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**SEMMELWEIS
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Development of Complex Curricula for Molecular Bionics and Infobionics Programs within a consortial* framework**

Consortium leader

PETER PAZMANY CATHOLIC UNIVERSITY

Consortium members

SEMMELWEIS UNIVERSITY, DIALOG CAMPUS PUBLISHER

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**Molekuláris bionika és Infobionika Szakok tananyagának komplex fejlesztése konzorciumi keretben

***A projekt az Európai Unió támogatásával, az Európai Szociális Alap társfinanszírozásával valósul meg.



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TÁMOP – 4.1.2-08/2/A/KMR-2009-0006



BIOMEDICAL IMAGING

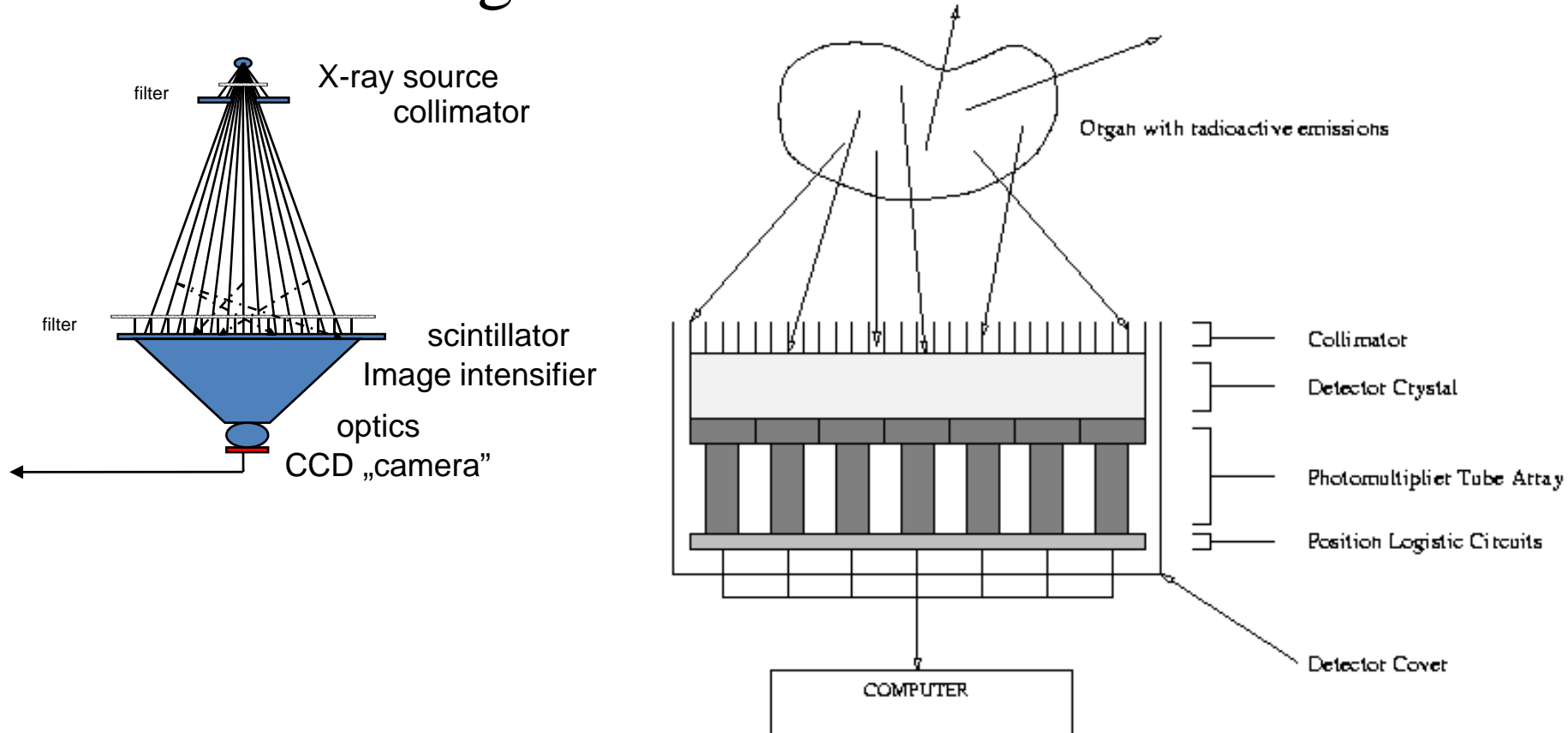
(Orvosbiológiai képalkotás)

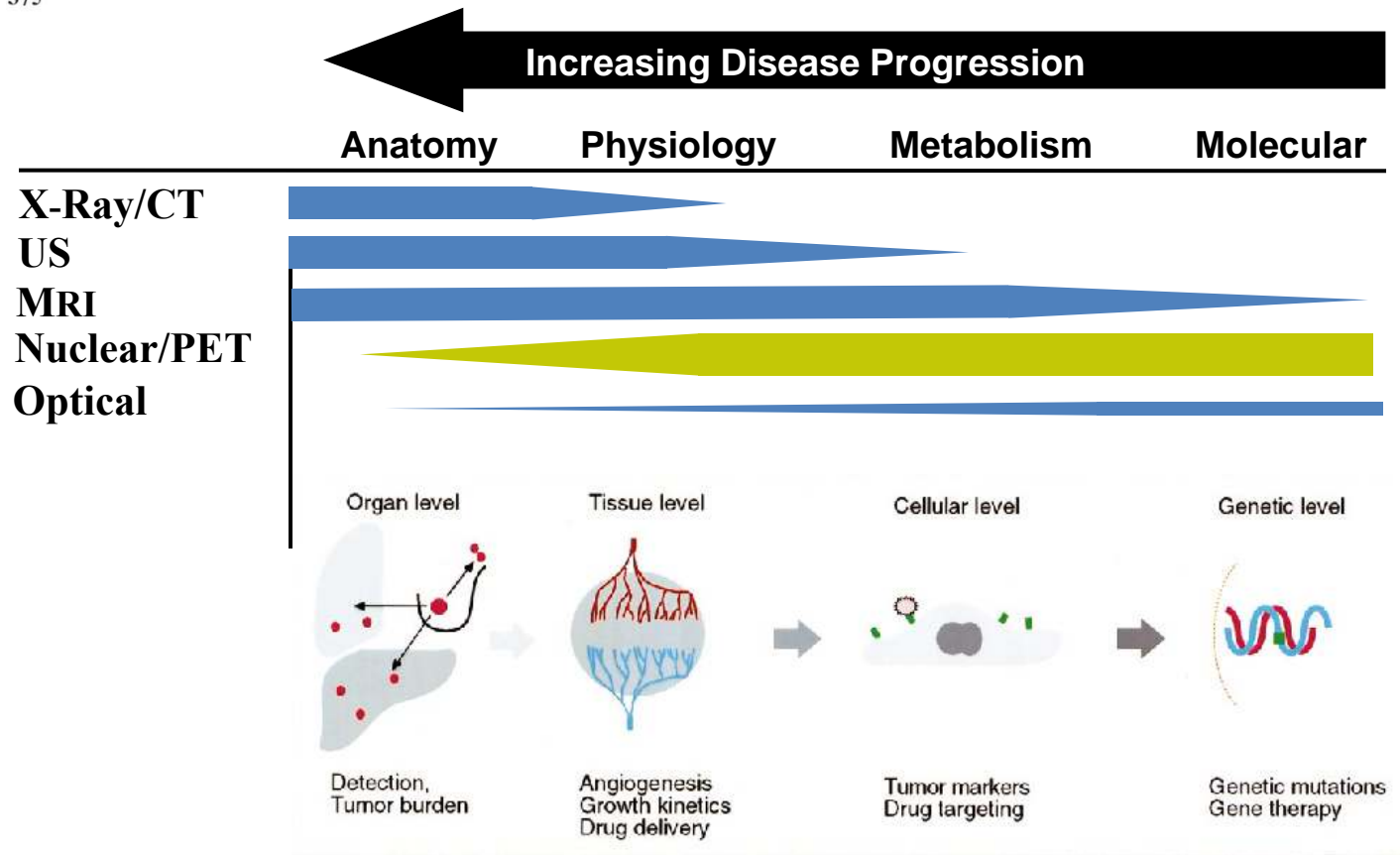
GAMMA CAMERA AND POSITRON EMISSION TOMOGRAPHY (PET)

(Gamma kamera és Pozitron emissziós tomográfia (PET))

GYÖRGY ERÖSS

Technical Background

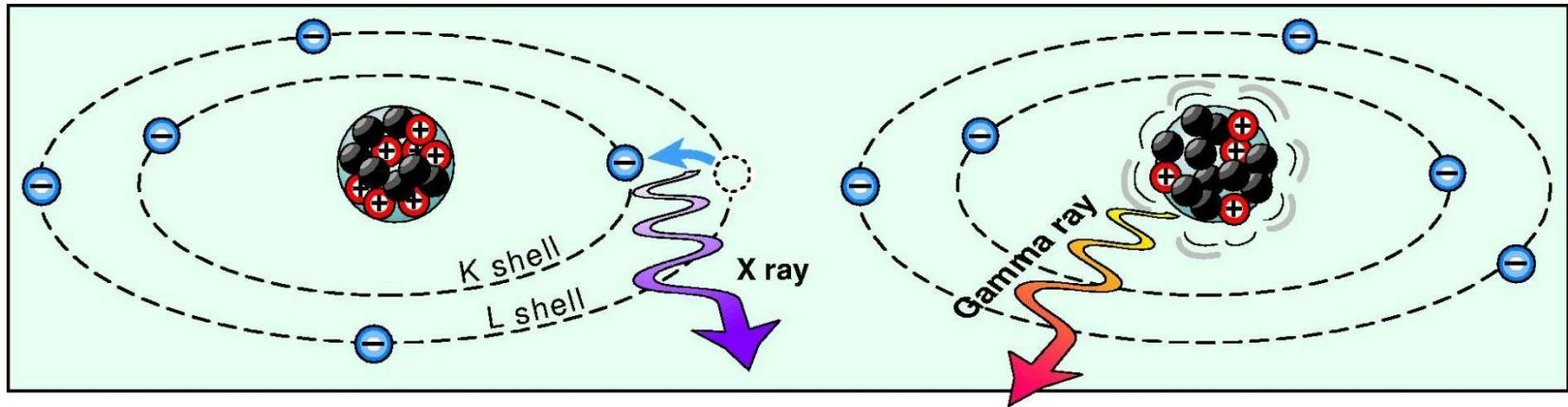




PET provides metabolic or functional information and may lead to detection of early onset of disease

