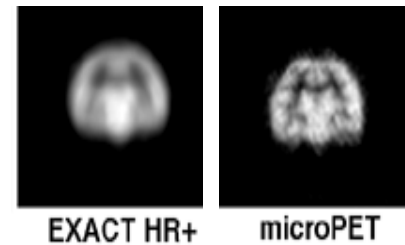
ECAT II
1977

NeuroECAT
1978

ECAT 931
1985

ECAT EXACT HR⁺
1995

Monkey brain



Animal PET
~1998

Image credits:
Crump Institute, UCLA

Image credits:
CTI PET Systems



PET Camera & Detector Design

- Typical Parameters
- Detector Module Design

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.

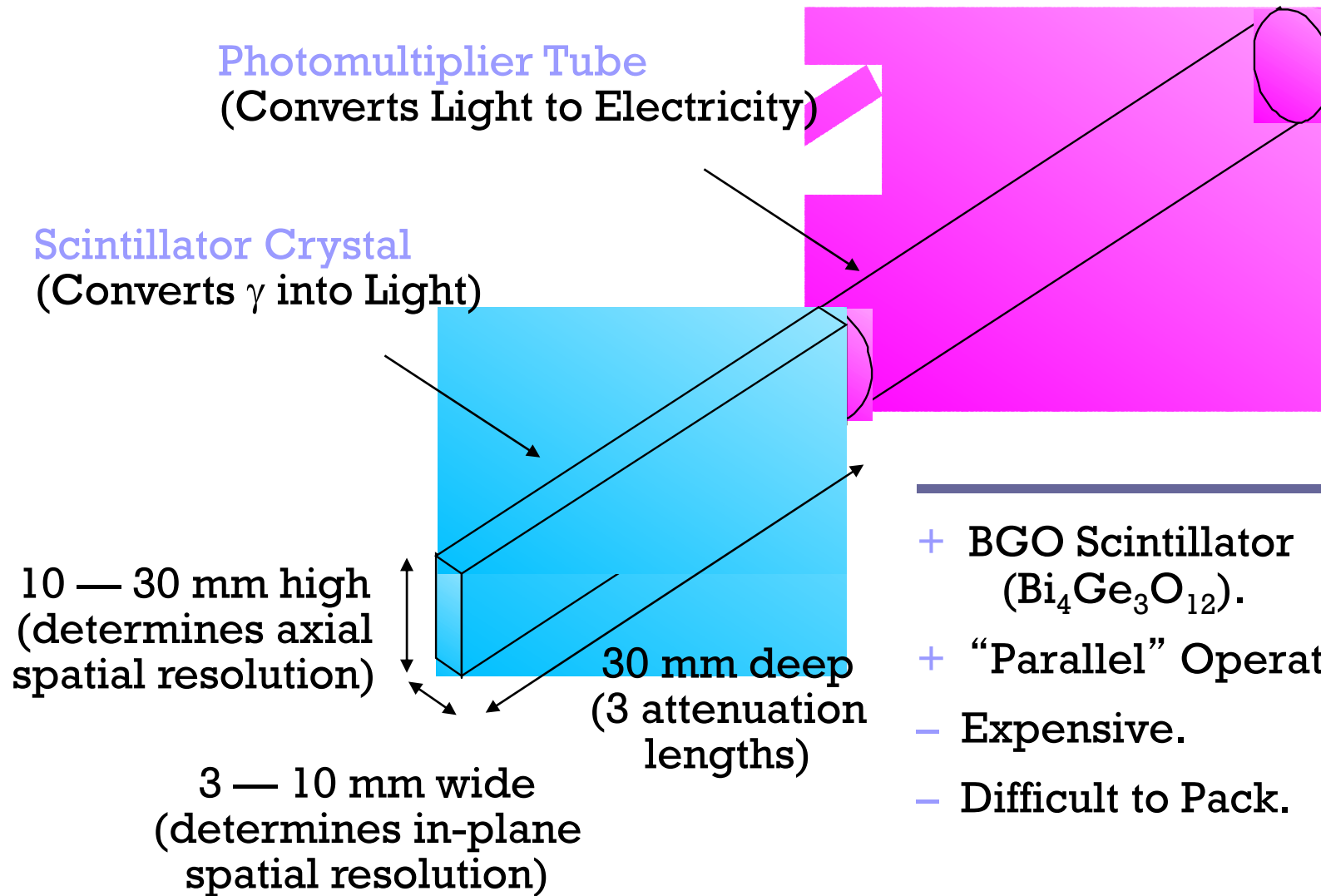
Images courtesy of GE Medical Systems and Siemens / CTI PET Systems



What Do We Need for PET Detector?

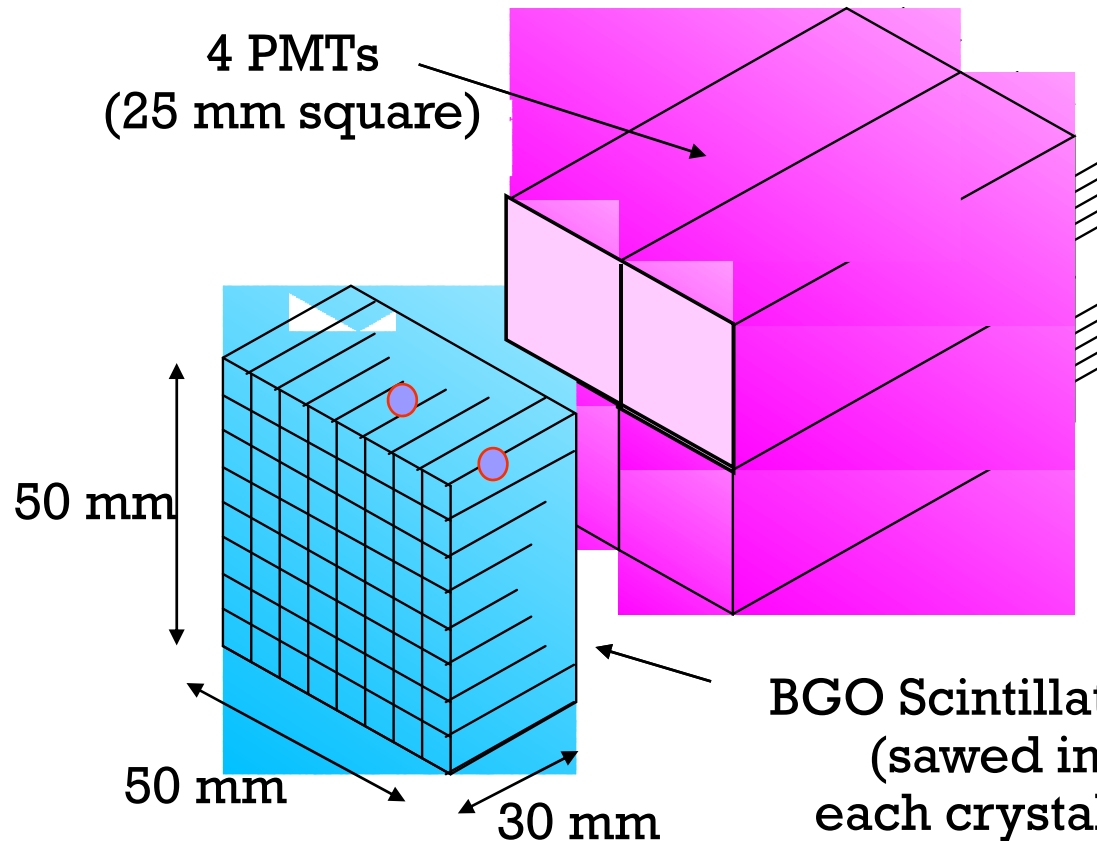
- Efficient – 511keV gamma rays are not easily stopped in detector.
- Excellent timing accuracy (typically a few ns) – for coincidence measurements.
- Capability of a very high counting rate (e.g. 0.5MC/s per cm²)
- High detector spatial resolution – for high imaging resolution.
- Cost-effective – very large detector volume is needed for practical PET systems.

Early PET Detector Module



- + BGO Scintillator ($\text{Bi}_4\text{Ge}_3\text{O}_{12}$).
- + “Parallel” Operation.
- Expensive.
- Difficult to Pack.

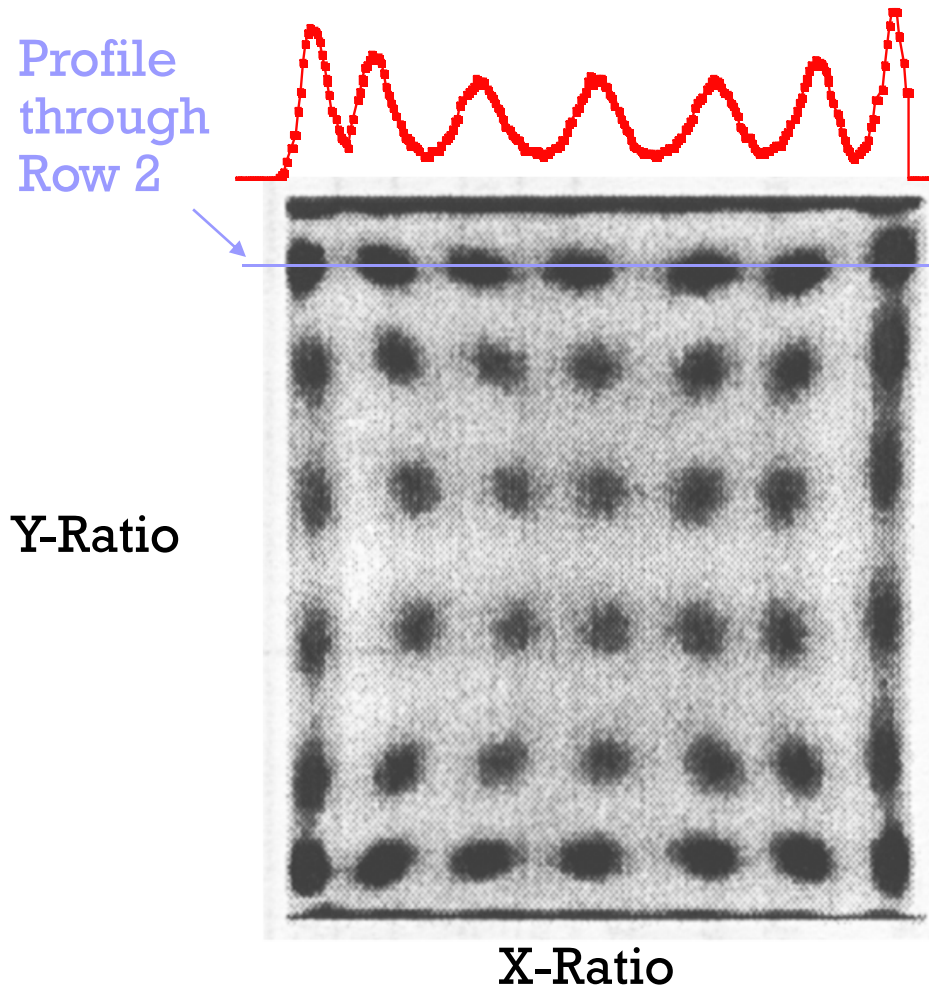
Block Design Using Anger Logic



- 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).

Good Performance, Less Expensive, Easy to Pack

Crystal Identification with Anger Logic



- Uniformly illuminate block.
- For each event, compute X-Ratio and Y-Ratio, then plot 2-D position.
- Individual crystals show up as dark regions.
- Profile shows overlap (i.e. identification not perfect).

Can Decode Up To 64 Crystals with BGO



Event Rates

Singles Events:

~3 ns timing accuracy

10^6 events / sec / module (25 cm^2)

200 modules $\Rightarrow 2 \times 10^8$ events / sec / camera

Coincidence Events:

Time window ~10 ns

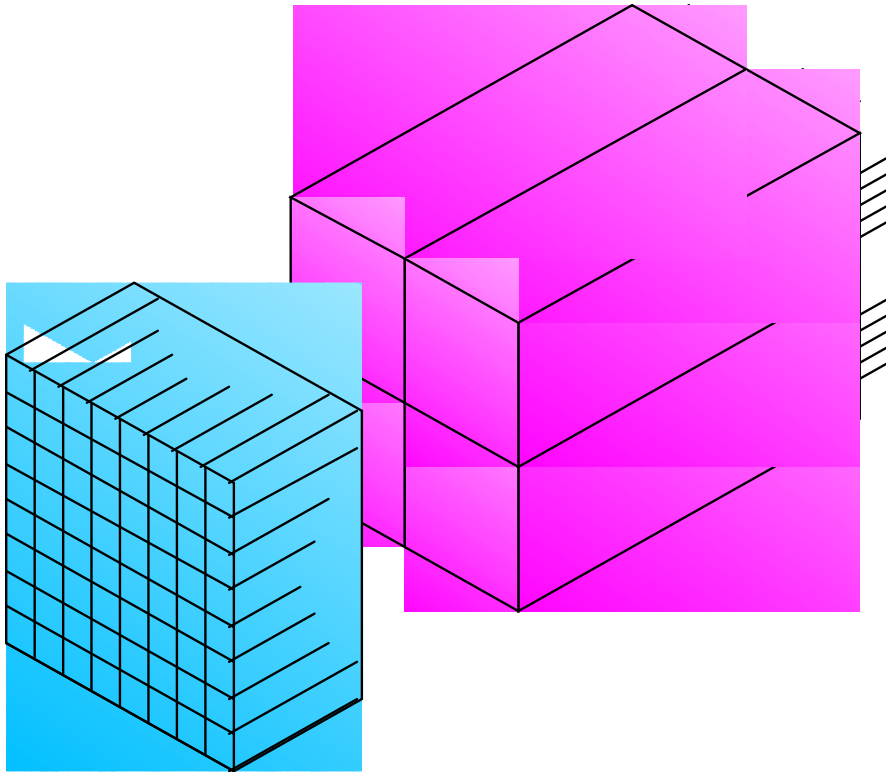
Lots of chords

(~280,000,000 in 48 layer camera with septa removed).

