Positron Emission Tomography
Present status and future prospects

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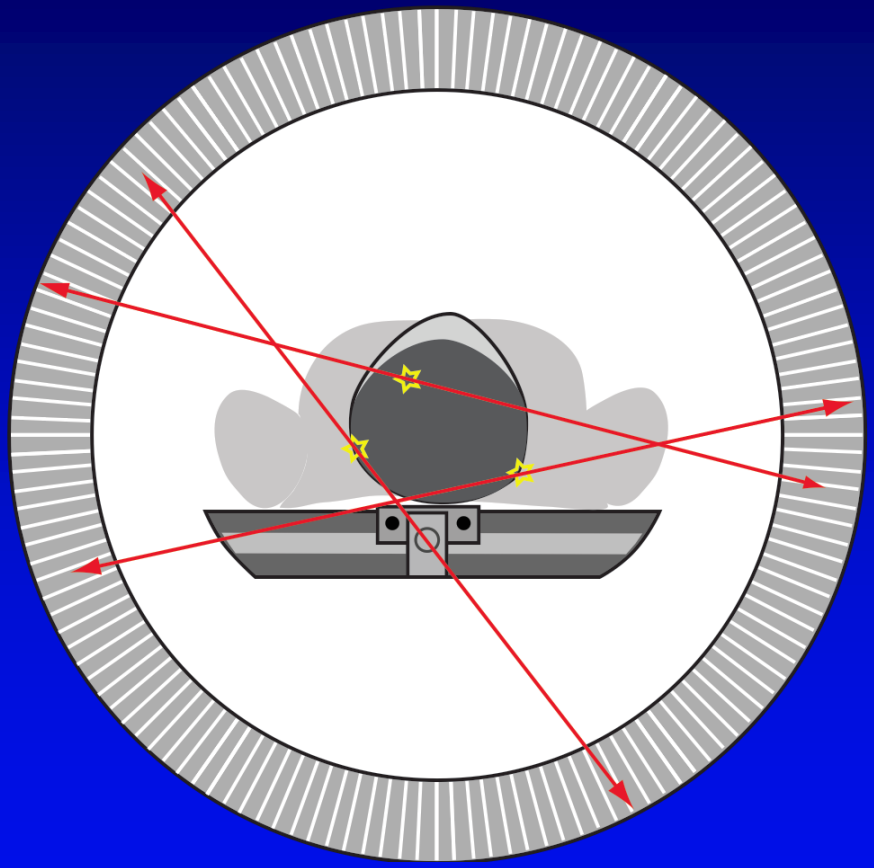
What is PET

Positron Emission Tomography is a non invasive method for imaging the distribution of a radioactively labelled compounds in the human body.

This is usually often to as “molecular imaging”, or functional imaging.

In Positron Emission Tomography a chemical compound is labelled with a positron emitting isotope. The labelled compound is injected in a patient.



After some time the isotopes decay. The emitted positron annihilates with an electron into two back-to-back gamma rays of 511 keV. Detecting the gamma rays reveals the position of the isotope.

The PET scanner is not observing space points, but a lines of response. The positron annihilation occurred somewhere along this line of response.

From a large set of lines of response, covering a sufficient number of directions around the patient, it is possible to reconstruct the 3-dimensional density distribution of the tracer.

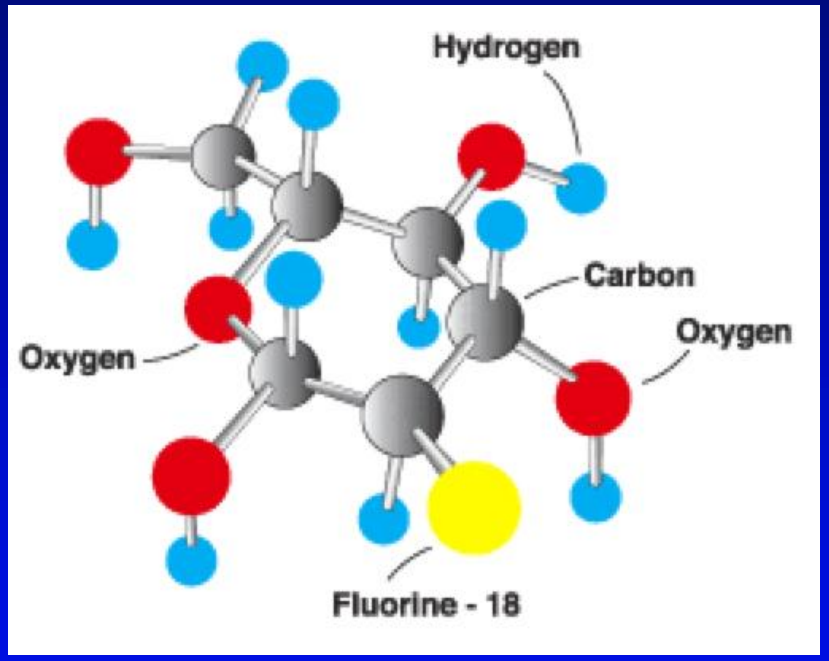
This is usually done with an iterative reconstruction algorithm, and is very computer intensive.

The most commonly used isotopes in PET are

Isotope	Decay time (1/2 life)
^{11}C	20 min
^{18}F	110 min
^{13}N	10 min
^{15}O	2 min

Producing these isotopes requires a cyclotron

By far the most commonly used radiopharmaceutical is FDG (Fluoro2-deoxy-D-glucose), a 18F labelled glucose analog.



FDG is transported in the body in a very similar way as normal glucose.
The metabolic product of FDG is trapped in the cell.
Therefore the activity distribution directly reflects the metabolic activity of the cells

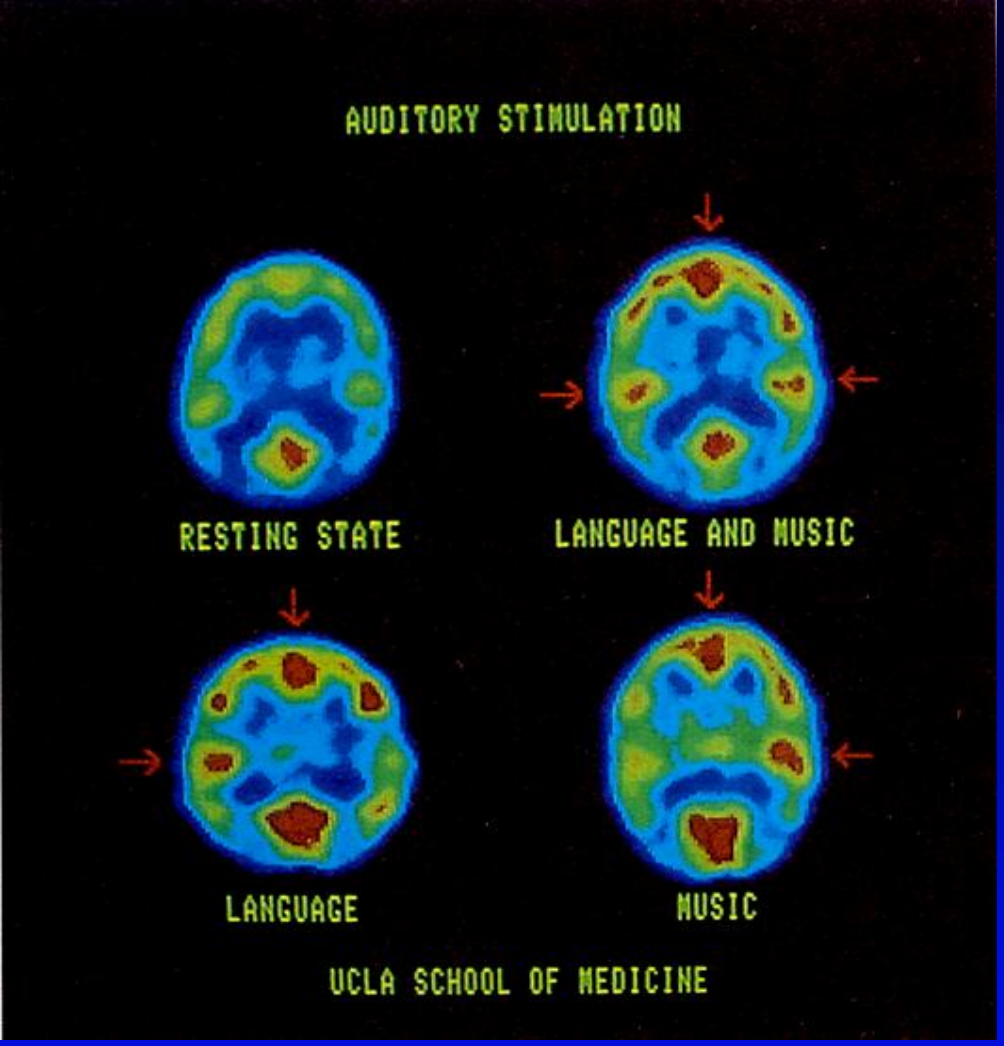
Functional information can also be obtained from MRI, but the most important advantage of PET is its sensitivity.

Useful images can be obtained with for pico-Mole concentrations of the tracer molecule.
A few pico-Mole is far below the concentration that has any pharmacological effect.