Nuclear Medicine

γ -ray & X-ray Production – what we image



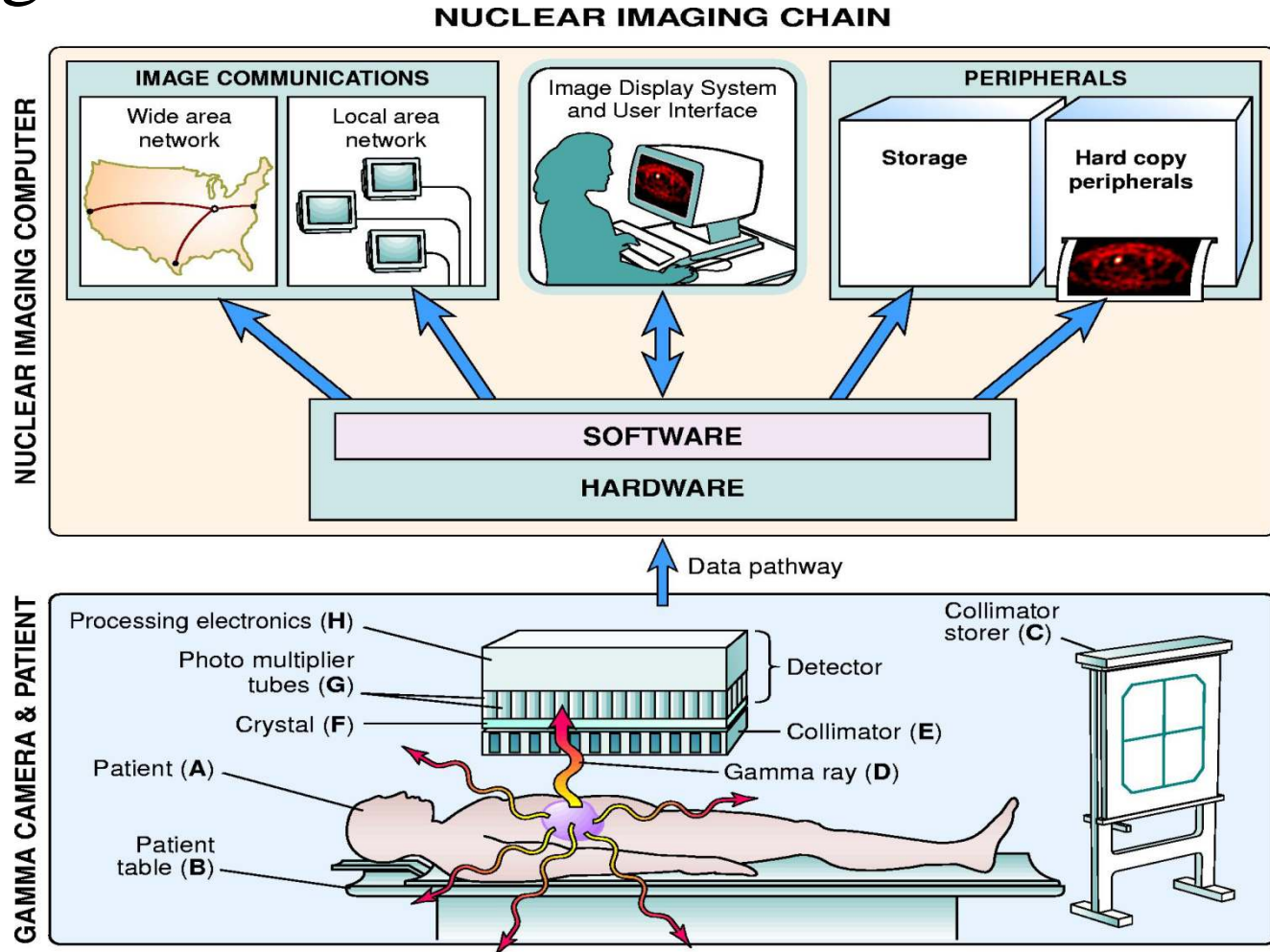
X-ray – high energy photon emitted by electron transition

Gamma ray – high energy photon emitted from nucleus

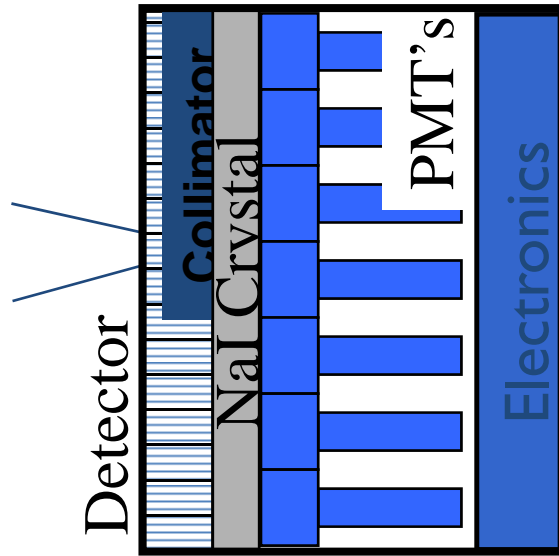
Nuclear Medicine Radionuclides

| | | |
|----------|------------------|------------|
| • Tc99m | 140.5 keV | 6.03 hours |
| • I-131 | 364,637 keV | 8.06 days |
| • I-123 | 159 keV | 13.0 hours |
| • I-125 | 35 keV | 60.2 days |
| • In-111 | 172, 247 keV | 2.81 days |
| • Th-201 | ~70, 167 keV | 3.044 days |
| • Ga-67 | 93, 185, 300 keV | 3.25 days |

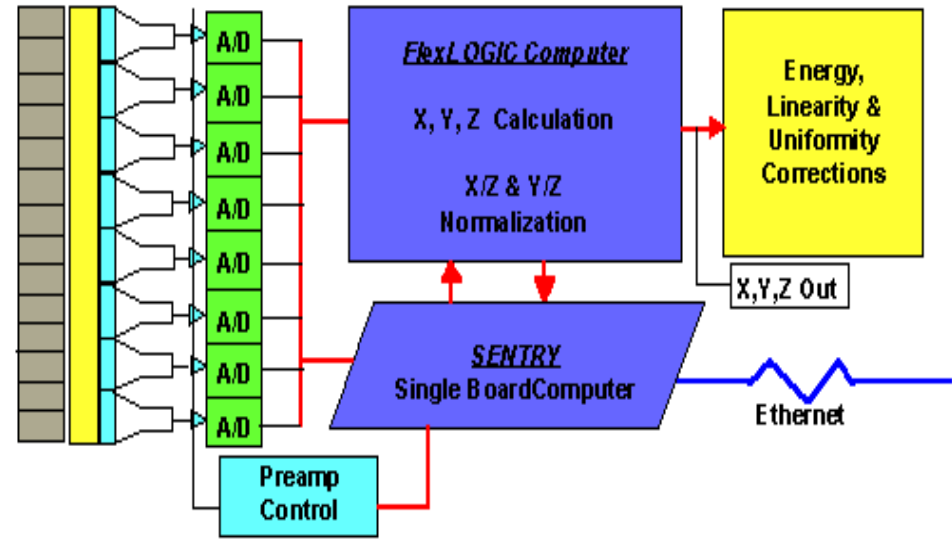
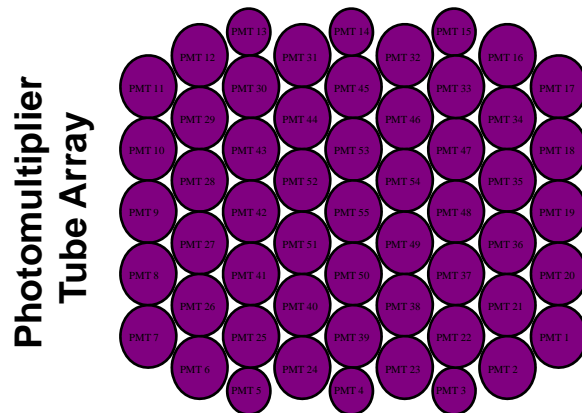
Planar gamma camera



Gamma Camera - Image Formation



- Lead collimator focuses photons (lens)
- NaI crystal scintillates
- PMTs detect scintillation
- Position calculation



Collimators

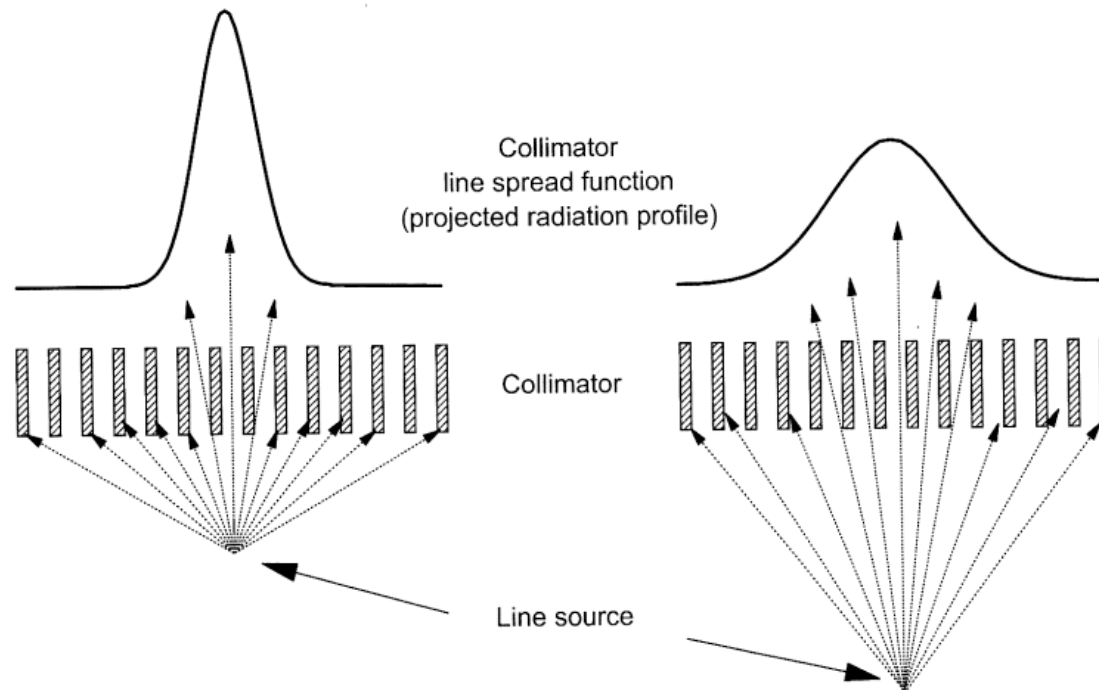


FIGURE 21-12. Line spread function (LSF) of a parallel-hole collimator as a function of source-to-collimator distance. The full-width-at-half-maximum (FWHM) of the LSF increases linearly with distance from the source to the collimator; however, the total area under the LSF (photon fluence through the collimator) decreases very little with source to collimator distance. (In both figures, the line source is seen “end-on.”)

Type of collimators

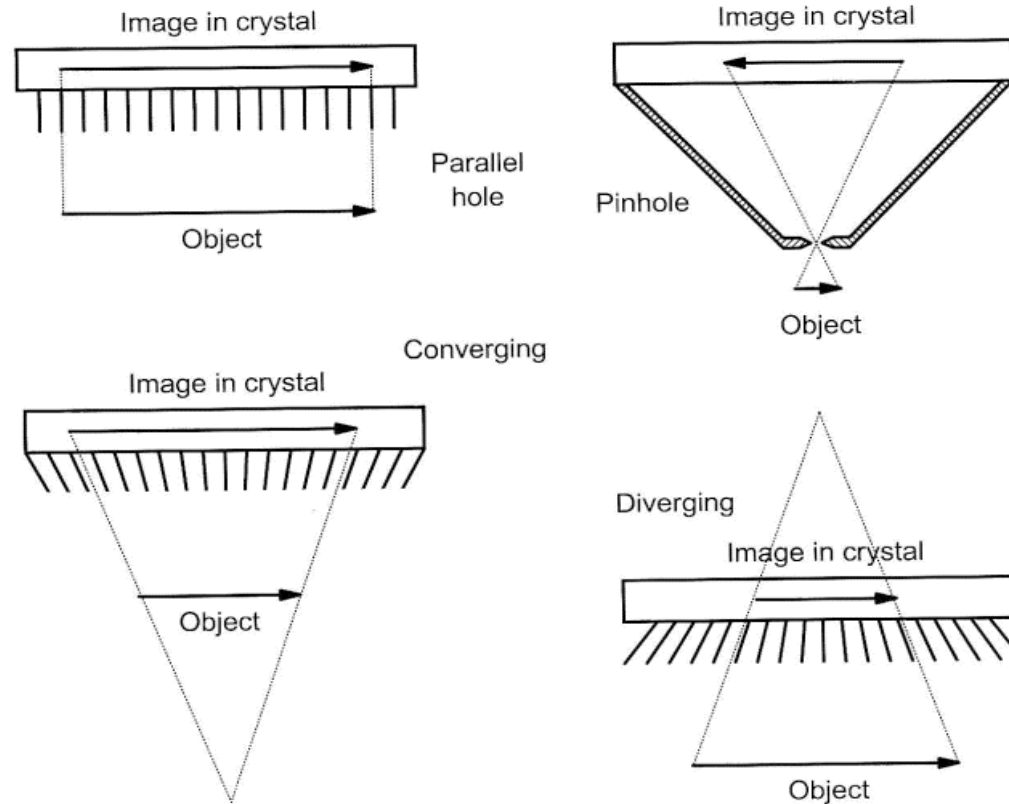


FIGURE 21-6. Collimators.