5×10^6 coincidence events / sec

Parallel Electronics is Necessary

Detector Requirements



Detect 511 keV Photons With
(in order of importance):

- >85% efficiency
- <5 mm spatial resolution
- “low” cost (<\$100 / cm²)
- “low” dead time (<1 μs cm²)
- <5 ns fwhm timing resolution
- <100 keV energy resolution

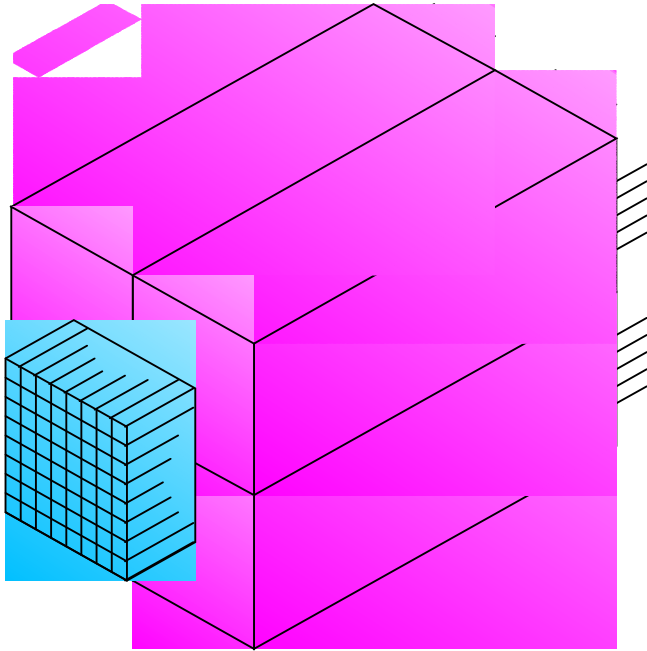
Based on Current PET Detector Modules



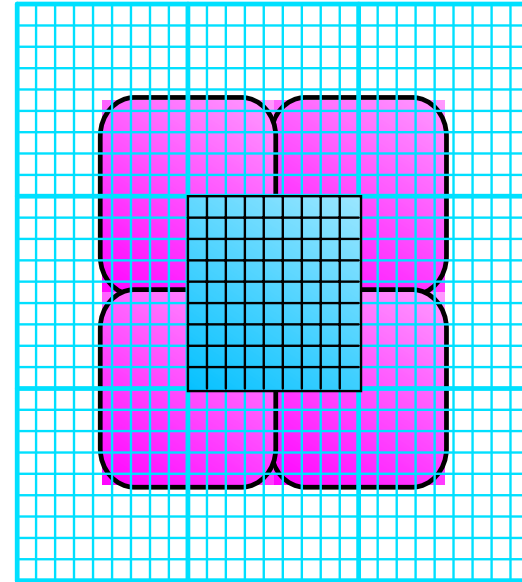
Variations (Present & Future)

- Quadrant Sharing
- Other Scintillators
- Partial Ring
- Animal PET
- Time of Flight
- PET / CT
- PET / SPECT

Quadrant Sharing



Perspective View



Front View

Each PMT Services 4 Crystal Blocks (Not 1)
(Number of PMTs = Number of Blocks)

- + Cost of PMTs Reduced 4x
- Dead Time Increased 9x

Scintillation Crystal Properties

TABLE 1 Properties of Common Scintillation Crystals Used in Small-FOV Imager Designs

Scintillator	Effective Z	Density (g/cc)	Radiation Length (mm) ^a	Relative Light Yield	Refractive Index	Decay Time (ns)	Peak Emission Wavelength (nm)	Hygroscopic?	Rugged?
NaI(Tl)	51	3.67	3.4	100	1.85	230	410	Yes	No
CsI(Tl)	54	4.51	2.2	135	1.79	1000	530	No	Yes
CsI(Na)	54	4.51	2.2	75	1.79	650	420	No	Yes
BGO	74.2	7.13	10.5	15	2.15	300	480	No	Yes
LSO(Ce)	65.5	7.4	11.6	75	1.82	40	420	No	Yes
CaF ₂ (Eu) ^b	16.9	3.17	N/A	50	1.43	940	435	No	Yes

^aRadiation lengths for NaI(Tl), CsI(Tl) and CsI(Na) are for 140-keV photons; Values for BGO and LSO are at 511 keV.

^bCaF₂(Eu) is used in beta imaging.

Lutetium Orthosilicate (LSO) Scintillator



Compared to BGO, LSO has:

Same Attenuation Length:

⇒ Good Spatial Resolution

Higher Light Output:

⇒ Decode More Crystals per Block

⇒ Better SNR for “Enhanced” Readout
(e.g. Depth of Interaction)

Shorter Decay Time:

⇒ Less Dead Time
(Allows Larger Block Areas)

⇒ Better Timing Resolution

Reduce Cost OR Increase Performance

Improvements In Scintillators Needed



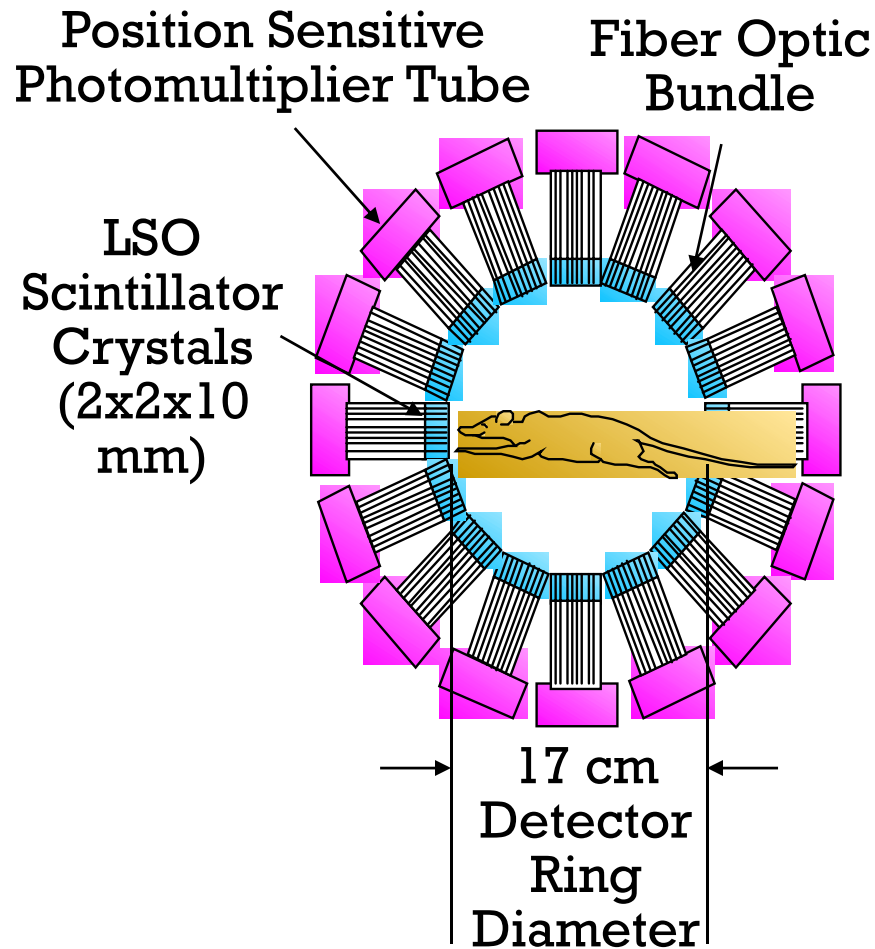
Image courtesy of Paul Lecoq, CERN

Combine Best Properties of:

- $\text{LaBr}_3:30\% \text{ Ce}$
 - Timing resolution $<100 \text{ ps}$
 - Energy resolution $<4\%$
- $\text{LuI}_3:\text{Ce}$
 - Light output $>100,000 \text{ ph/MeV}$
- PbWO_4
 - Density $>8 \text{ g/cc}$
 - High atomic number
 - Inexpensive

PET Performance Determined by Scintillator

Animal PET Camera

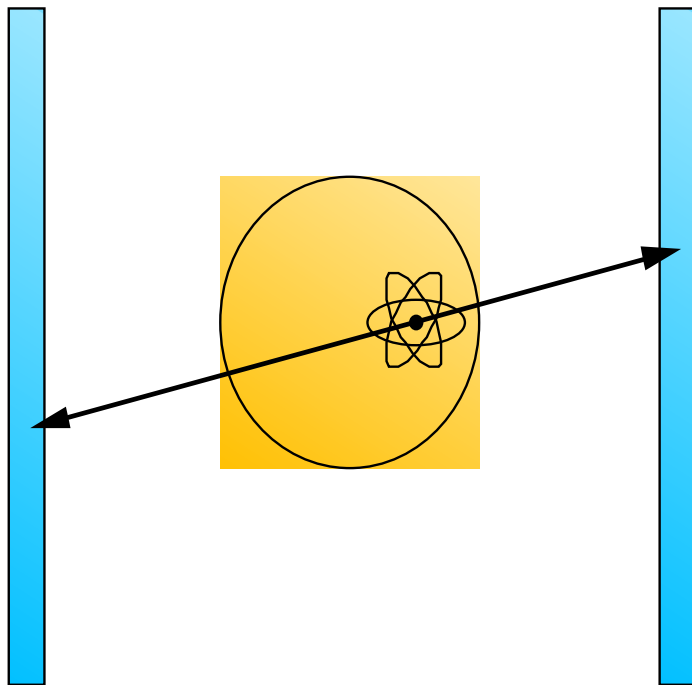


*Image courtesy of Simon Cherry, UC Davis

Miniature Version of "Standard" PET Camera

Dual Modality: PET / SPECT

Use SPECT Camera for PET)

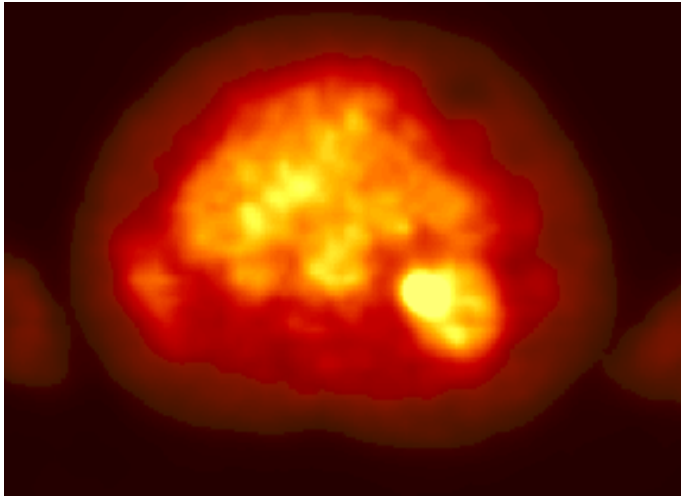


- **SPECT cameras optimized to image 140 keV (not 511 keV) photons.**
- **Detectors are “thin” (0.8 attenuation lengths) NaI:Tl.**
 - ☐ lower efficiency
 - ☐ higher scatter fraction
- **Large gaps in angular coverage**
 - ☐ rotate for complete sampling
 - ☐ lower solid angle coverage.
- **Detector area**
 - ☐ large dead time effects

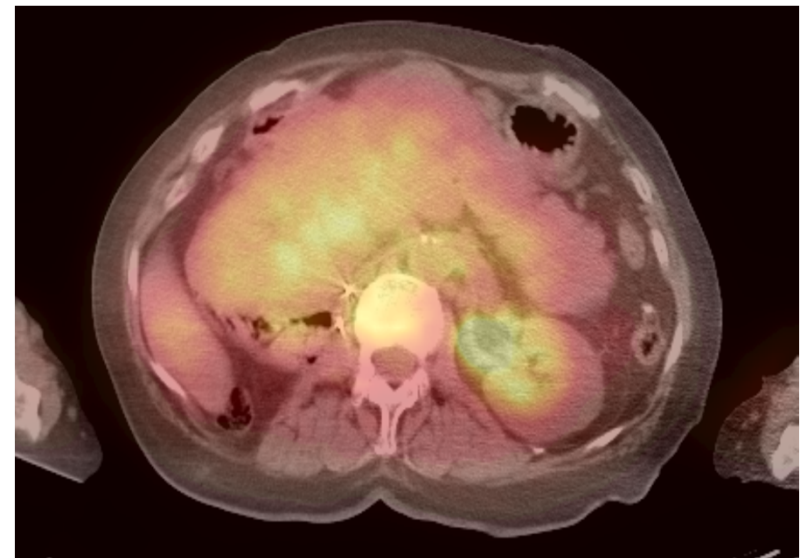
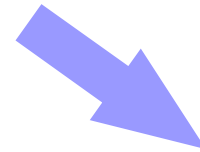
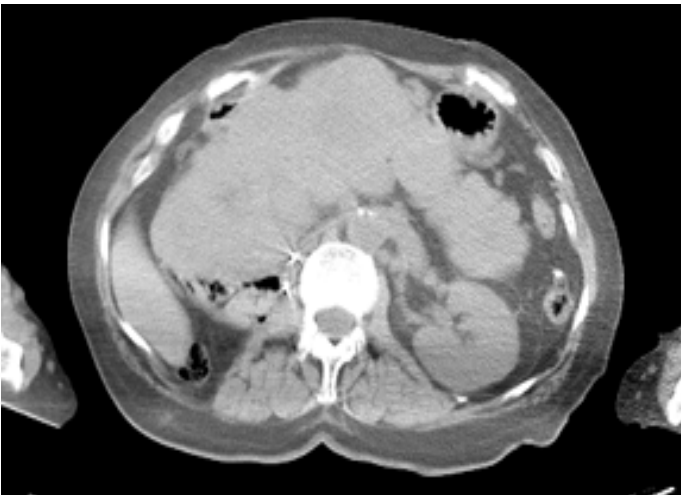
Less Expensive, But Not Optimized for PET