Applications of PET

The most important applications of PET are

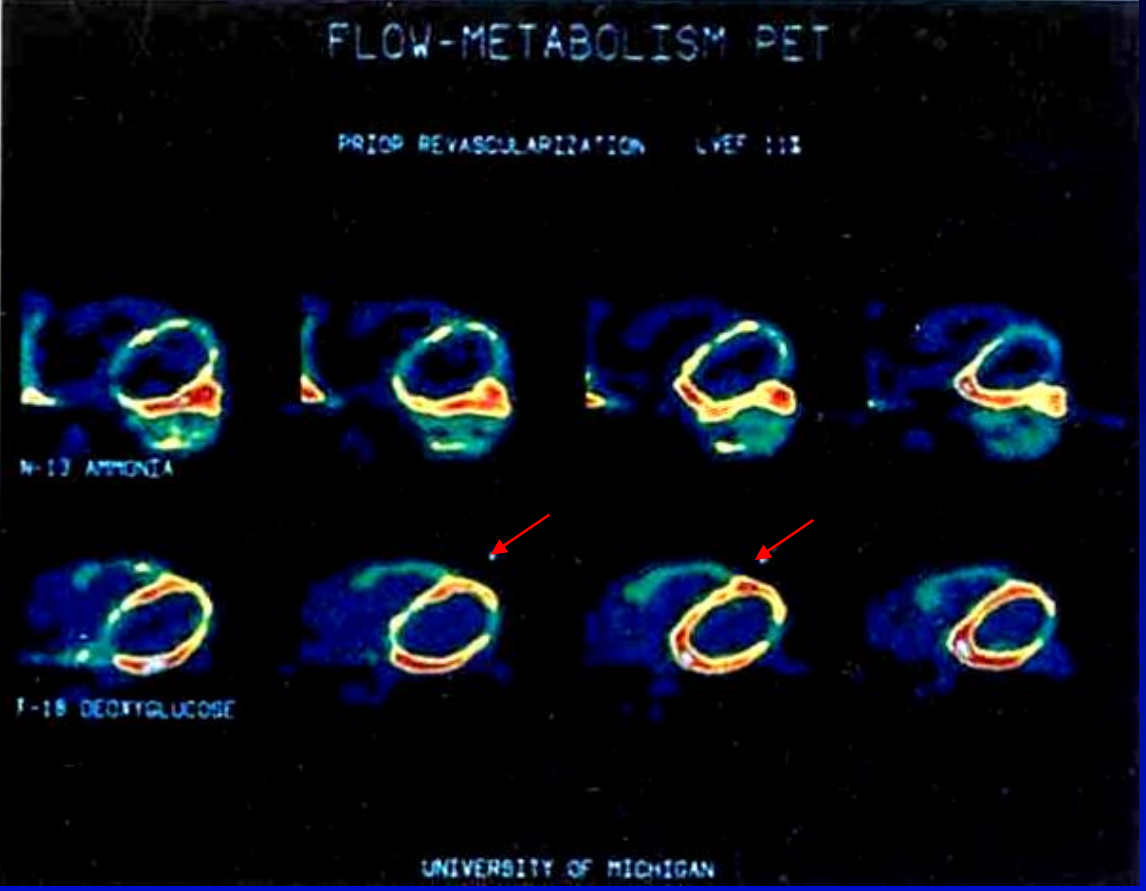
- neurology
- cardiology
- oncology
- biomedical research (small animal PET)



Normal volunteers were injected with FDG. PET scans show the activity of the brain in response to different auditory stimuli. The glucose concentrates in areas where there is increased metabolic activity in the brain.

Language = Sherlock Holmes story.
Music = a Brandenburg concerto

Clinical use: early detection of Alsheimer's and Huntington's disease



PET in cardiology

N-13 Amonia-perfusion

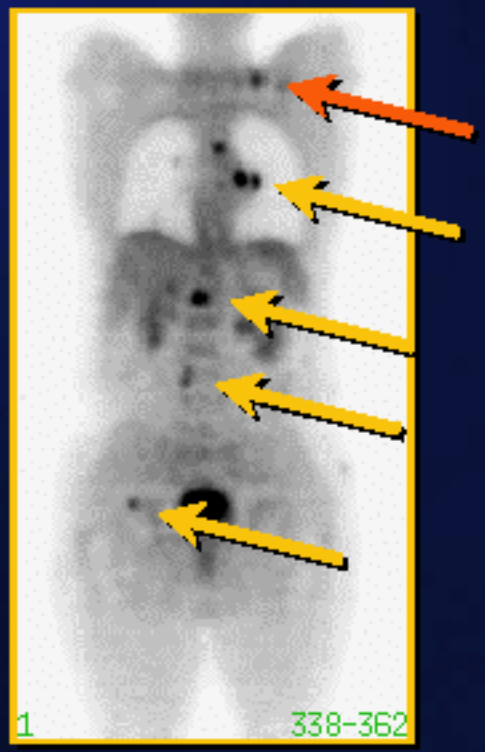
FDG metabolism

In patients with CAD, PET studies allow discrimination between necrotic and viable ischemic myocardium. When viable myocardium tissue still exists, surgery (a by-pass) may be indicated, whereas if there is no FDG metabolism, a heart transplant would normally be chosen as treatment

PET Case Study: Melanoma Staging & Follow-up

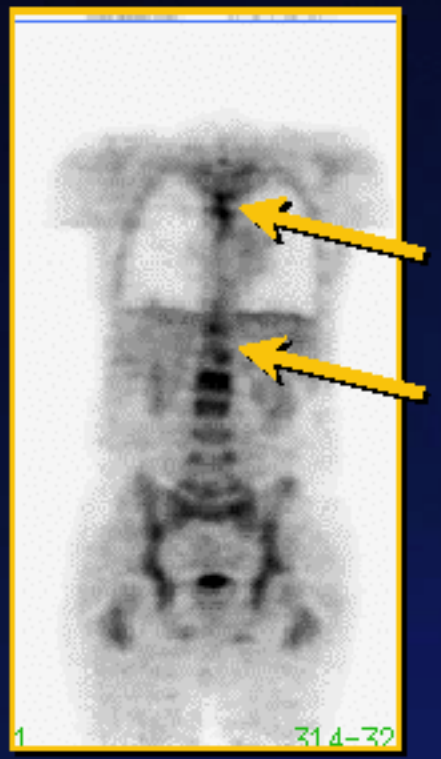
PET in oncology

Before Therapy PET on 11/20/00



CT showed mass in left shoulder
But missed abdominal lesions

After Therapy PET on 2/18/01

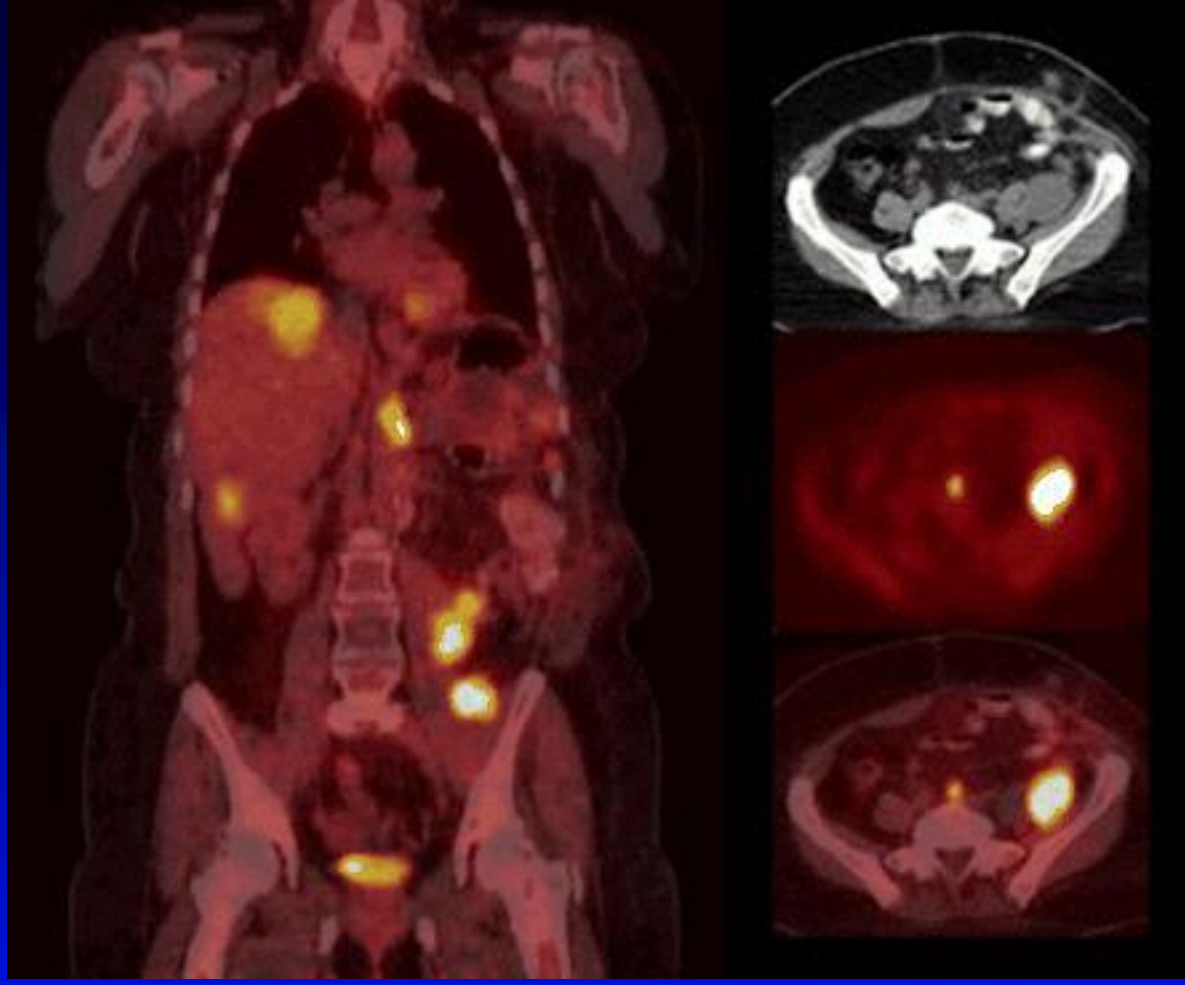


Normal post-therapy
bone marrow uptake

The PET image shows only limited anatomical information. Nearly all whole body PET scanners today are combined PET – CT scanners.