Collimator: Resolution and Sensitivity

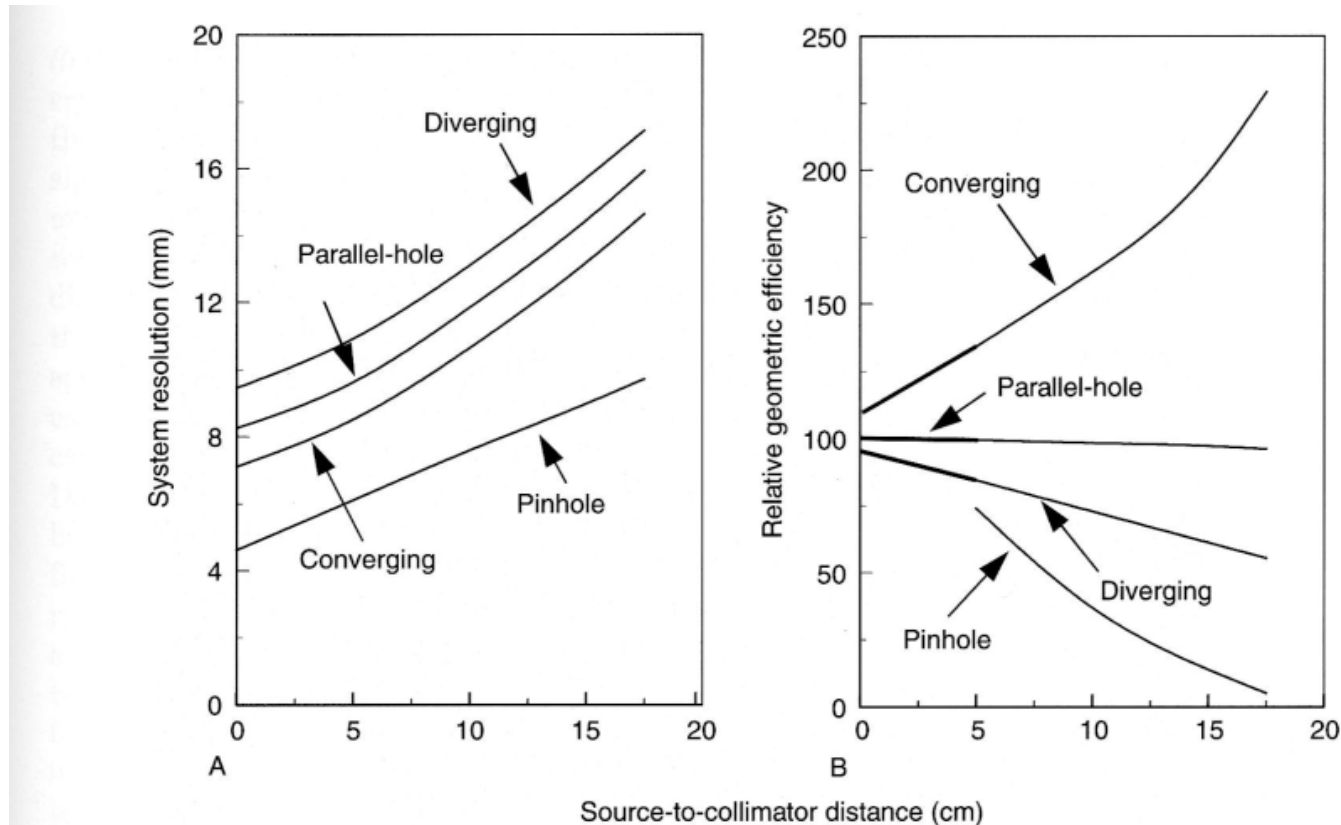
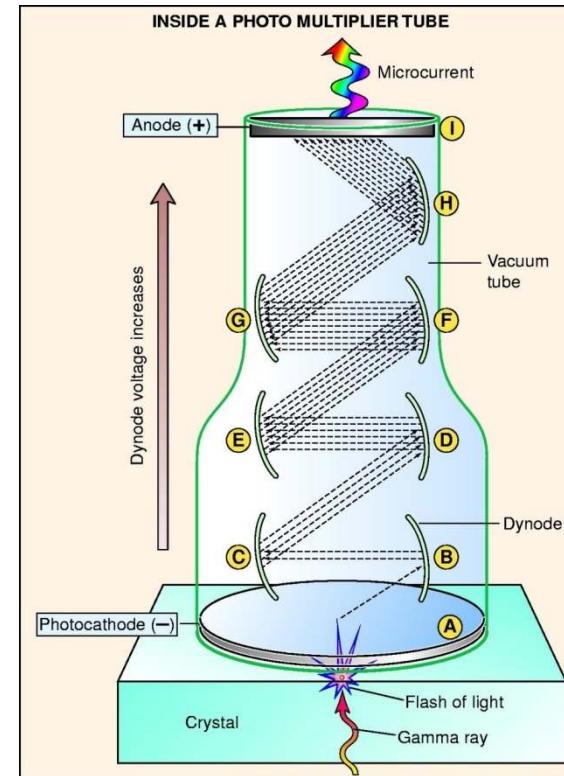
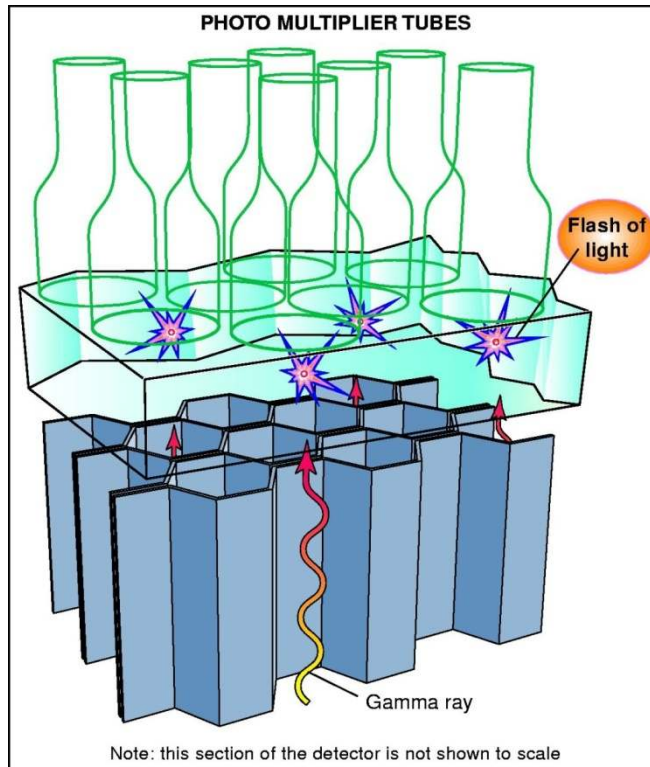


Figure 14-21. Performance characteristics (A, system resolution; B, point-source geometric efficiency in air) versus source-to-collimator distance for four different types of gamma camera collimators. (Reprinted by permission of the Society of Nuclear Medicine from Moyer RA: A low-energy multihole converging collimator compared with a pinhole collimator. *J Nucl Med* 15:59-64, 1974.)

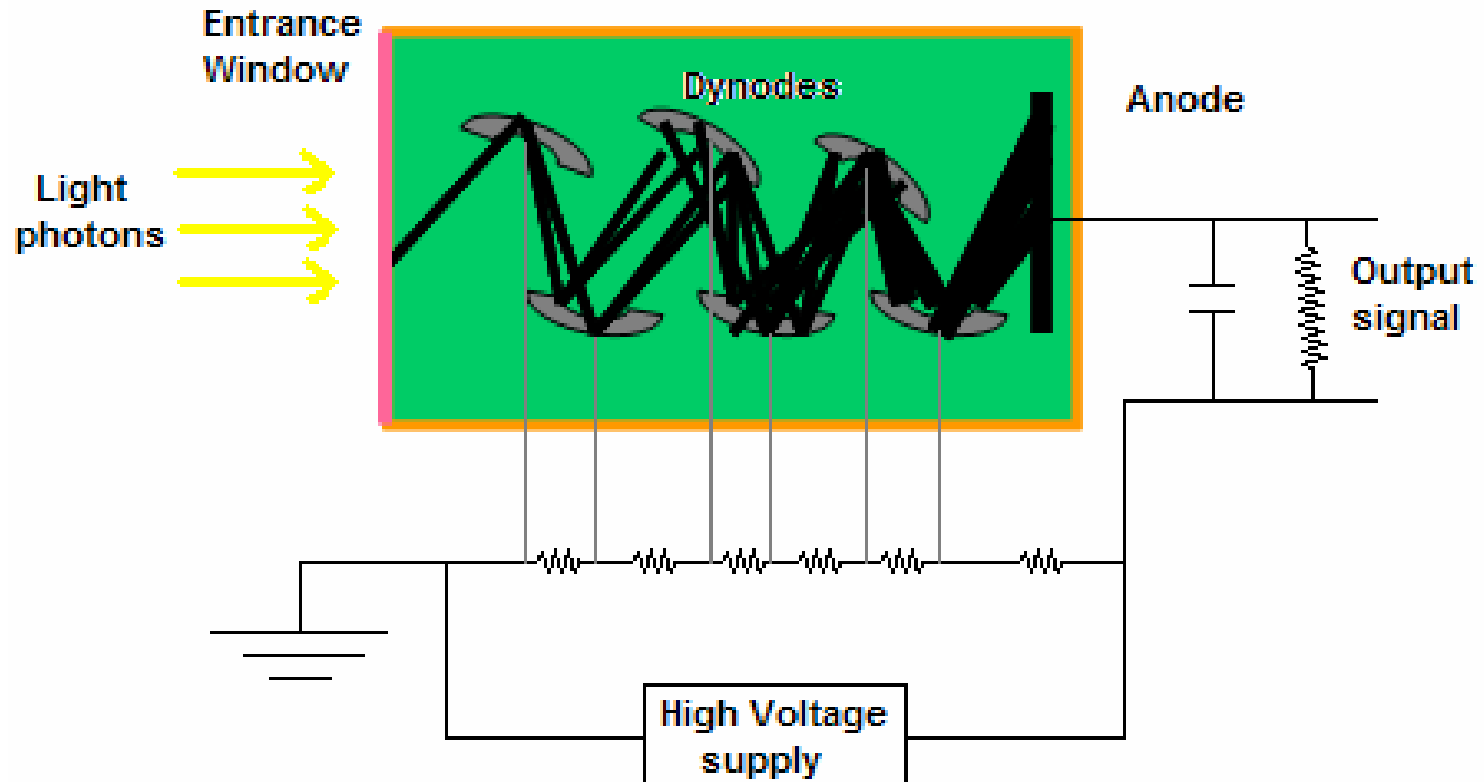
Scintillator material

| | NaJ | GSO | LSO | LYSO | BGO | LaBr3 | |
|--------------------|--------|------------|------------|---------|---------|---------|---------------------------------------|
| | NaJ:Ti | Gd2SiO5:Ce | Lu2SiO5:Ce | | Bi4Ge3O | | |
| Density | 3.67 | 6.7 | 7.4 | 7 | 7.1 | 5.3 | |
| Effective Z | 51 | 57/59 | 65/66 | 64 | 73/75 | 47 | |
| Attenuation length | | 1.4 | 1.15 | 1.2 | 1.04 | 2.1 | sensitivity / dose |
| Light Yield | | <0.5 | 1 | 1.2 | <0.2 | 2 | image quality / detection accuracy |
| Decay Time | 230 ns | 60 ns | 40 ns | 40 ns | 300 ns | 35 ns | coincidence window (sc&rnd) |
| Energy Resolution | | 8.50% | 11% | 10% | >13% | 3% | scatter & random reduction |
| Timing Resolution | N/A | N/A | N/A | <450 ps | N/A | <400 ps | |
| photon/MeV | 41000 | 8000 | 26000 | | 9000 | | |