Dual Modality (PET / X-Ray CT)

PET



CT



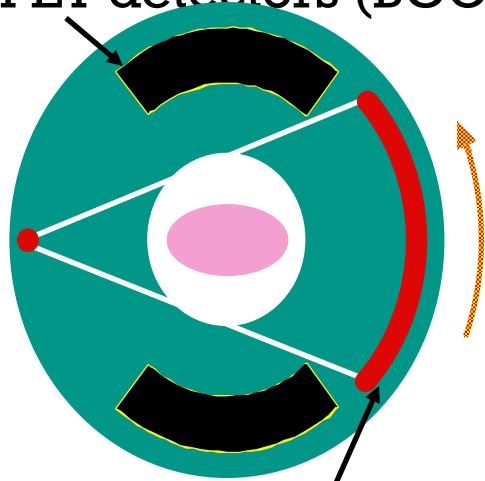
Fused PET + CT

***Data courtesy of David Townsend, U. Tenn.**

PET / X-Ray CT

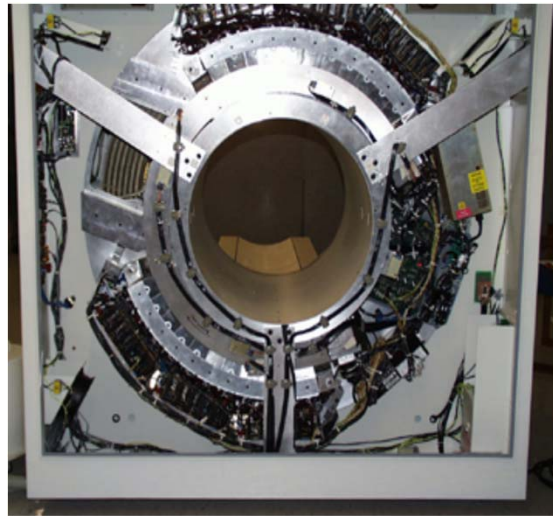
Artist's Conception

PET detectors (BGO)

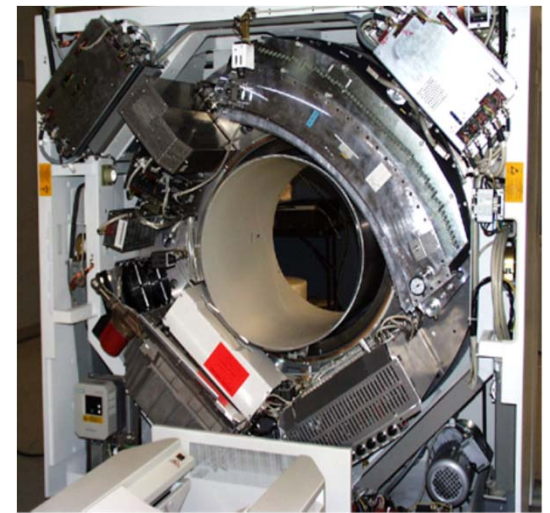


CT detectors (Xe)

Reality



ECAT ART



Somatom AR.SP

PET & CT Scanners Must Be Separated Axially
⇒ Cannot Image Same Slice Simultaneously!

*Data courtesy of David Townsend, U. Tenn.



“Standard” Performance Evaluation

NEMA Standards Publication NU 2-2001:
“Performance Measurements of Positron Emission
Tomographs”

- ☐ Spatial Resolution
- ☐ Scatter Fraction
- ☐ Sensitivity
- ☐ Count Losses & Randoms
- ☐ Uniformity
- ☐ Correction (Scatter, Count Rate, Attenuation)

<http://www.nema.org/>



Real World Effects Limiting the Performance of PET

- Photon Attenuation
- Random Coincidences
- Scatter
- Radial Elongation



Photon Attenuation

- Attenuation length of 511 keV photons in water (*i.e.* tissue) is 10 cm.
- Brain is 20 cm diameter.

⇒ up to $e^{-2} = 86\%$ of the events are lost.

- Loss fraction depends on position in patient.

⇒ Need to correct for attenuation.

PET: Impaired Image Quality in Larger Patients

Slim Patient



Large Patient

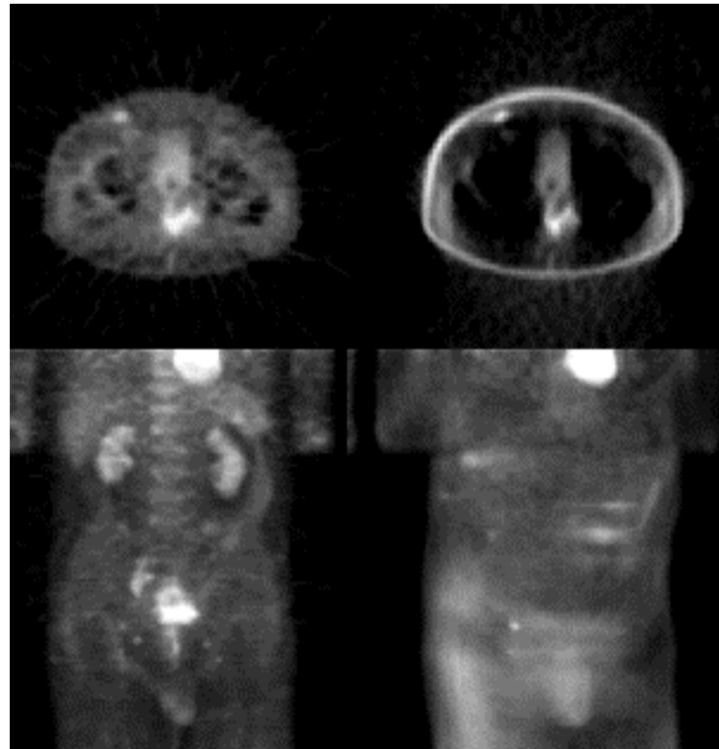


- For an equivalent data signal to noise ratio, a 120 kg person would have to be scanned 2.3 times longer than a 60 kg person ¹⁾

1) Optimizing Injected Dose in Clinical PET by Accurately Modeling the Counting-Rate Response Functions

Specific to Individual Patient Scans. Charles C. Watson, PhD et al Siemens Medical Solutions Molecular Imaging, Knoxville, Tennessee, JNM Vol. 46 No. 11, 1825-1834, 2005

Attenuation Correction $\Rightarrow$ Quantitation



Transverse

Volume
Rendered

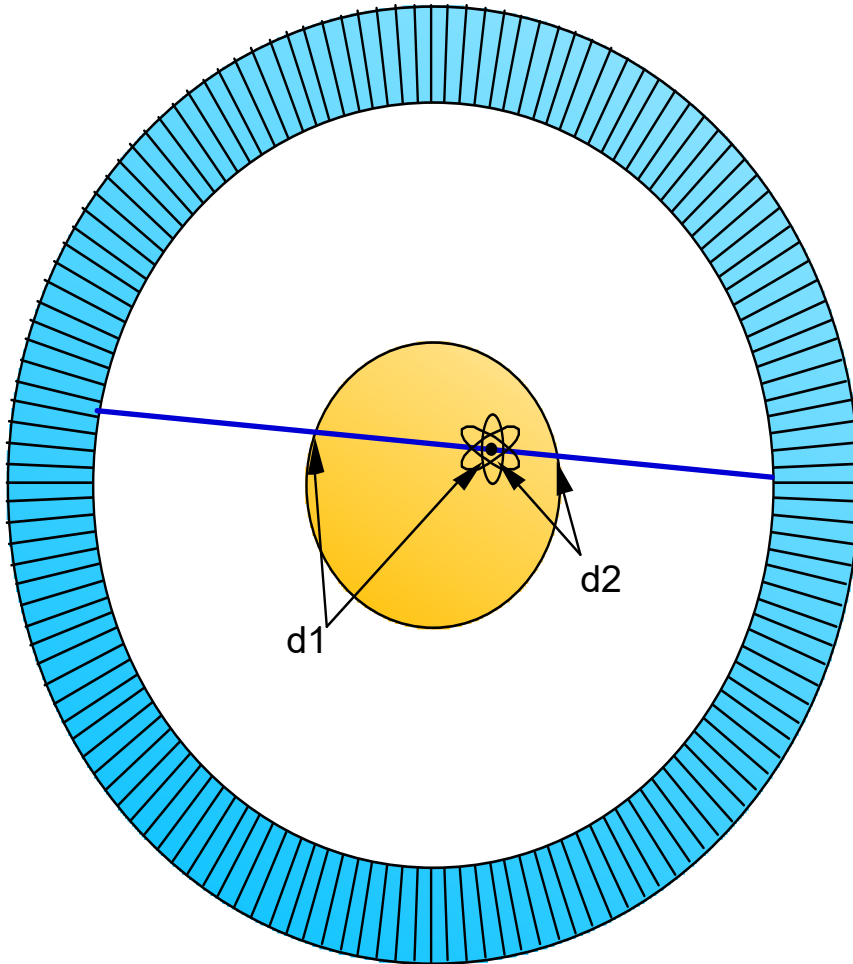
Corrected

Uncorrected

*Data courtesy of Duffy Cutler, Washington University

- | |
|--|
| <ul style="list-style-type: none">+ Accurate Quantitation ($\mu\text{Ci/cc}$) Possible- Doubles Image Acquisition Time |
|--|

Attenuation of Internal Source



$$P_1 = e^{-\mu \cdot d_1} \quad P_2 = e^{-\mu \cdot d_2}$$

$$P = e^{-\mu \cdot (d_1 + d_2)}$$

Event detection probability is product of individual photon detection probabilities.

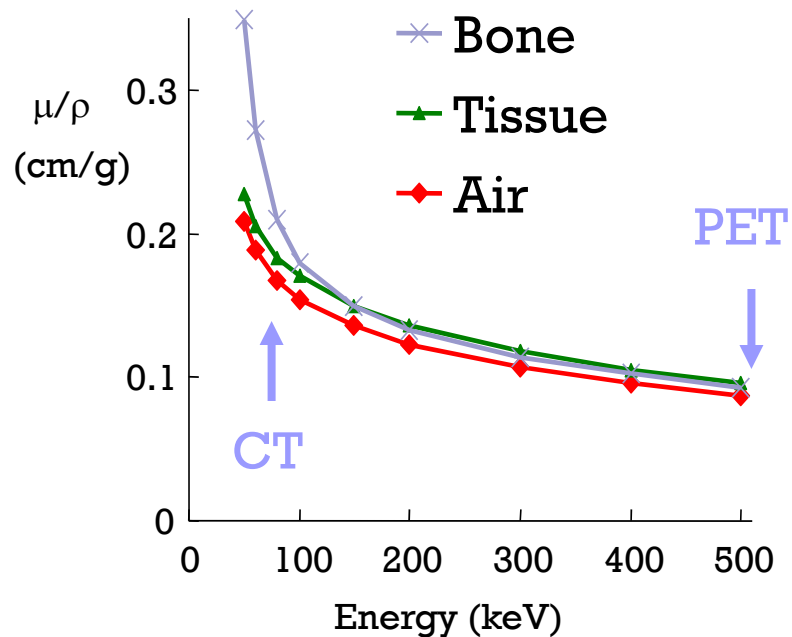
Transmission Scan Using an Isotopic Source



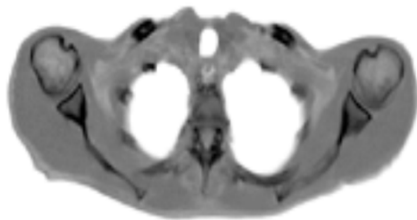
XBB 887-6863

- Can reconstruct an image of the attenuation.
- Essentially a 511 keV x-ray CT image.

