PET and PET/CT
Principles and Instrumentation

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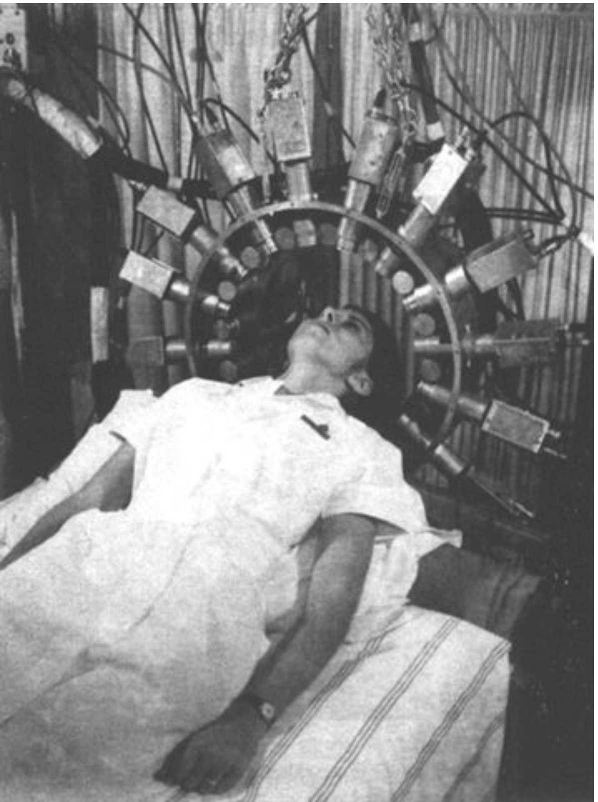
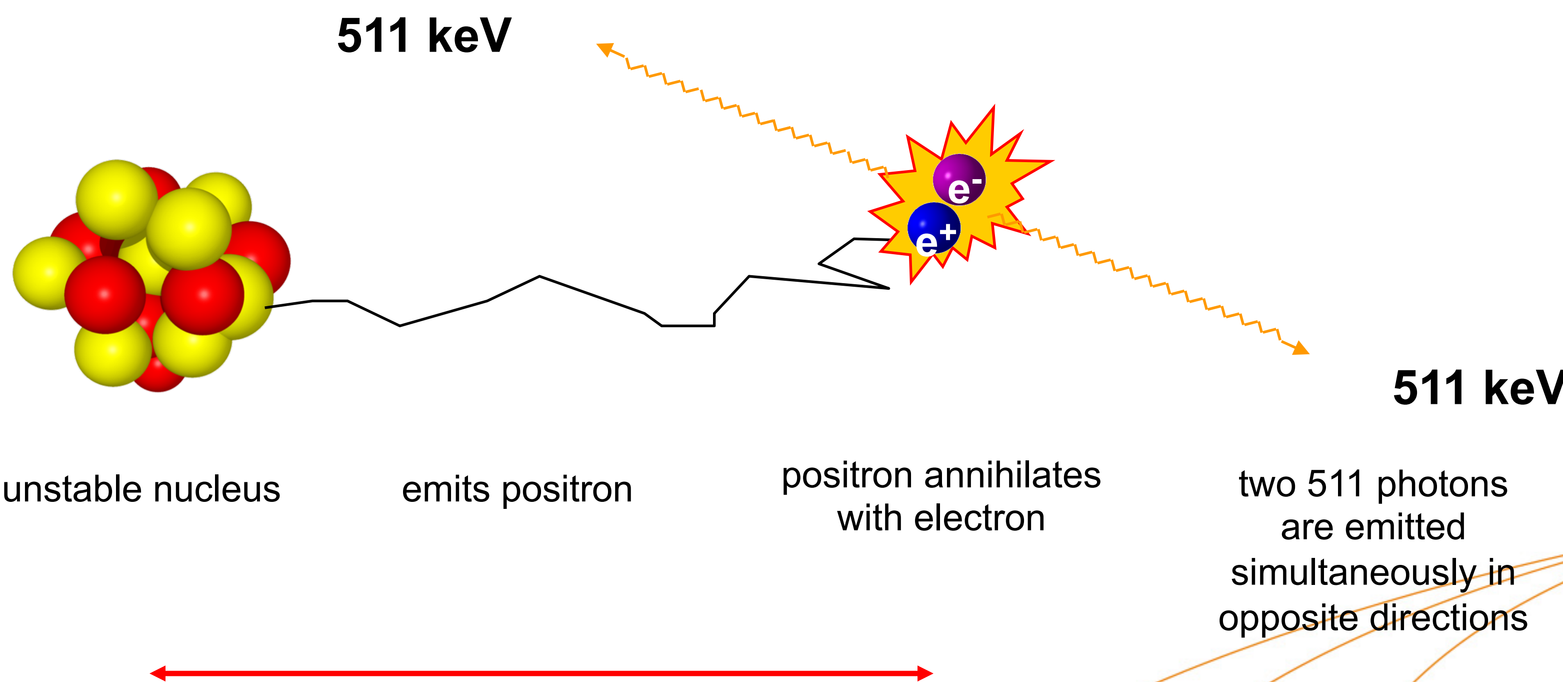


IEEE NPSS
Nuclear and
Plasma Sciences Society

PET detection basis

2 photons of 511 keV simultaneous (in coincidence)
almost on a straight line that
almost contains the point of the decay



Range of positron before annihilation depends on energy

Typical values: few (1-3) mm

Positron emitters: production process

Cyclotron

Cyclotrons combine:

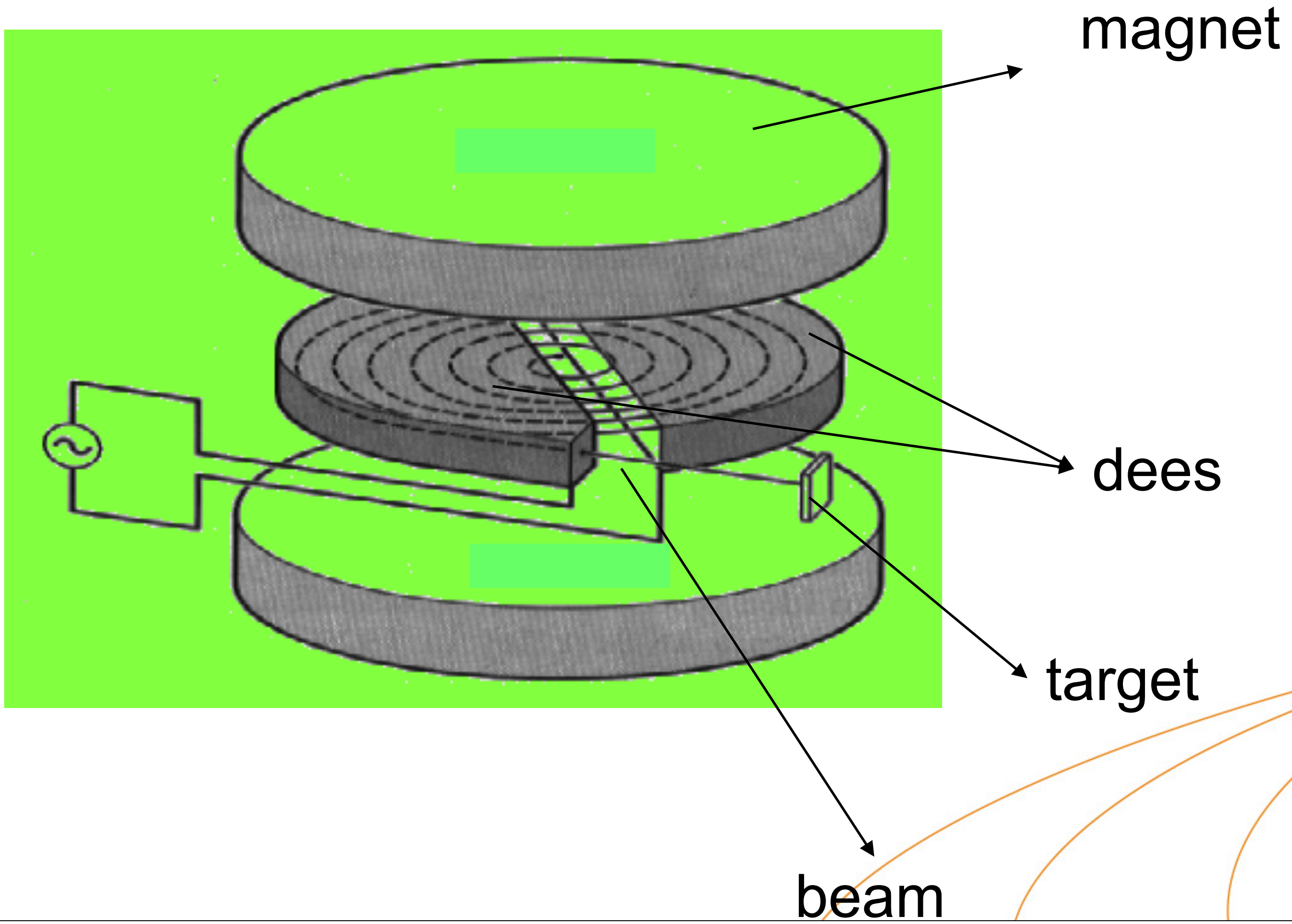
- a strong axial magnetic field

- a high frequency alternative electric field between two elements of a semi-circular form (known as dees)

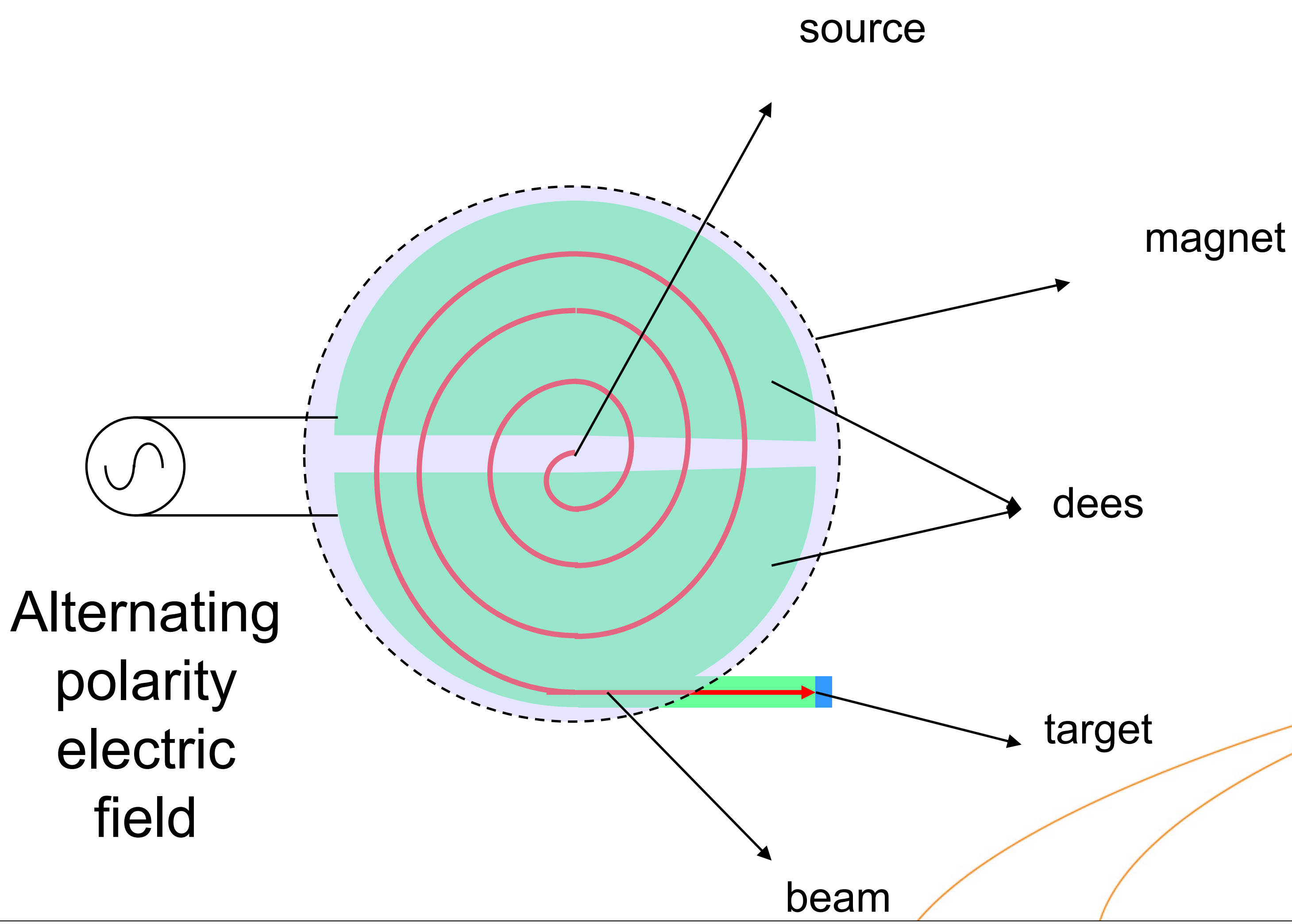
- an ion source (protons ou deuterons (proton + neutron))

- a target

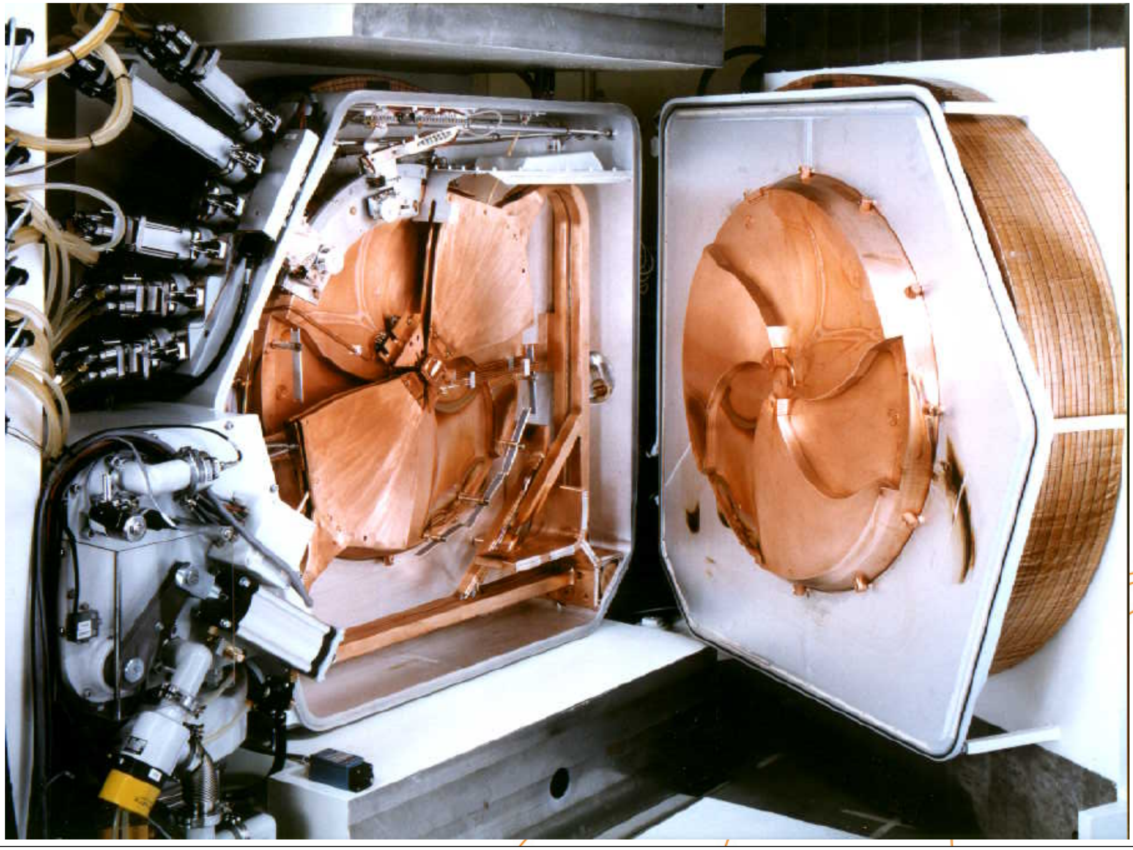
Cyclotron



Cyclotron


source
magnet
dees
target
beam
Alternating polarity electric field

Cyclotron



Nuclear Reactions of interest

$$_{Z}X^{A} + p \rightarrow {}_{Z+1}Y^{A} + n \qquad X^{A}(p,n)Y^{A}$$

$$_{Z}X^{A} + d \rightarrow {}_{Z+1}Y^{A+1} + n \qquad X^{A}(d,n)Y^{A+1}$$

Examples:

$N^{14}(d,v_e)O^{15}$

$O^{16}(p,\alpha)N^{13}$

$N^{14}(p,\alpha)C^{11}$

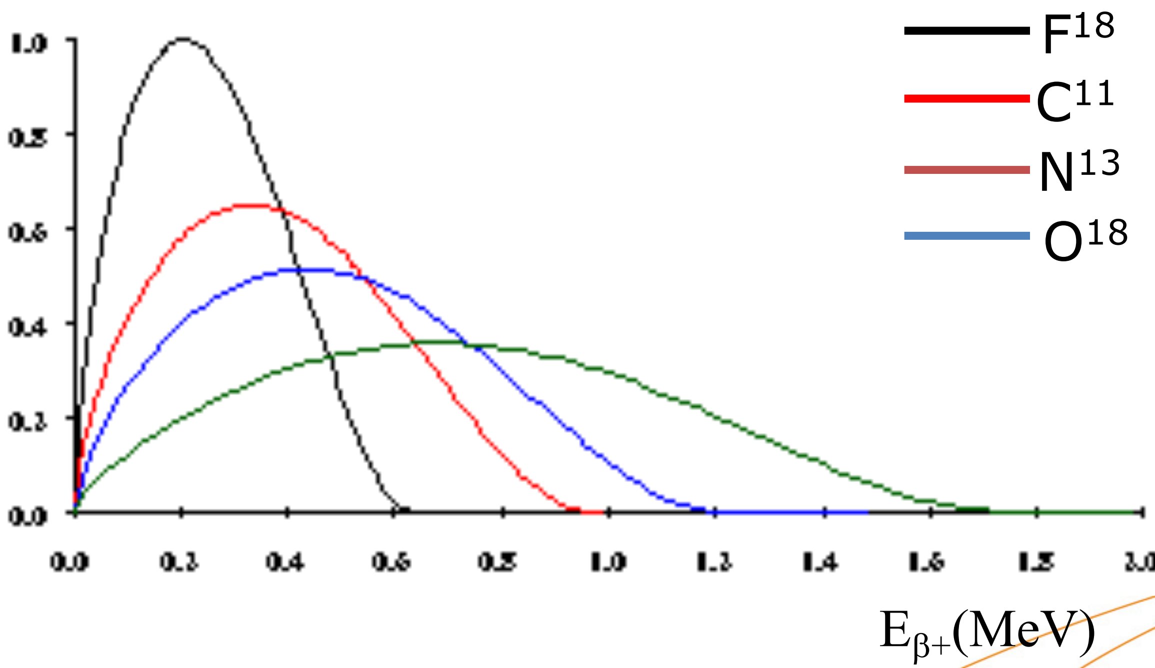
$O^{18}(p,v_e)F^{18}$

Isotopes

disintégration	period ($T_{1/2}$)	yield(%)	E_{max}(keV)
$_9F^{18} \rightarrow {}_8O^{18}$	109.8^m	97	633.5
$_6C^{11} \rightarrow {}_5B^{11}$	20.38^m	99.8	960.5
$_8O^{15} \rightarrow {}_7N^{15}$	122^s	99.9	1731.9
$_7N^{13} \rightarrow {}_6C^{13}$	9.96^m	100	1198.4
$_{31}Ga^{68} \rightarrow {}_{30}Zn^{68}$	68.1^m	89	1899.1
$_{29}Cu^{64} \rightarrow {}_{28}Ni^{64}$	12.7^h	19	653.1

Isotopes

Energy distribution of protons



Isotopes

β^+ range

Isotope	Average E_k (MeV)	Effective range in water (mm)
^{18}F	0.242	0.54
^{11}C	0.385	0.92
^{15}O	0.735	2.4
^{68}Ga	0.740	2.8

Radio-pharmaceutical in PET

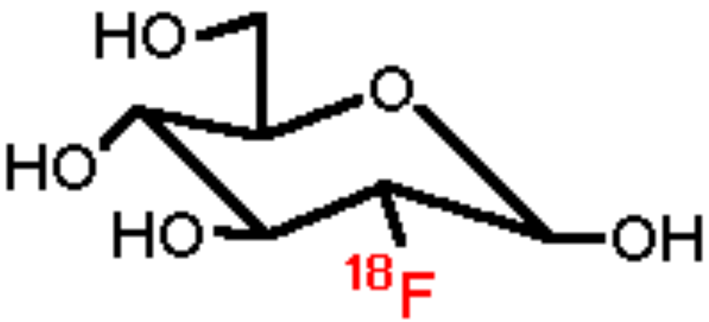
$_9F^{18}$ fluorodéoxyglucose

$_6C^{11}$ déoxyglucose

$_8O^{15}$ oxygène (gaz)

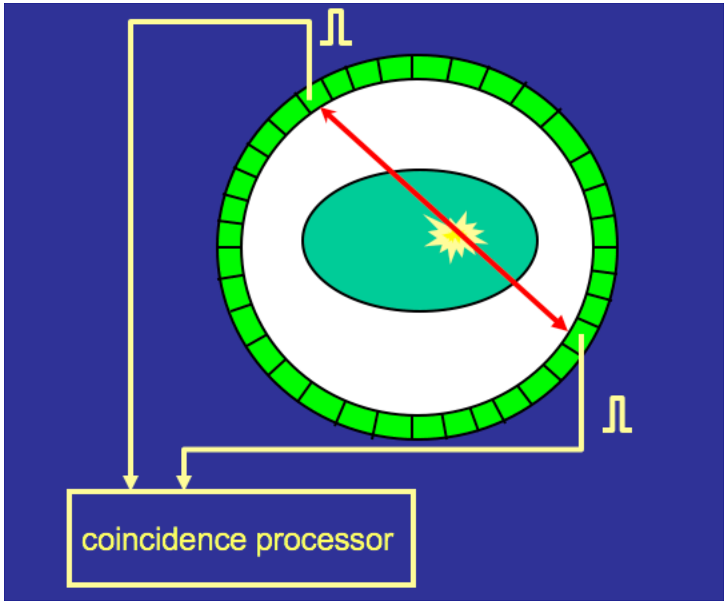
$_6C^{11}$ dioxyde de carbone

$_8O^{15}$ dioxyde de carbone

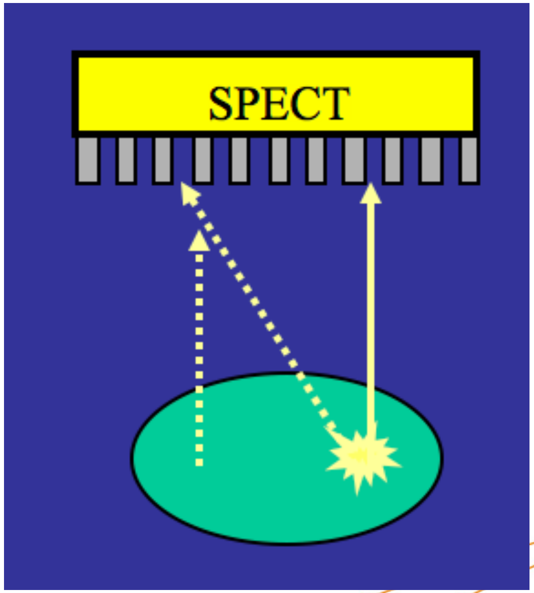


PET vs SPECT

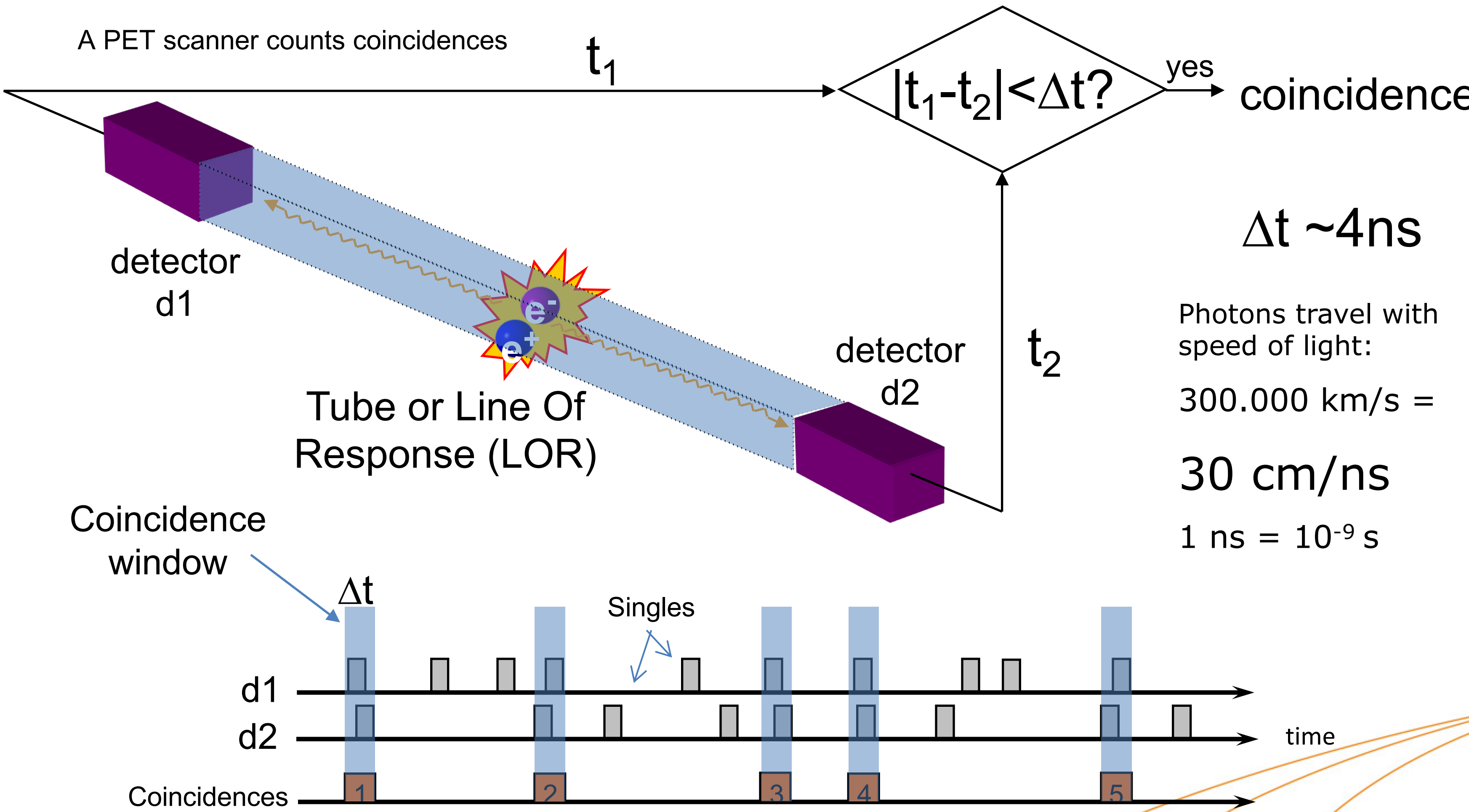
Collimation
électronique



Collimation
physique



PET detection



Δt ~4ns

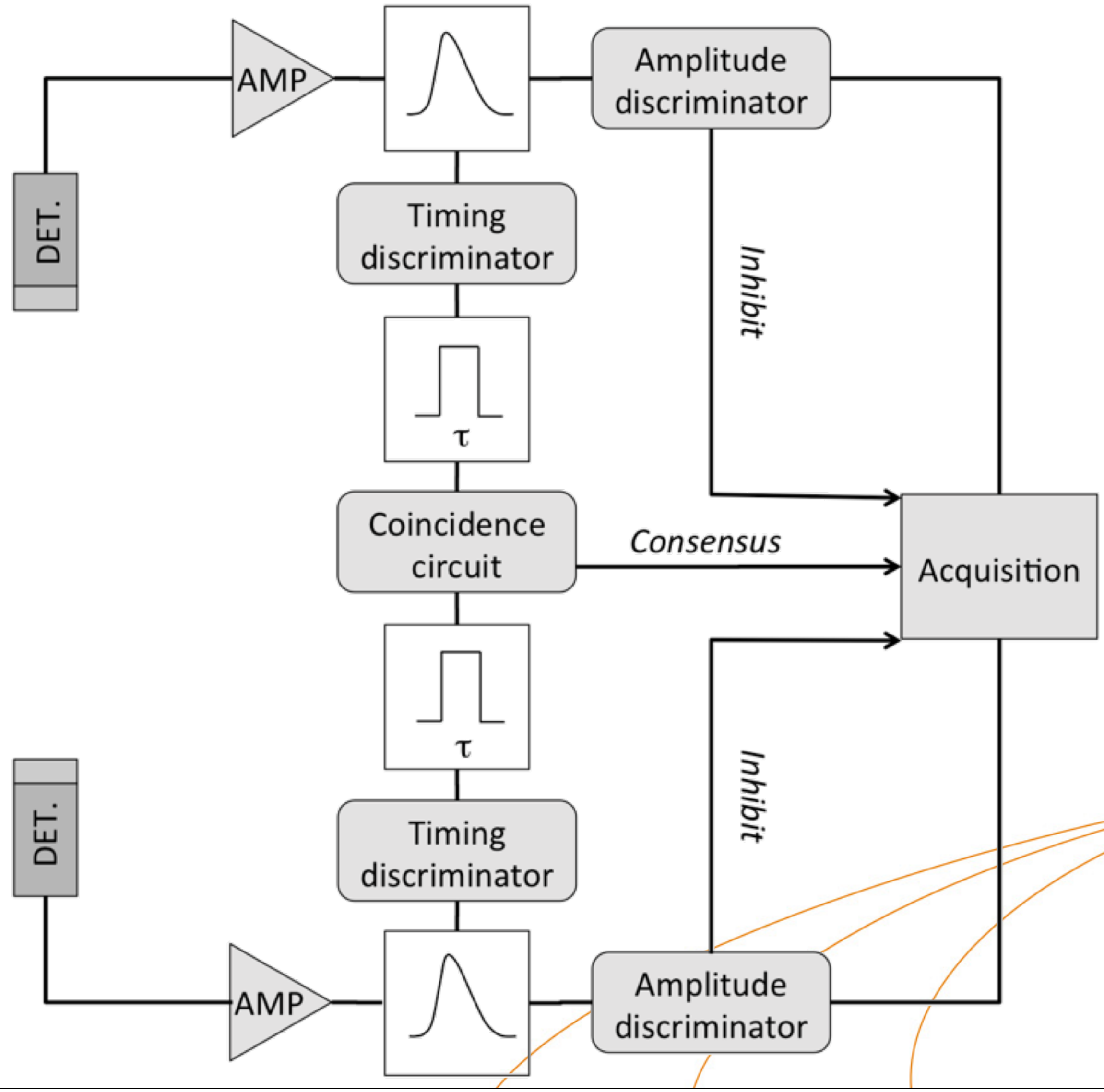
Photons travel with speed of light:

300.000 km/s =

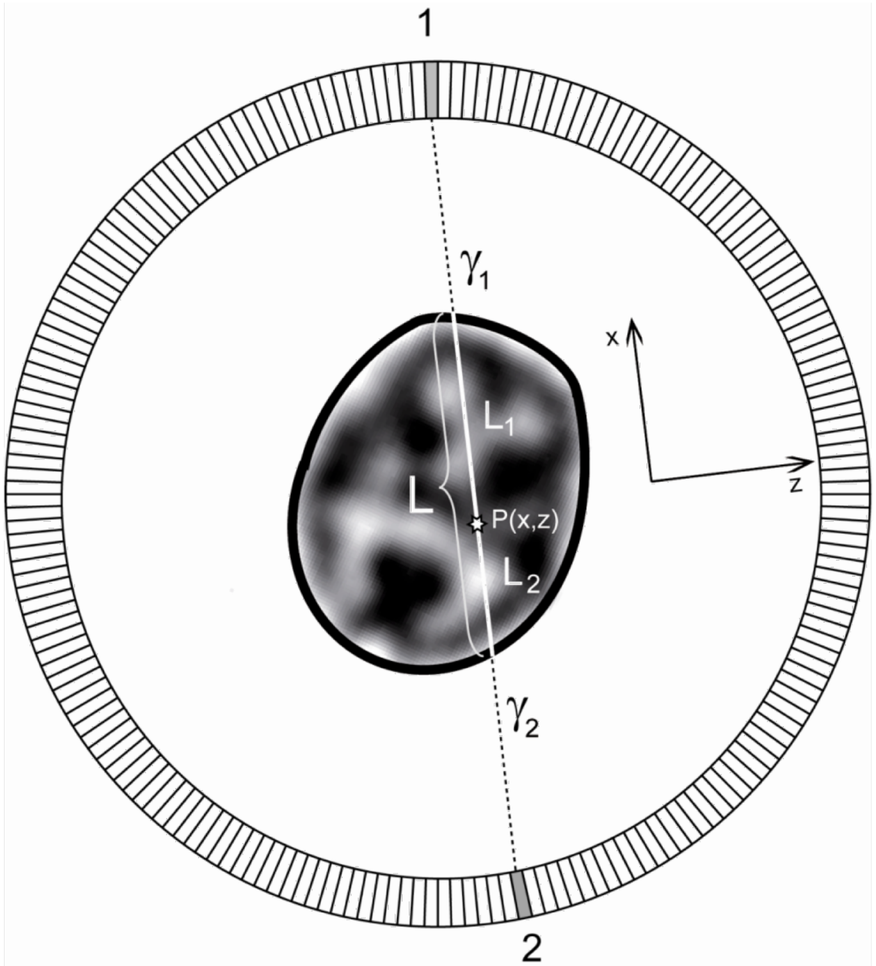
30 cm/ns

1 ns = 10^{-9} s

Event detection



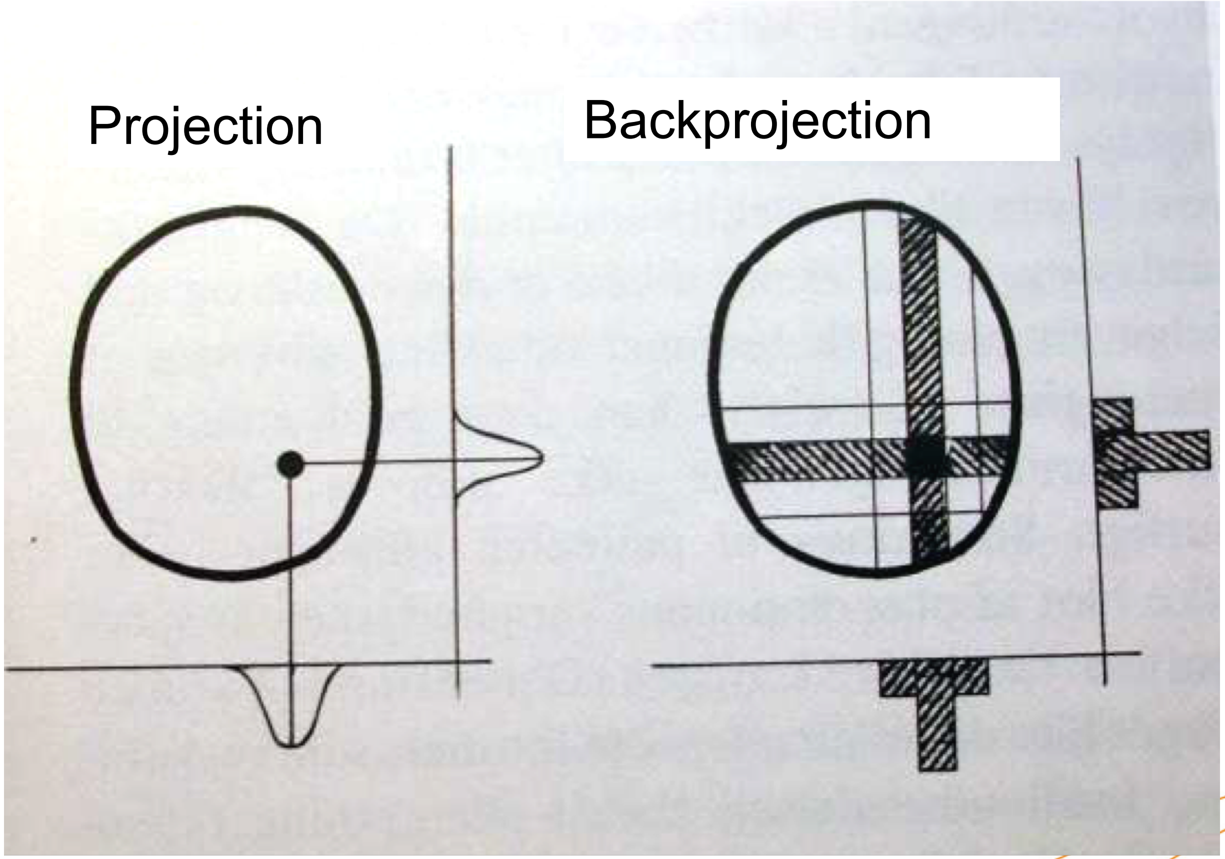
Linear integral model



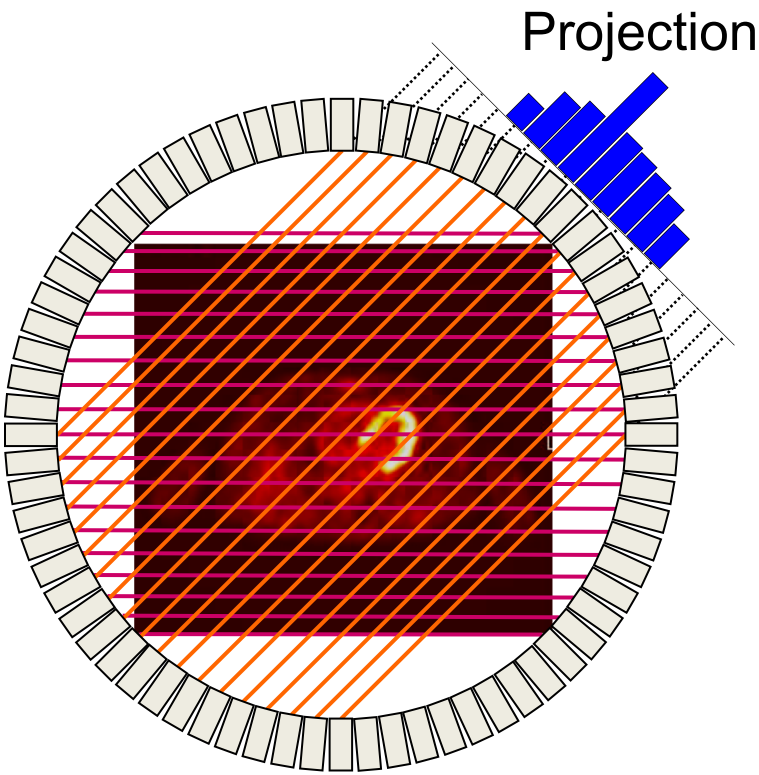
$$N_{\gamma-\gamma} = k \int_L \rho(x,y,z)\, dl$$

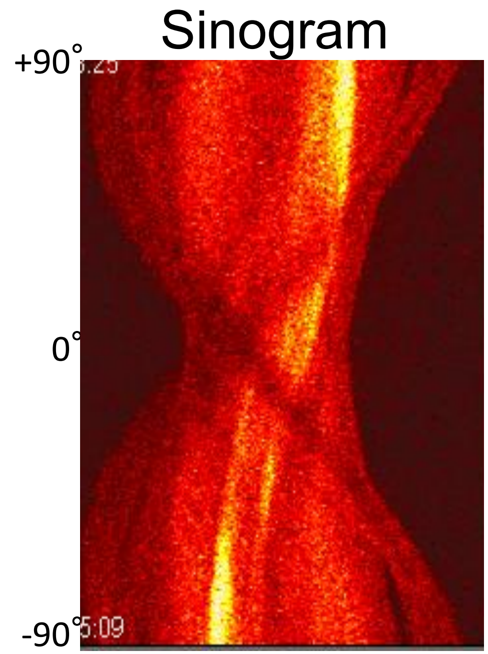
- **The activity distribution ρ(x,y,z) is measured in terms of projections (Nγ) along lines L**
- **Each projection is obtained from the activity distribution with the line integral operator**
- **Ideal model**

Simplest principle of tomographic image formation!



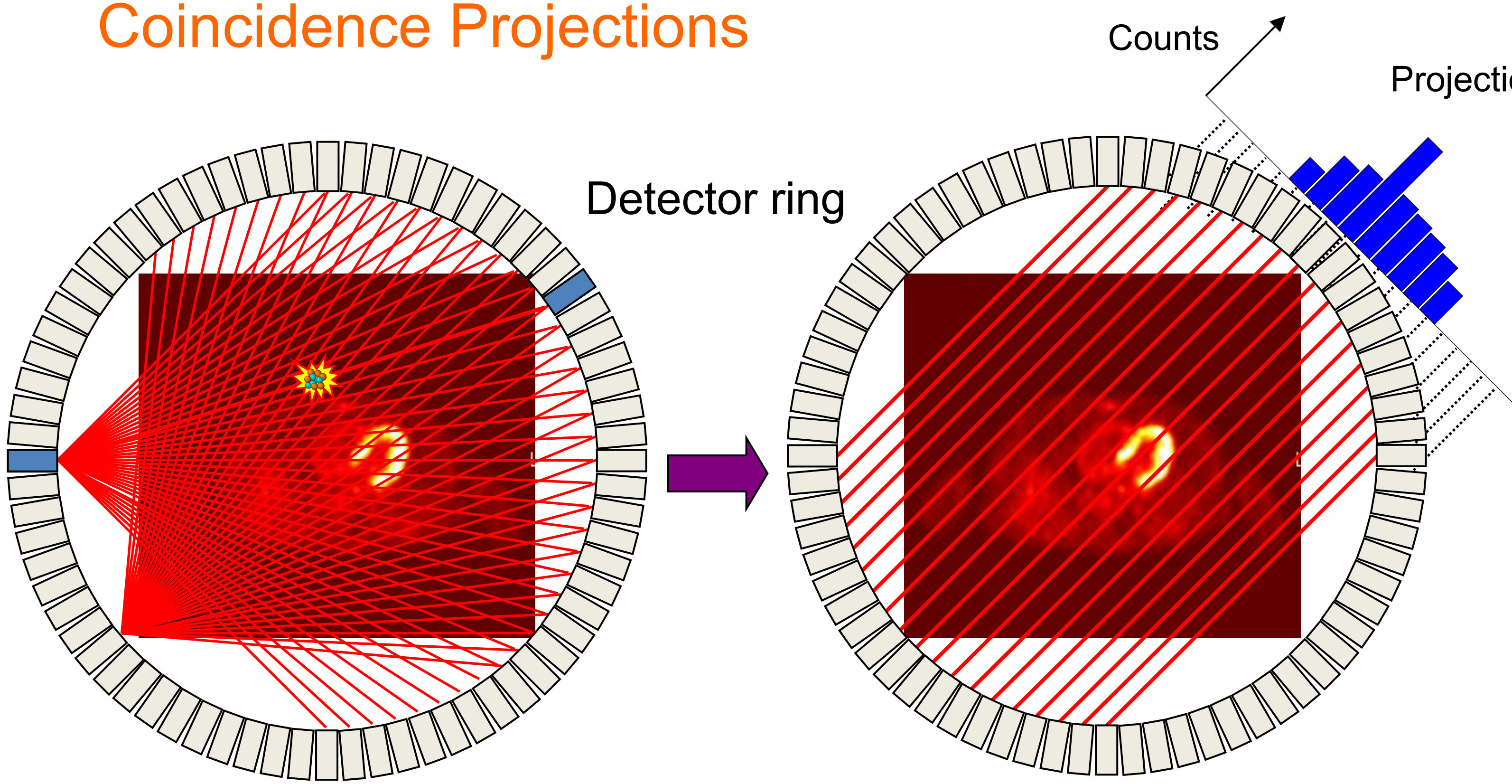
Data-Sorting into Sinogram





Each **projection** is entered as a row into a **sinogram**. A sinogram is an array which stores the number of coincidence events for each detector **position** and each **angle**.