Detector system



Photon Multiplier Tube (PMT)



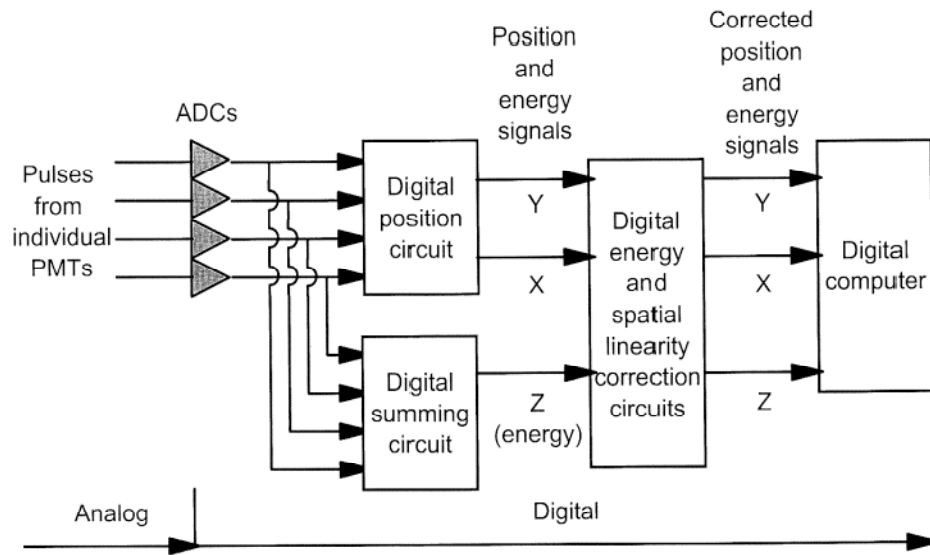
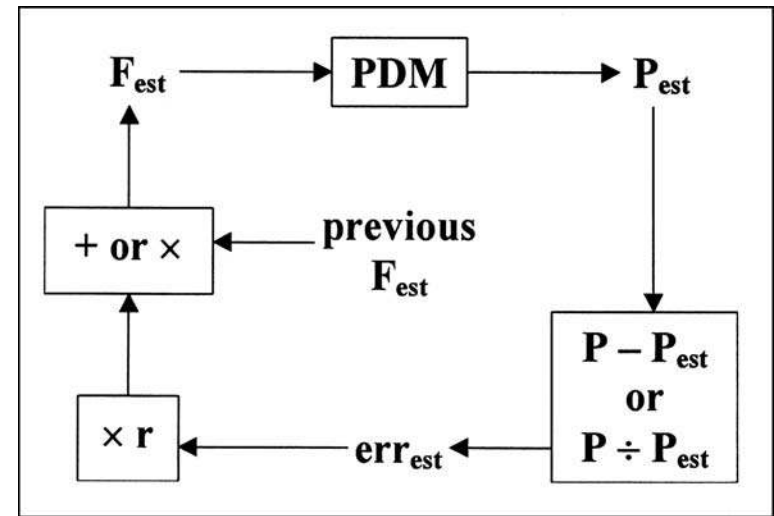


FIGURE 21-5. Electronic circuits of a modern digital scintillation camera.

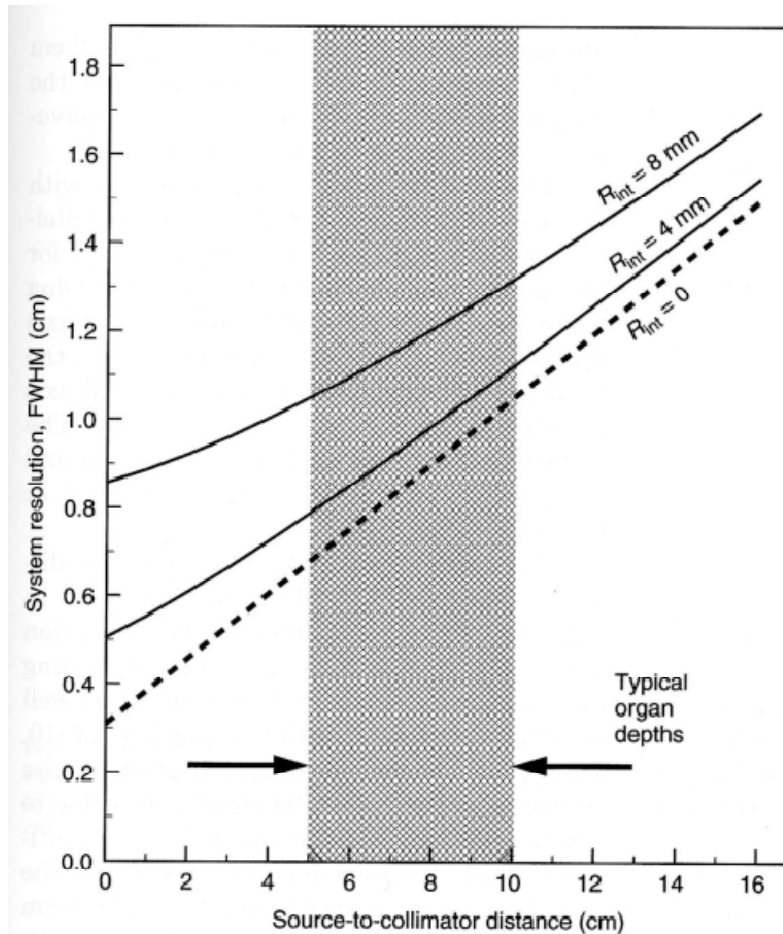
Image reconstruction:
backprojection with iteration