PET-CT image fusion

55 year old female
Renal metastases

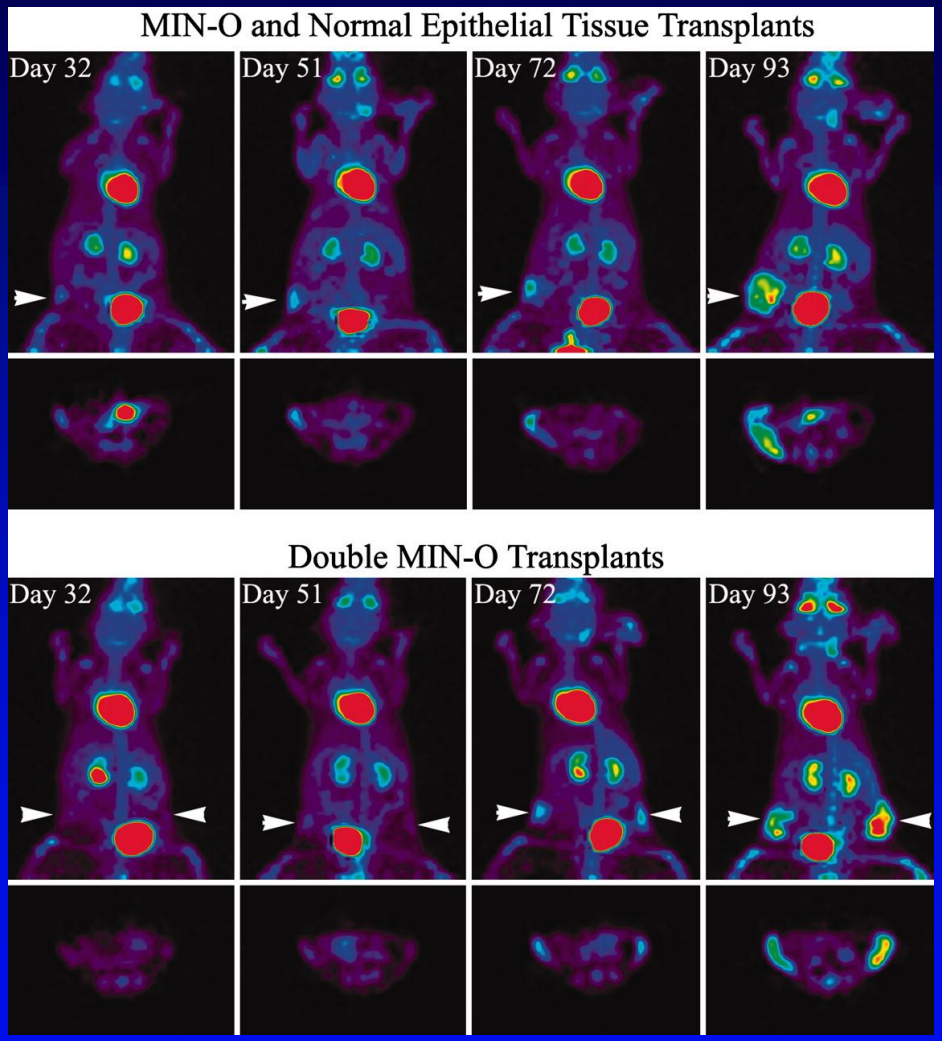


Small animal PET (preclinical PET)

Biologists have established rodent models for studying the human biology and diseases. Therefore there is a big demand for imaging small animals for research purposes.

Example: in the process of the development of a new drug, one wants to know the pharmacokinetics of the new drug early on.

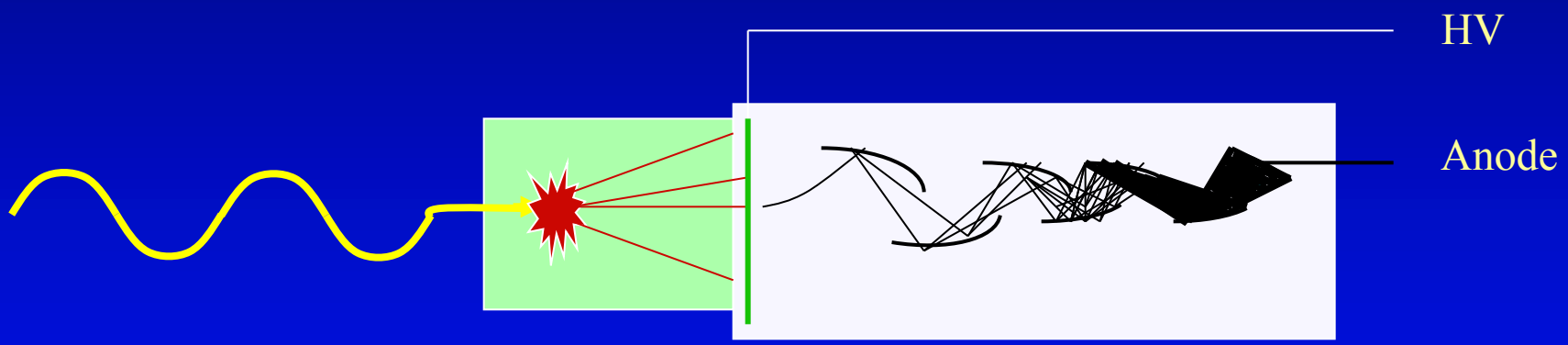
In vivo positron-emission tomography imaging of progression and transformation in a mouse model of mammary neoplasia



Abbey C K et al. PNAS 2004;101:11438-11443

Performance of PET scanners

From the engineering point of view a PET scanner is a detector for 511 keV gamma rays that surrounds the patient.



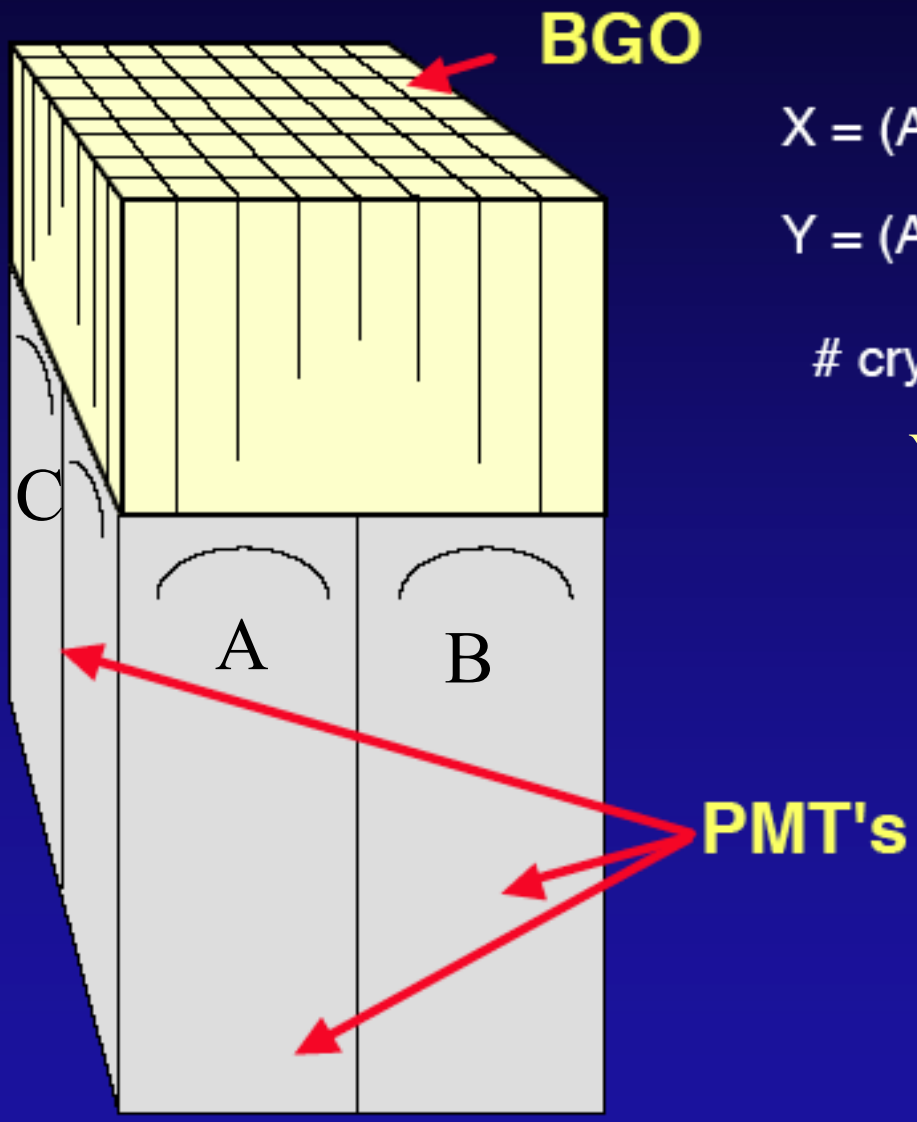
Gamma ray Scintillator Photomultiplier tube

Nearly all PET scanners use photomultiplier tubes for cost reason.

At 100 €/cm^2 the cost of the photodetectors will add up to ≈500'000 € in a typical whole body PET scanner.