Attenuation Correction w/ X-Ray CT



- Can use x-ray CT data to obtain attenuation data
 - Attenuation coefficients μ are energy dependent
- ⇒ μ at 70 keV (x-ray CT energy) not equal to μ at 511 keV
- “Scale” data — use CT to classify voxels as either air, tissue, or bone, then multiply by known ratio of μ_{511} / μ_{70} to do correction



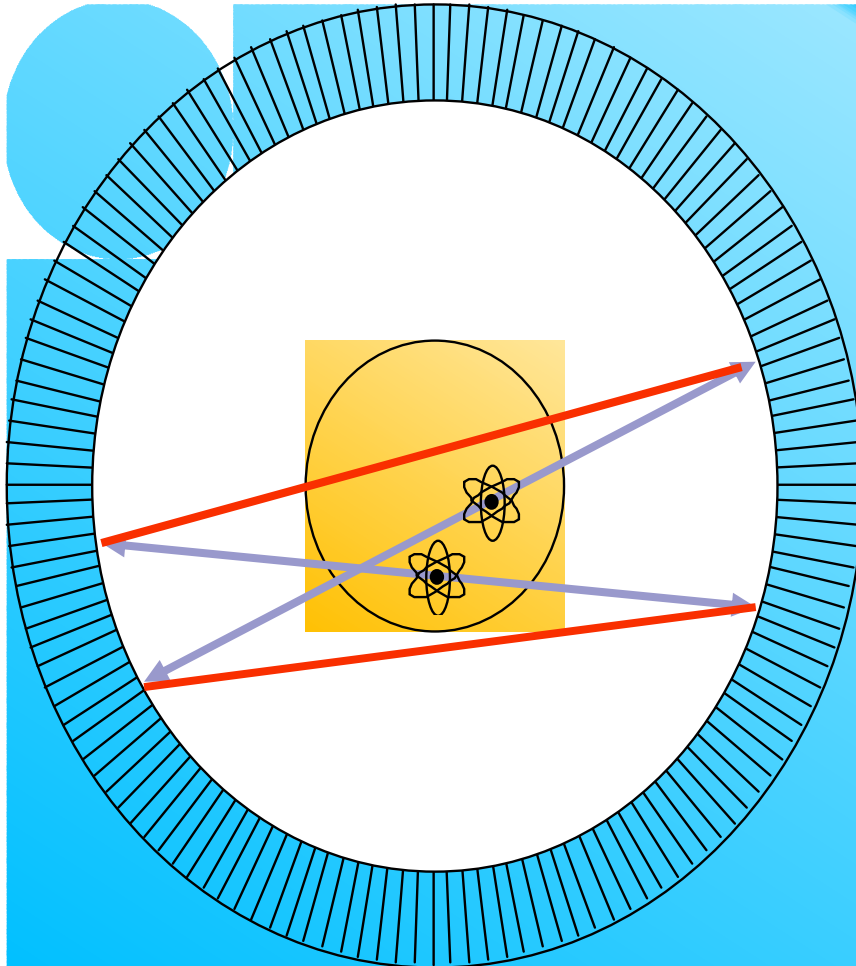
CT:
70 keV



Scaled:
511 keV

*Data courtesy of David Townsend, U. Tenn.

Random Coincidences



- Simultaneous decays can cause erroneous coincident events called Randoms.
- For 3-D PET, randoms can be as high as 50% of image.
- Random Rate is $\text{Rate}_1 \times \text{Rate}_2 \times 2 \Delta t$
- Randoms reduced by narrow coincidence window Δt .
- Time of flight across tomograph ring requires $\Delta t > 4 \text{ ns}$.

$$\text{Random Rate} \propto (\text{Activity Density})^2$$



What Is Actually Reconstructed?

3 Scans Taken:

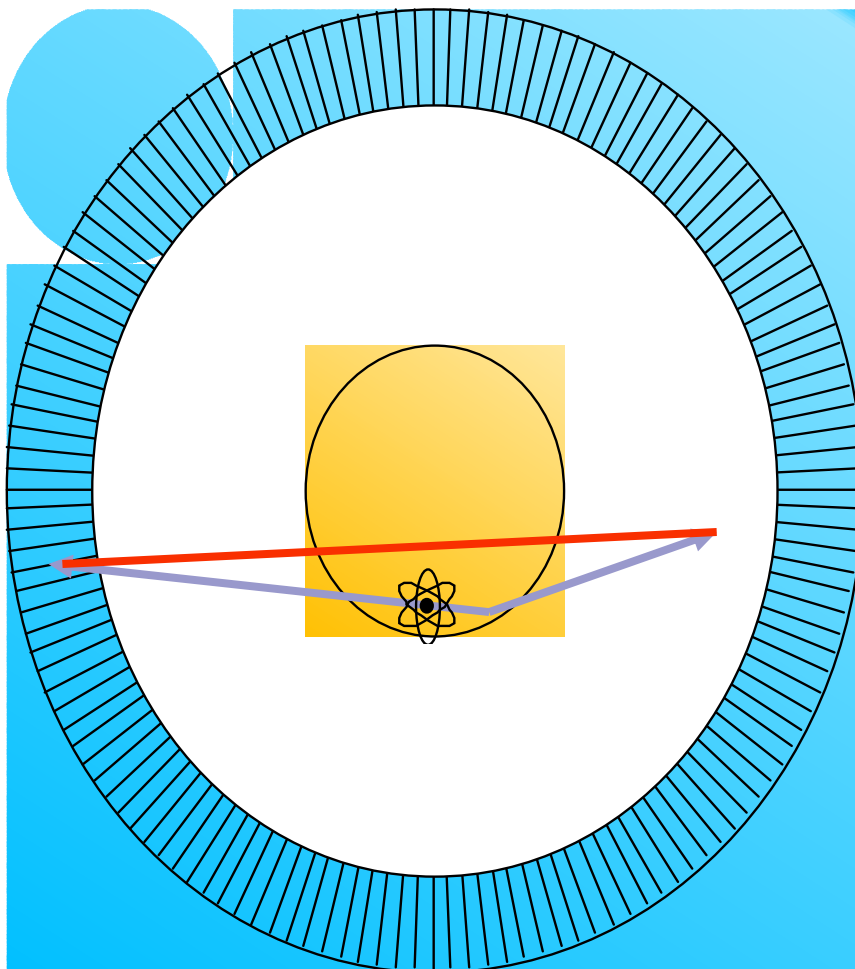
- Hoop (external source with nothing in ring).
- Transmission (external source with patient in ring).
- Emission (patient after isotope injected).

$$\text{Recon.} = (\text{Emission} - \text{Randoms}) / \text{Attenuation} / \text{Efficiency}$$

$$\text{Attenuation} = \text{Transmission} / \text{Hoop}$$

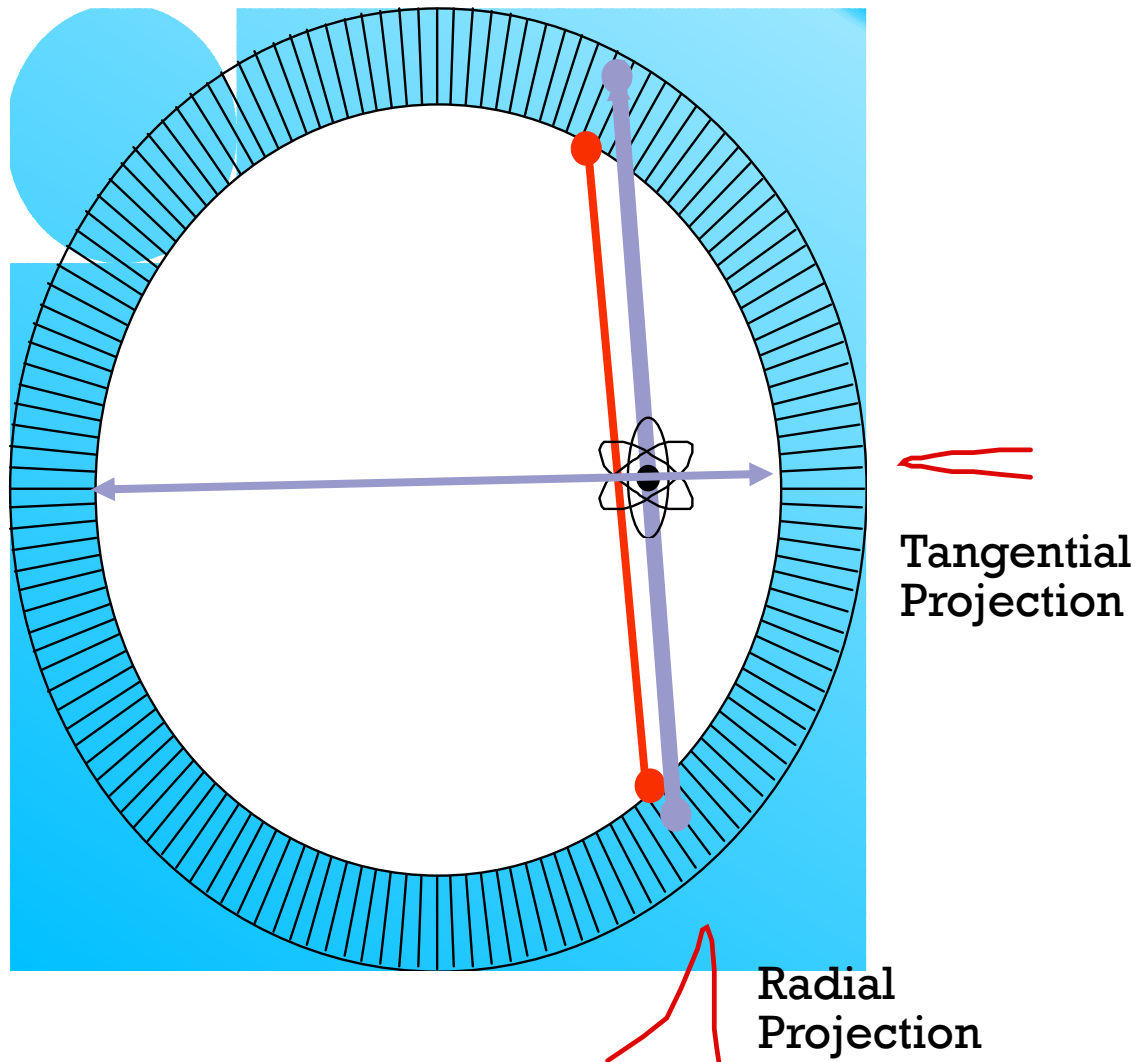
$$\text{Efficiency} = \text{Hoop} / \text{Hoop_Average}$$

Scattered Events



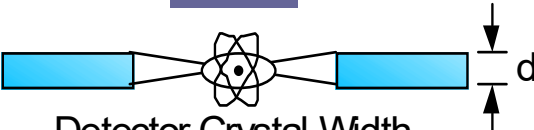
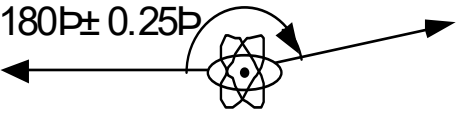
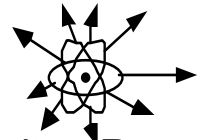
- Compton scatter in patient produces erroneous coincidence events.
- ~15% of events are scattered in 2-D PET (i.e. if tungsten septa used).
- ~50% of events are scattered in 3-D Whole Body PET.
- ~30% of events are scattered in 3-D Brain PET.

Radial Elongation



- Penetration of 511 keV photons into crystal ring blurs measured position.
- Blurring worsens as attenuation length increases.
- Effect variously known as Radial Elongation, Parallax Error, or Radial Astigmatism.
- Can be removed (in theory) by measuring depth of interaction.

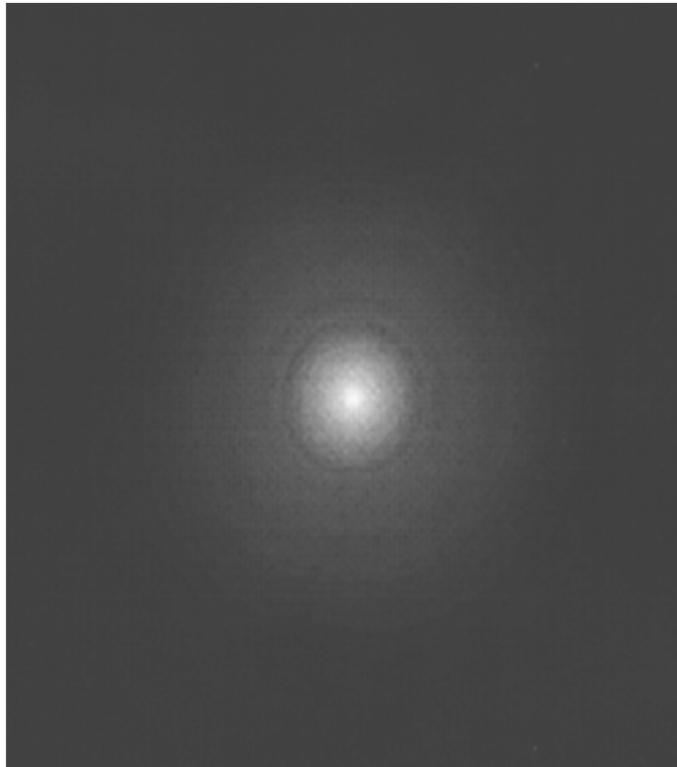
Spatial Resolution

Factor	Shape	FWHM
 Detector Crystal Width		$d/2$
 Anger Logic		0 (individual coupling) 2.2 mm (Anger logic)* *empirically determined from published data
 Photon Noncollinearity		1.3 mm (head) 2.1 mm (heart)
 Positron Range		0.5 mm (^{18}F) 4.5 mm (^{82}Rb)
Reconstruction Algorithm	multiplicative factor	1.25 (in-plane) 1.0 (axial)