Gamma Camera

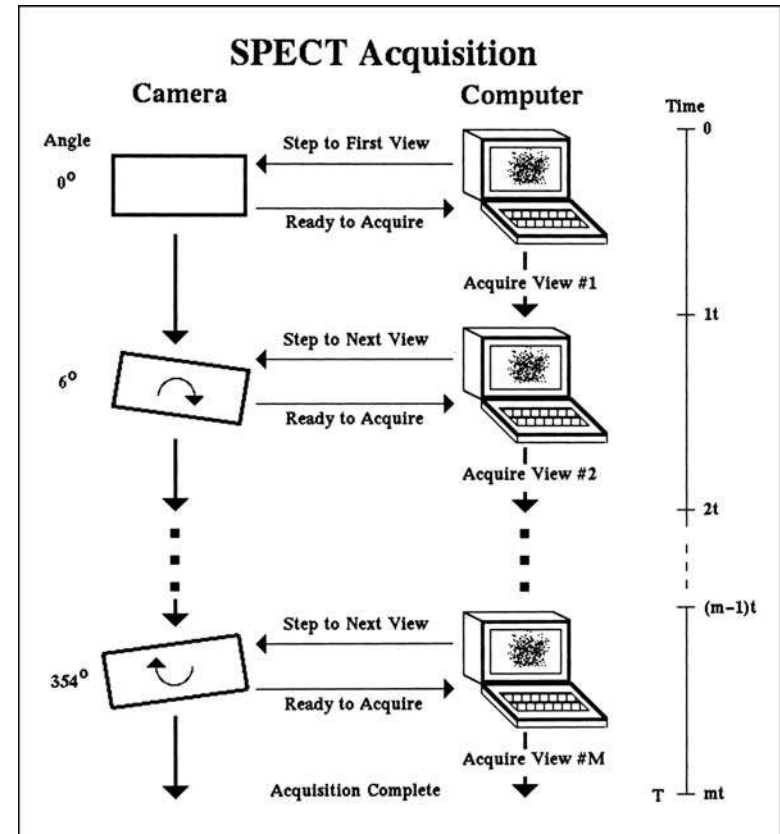


Gamma Camera - spatial resolution

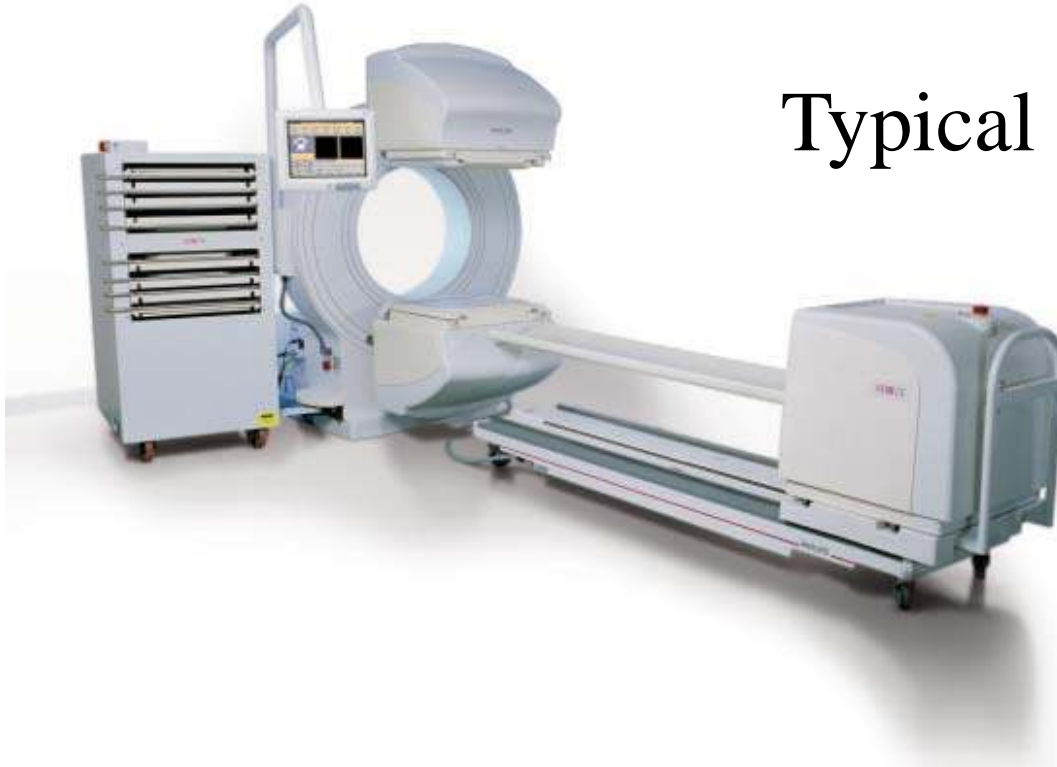


Single Photon Emission Computed Tomography

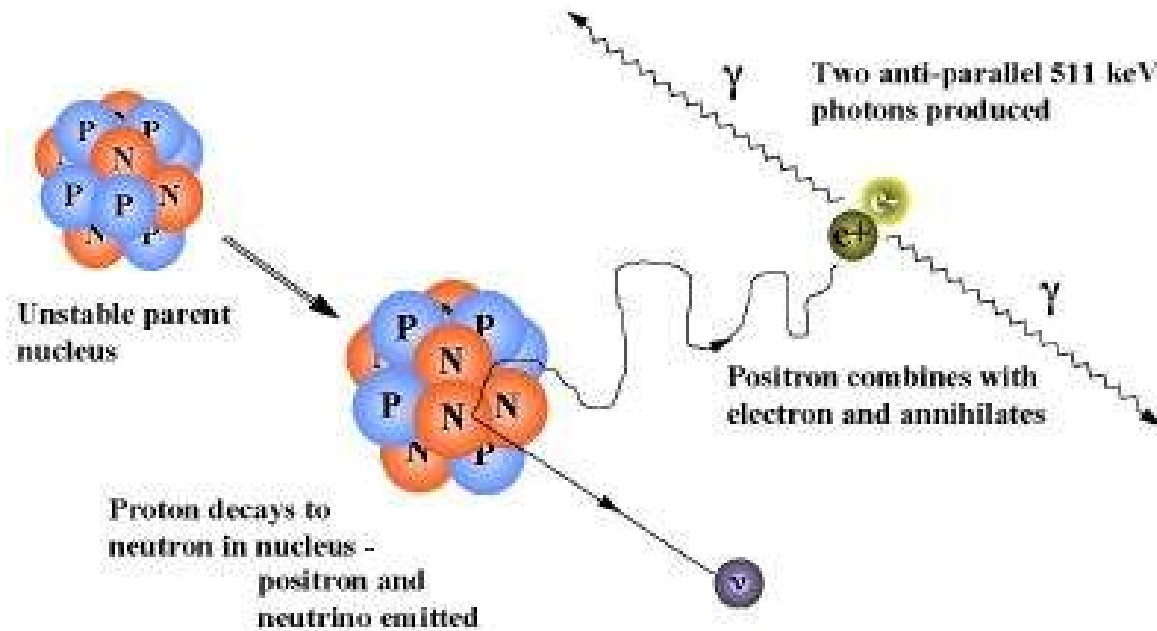
SPECT imaging is performed by using a gamma camera to acquire multiple 2-D images (also called projections), from multiple angles. A computer is then used to apply a tomographic reconstruction algorithm to the multiple projections, yielding a 3-D dataset.



Typical SPECT cameras



Positron Emission Tomograph



Positron emission and annihilation

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 |

http://depts.washington.edu/nucmed/IRL/pet_intro/intro_src/section2.html

Radionuclide Imaging Radiochemistry

- Radioactivity is the means by which we measure the concentration of something
- **metabolic** *in vivo*.
- What would we want to measure?

Location of drugs, receptors, proteins, genes...

| | | | |
|-----------------|---------------------------|--------------------|--------------------|
| Oxygen | O ₂ metabolism | Fluorodeoxyglucose | Glucose metabolism |
| Water | Perfusion | FESP | D2 receptor |
| Ammonia | Perfusion | FMISO | Hypoxia |
| Carbon monoxide | Blood volume | FCZ | Beta-AR |

Common PET tracers

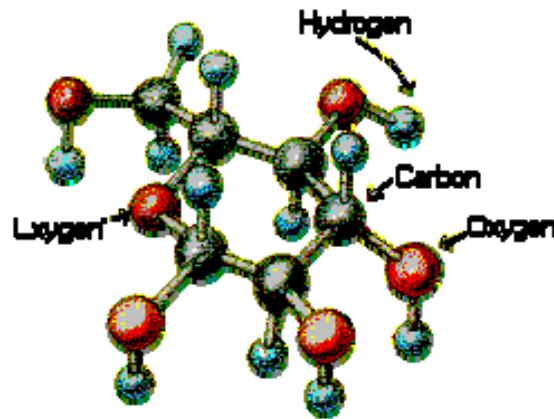
Different Radio-pharmaceuticals provide information on different *metabolic* processes

How is a PET image formed?

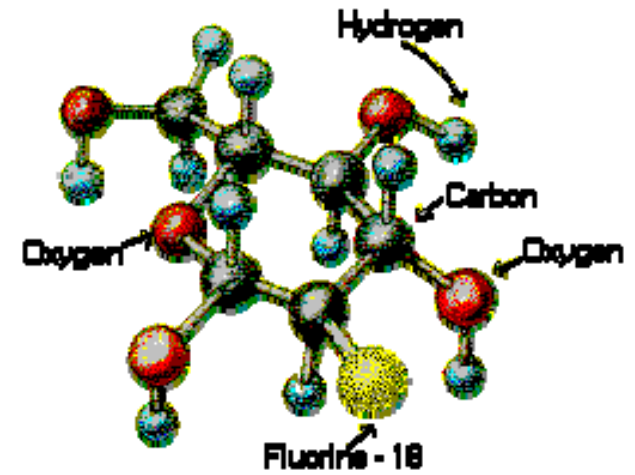
1. Patient is injected with radio-pharmaceutical (usually FDG)
2. Wait for uptake (usually ~60 minutes)
 - FDG taken up by cells that metabolize glucose



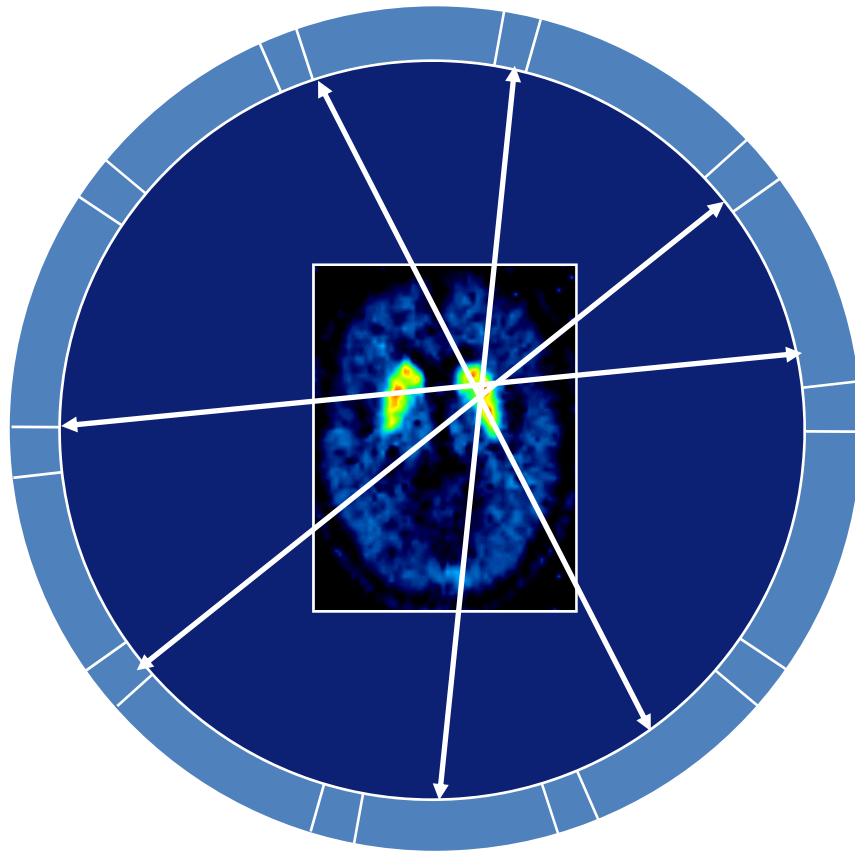
glucose



2-fluoro-
2-deoxy-D-glucose
"FDG"



How is a PET image formed?

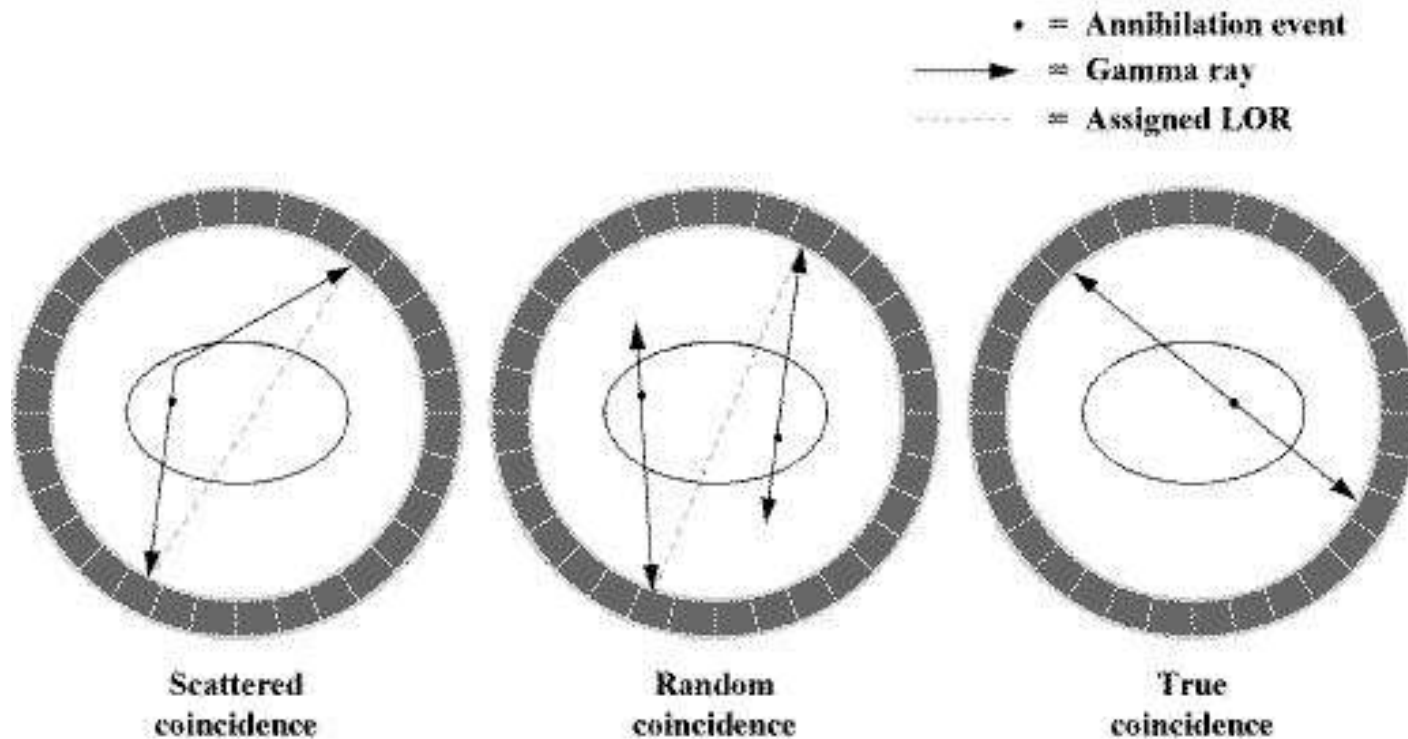


3. Radioactive isotope emits positrons
 - Collide with and “Annihilate” an electron
 - Two 511 keV photons emitted 180 degrees apart
4. Millions of Coincidence pairs recorded to form image
More annihilation (coincidences) – more intensive image