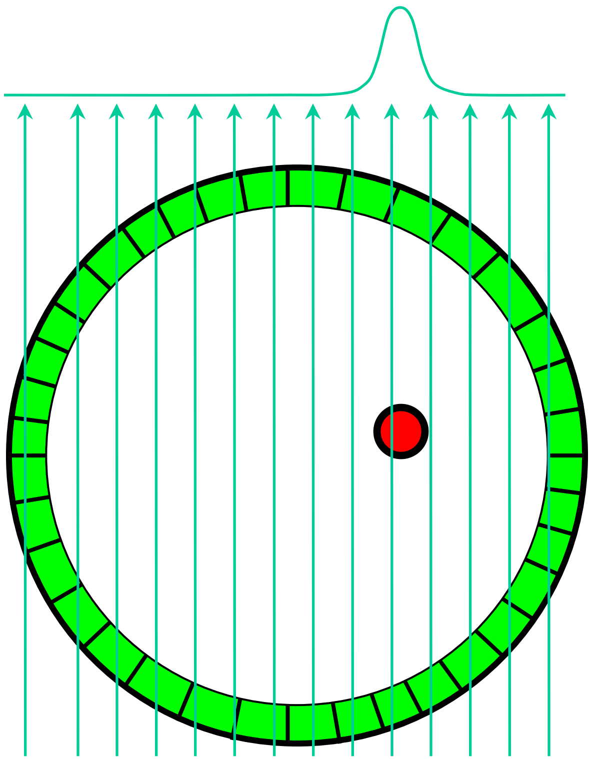
Coincidence Projections

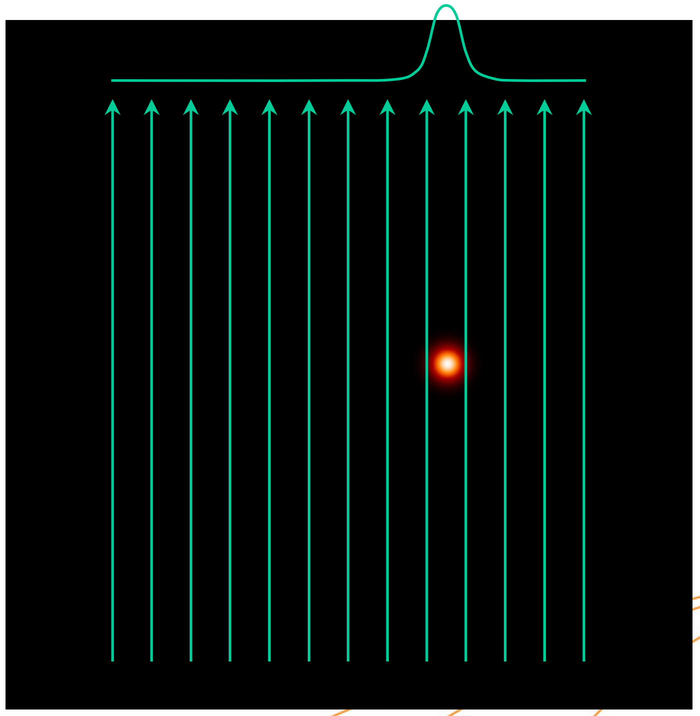


Pair of detectors determine sampling paths (**Lines Of Response, LORs**)

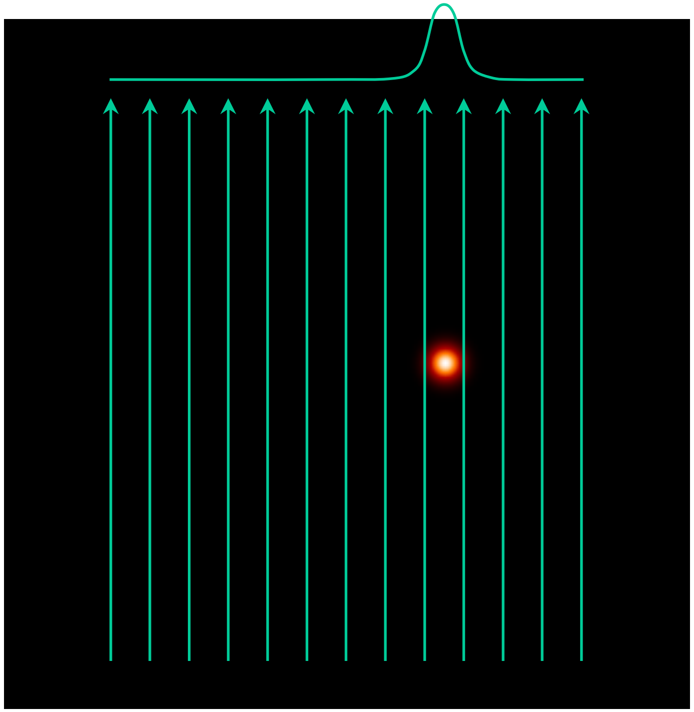
Parallel Lines Of Response are sorted into a row of count numbers (**Projection**), representing the number of 511 keV photon pairs detected.