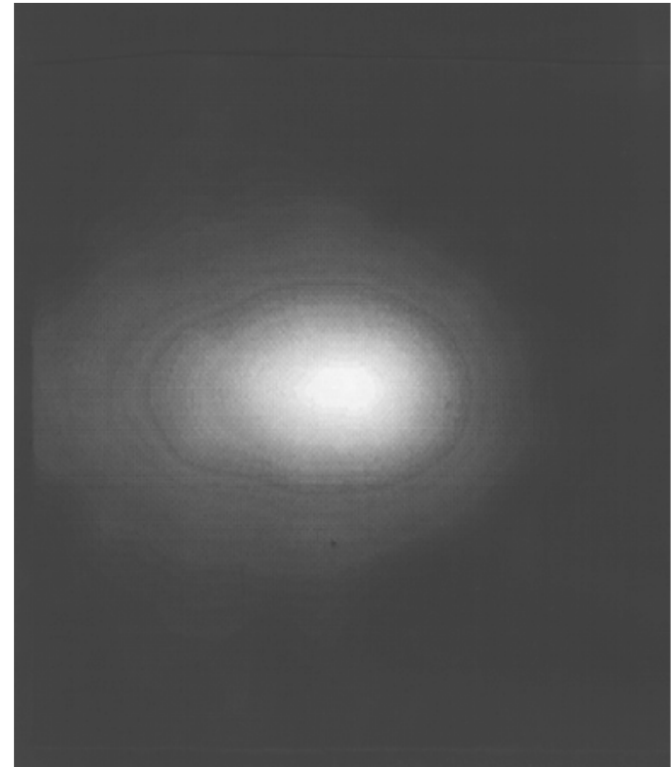
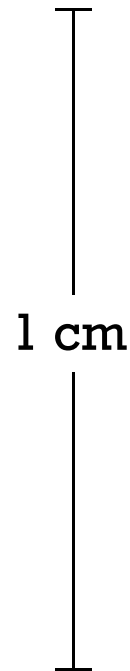
- Dominant Factor is Crystal Width
- Limit for 80 cm Ring w/ Block Detectors is 3.6 mm

Spatial Resolution Away From Center

Point Source Images in 60 cm Ring Diameter Camera



Near Tomograph Center

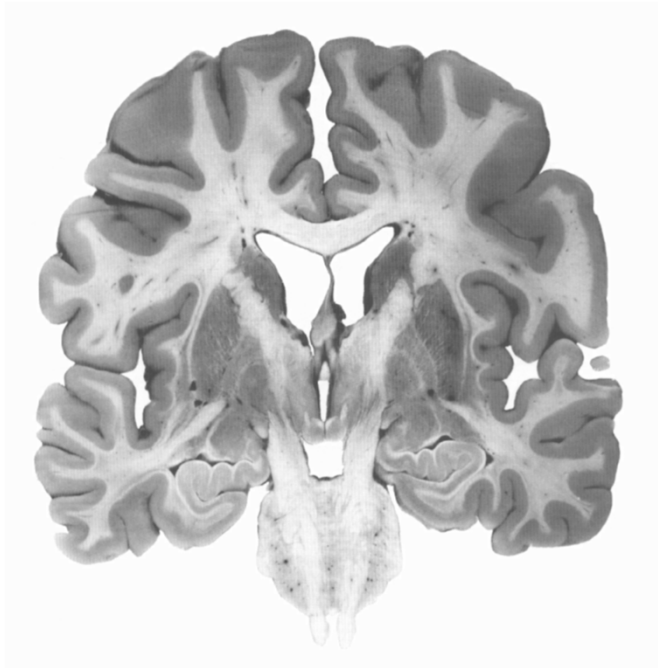


14 cm from Tomograph Center

Resolution Degrades Significantly...

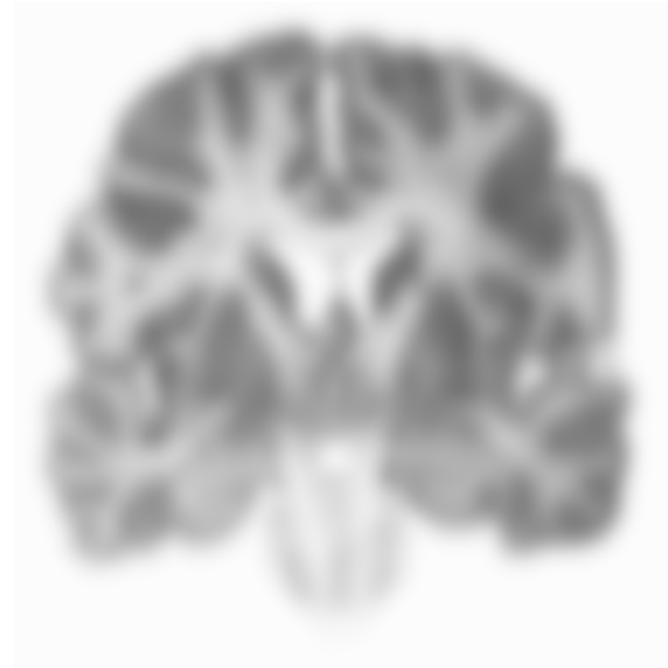
Loss in Spatial Resolution

Underlying Distribution



Gray / White Ratio = 4:1

Measured Distribution



Gray / White Ratio = 2.5:1

Controlled Charge Collection

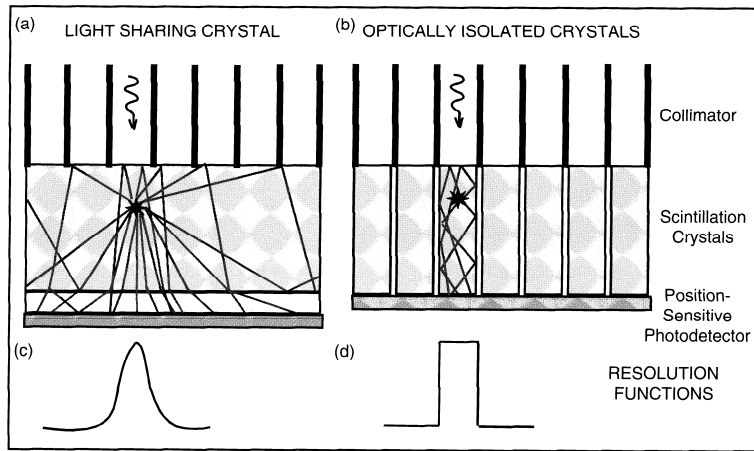
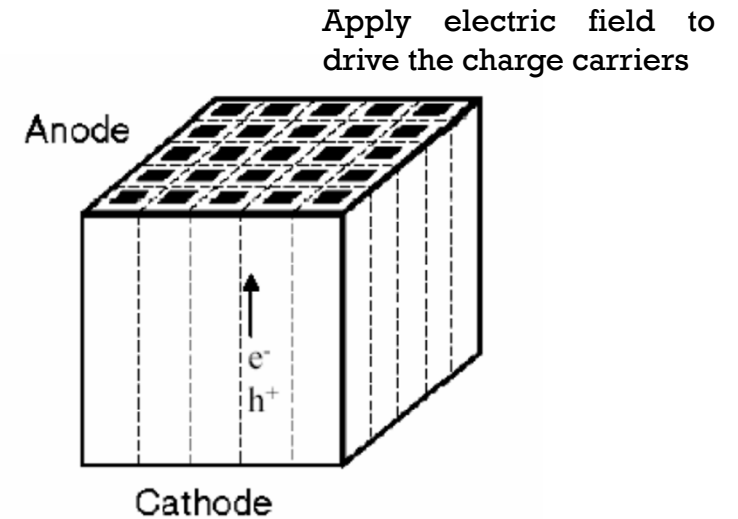


FIGURE 6 Schematic drawings of the light ray propagation for typical (a) single and (b) multiple scintillation crystal camera designs. For the pixellated design, scintillation light is confined to one crystal and focused on one spot of the photodetecting array. (c,d) Approximate shapes of the resulting theoretical intrinsic point spread functions for single-photon imaging.

Collection of visible photons in scintillator

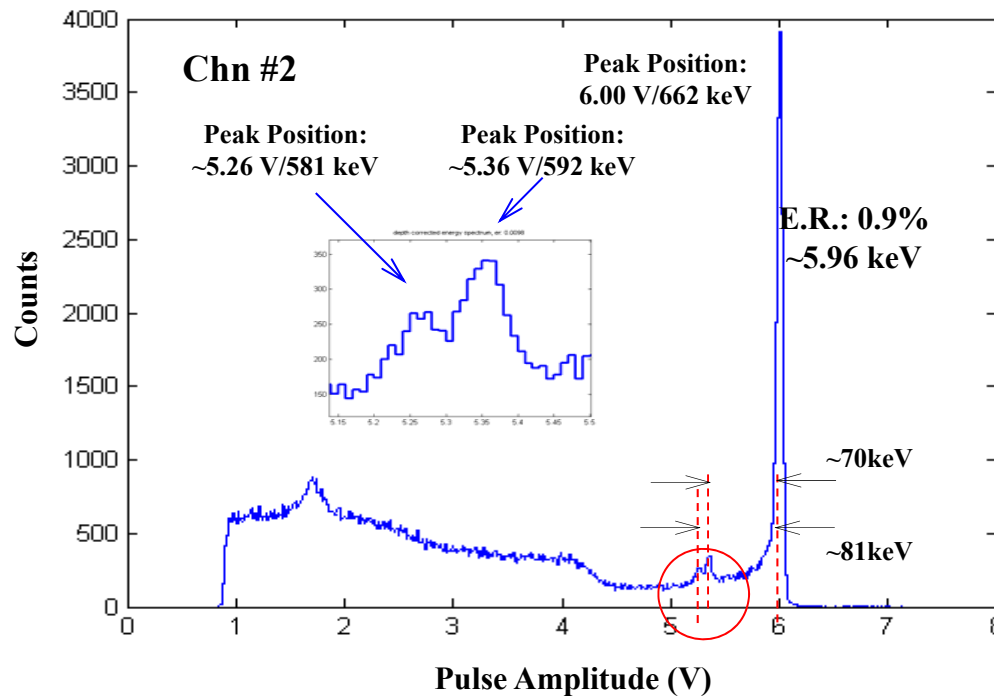


Collection of charge carriers in semiconductor

In semiconductor, electron and holes are driven by electric field.

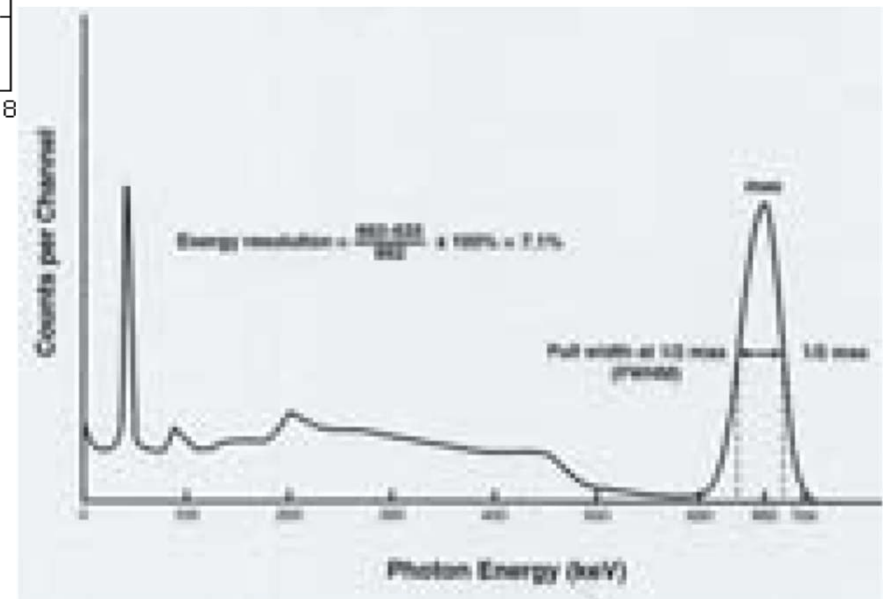
Spatial spreading of the charge carriers can be better controlled, so that a better spatial resolution can be achieved.