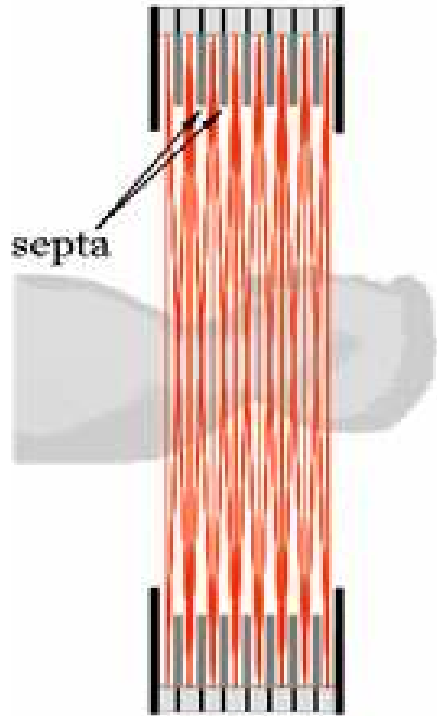
**Positron Emission
Tomography**

Coincidence events in PET

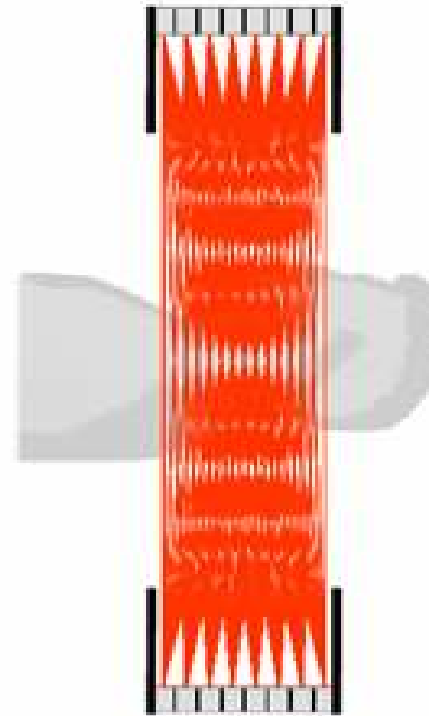


PET 2D and 3D Acquisition Modes

2D
(= with septa)



3D
(= no septa)

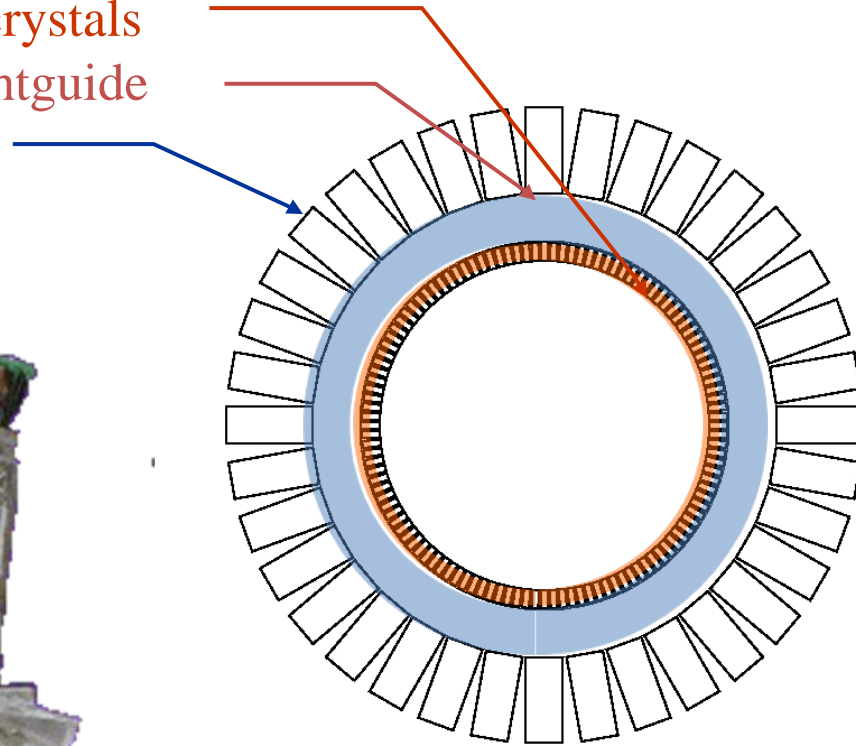
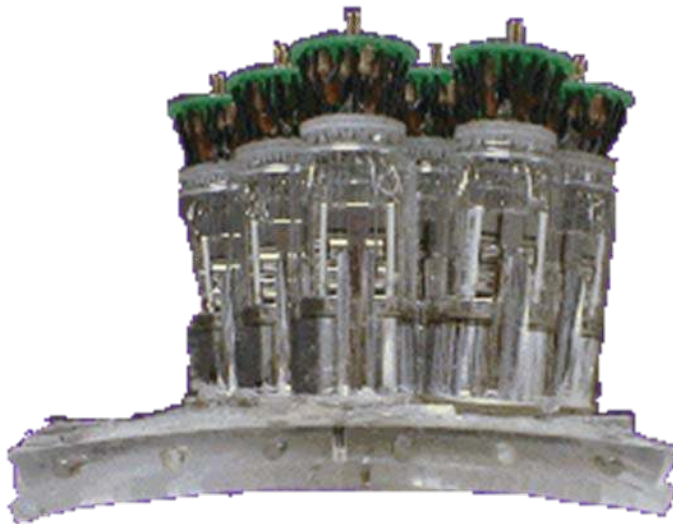


Sensitivity ↑

Scatter ↑

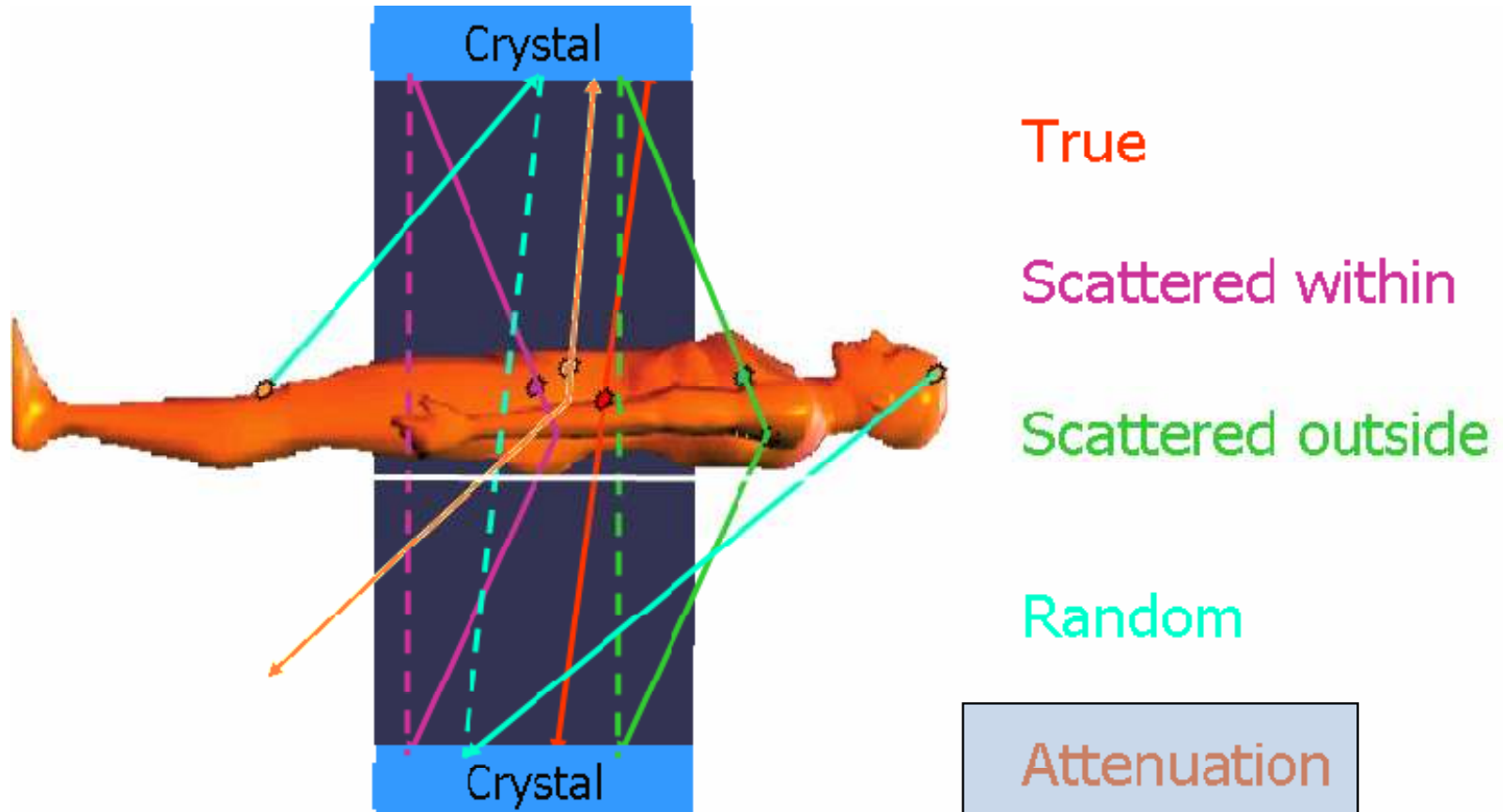
Pixelated-continuous PIXELAR technology:

- individual scintillating crystals
- optically continuous lightguide
- closely packed PMTs



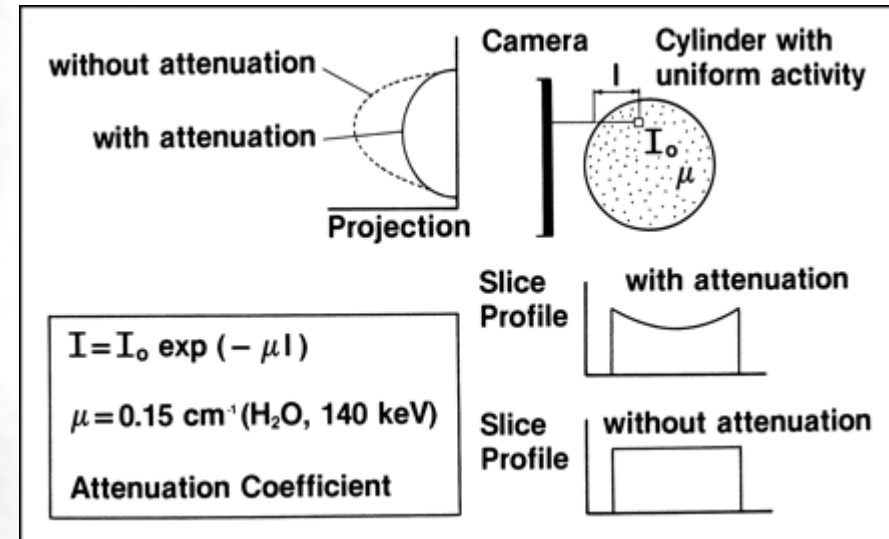
Typical PET image





Small Patient

Large Patient



Attenuation correction => density from external source
 => CT scan



CT by itself provides excellent anatomical detail, but limited functional / metabolic information