In small animal PET scanners one can afford a more expensive photodetector

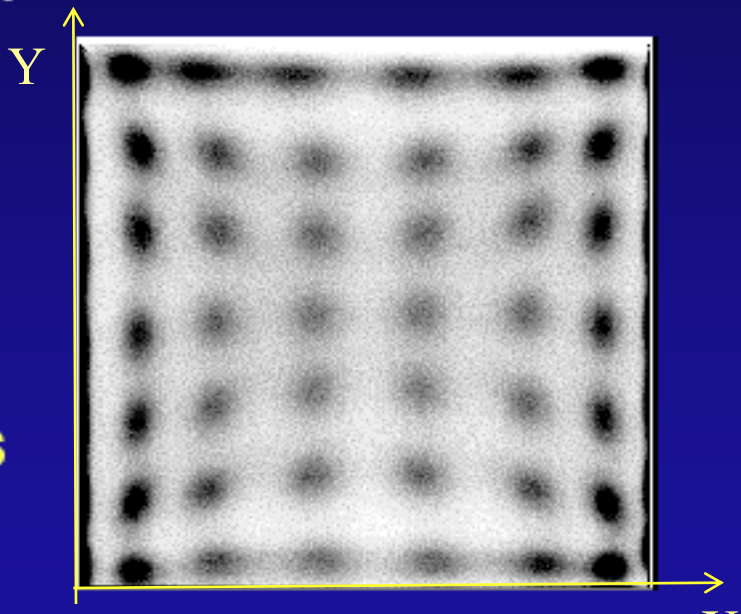
PET Block Detector



$$X = (A + B - C - D) / (A + B + C + D)$$

$$Y = (A - B + C - D) / (A + B + C + D)$$

crystals / # PM tubes = 9 to 16



Flood Source Response:
CTI/Siemens EXACT HR Block

Scintillators for PET

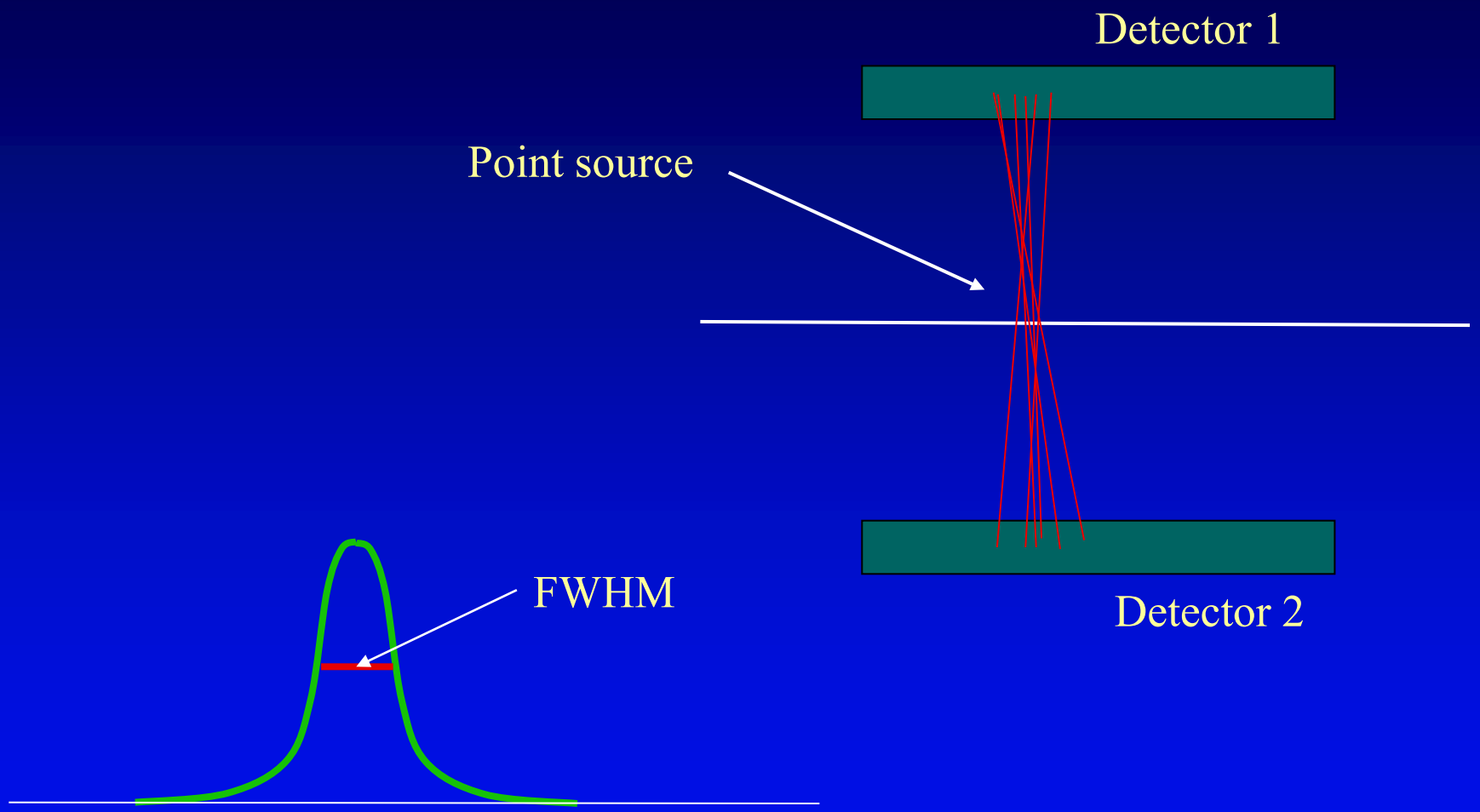
Crystal	Att. length [mm]@522keV	Light Yield	λ [nm]	Decay time [ns]
BGO	10.4	15	480	300
NaI	28.6	100	410	230
GSO	14.1	30	440	60
LSO	11.4	75	420	40

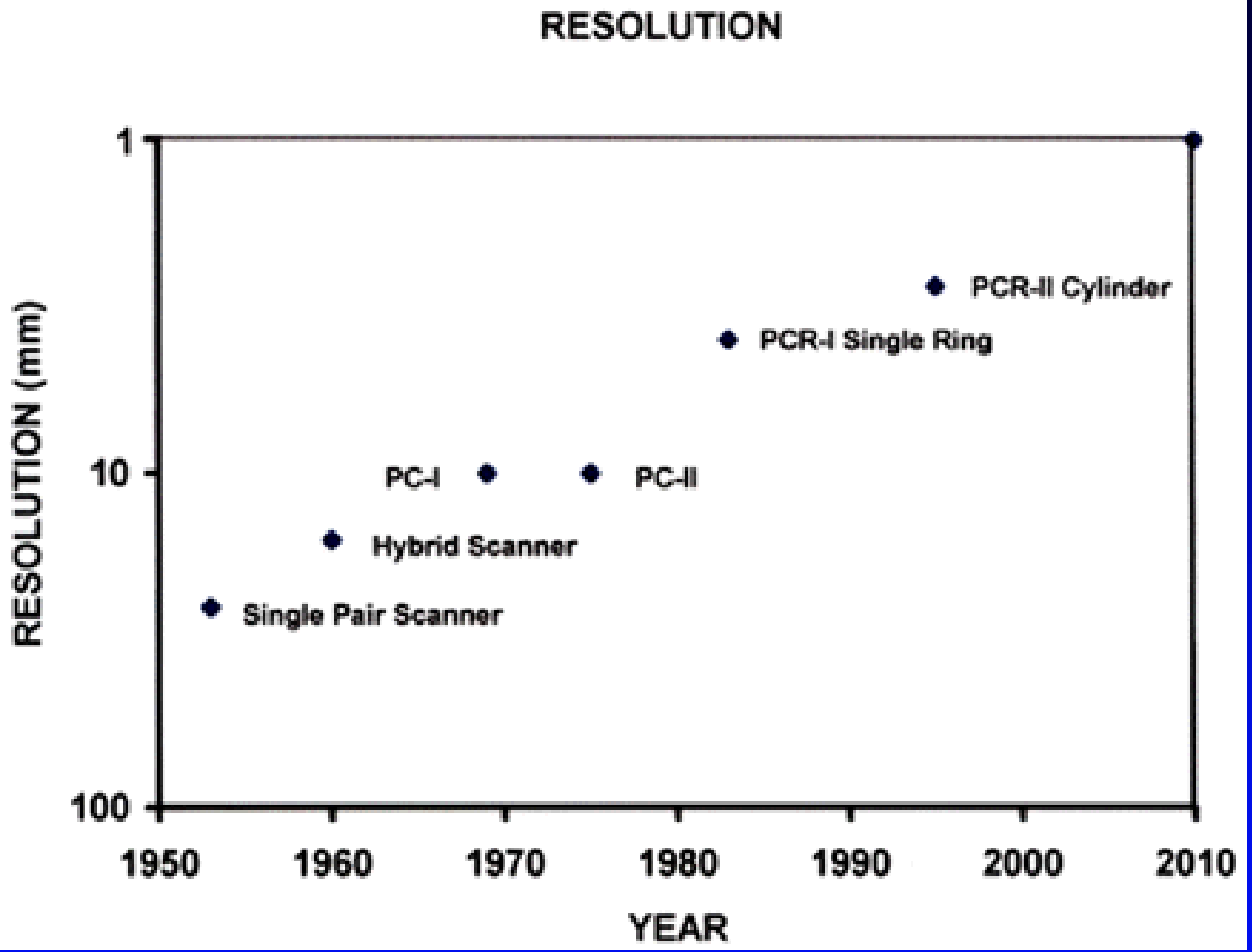
The most important physical characteristics of a PET scanner are:

- spatial resolution in the image
- sensitivity: number of counts/s for a given activity in the patient.
- time resolution
- energy resolution

Of course: cost, reliability, support, ease of use, patient comfort, etc. are very important too, but we will concentrate on the physical properties.