A Typical Measured Energy Spectrum



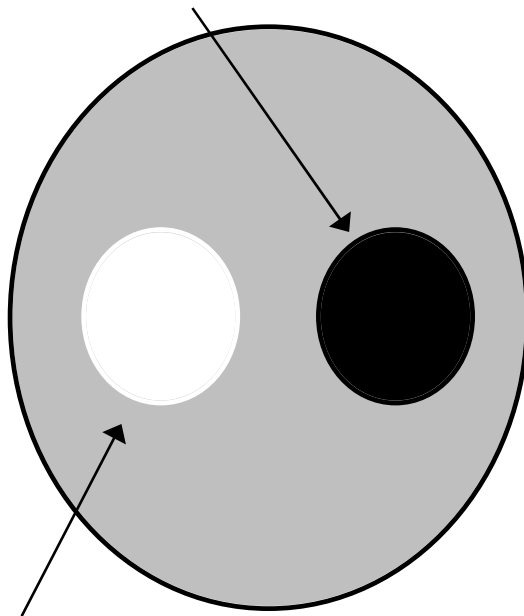
Measured energy spectrum from HgI_2 semiconductor, 1mm thick, $1 \times 1 \text{ mm}^2$ pixels

Typical energy spectrum from a 3 inch NaI(Tl) scintillation counter

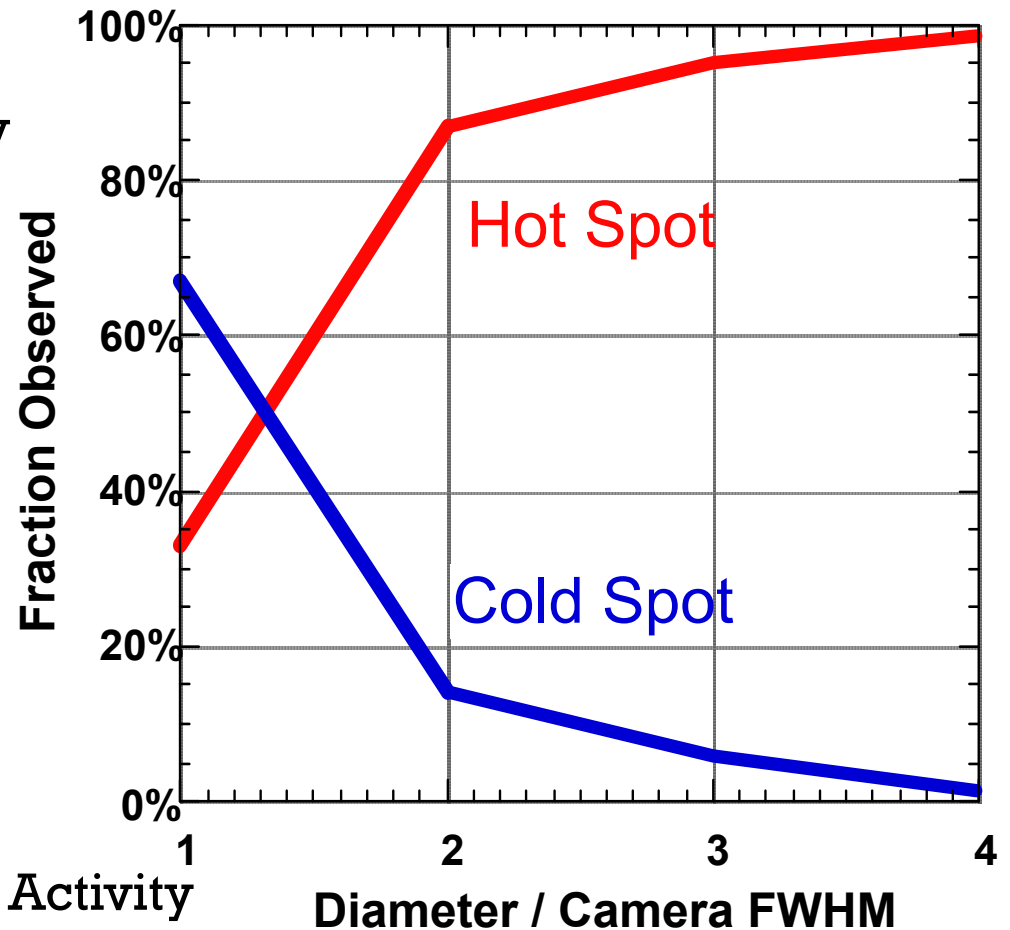


Accurate Quantitation $\Rightarrow$ Large Regions

Hot Spot Fraction =
Activity Measured / True Activity

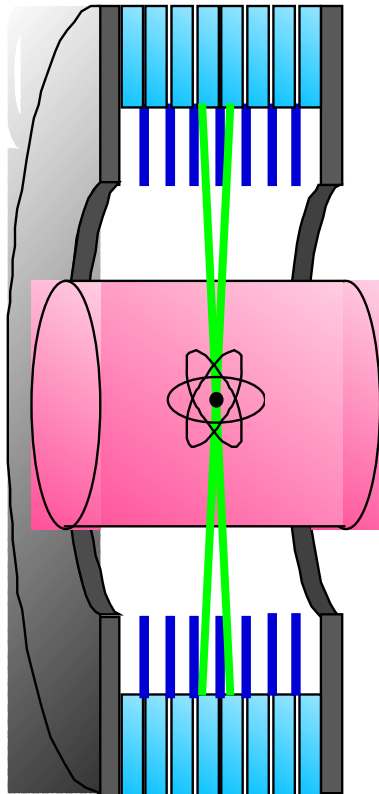


Cold Spot Fraction =
Activity Measured / Background Activity



Object Must Be 2x–4x Larger Than Scanner FWHM

Low Image Noise $\Rightarrow$ High Sensitivity

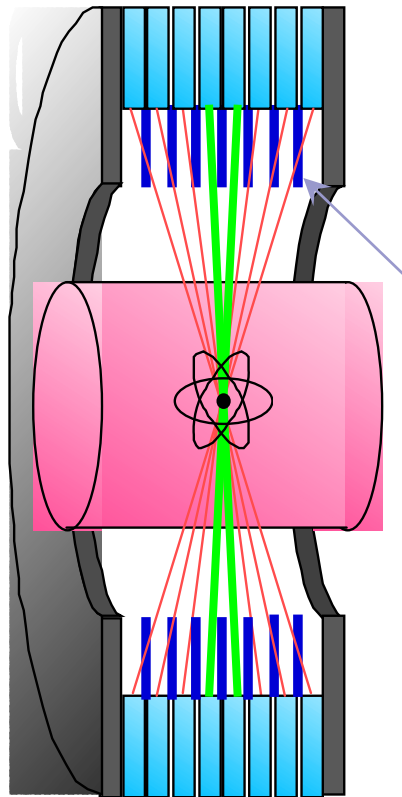


Sensitivity Definition:

- Place 20 cm diameter phantom in camera.
- Measure True Event Rate.
- Sensitivity =
True Event Rate / μCi / cc.

- Sensitivity Measures Efficiency for Detecting Signal
 - Increased Axial Extent Increases Sensitivity

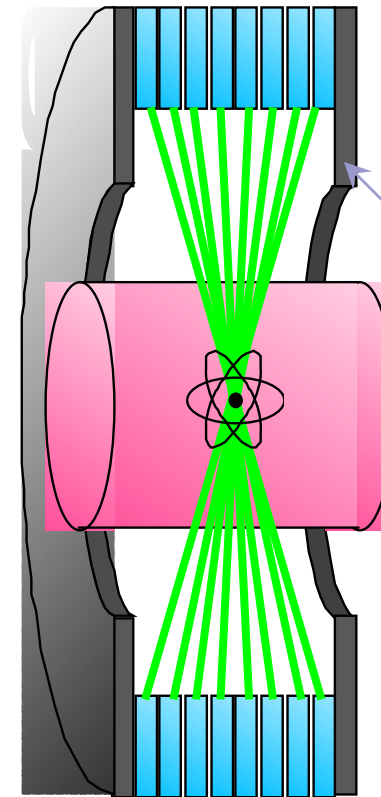
Increase Sensitivity by Removing Septa



Inter-Plane
Septa

2-D (w/ Septa)

- + Septa Reduce Scatter
- Smaller Solid Angle for Trues

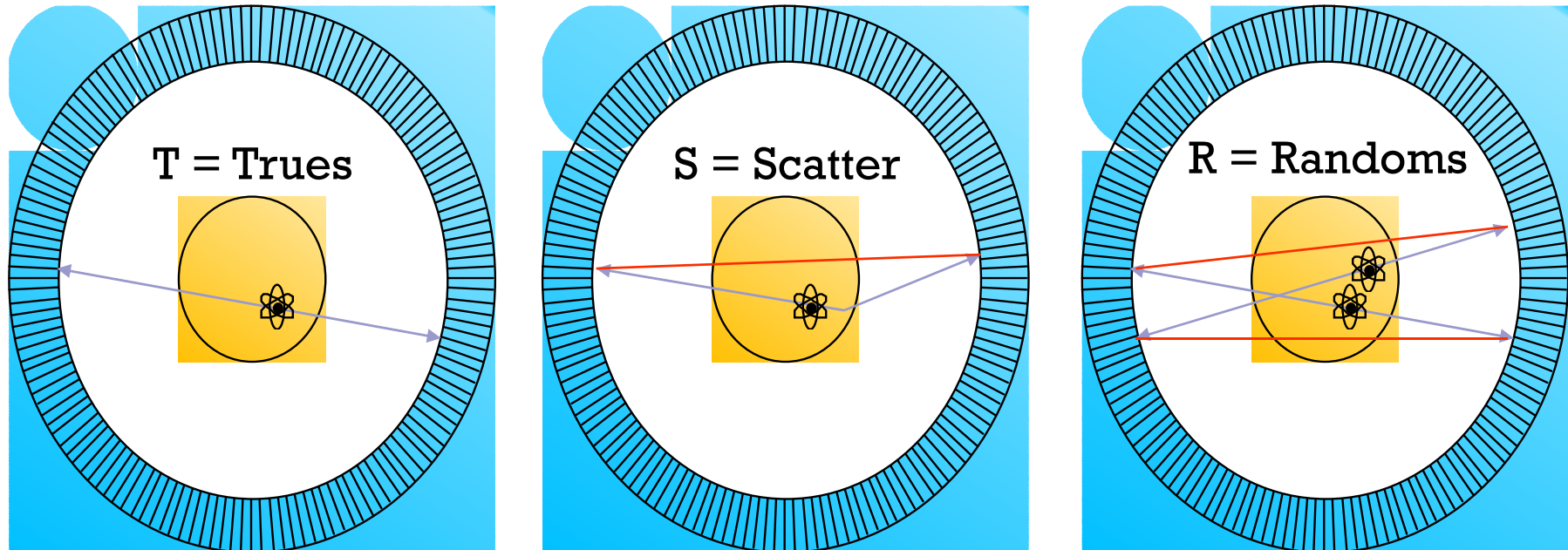


No
Septa

3-D (w/o Septa)

- No Scatter Suppression
- + Larger Solid Angle for Trues

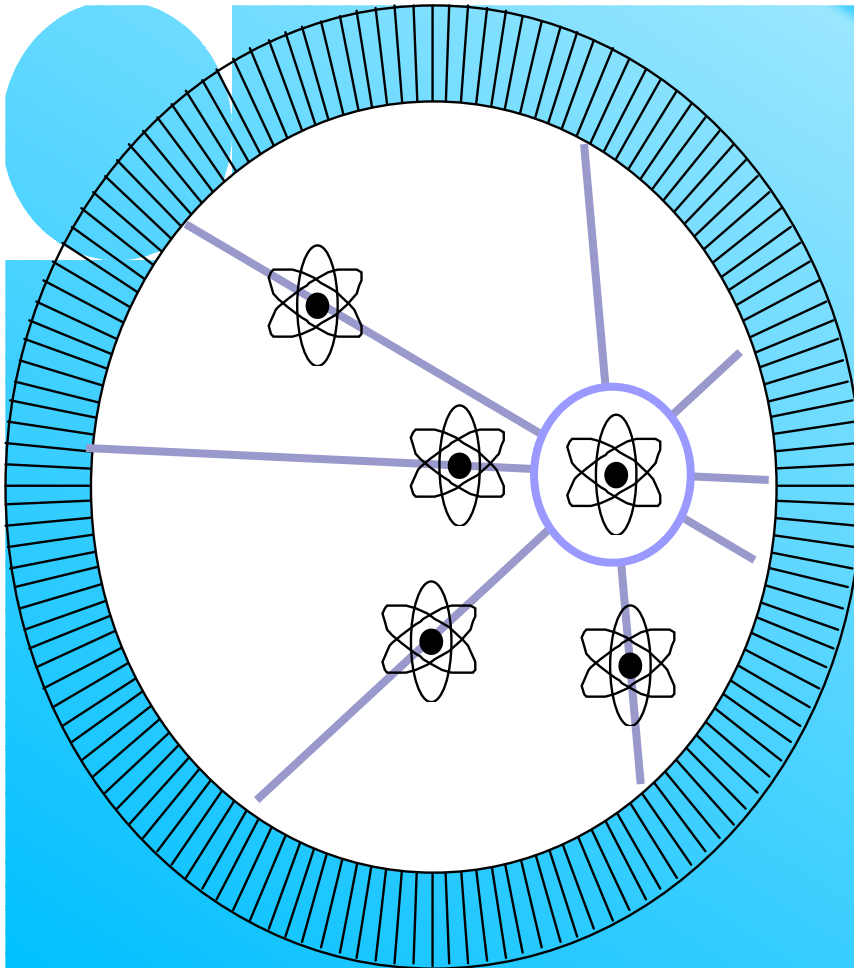
Sensitivity Includes Noise from Background



Even when you do background subtraction,
statistical noise from the background remains.

Image Noise Not Determined by Sensitivity Alone!