Coincidence Projections

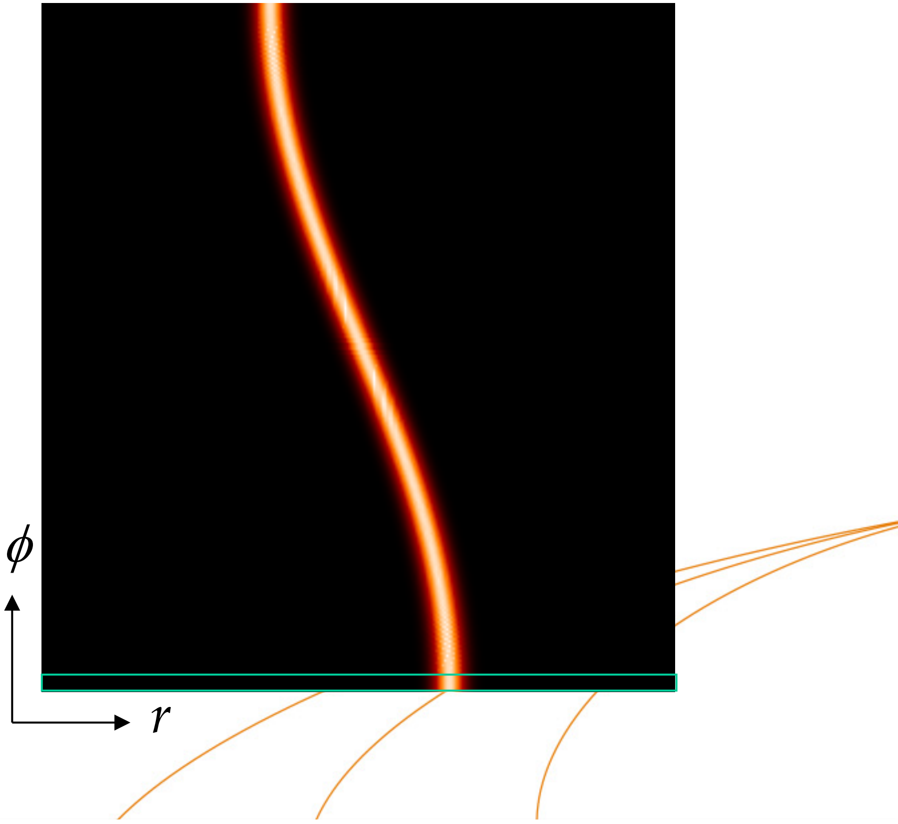


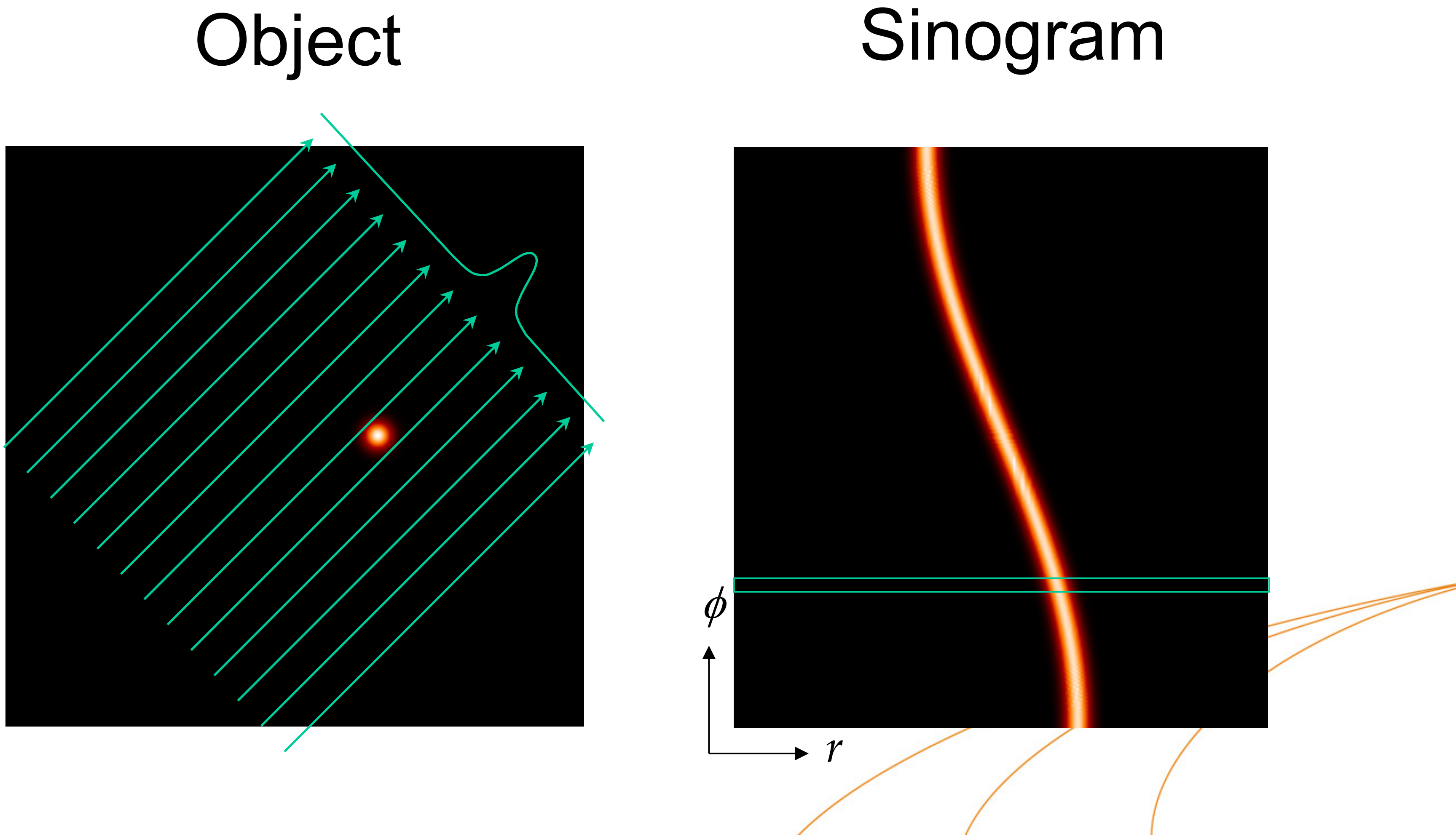


Object

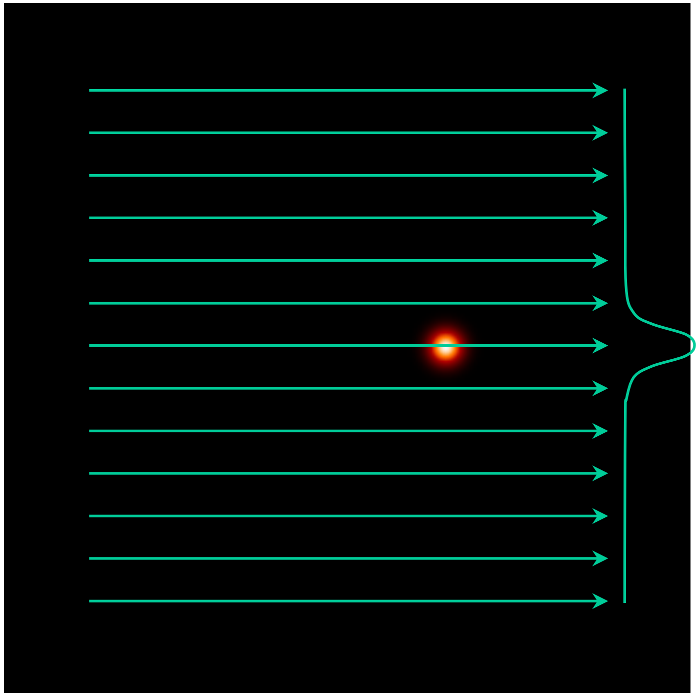


Sinogram

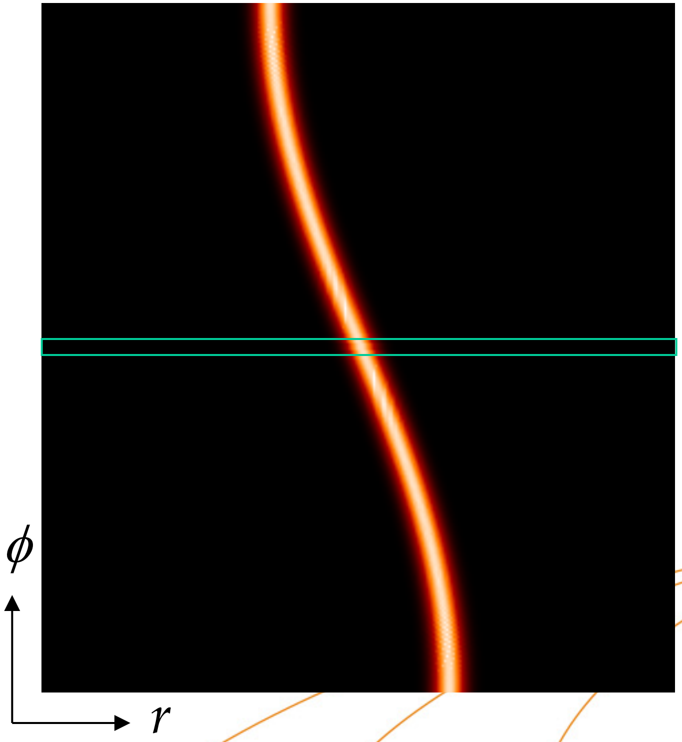


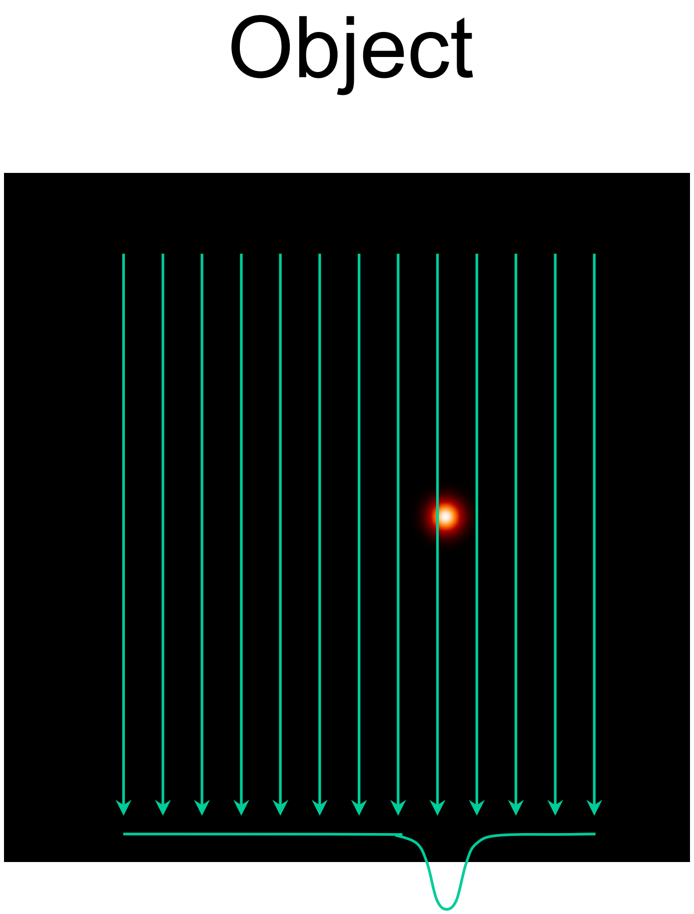

Object
Sinogram
ϕ
r

Object



Sinogram




Object

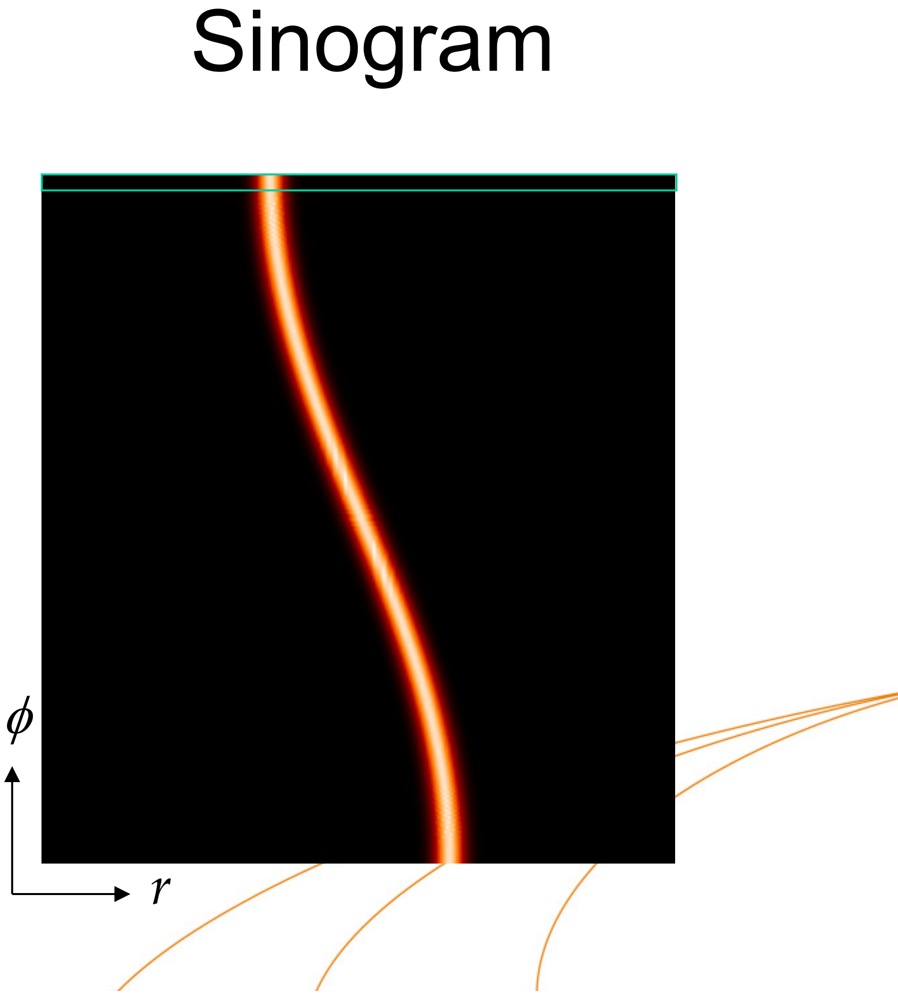
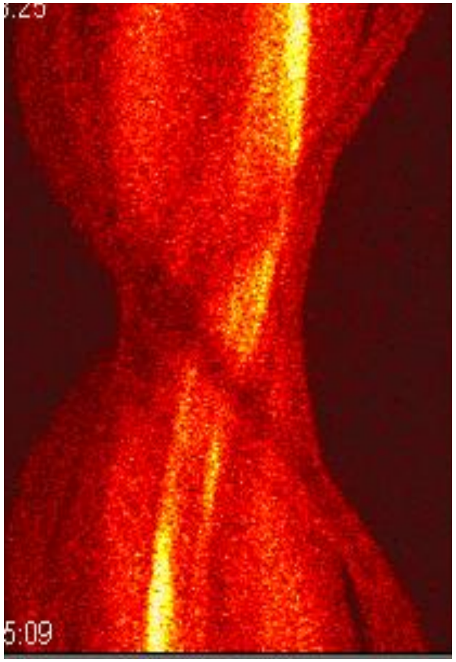

Sinogram
ϕ
r

Image Reconstruction



Sinogram

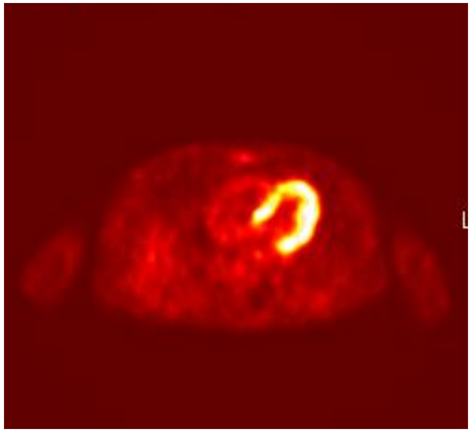
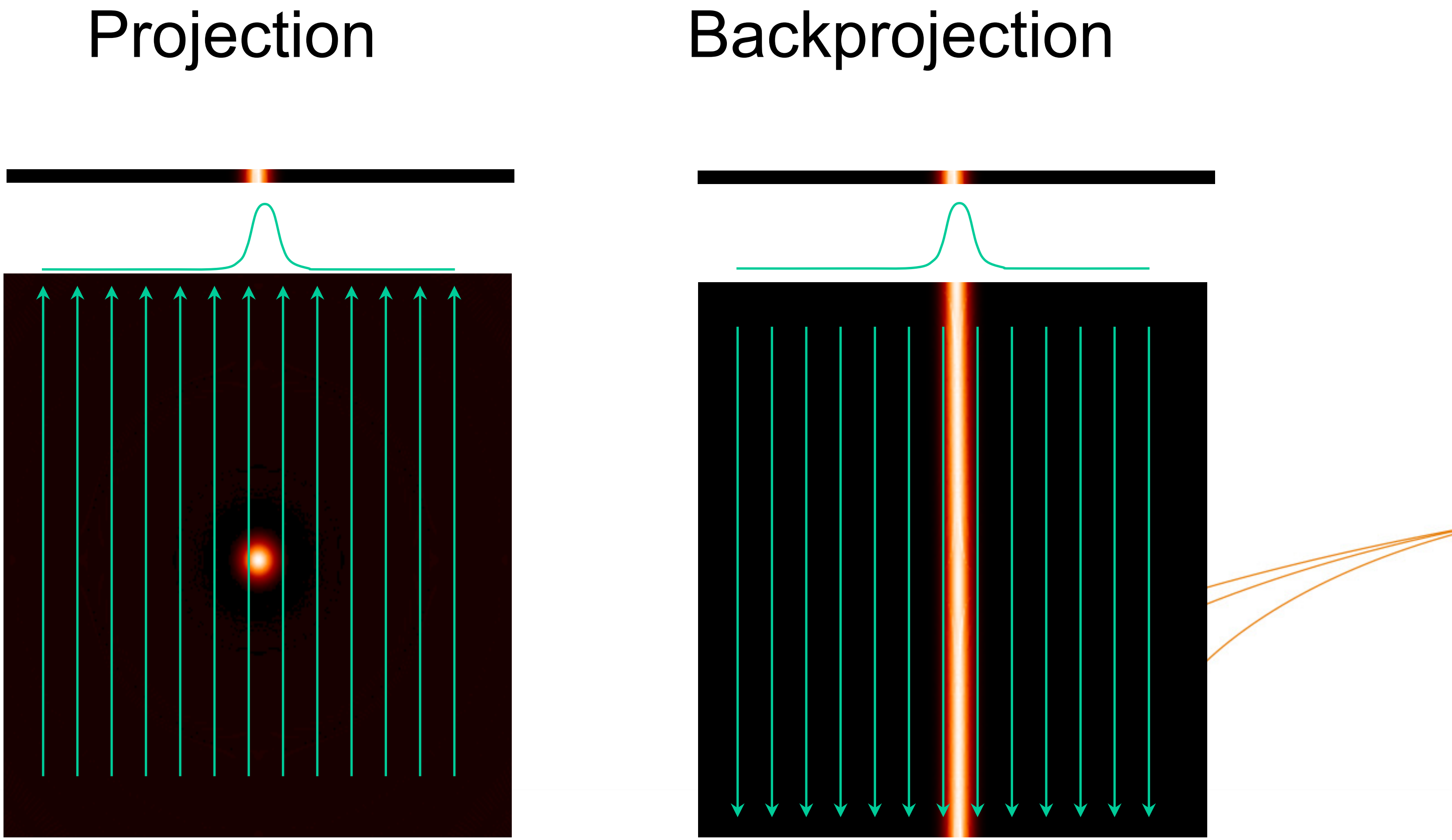
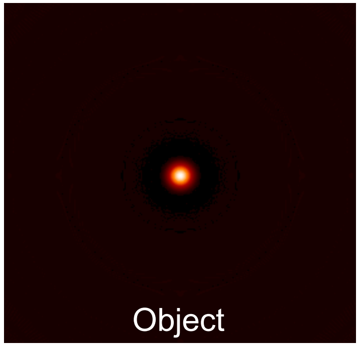