Spatial resolution in PET




RESOLUTION
RESOLUTION (mm)
1
10
100
PCR-II Cylinder
PCR-I Single Ring
PC-I
PC-II
Hybrid Scanner
Single Pair Scanner
1950
1960
1970
1980
1990
2000
2010
YEAR

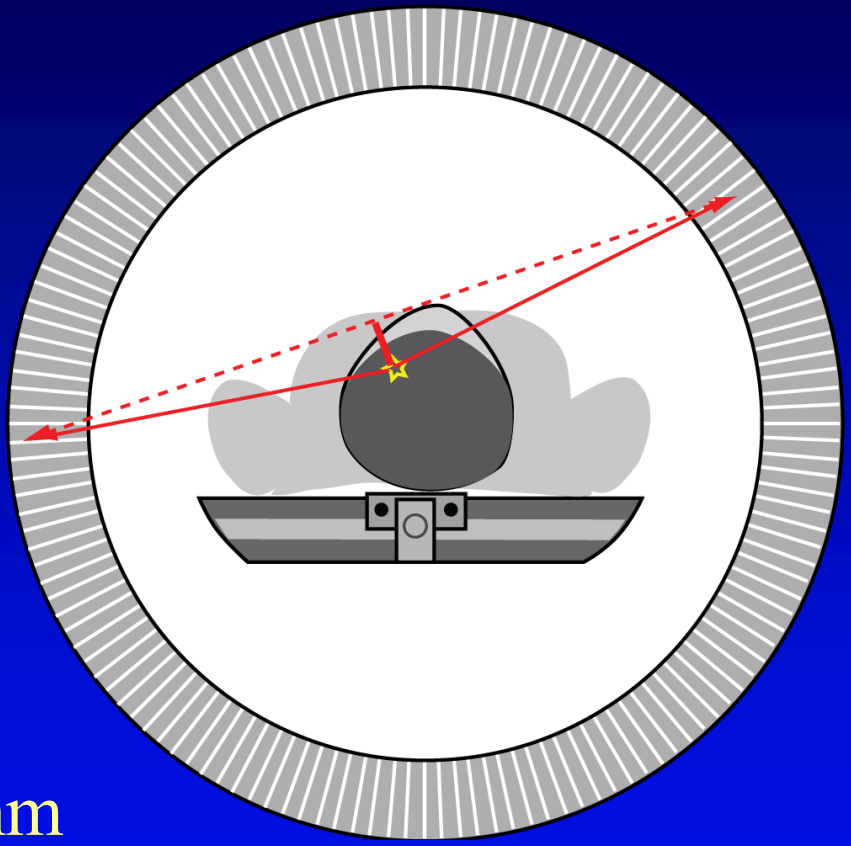
Will the trend of improving resolution continue?

Two physical effects limit the resolution
which can be achieved in PET

- Non-collinearity
- Positron range

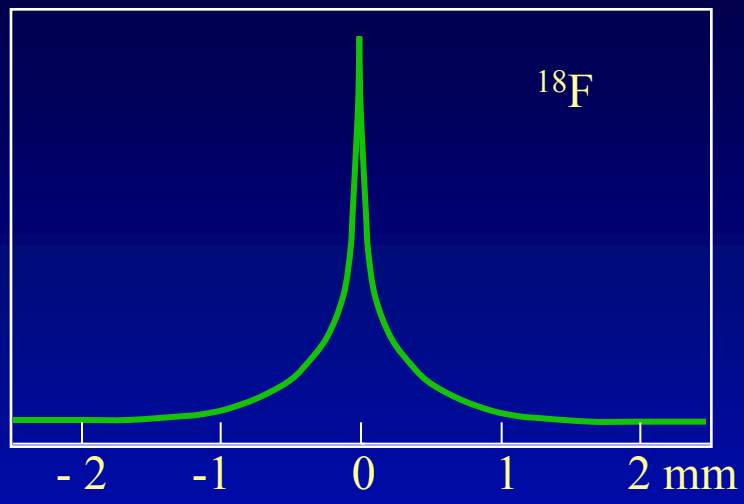
The two 511 gamma rays are not exactly back-to-back

FWHM = 0.0022 Ring Diameter

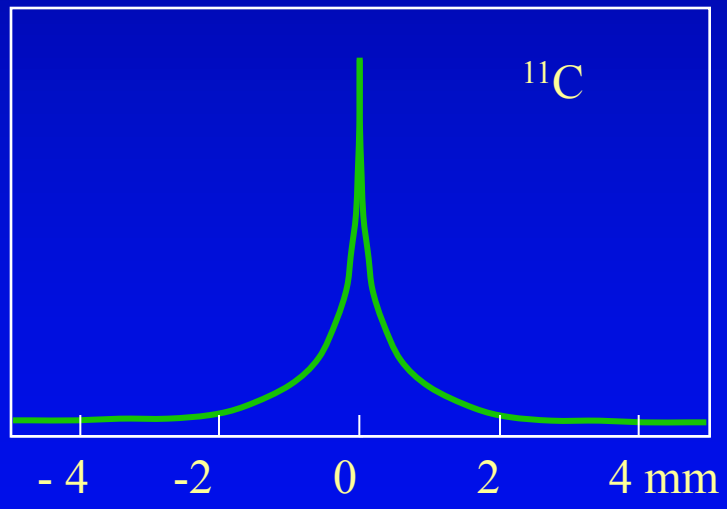


For ≈90 cm diameter ≈ 2.0 mm
For ≈15 cm diameter ≈ 0.3 mm

Positron range



FWHM = 0.102 mm
FWTM = 1.03 mm



FWHM = 0.188 mm
FWTM = 1.86 mm

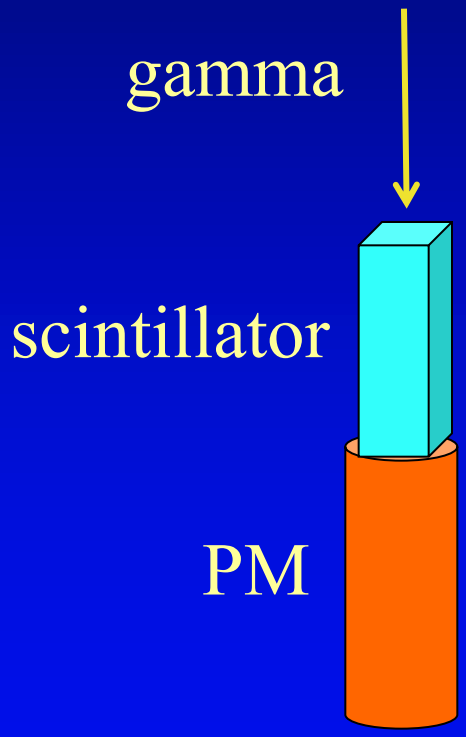
$$FWHM = \sqrt{Range^2 + Collinearity^2}$$

The ultimate resolution possible in clinical whole body scanners is about 2 mm

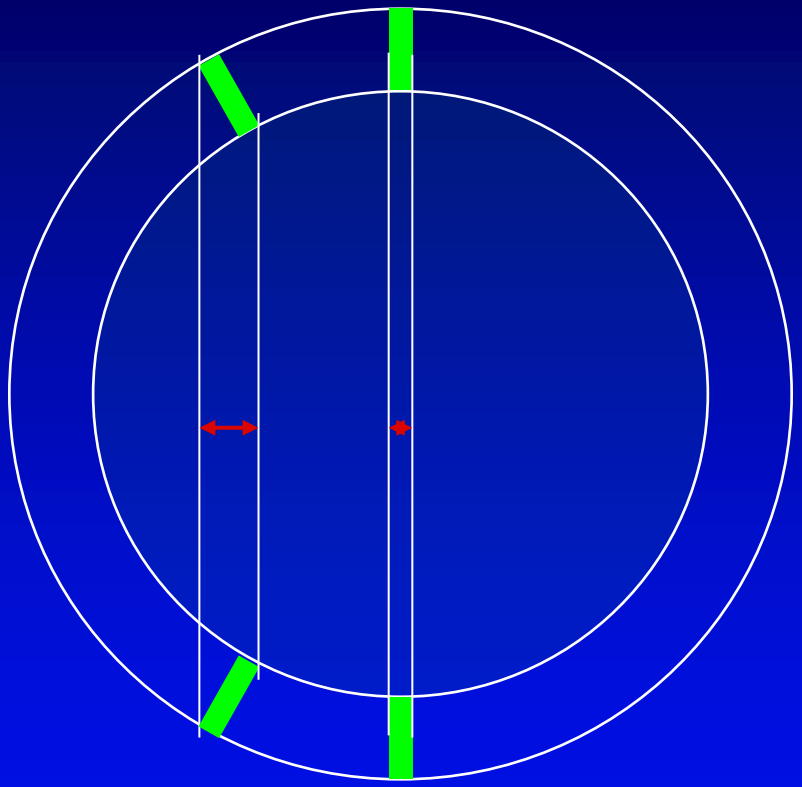
In small animal PET it is about 0.5 mm.