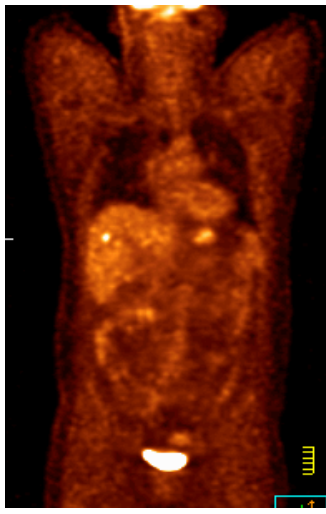
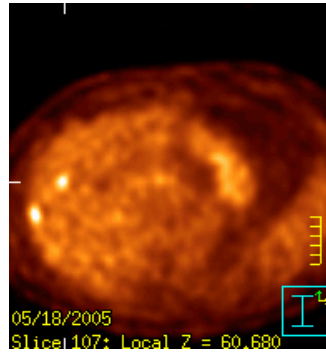
PET by itself provides useful information on functional / metabolic activity, but limited detail on anatomic structures and location

PET/CT combines metabolic and anatomic information in one dataset, in one episode of care

Clinical Need

- Assessment of metabolic activity
- Structural detail
- Localization

Resulting in increased diagnostic confidence



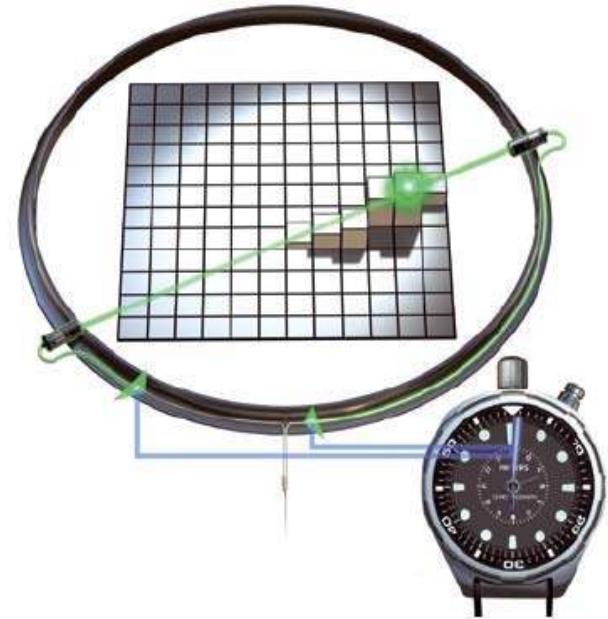
SPECT-CT



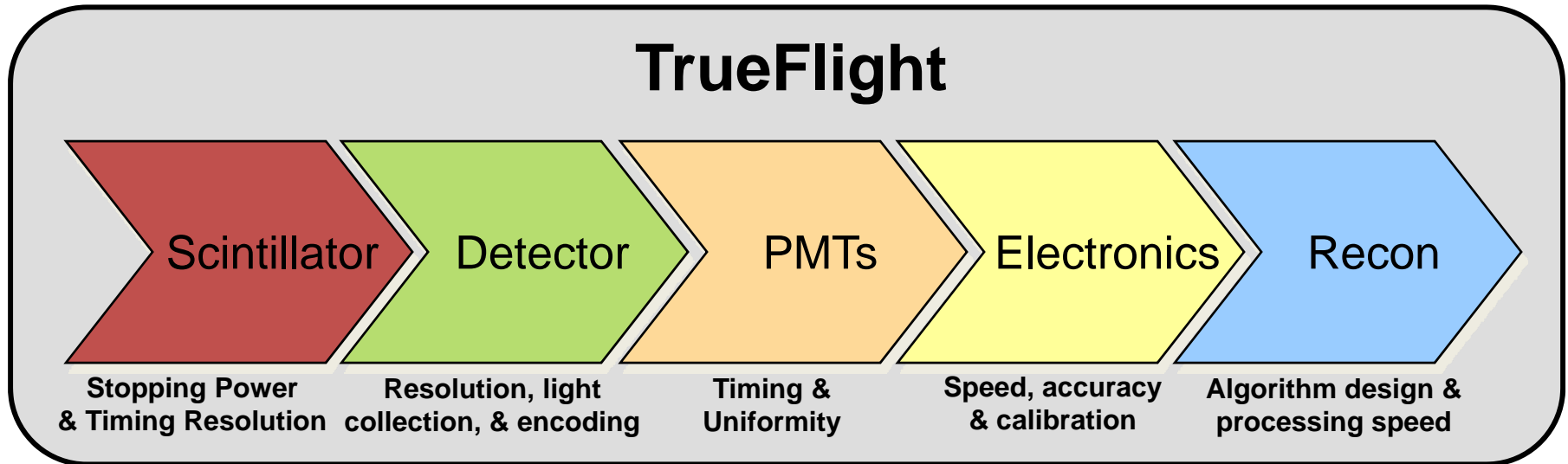
Latest Generation PET – Time of Flight (TOF)



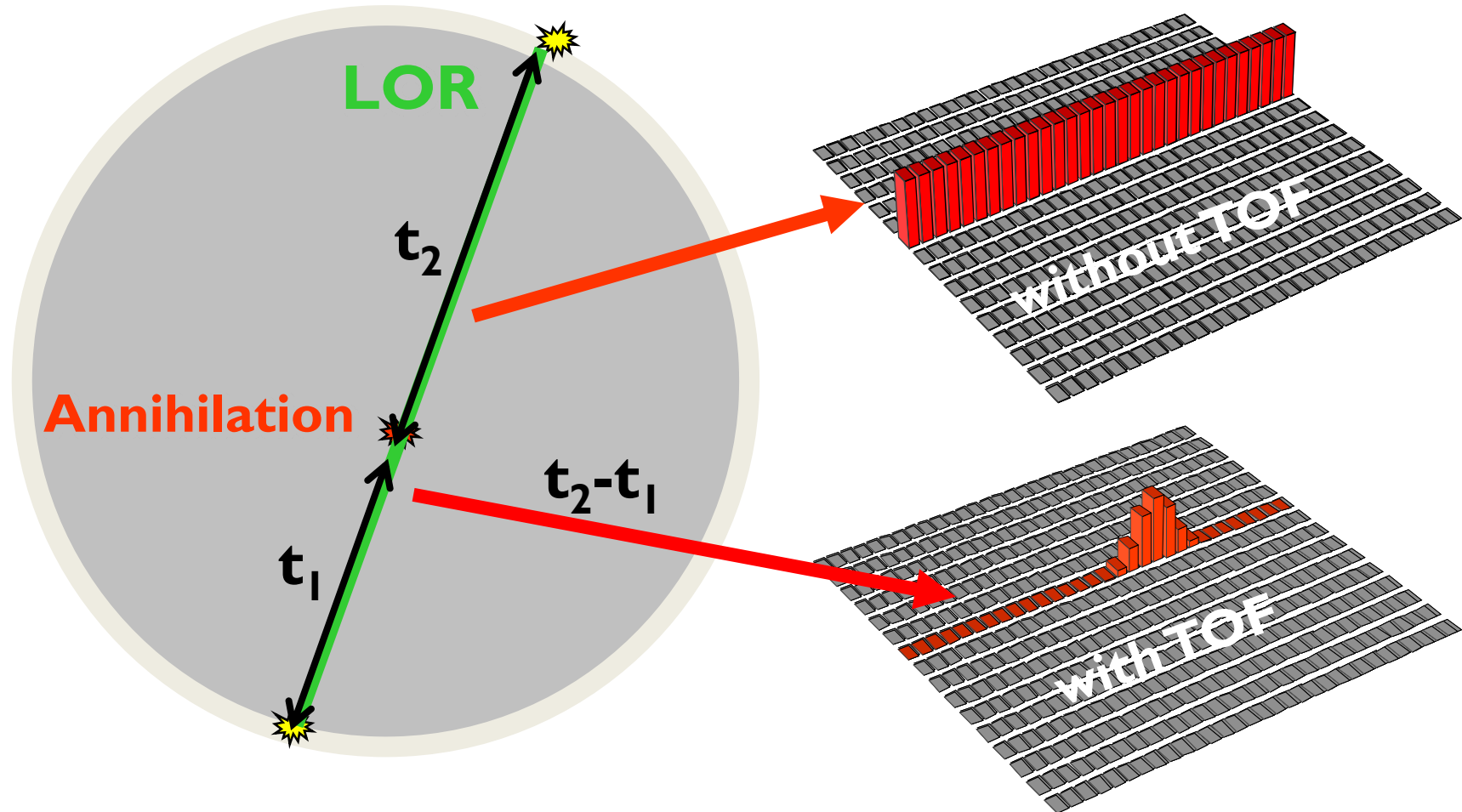
A coincidence event is assigned to a line of response



Time-of-Flight information is used in the data reconstruction to more accurately localize the origin of the annihilation



Concept of Time of Flight PET



Clinical Benefits I

How can your observers benefit from reduced noise and higher sensitivity?