Image slice

PET Image reconstruction: filtered backprojection



PET Image reconstruction

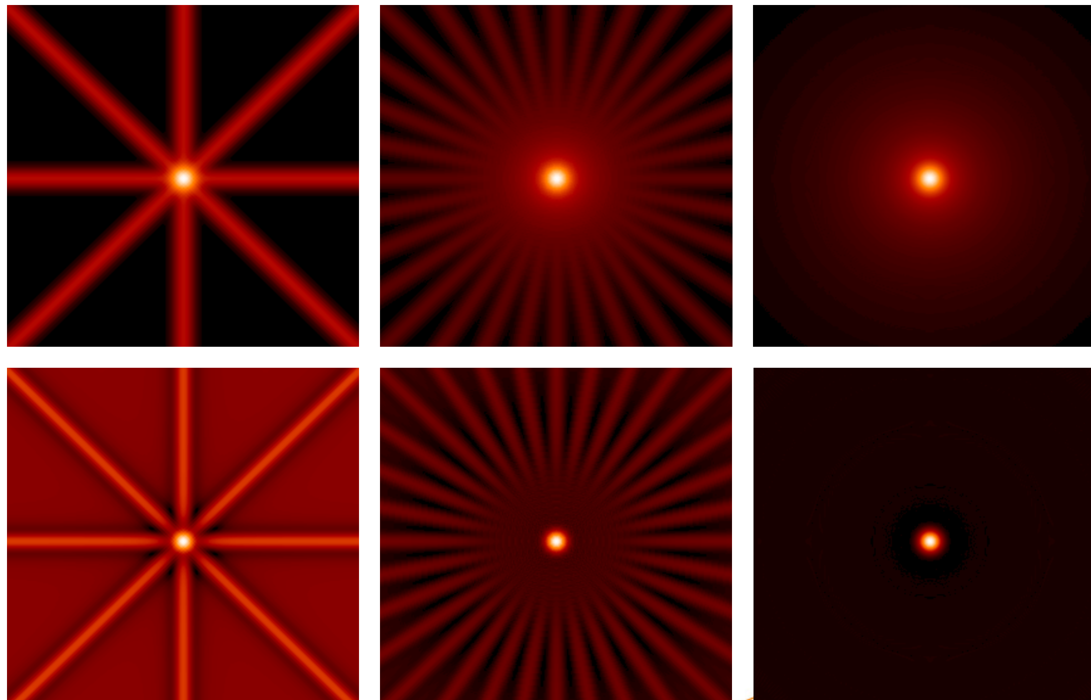


Backprojection

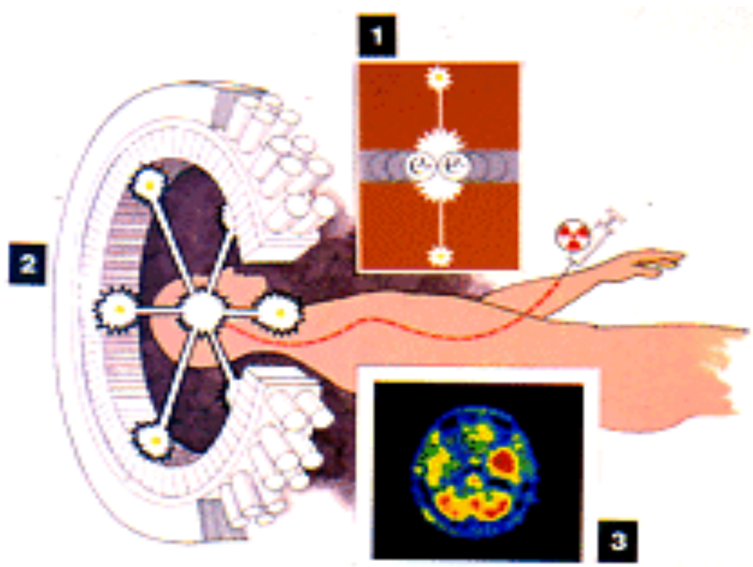
Filtered Backprojection

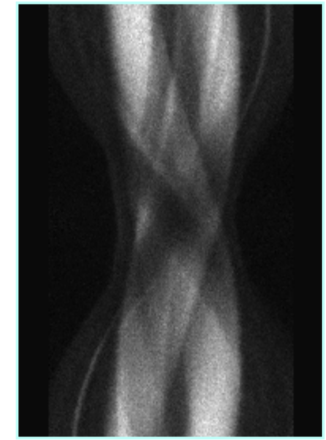
FBP

4 projections | 16 projections | 128 projections



PET Reconstruction





Data acquired as sinograms

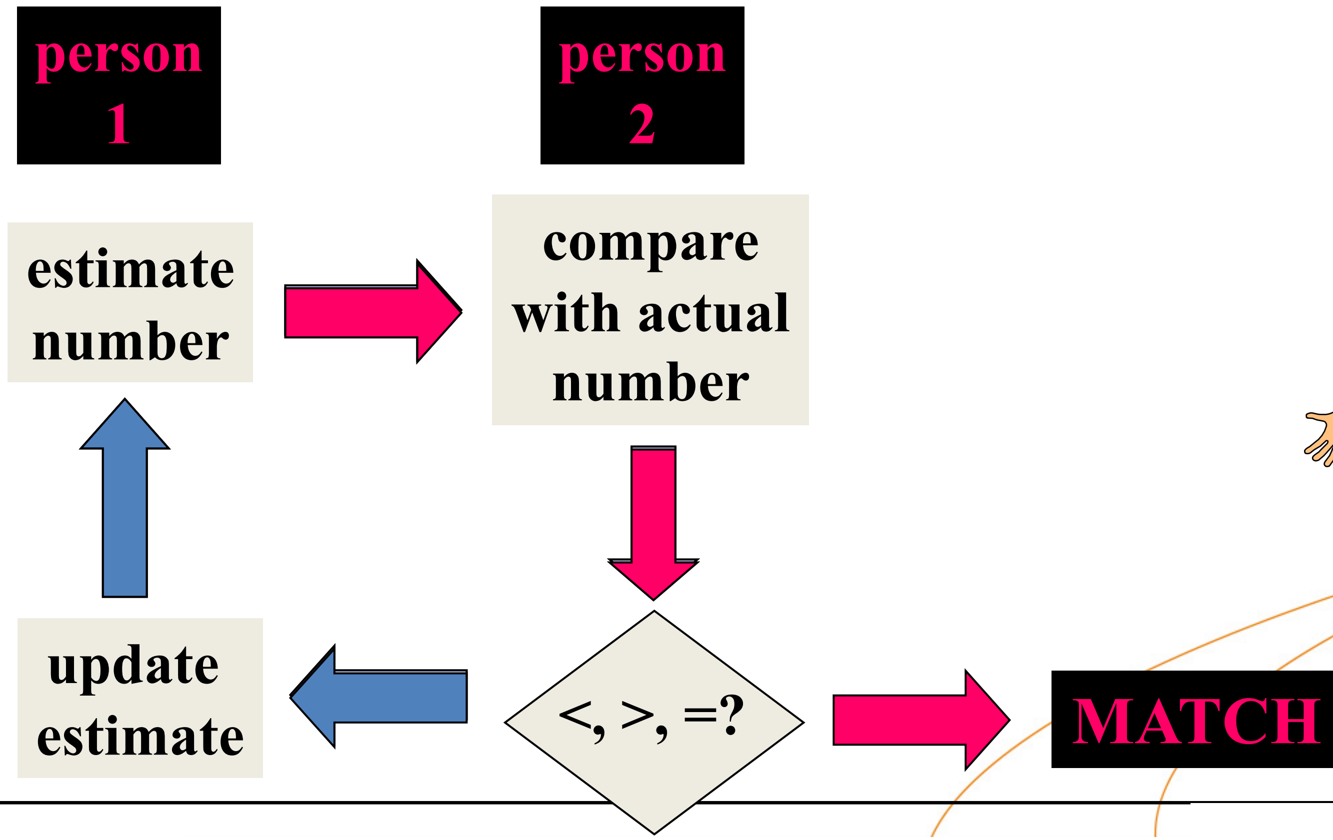
Filtered back projection

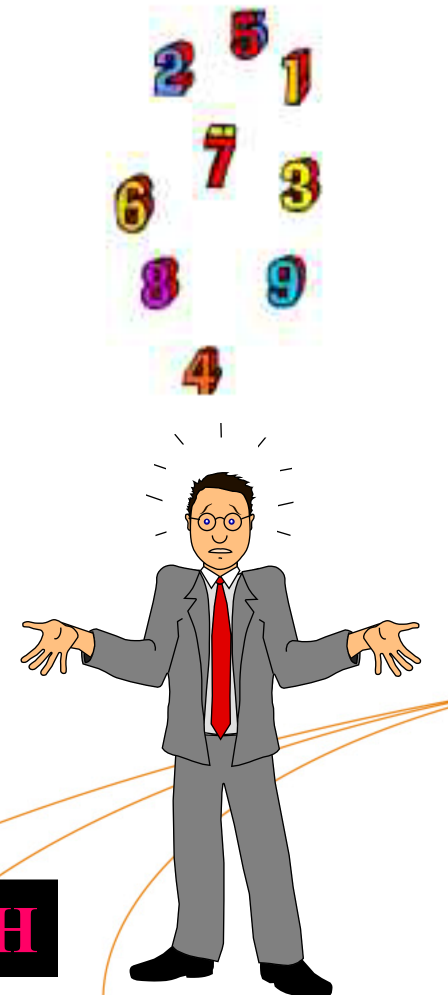
1 angle 2 angles 4 angles 16 angles 128 angles

OR iterative reconstruction

What does iterative mean?

- choose a number between 1 and 20





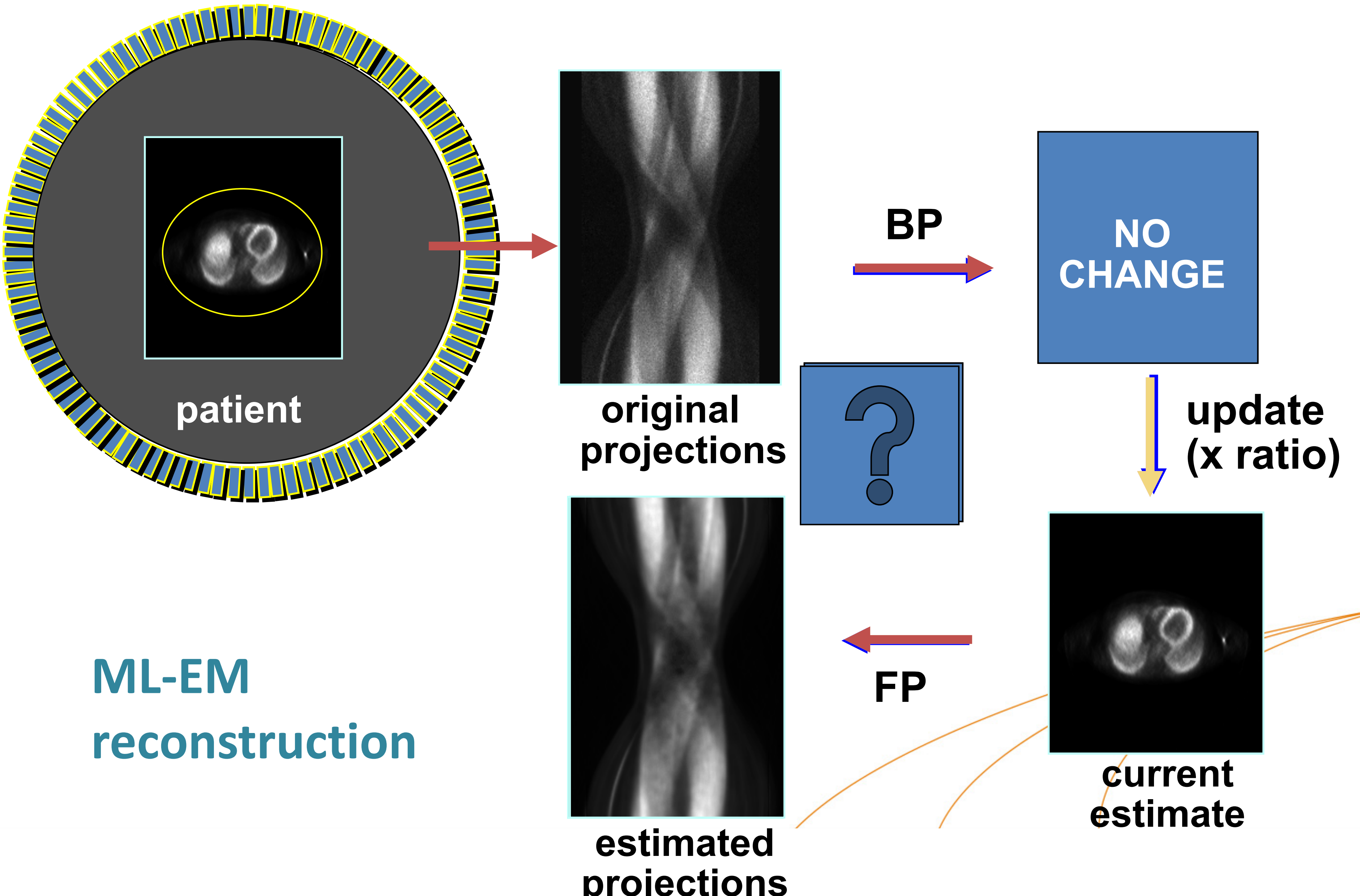
Tomographic reconstruction: terminology

Maximum likelihood reconstruction (ML-EM)
Find the 'most likely' distribution of activity, given the set of measurements.
- assumes Poisson probability of emission; i.e. no negative values

- **EM** (expectation maximization) is the name of the algorithm normally used to find the 'most likely' solution

- **OS-EM** (ordered subsets EM) is an accelerated form of EM

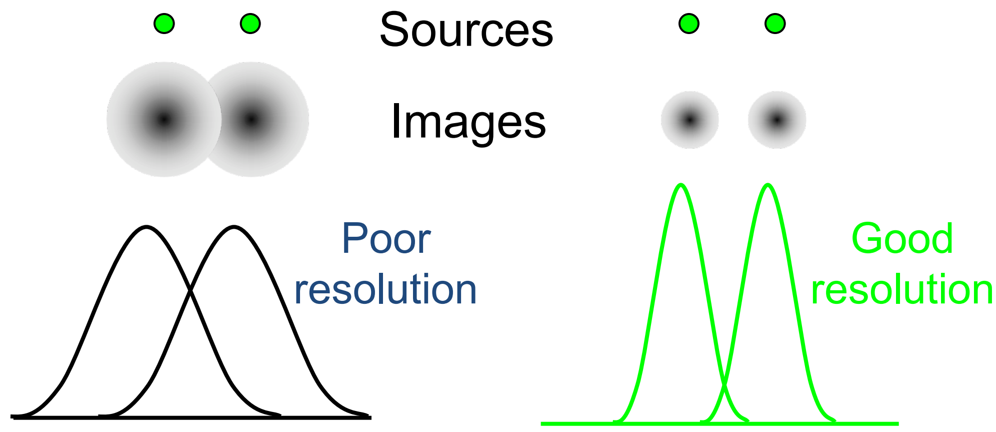
- **MAP** (maximum a-posteriori) incorporates a prior or penalty term



ML-EM reconstruction

Spatial Resolution

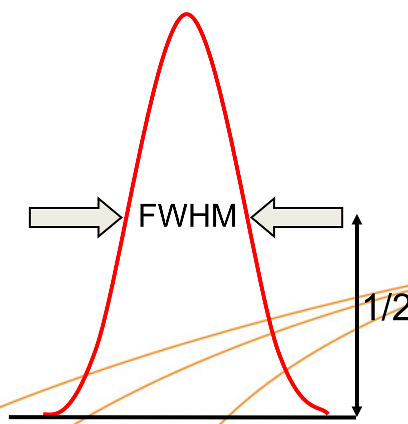
- ~~How small an object can you see in PET?~~



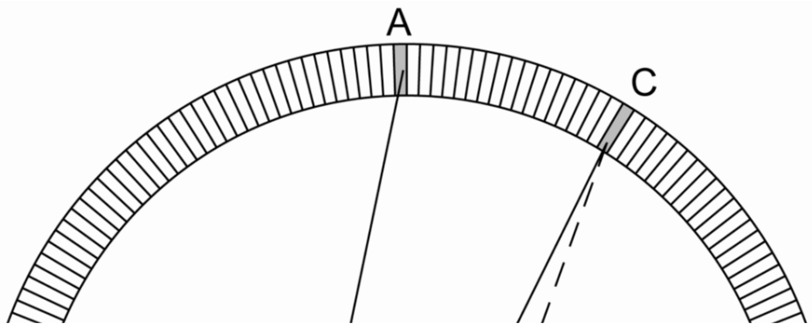
- Ability to separate two objects close together: ***Resolution***

Line profile of a point source (PSF)

- Full Width at Half Maximum (FWHM) is the measure of resolution (unit: mm).
- Depends on position and direction in the field.
- Typical PET resolution: FWHM ≈ 5 mm.

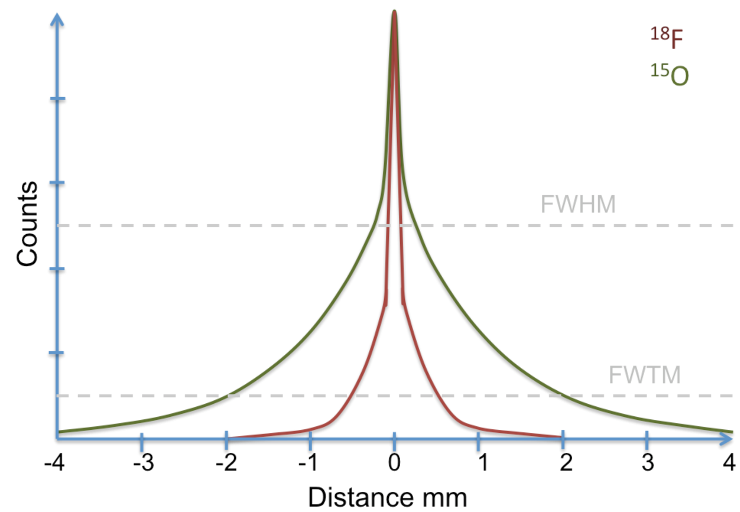


Spatial resolution issues: β⁺ range

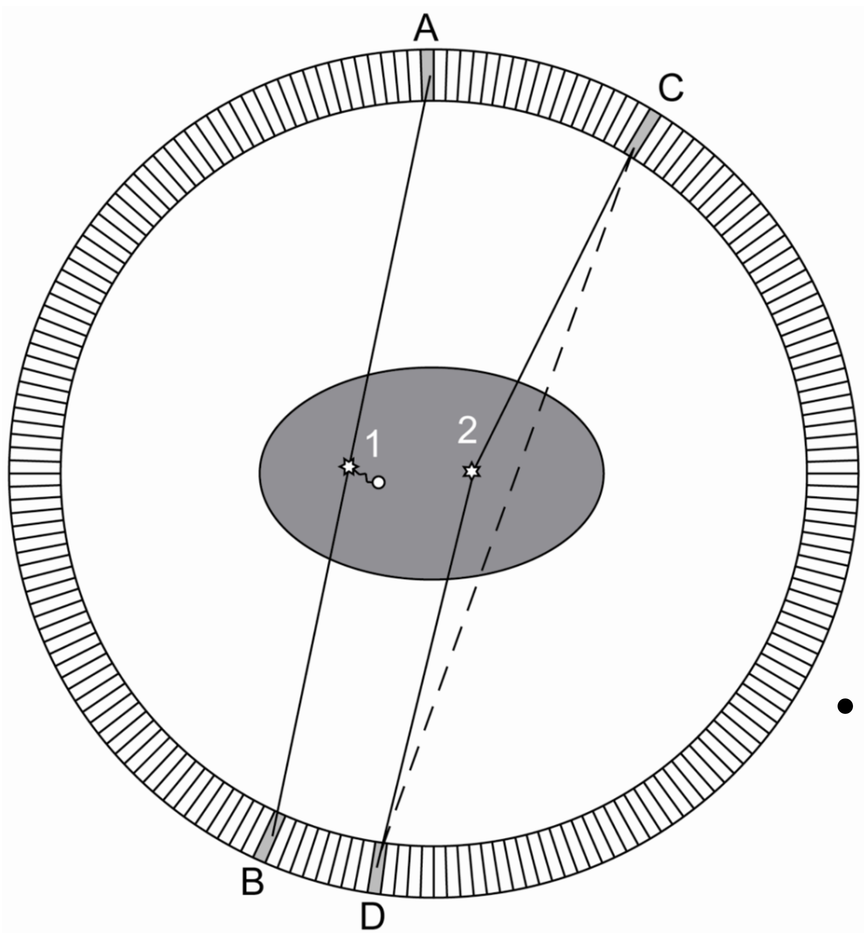


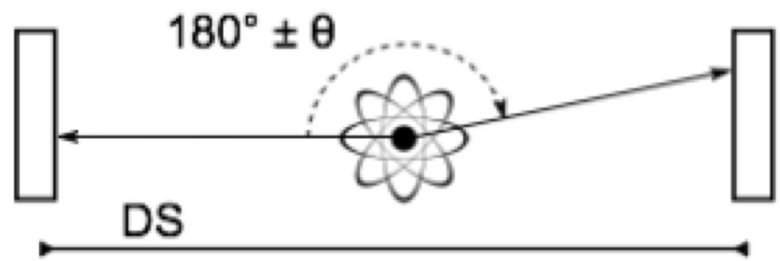
Isotope	Average E_k (MeV)	Effective range in water (mm)	FWHM (mm)	FWTM (mm)
^{18}F	0.242	0.54	0.10	1.03
^{11}C	0.385	0.92	0.28	1.86
^{15}O	0.735	2.4	0.50	4.14
^{68}Ga	0.740	2.8	0.58	4.83

D



Spatial resolution issues: non-collinearity



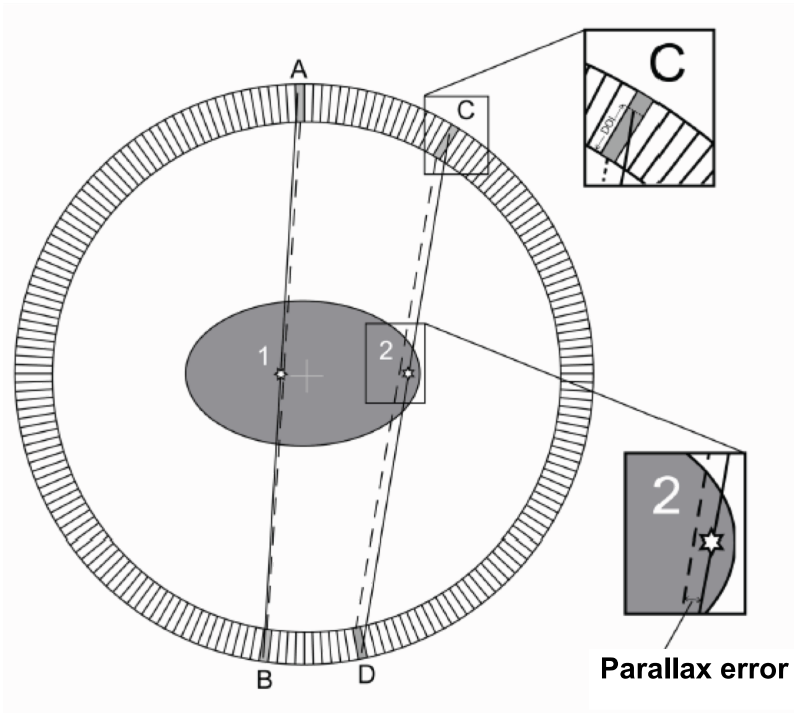


Contribution to FWMH: $FWHM_{\Delta\theta} \approx \Delta\theta \times \frac{D}{4} = 0.0022D$

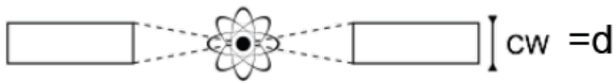
(1,7mm @ 80cm ∅ detector-ring !)