Real PET scanners have a number of instrument related limitations on the resolution

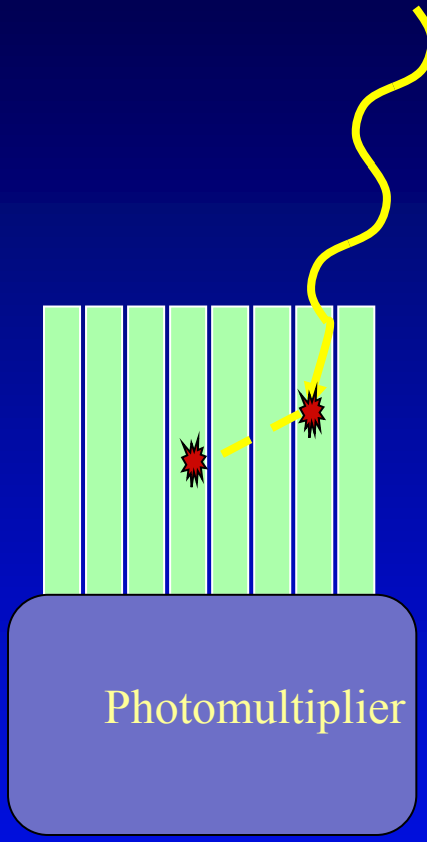
- crystal size
- depth of interaction
- compton scatter in crystal



One one cannot use very long crystals; needs to compromise between resolution and sensitivity



Depth of interaction



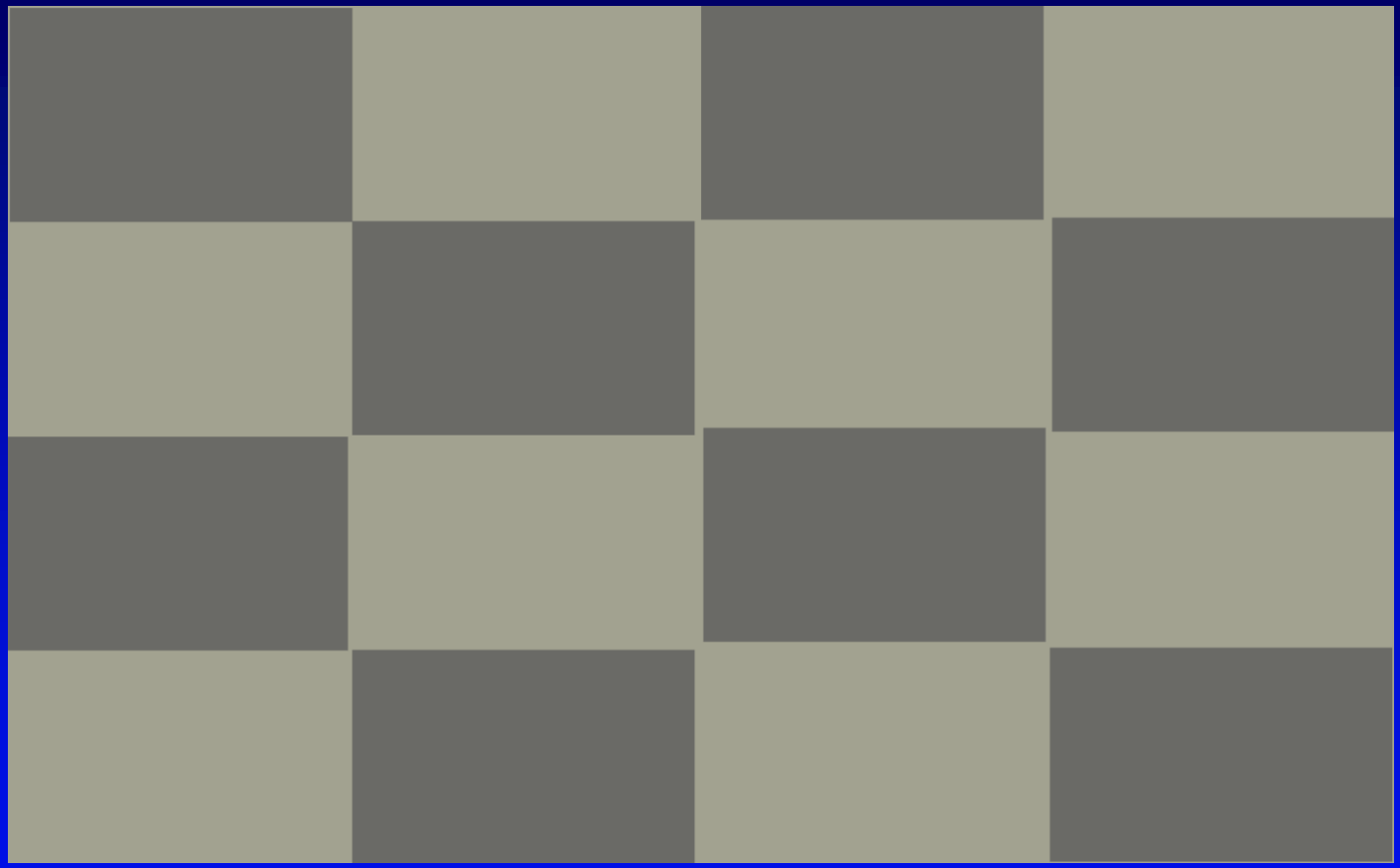
Compton scatter in detector

Other important effects : patient motion!!

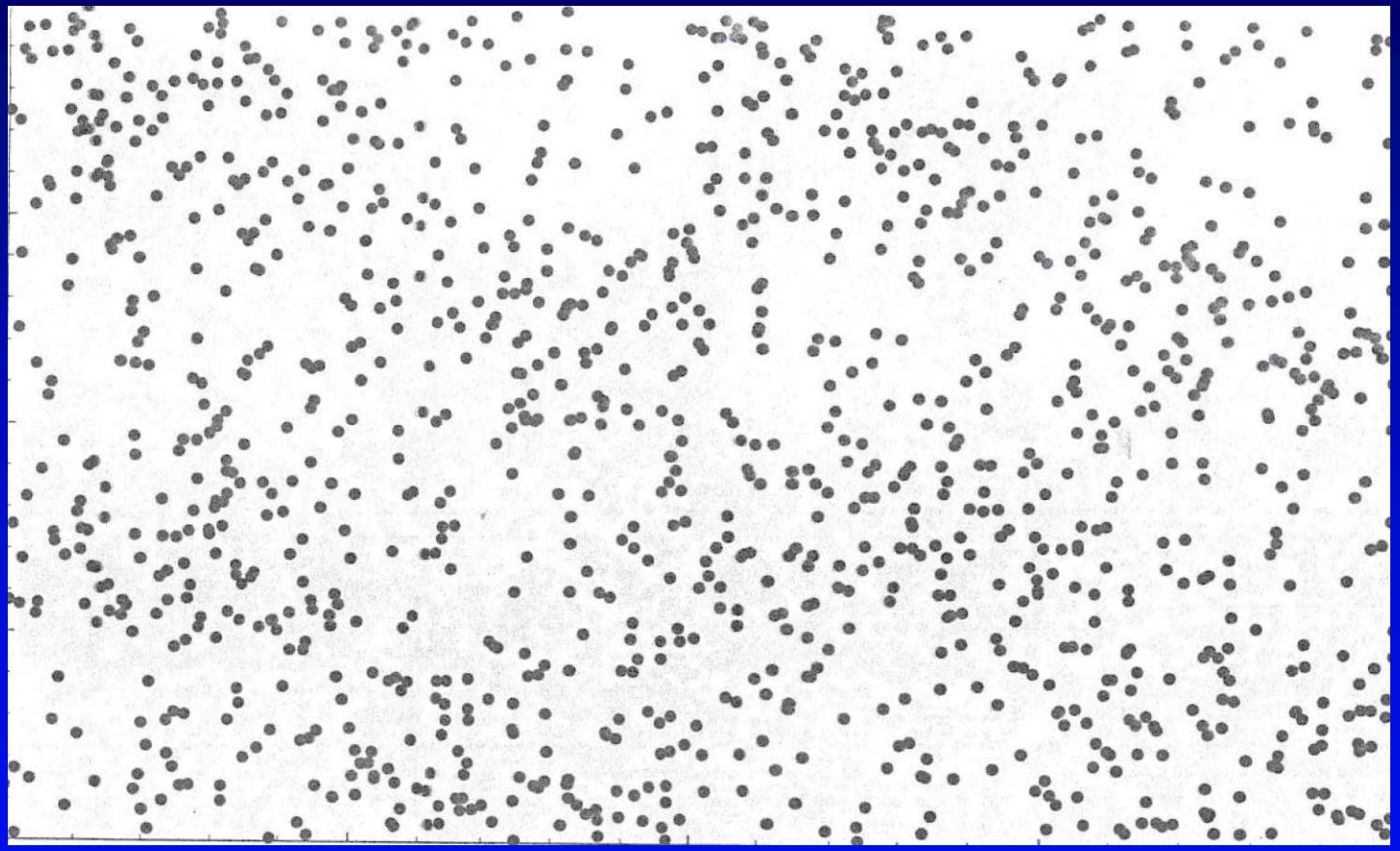
In whole body PET a resolution better than 4 mm is maybe possible but very difficult

In small animal PET a resolution of <1 mm is maybe possible but very difficult

The importance of sensitivity



Resolution is useless if you do not have enough counts!



How many annihilation events one needs to make a PET image with resolution Δ?

$$N = \left(\frac{A}{\sigma\{A\}}\right)^2 \left(\frac{L}{\Delta}\right)^3 \left(\frac{L}{\Delta}\right)$$