Statistical Noise in PET



If there are N counts in the image,

$$\text{SNR} = \frac{N}{\sqrt{N}}$$

Signals from Different Voxels are Coupled
⇒ Statistical Noise Does Not Obey Counting Statistics



Noise Equivalent Count Rate (NECR)

$$NECR = \frac{T^2}{T + S + R}$$

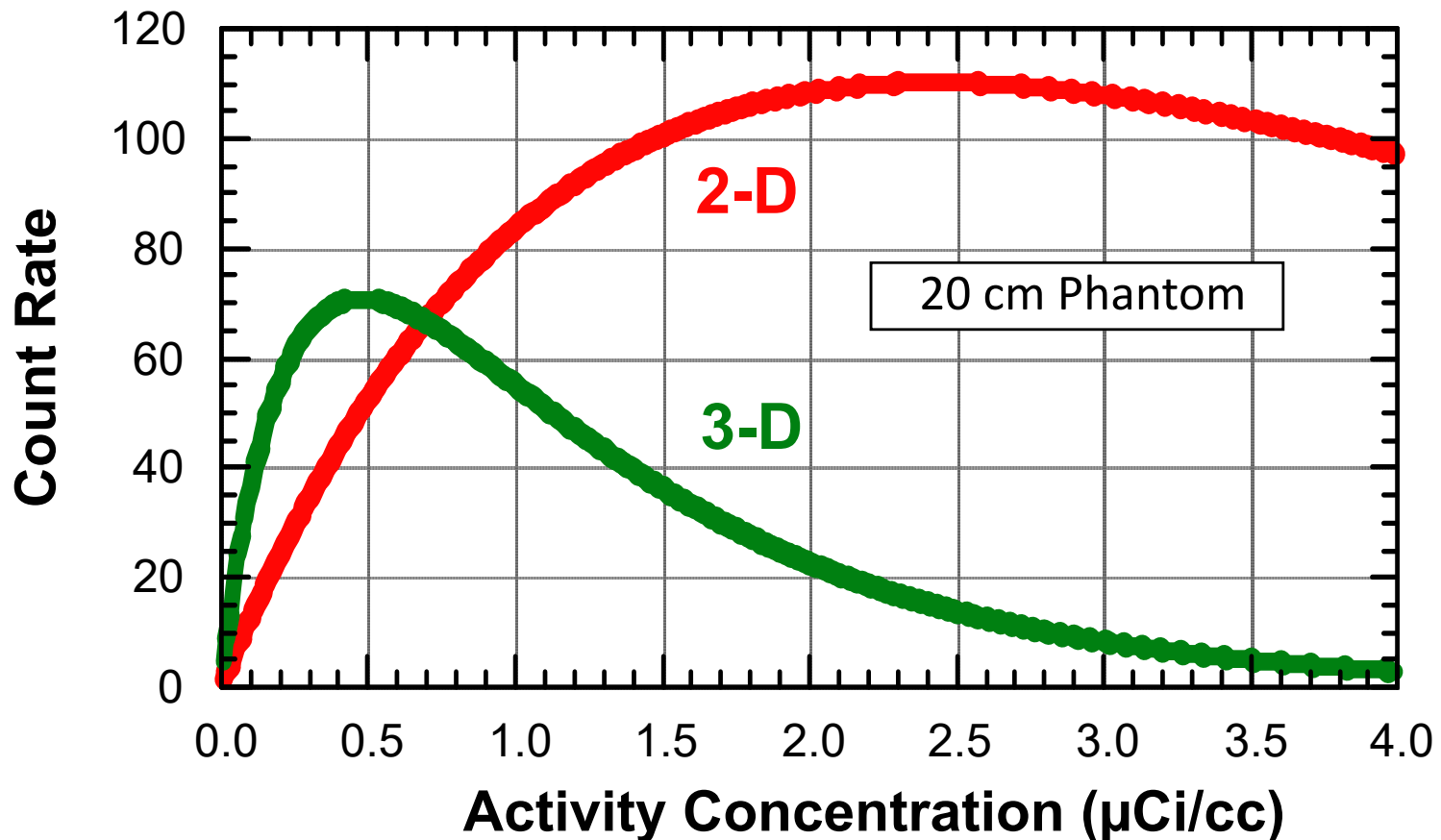
T: true count-rate, S: scattered count-rate, R: random count rate

NECR Properties:

- Like a Signal / Noise Ratio
(Sensitivity only Includes Signal).
- Includes Noise from Backgrounds.
- Statistical Noise Variance $\propto$ NECR.

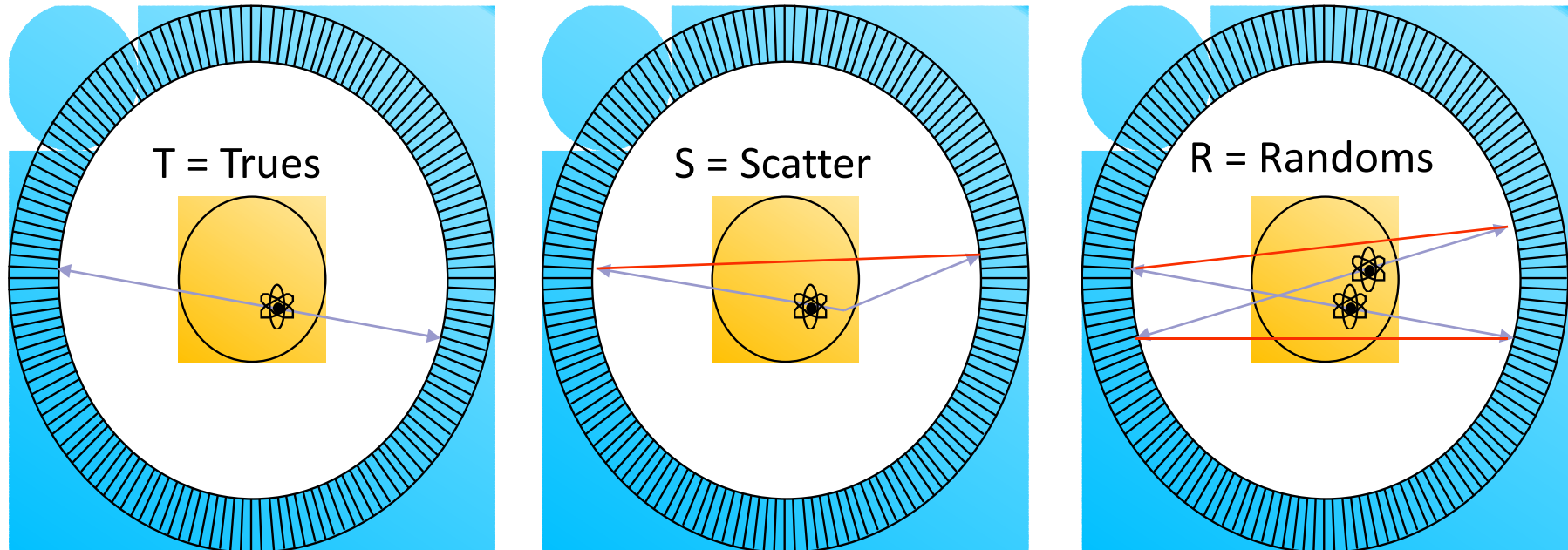
Maximize NECR to Minimize Image Noise

NECR Depends On Activity Density



- At Small Activities, 3-D has Higher NECR
- Peak NECR in 2-D > Peak NECR in 3-D
- Very Sensitive to Scanner, Definitions, & Phantom Size!

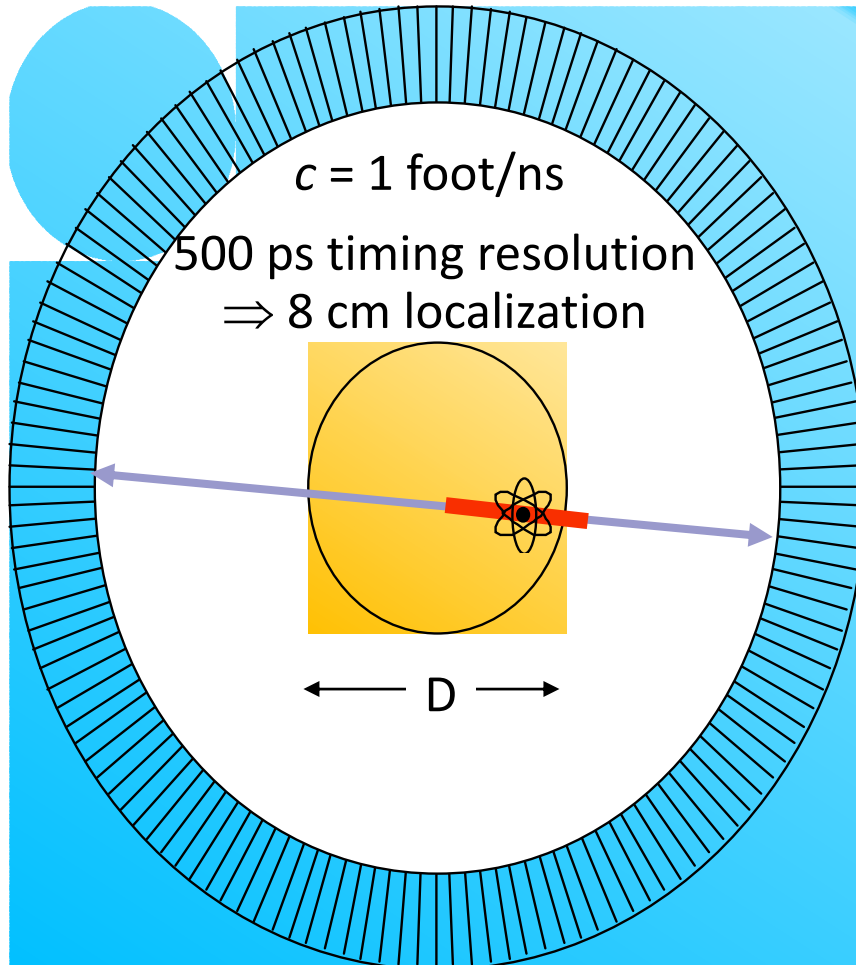
Sensitivity Includes Noise from Background



Even when you do background subtraction,
statistical noise from the background remains.

Image Noise Not Determined by Sensitivity Alone!

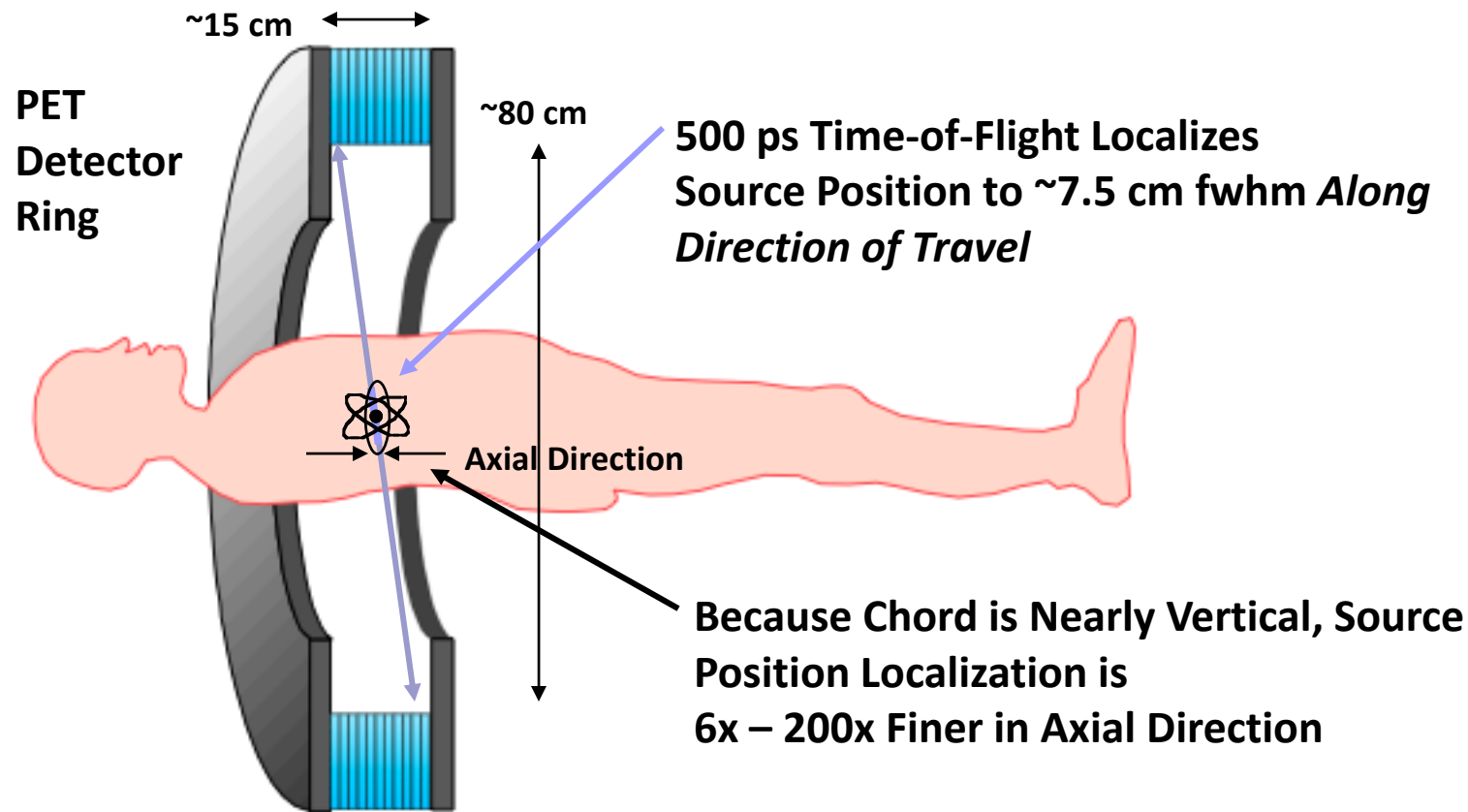
Time-of-Flight Tomograph



- 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 .
- Difficult to keep all detectors in accurate time coincidence.

- Variance Reduction Given by $2D/c\Delta t$
- 500 ps Timing Resolution $\Rightarrow$ 5x Reduction in Variance!