- **As a consequence, the two photons are not emitted at exactly 180, but they have an angular deviation from collinearity of ±0.25°**

Spatial resolution issues: parallax error



- Crystal pitch

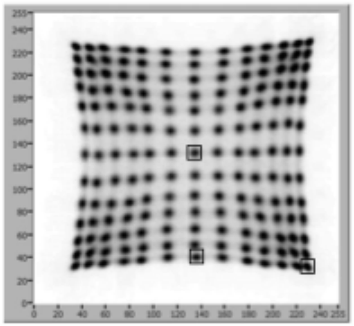


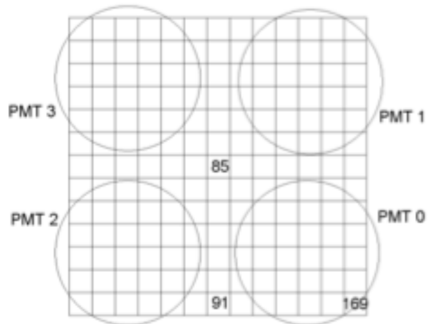
Contribution to FWMH: $\sim \frac{d}{2}$

The best spatial resolution achievable is also limited by other factors, i.e.,

- No information of the depth-of-interaction
- Crystal position readout coding
- Image reconstruction algorithm

Spatial resolution issues: detection system





> Coding

When the crystal position is identified via "light sharing" technique, i.e., by calculating the centroid of the light spot emerging from the crystal with a high granularity position-sensitive photodetector, there is a nonnegligible, position-dependent error. The average contribution is usually called **"coding error".**

Spatial resolution limitations in PET

$$FWHM = 1.2\sqrt{\left(\frac{d}{2}\right)^2 + b^2 + (0.0022D)^2 + r^2 + p^2}$$

Reconstruction

Crystal pitch

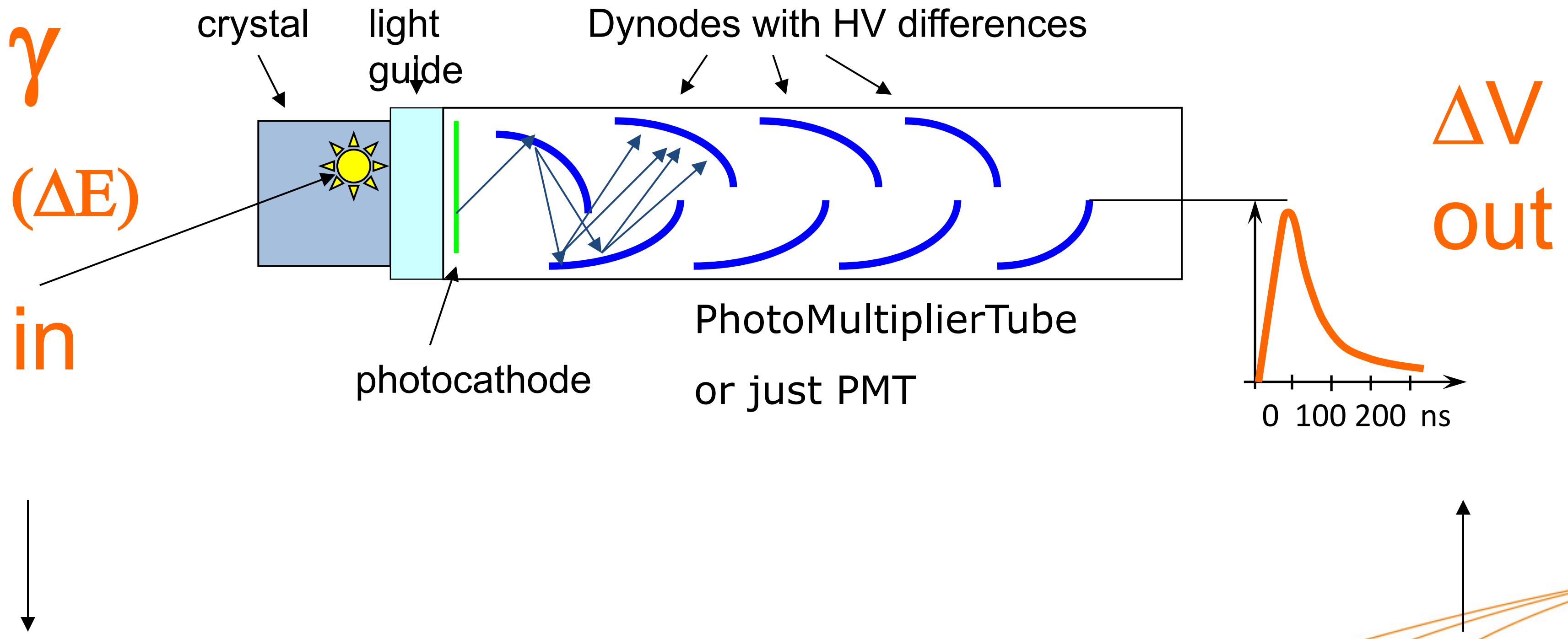
Coding

Non-collinearity

Positron range

Parallax

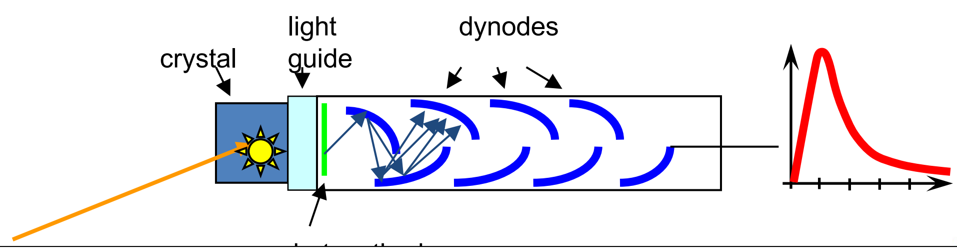
Scintillation detector



(γ) - photon absorbed - converted to light – starts cascade af electrons

The ideal scintillation detector has

- High element no (Z) .... Good absorption
- High density (ρ)
  - ⇒ High sensitivity
- Short decay of light .... ⇒ Less Deadtime, fast counting
- High light output .... ⇒ Narrow coincidence window
  - ⇒ less Randoms
  - ⇒ Good energy resolution
  - ⇒ Scatter rejection
- Low price

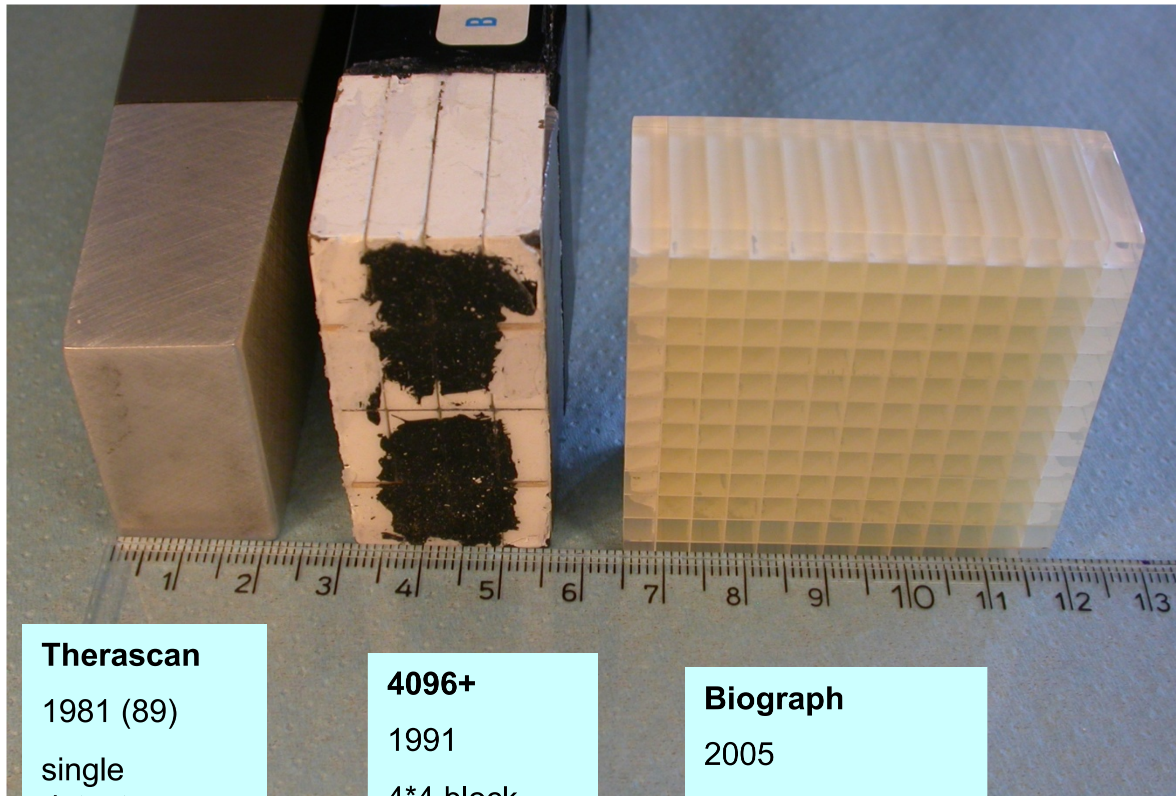


PET Detector Scintillator Materials

Crystal material	max Z	effective Z	density g/cm^3	output photons/keV	decay time ns
NaI:Tl	53	51	3.7	**40**	230
BGO	**83**	**73**	7.1	8	300
LSO:Ce	71	66	**7.4**	28	**40**
LYSO	71	54	5.4	28	53
GSO:Ce	64	59	6.7	7.5	56
BaF_2	55	54	4.1	2	**0.8**

Evolution of PET-detectors

1975



Therascan

1981 (89)