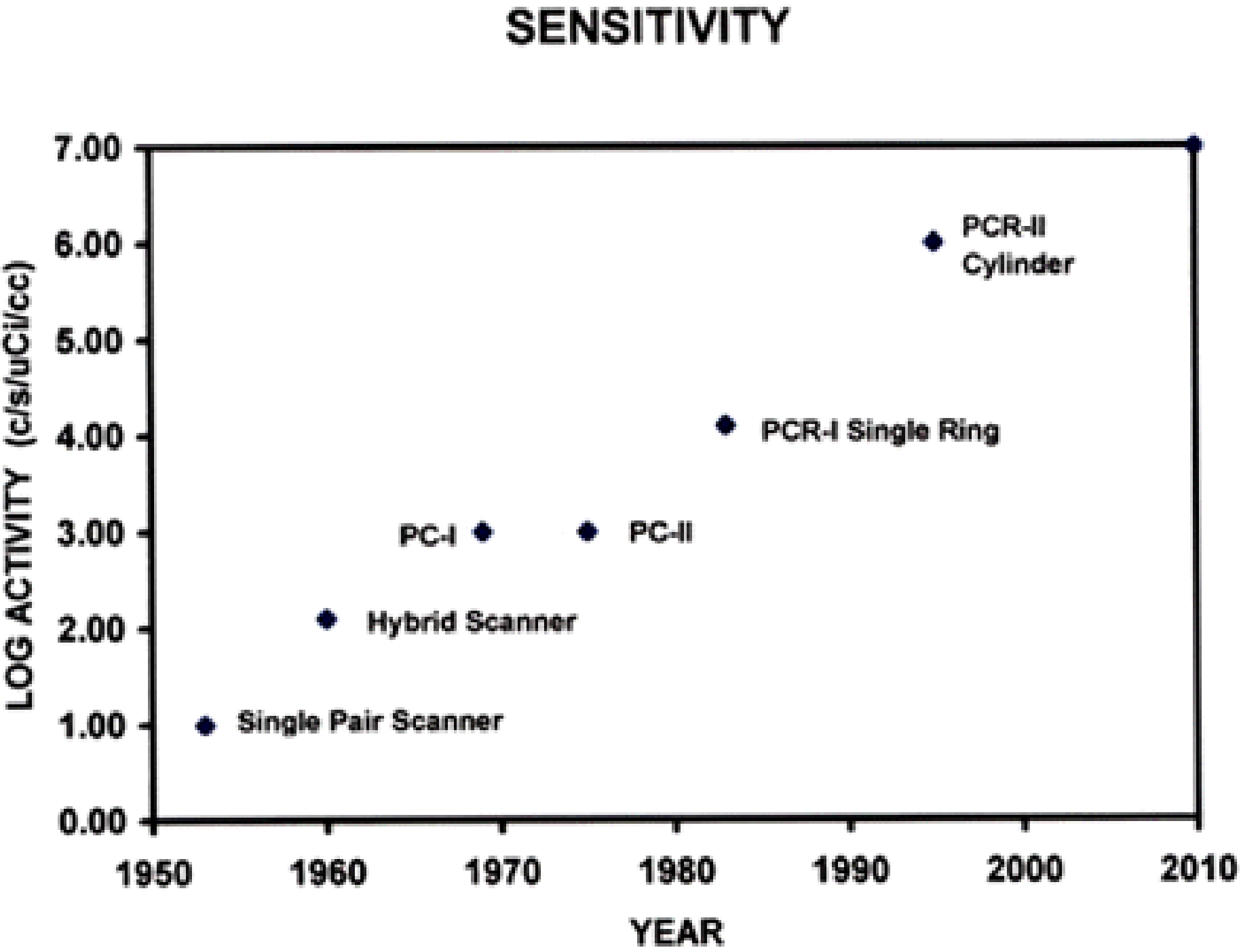
A cube of dimension L^3 is divided in voxels of dimension Δ^3.

Brain (20 cm) resolution Δ=2mm $\sigma\{A\}/A$= 10%
$\approx 10^{10}$ events ,

Imaging time 15 min >>> rate $\approx 10^7$ counts/s

If the data rate is limited to 10^6 cps, the resolution is limited to ≈ 8 mm!

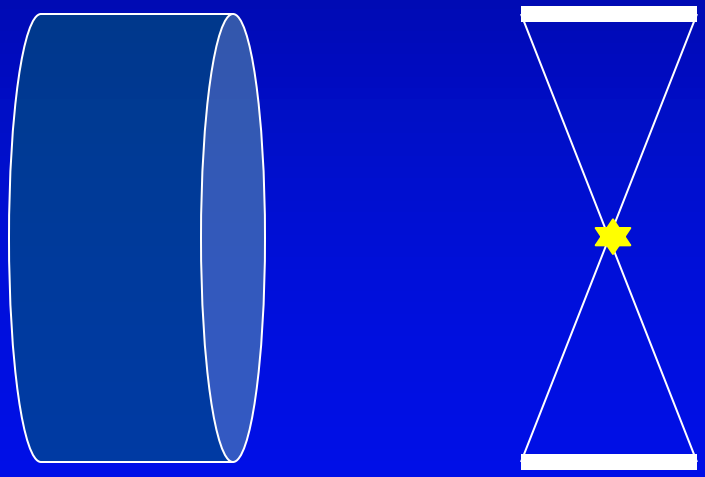
In practical clinical situations the image quality is usually more affected by lack of sensitivity than by lack of spatial resolution


SENSITIVITY
LOG ACTIVITY (c/s/uCi/cc)
7.00
6.00
5.00
4.00
3.00
2.00
1.00
0.00
PCR-II
Cylinder
PCR-I Single Ring
PC-I
PC-II
Hybrid Scanner
Single Pair Scanner
1950
1960
1970
1980
1990
2000
2010
YEAR

Sensitivity ?

For a point source in the centre,

Sensitivity = Solid angle x (efficiency)^2 = $\Omega.\varepsilon^2$



Sensitivity = Solid angle x $(\text{efficiency})^2 = \Omega.\varepsilon^2$

In principle sensitivity of several 10 % is possible

….. in practice that is very difficult

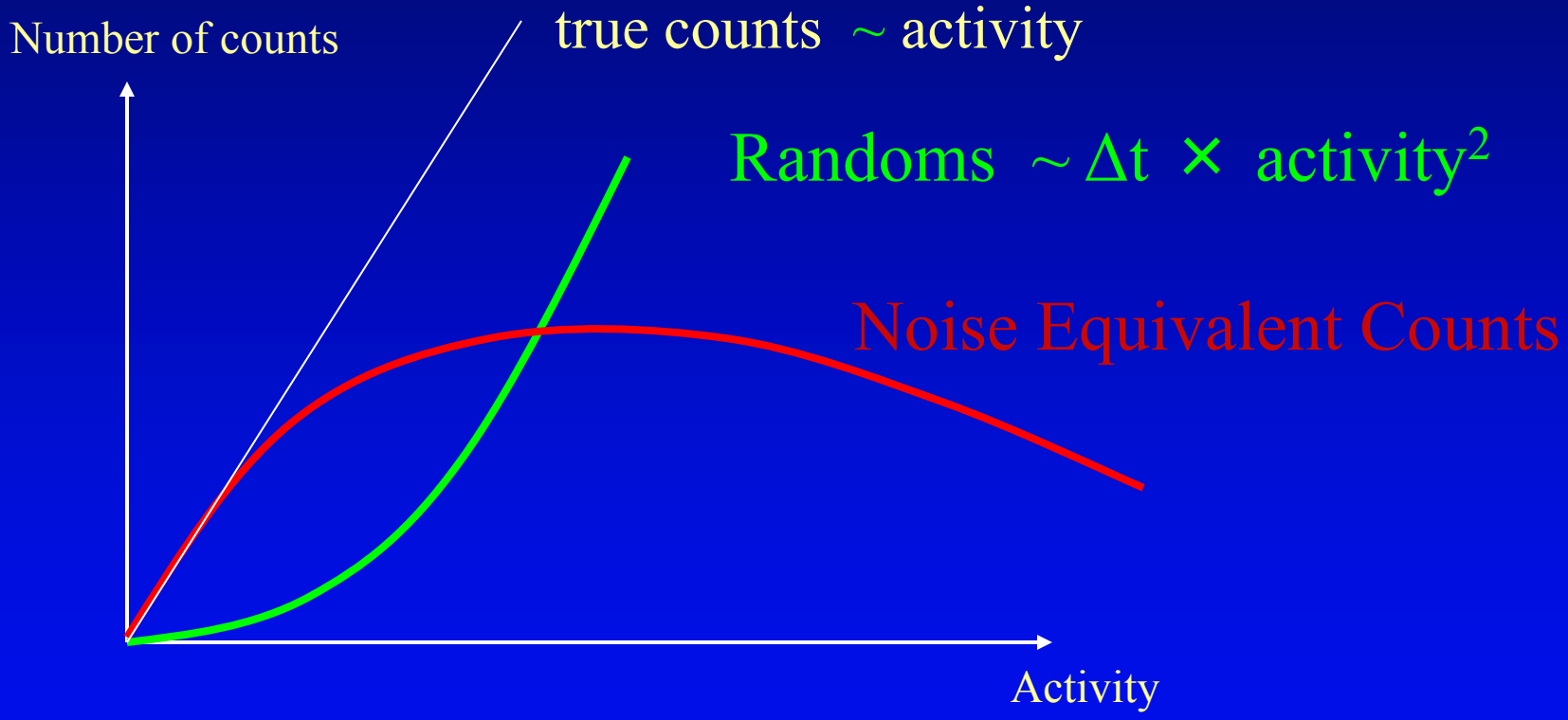
solid angle ≈ 20% (cost!)
detection efficiency ≈50%
(30 mm LSO 64% in photopeak)

Point source sensitivity 5%

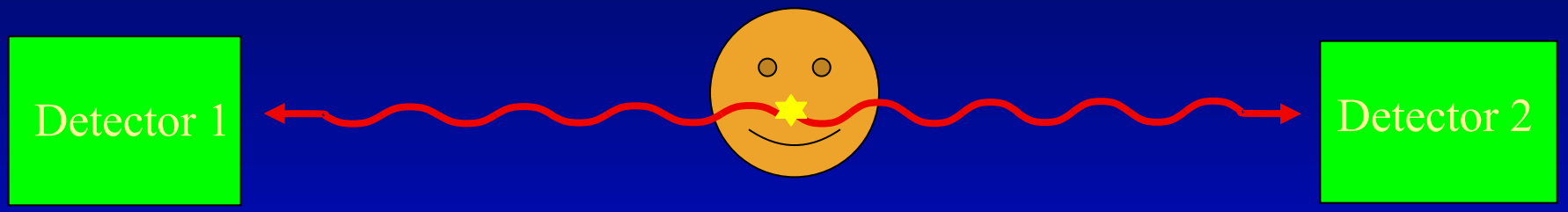
For real clinical scanners sensitivity for a point source in the middle is typically only a few %. In addition, there is scatter, reducing the true sensitivity further by a factor ≈ 7, and annihilations are usually not exactly in the centre of the scanner.