Exceptional Image Quality

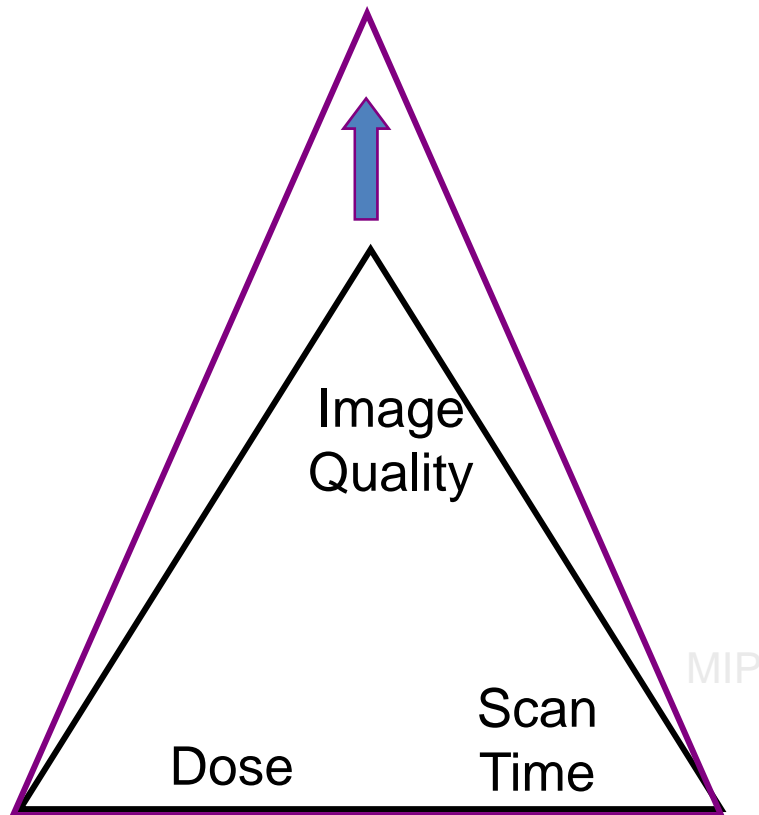


Image courtesy of J Karp, University of Pennsylvania

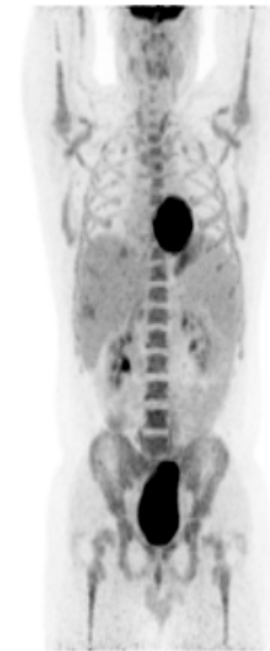
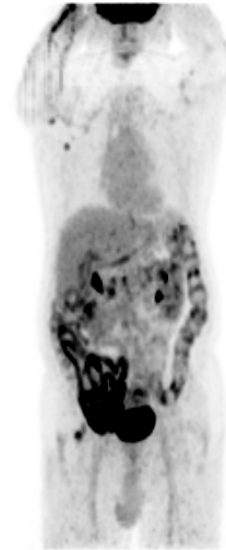
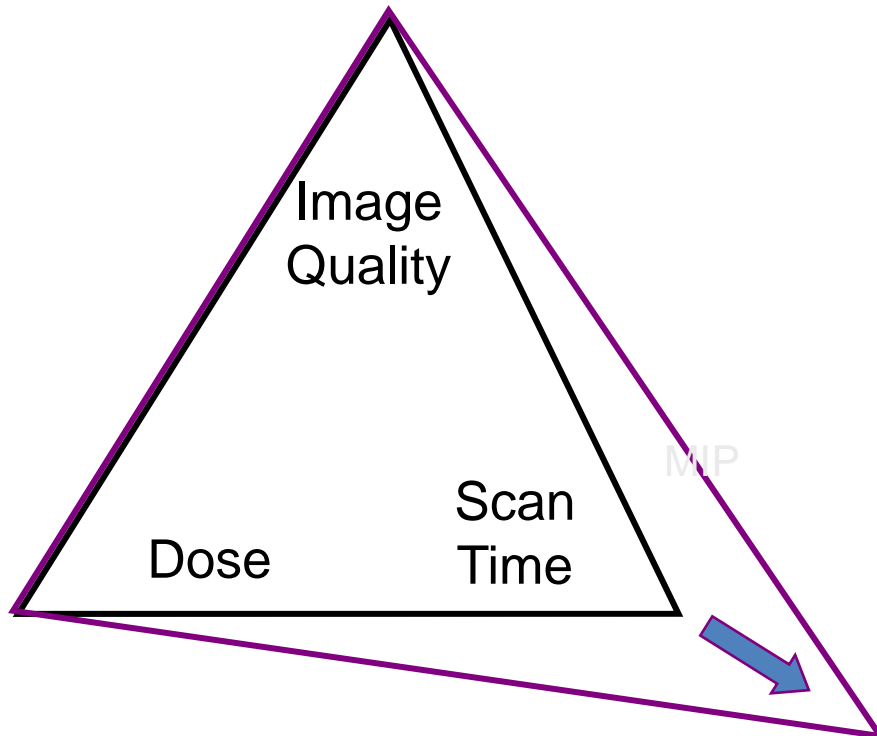


Image courtesy of University Hospitals, Cleveland

Clinical Benefits II

How can your observers benefit from reduced noise and higher sensitivity?

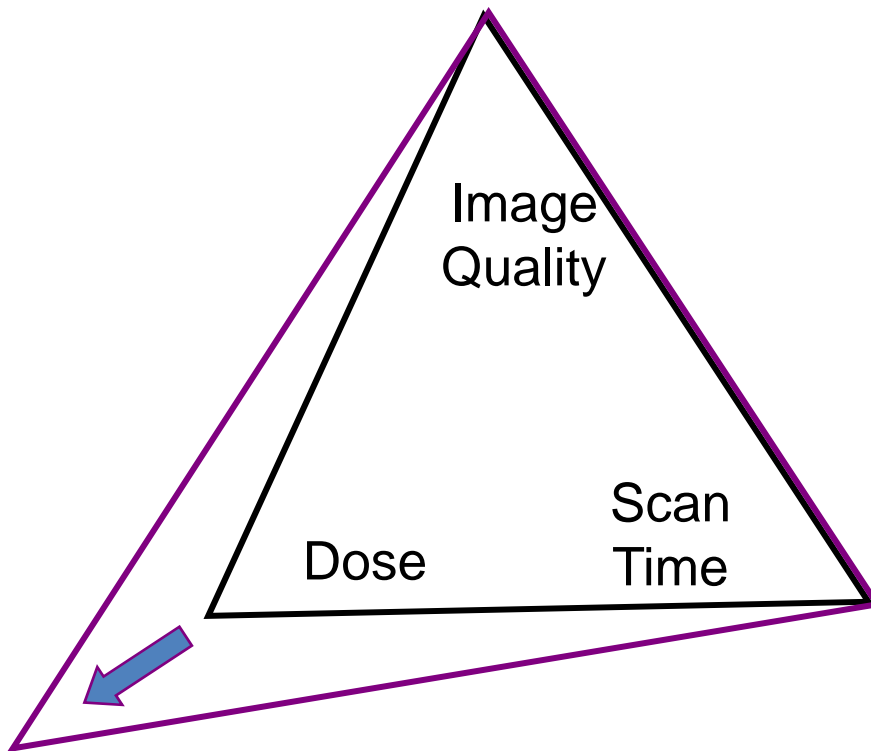
Faster Scan Times



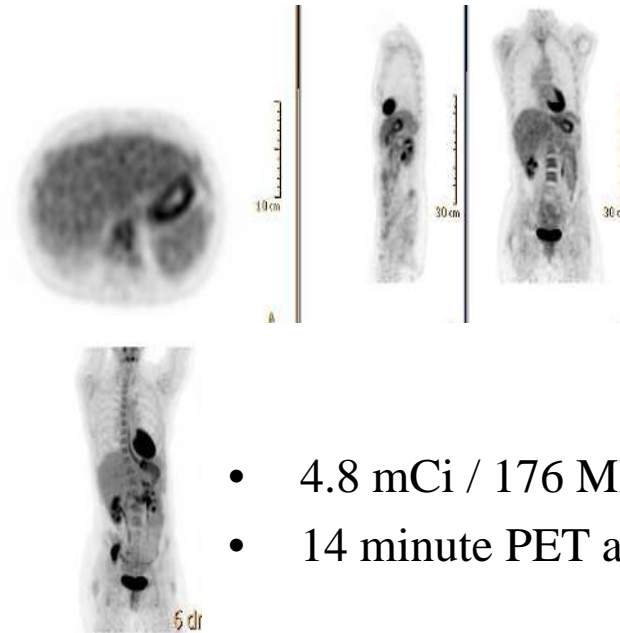
- 11.3 mCi / 418 MBq FDG
- 9 minute PET acquisition
- 76 kg / 168 lb Patient

Clinical Benefits III

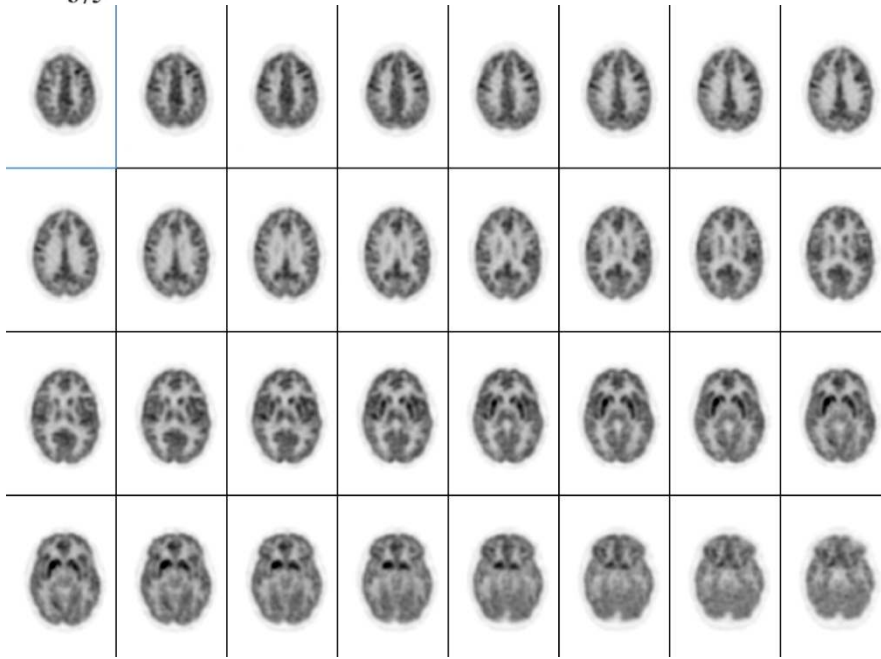
How can your customers benefit from reduced noise and higher sensitivity?



Lower Doses

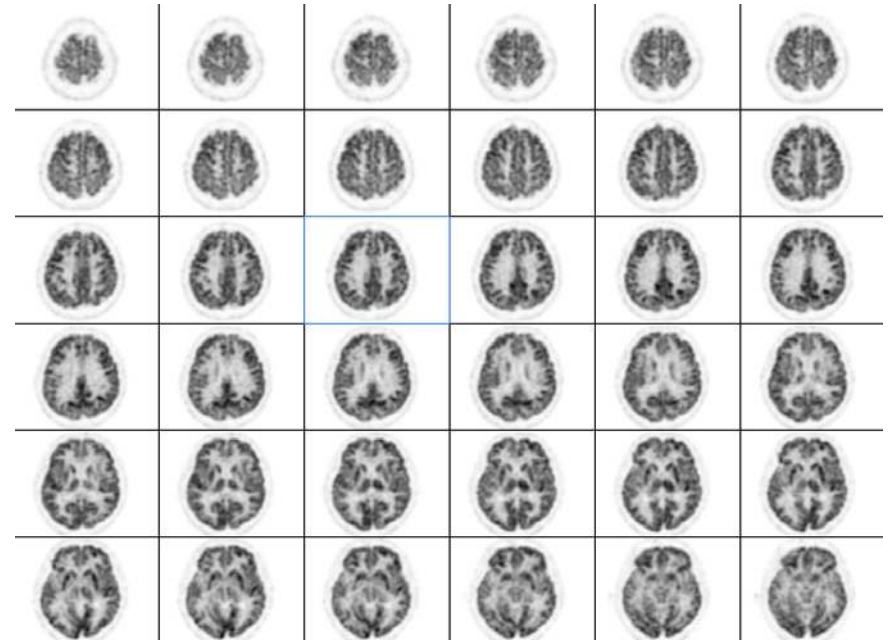


- 4.8 mCi / 176 MBq FDG
- 14 minute PET acquisition



TrueFlight

Non-TF





PET in the neuroimaging:

Before fMRI technology PET scanning was the preferred method of functional brain imaging (basic motor, sensory processes and complex cognitive processes).

The images generated by PET represent physiological parameters, such as the rate of glucose uptake or the rate of blood flow, which are inferred from the distribution of positron-emitting radiopharmaceuticals.

Radiotracers:

-ligands for specific neuroreceptor subtypes such as [11C] raclopride and [18F] fallypride for dopamine D2/D3 receptors, [11C] McN 5652 and [11C] DASB for serotonin transporters, or enzyme substrates (e.g. 6-FDOPA for the AADC enzyme).

-These agents permit the visualization of neuroreceptor pools in the context of a plurality of neuropsychiatric and neurologic illnesses.



PET in the neuroimaging:

Activation experiment: increases in local synaptic activity generate increases in local glucose uptake and blood flow.

H215O autoradiographic technique: the short half-life of ^{15}O permitting both successive measurements of cerebral blood flow in a single session and the acquisition of experimental and control images with the same subject .

Tracer kinetics limitation: temporal resolution of PET is several orders of magnitude slower than the neuronal events of interest.

Temporal resolution improvement: experimental designs

-Task repetition

- repetitive performance within the period of time in which a single measurement is taken
- repeated blocks of tasks.