Axial Position Determined Accurately w/ TOF



- Can Assign Chord to Correct Axial Plane
- Reduces Axial Blur in Reconstructed Image
- Turns 3-D Reconstruction into 2-D — *Much Faster!*

Whole-Body TOF Simulations

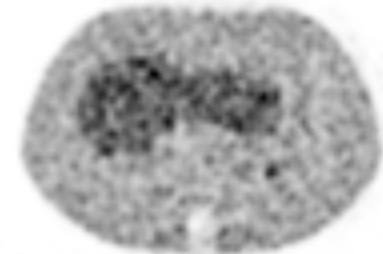
**2×10^6 Trues, 1×10^6 Randoms, Attenuation Included
OP-OSEM w/ TOF Extensions, 2 Iterations, 14 Subsets**



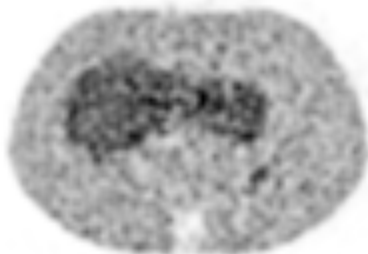
Phantom
(1:2:3 body:liver:tumor)



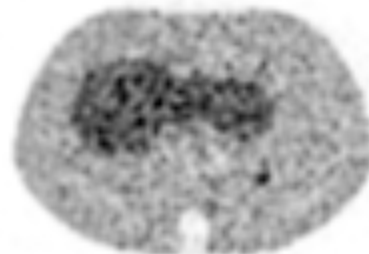
Conventional



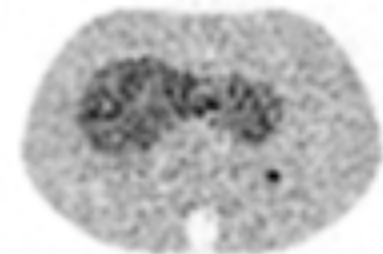
1.2 ns



700 ps



500 ps

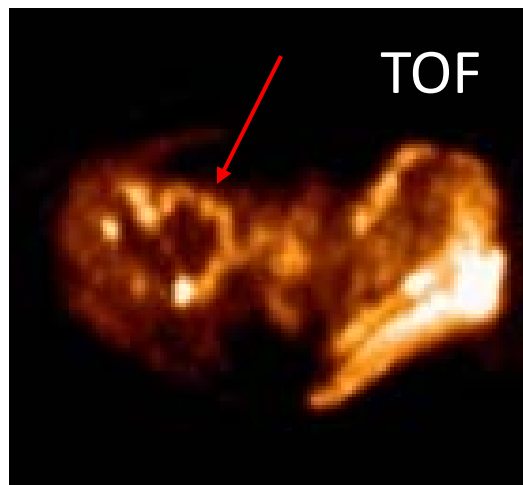
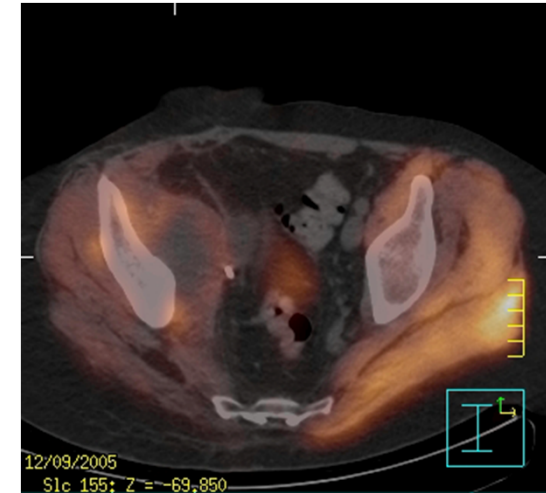
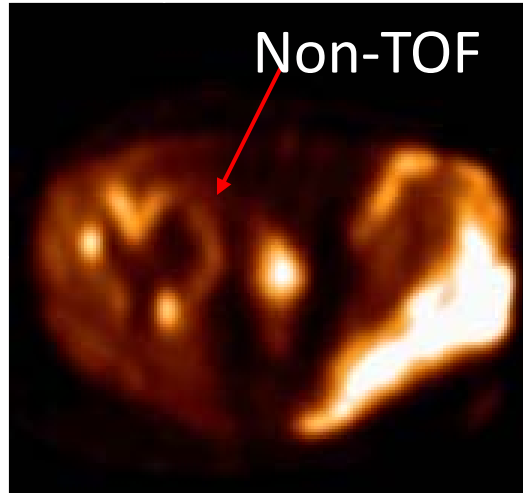
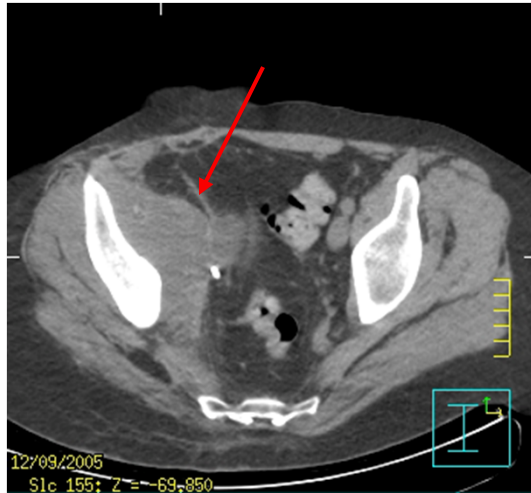


300 ps

Clear Improvement Visually

***Data courtesy of Mike Casey, CPS Innovations**

TruFlight™: Enhanced Diagnostic Confidence



Lymphoma within right iliopsoas muscle with central area of necrosis

improved delineation of lymphoma activity

116 kg; BMI = 31.2
14 mCi; 2 hr post-inj



Clinical Uses

- Brain Dysfunction

Tumor vs. Necrosis

Alzheimer' s Disease

Epilepsy

- Heart Tissue Viability

- Cancer / Oncology

Tumor vs. Necrosis



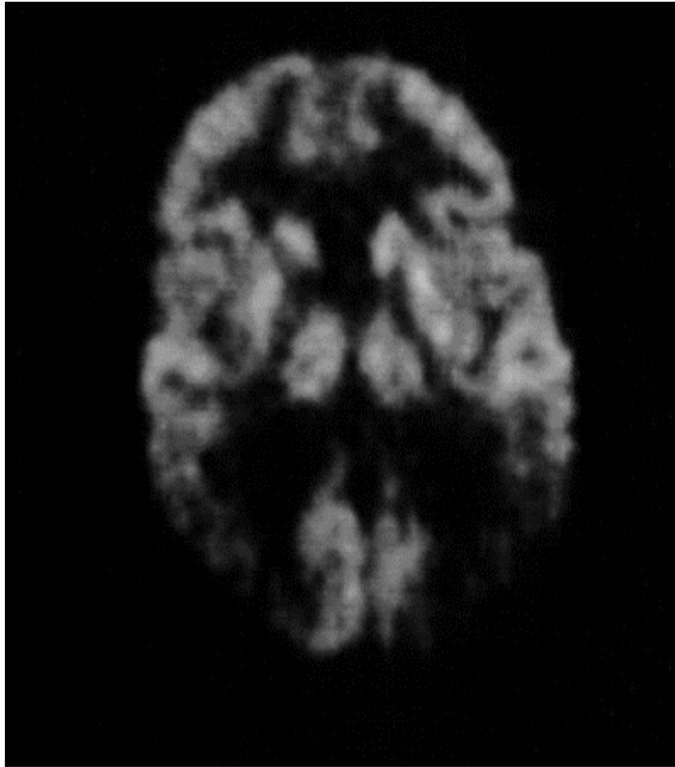
XBB 884-2937

- Brain tumor patient given radiation therapy.
- Symptoms recur.
- Too much or too little radiation?
- Check with PET.

Too much radiation
⇒ dead area.

Too little radiation
⇒ rapid metabolism.

Alzheimer's Disease



XBB 883-2443

- Decreased uptake in temporal and parietal regions.
- No known cure, but can tell if a curable disease is mis-diagnosed as Alzheimer's disease.

Epilepsy



XBB 893-2245A

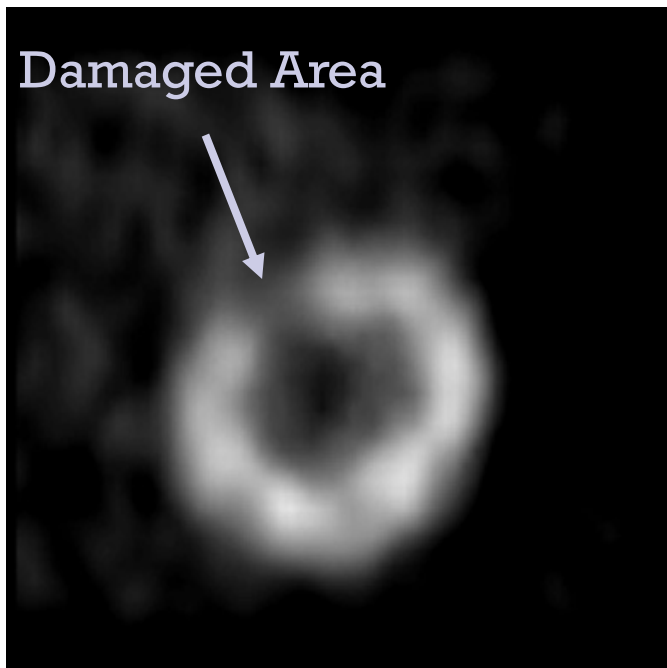
NMR



PET

- PET used to identify “focal centers” causing epilepsy.
- Focal centers surgically removed.

Heart Tissue Viability

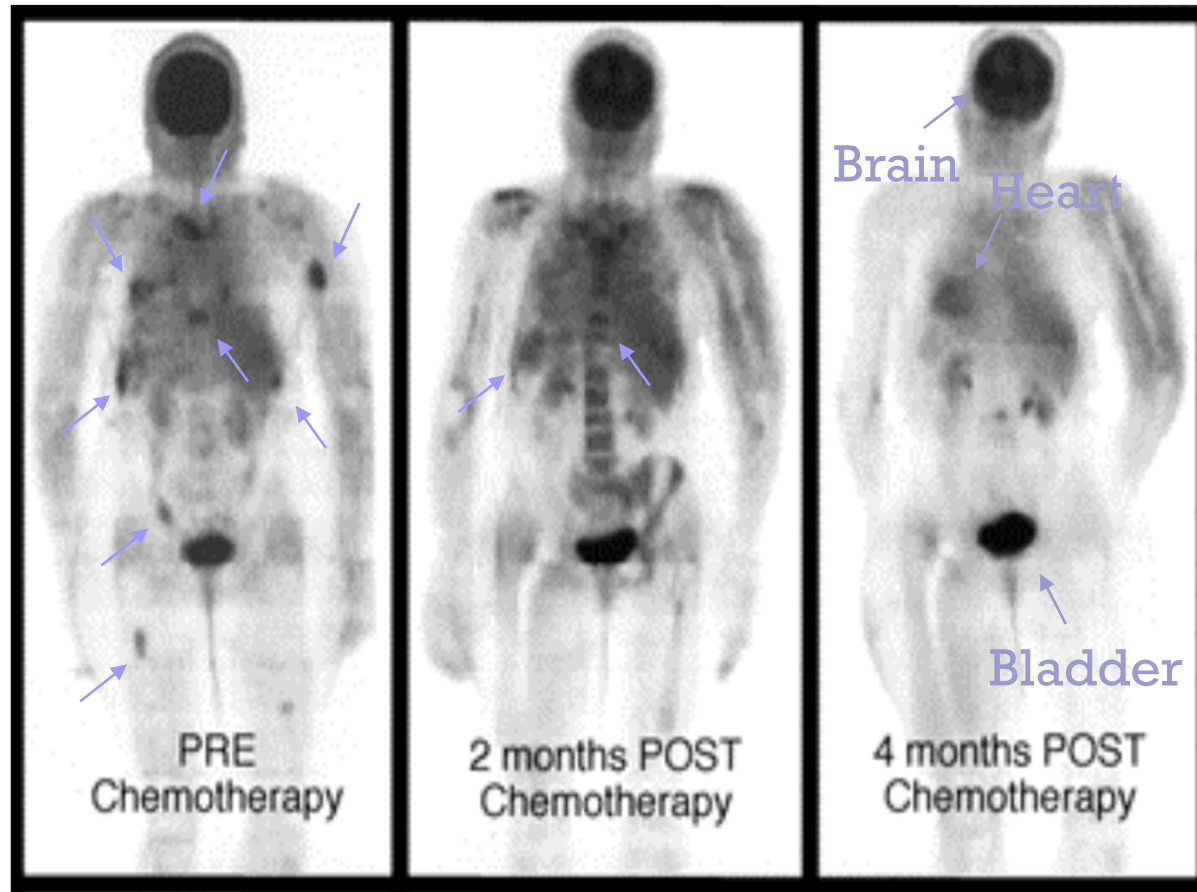


Human Heart

- Patient has heart attack but lives.
- Heart *always* sustains some damage.
- How badly is the heart damaged?
 - Badly $\Rightarrow$ Coronary bypass.
 - Not Badly $\Rightarrow$ No surgery.
- PET measures *degree* of damage.

Cancer / Oncology

Metastases
Shown with
Arrows



Normal Uptake
in Other Organs
Shown in Blue

- Many tumors have higher than normal uptake.
- Image the whole body to find metastases.