The importance of time resolution

Data rates in PET are quite large ($\geq 10^6$/s)
A time resolution of a few ns is essential.



Time Of Flight (TOF)? Δx=15 cm => Δt =1 ns !



If $\Delta t \approx$10 ps events would be space points !

$$N = \left(\frac{A}{\sigma\{A\}}\right)^2 \left(\frac{L}{\Delta}\right)^3 \left(\frac{L}{\Delta}\right)$$

This factor no longer needed

Time of flight gives an effective gain in sensitivity => $\approx 1\ \mathrm{ns}/\Delta t(\mathrm{FWHM})$

Some commercial scanners today reach $\Delta t \approx 500$ ps. There is a huge potential for improvement of the PET sensitivity by improving the time resolution.

Challenges for the near future in PET

a) Time of flight with $\Delta t << 500$ ps

b) Simultaneous PET- MR registration
The idea: get the structural information from a MRI rather than from a CT. Advantages
- avoids radiation dose from CT scan
- much better soft tissue contrast
- patient motion correction from MRI image

It will remain to be seen if these advantages justify the additional cosy

Conclusion

The PET instrumentation is now a mature technology, and it has found many applications, both in the clinic and in biomedical research.

For the PET instrument the main challenges are
- developing PET/MR co-registration
(now well under way)
- developing true Time Of Flight PET
(still along way to go)

In both cases the PMT will need to replaced by another photodetector

Reaching Time of Flight resolution in PET in the few 10 ps range is an enormous challenge. However, reaching 100 ps would already be an very big improvement.

The solution, no doubt, will require important developments in photodetector technology.

I hope that, at this conference, we will hear about developments that bring this goal a little bit closer.

Simulated images, based on a baby monkey brain phantom

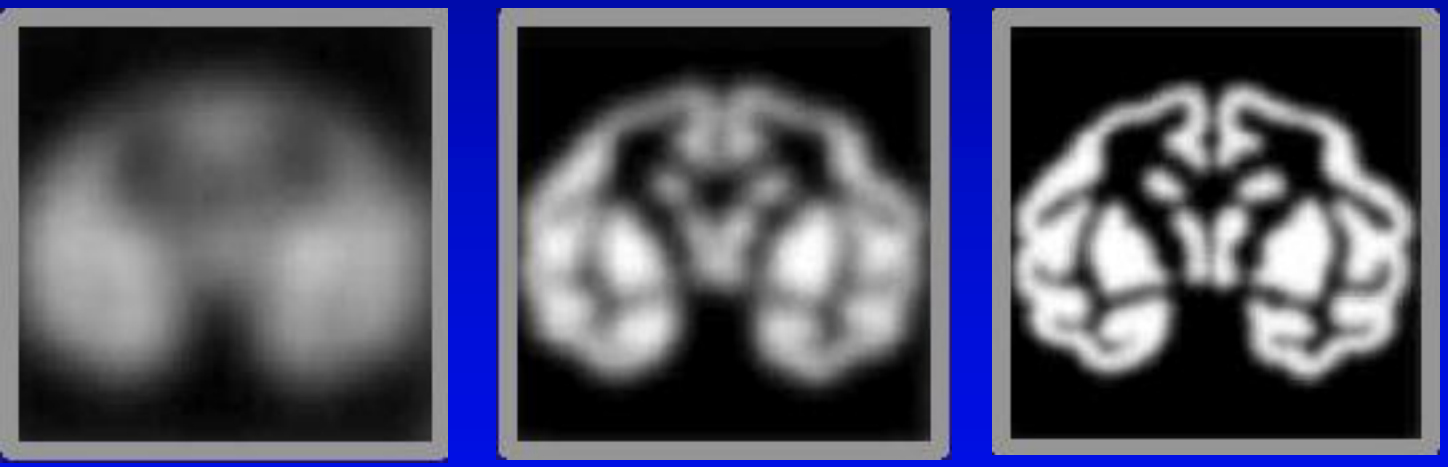
Clinical scanner Exact HR+

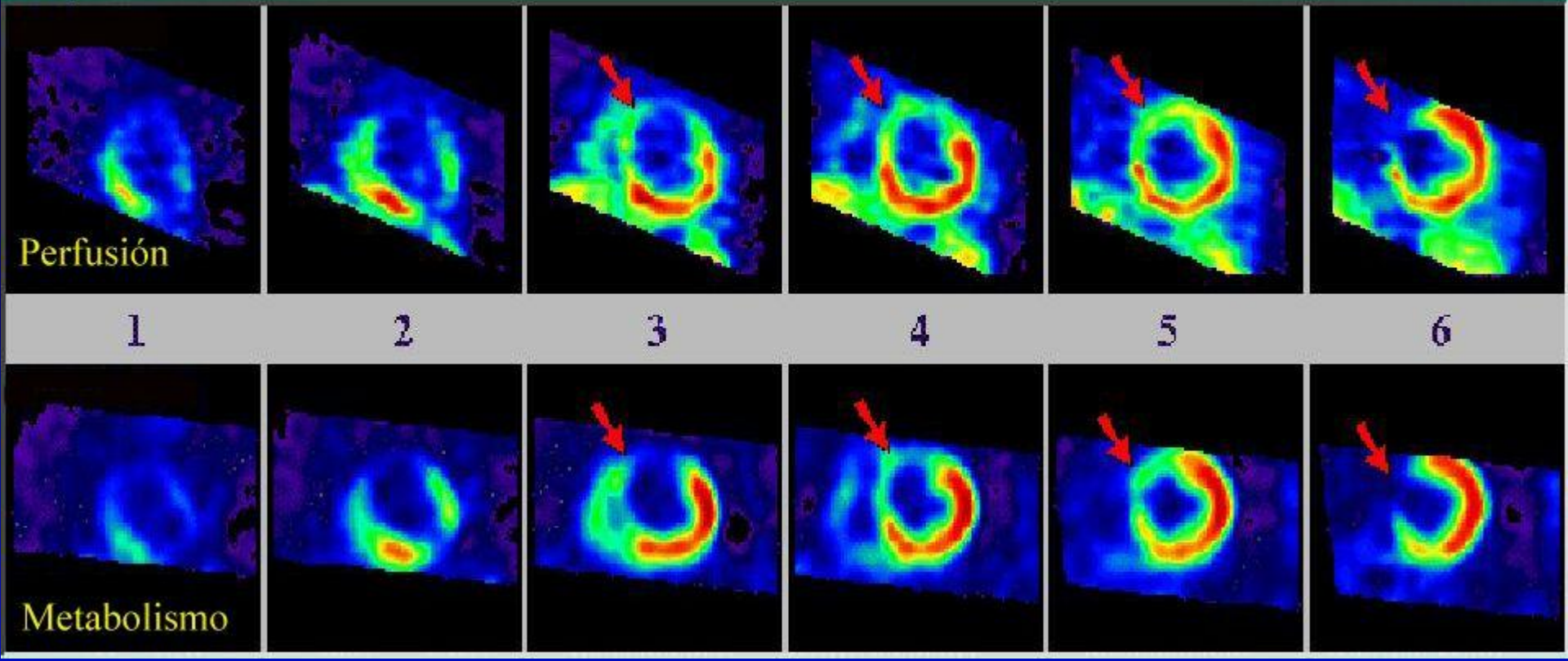
Dedicated small animal PET

4 mm

2 mm

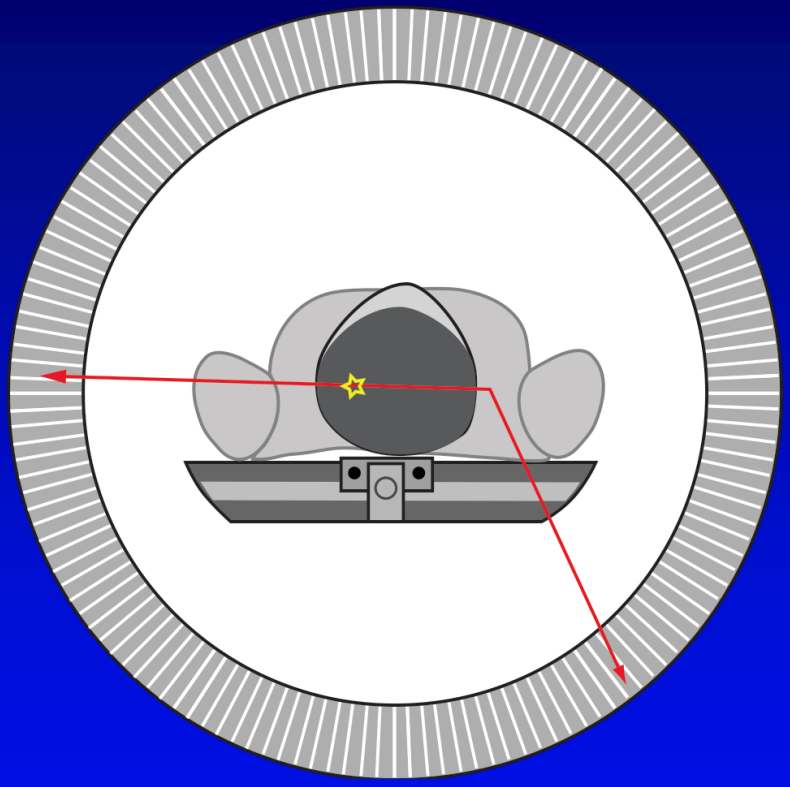
1 mm





This patient will not benefit from a bypass operation

The importance of energy resolution



In a whole body PET, only ≈15% of the annihilations the two gamma rays leave the body without Compton scatter in the patient.

Energy resolution allows rejecting scatter events.
FWHM{E}≈ 15%