single detector

20*35 mm

total # 256

4096+

1991

4*4 block

6*12 mm

total # 4096

Biograph

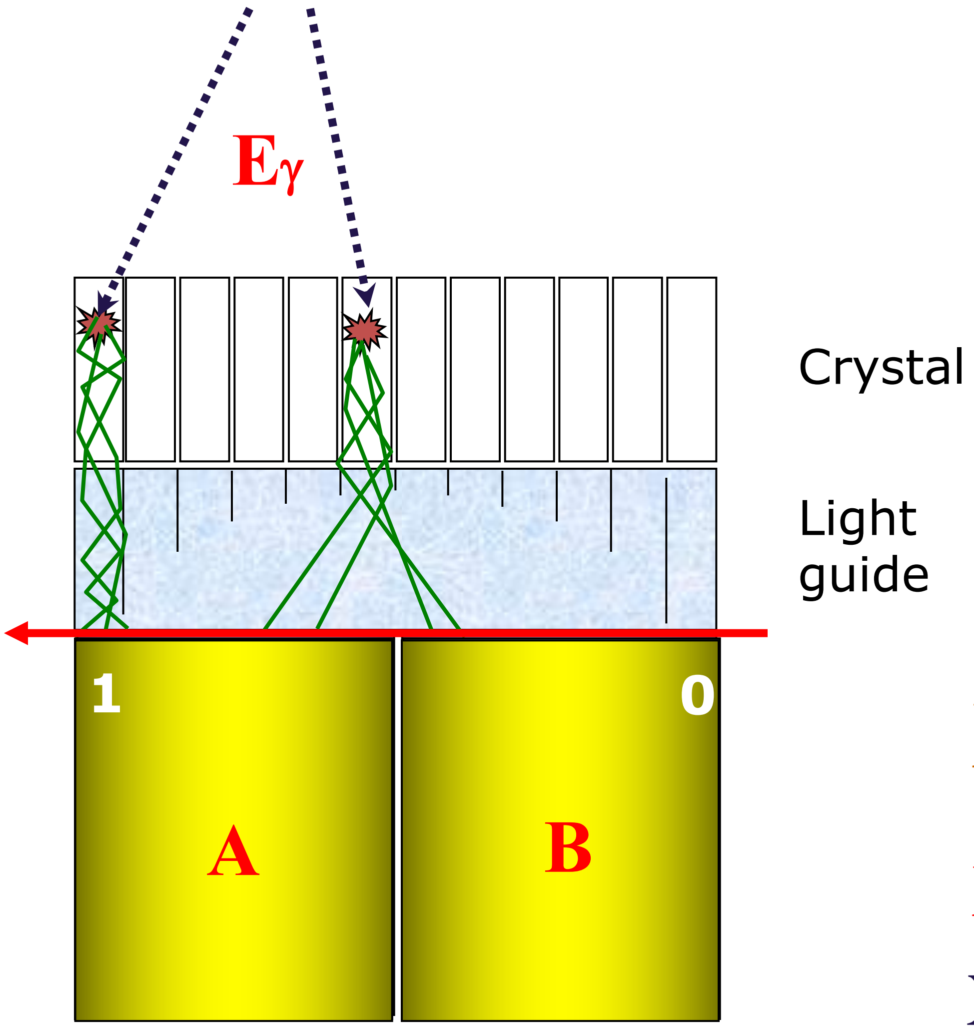
2005

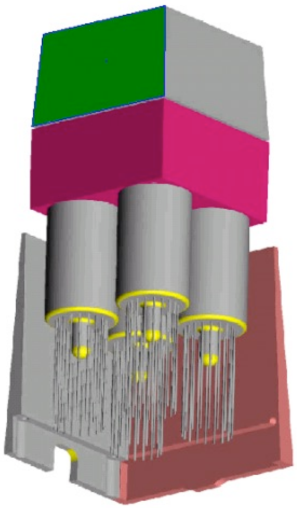
13*13 block

4*4 mm

total # 24336

Block-detector principle





$$X = A / (A + B)$$

$$X_1 = 100 / (100 + 0) = 1.0$$

$$X_2 = 55 / (55 + 45) = 0.55$$

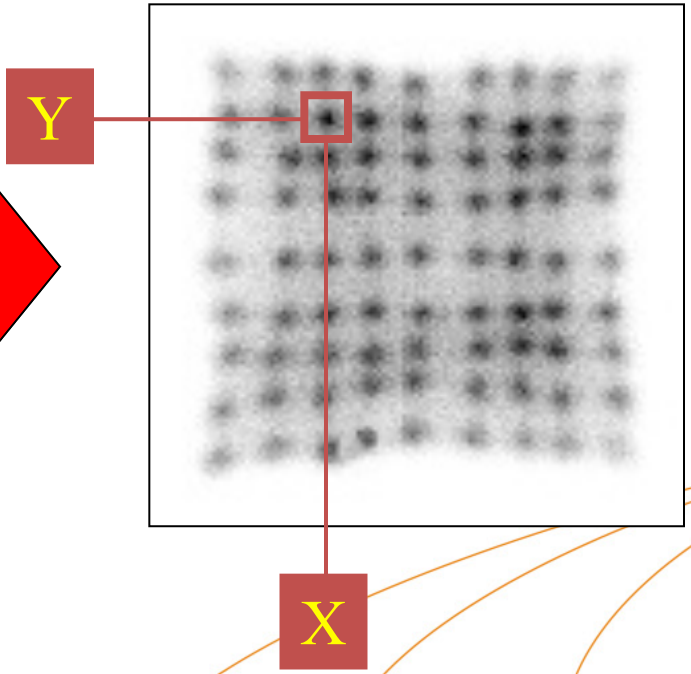
Flood Histogram / Position Map

Anger Logic

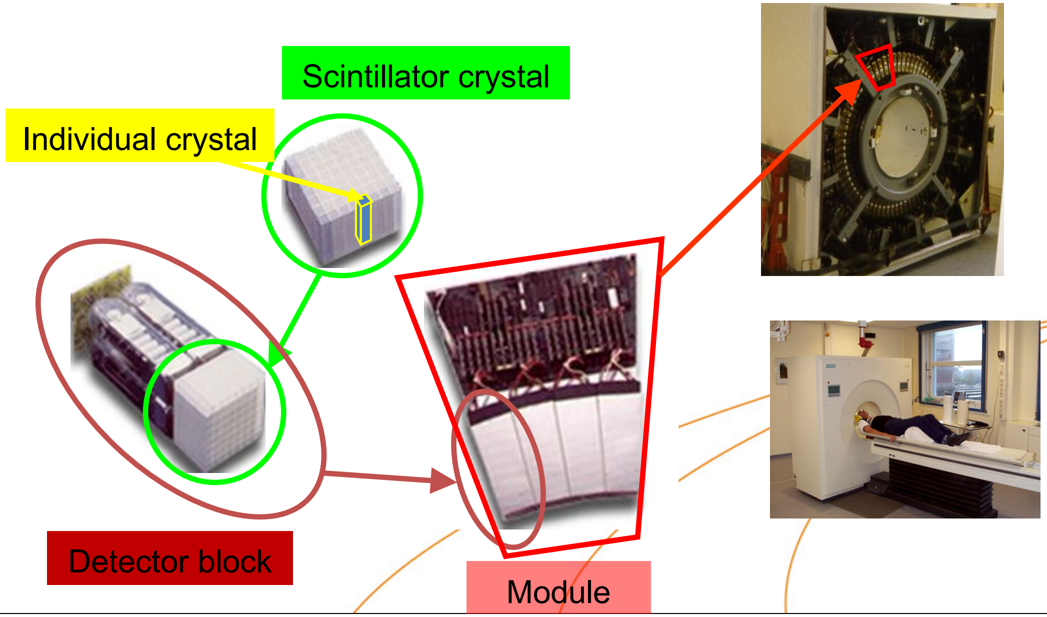
$$X = \frac{A}{A + B}$$

$$Y = \frac{C}{C + D}$$

"Crystal identification pattern"



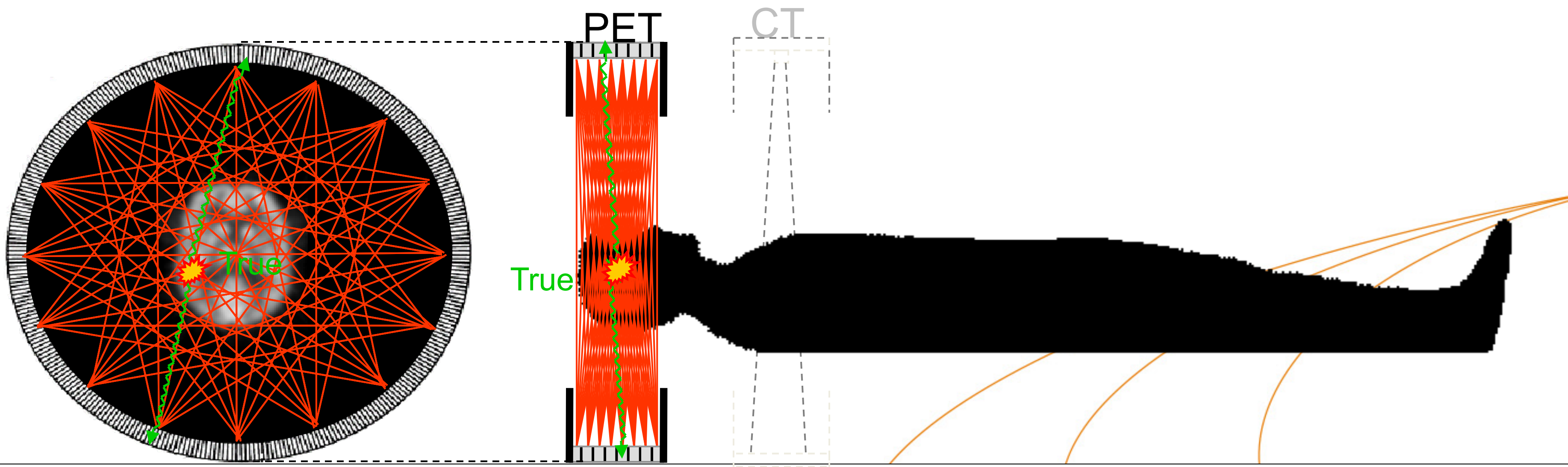
Assembly of a PET scanner



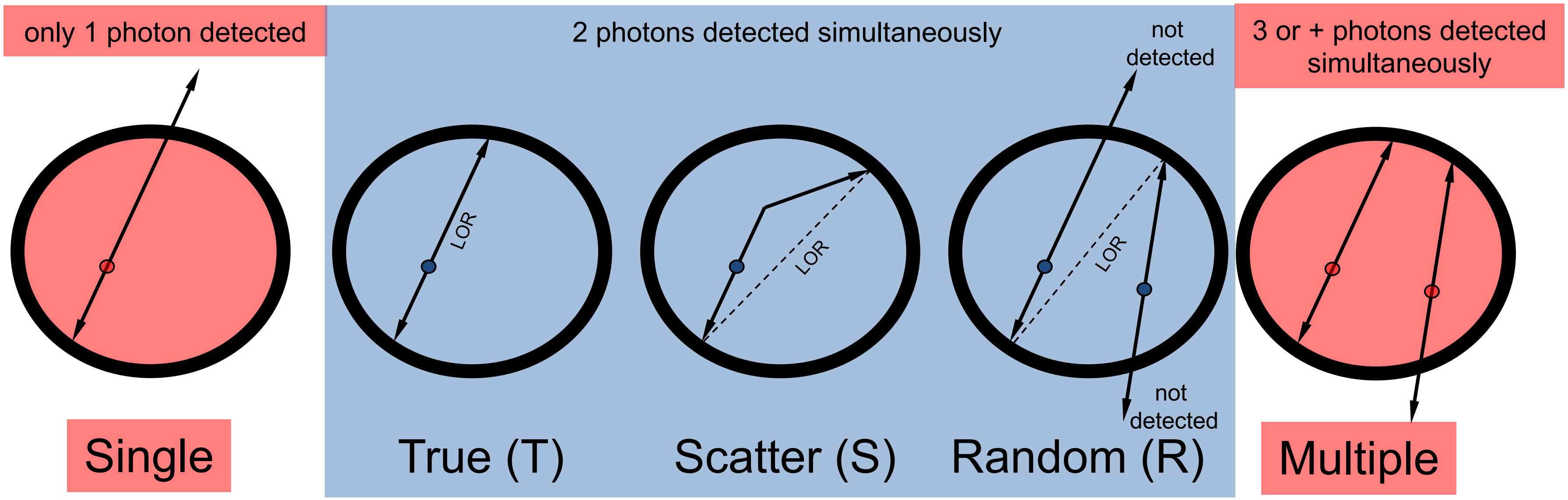
Typical configuration

whole-body (patient port ∅~70-85 cm; axial FOV~15-26 cm)

- scintillator crystals coupled to photomultiplier tubes (PMTs)
- cylindrical geometry
- ~12-52 rings of detector crystals
- hundreds of crystals/ring
- several millions of LORs
  (only a few are shown)



Types of "events"



Total coincidences measured in a given LOR: $T + S + R$

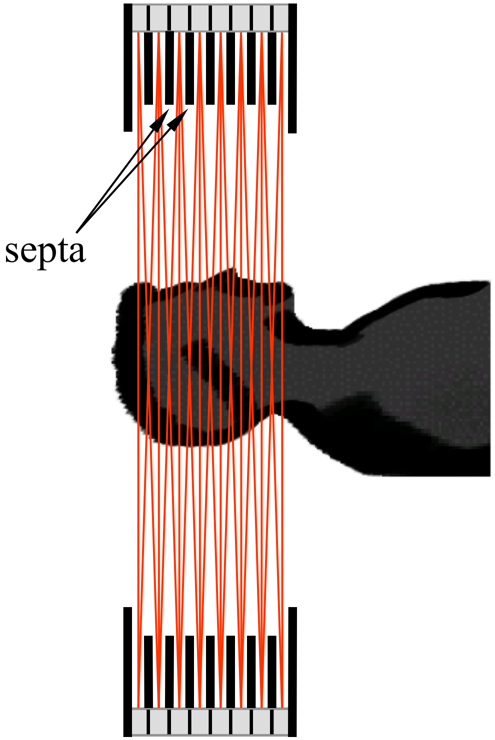
We only obtain an <u>estimate</u> of the trues: $\hat{T} = T + S + R - \hat{S} - \hat{R}$ (estimates)

Note that with low counts $\hat{T}$ can be negative (statistical process)

”2D” and ”3D” - nobody *uses* 2D anymore

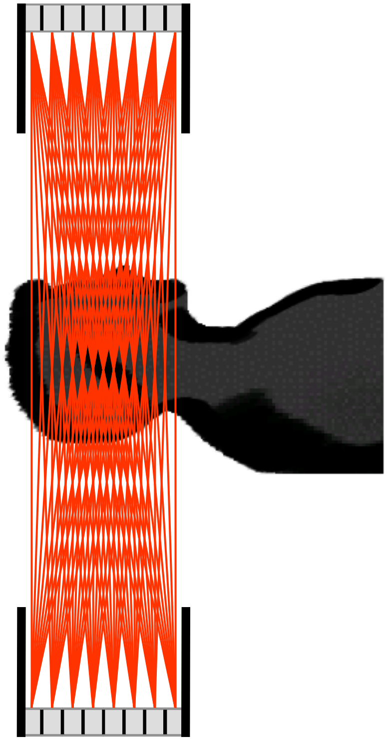
2D mode

(= with septa)



3D mode

(= no septa)



In 2D, detector rings were handled separately

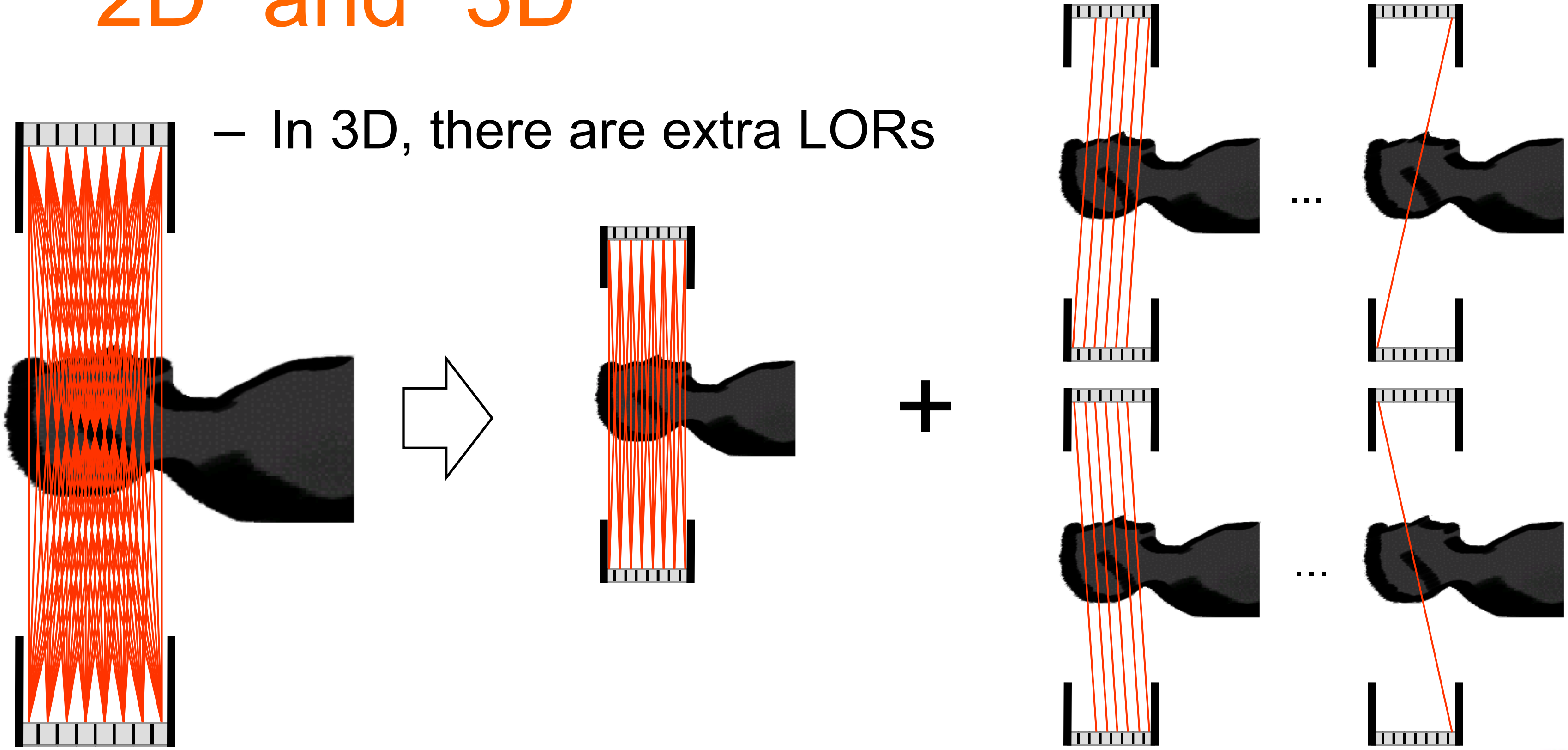
In the 3D mode there are no septa: photons from a larger number of incident angles are accepted, ***increasing the sensitivity***.

The increase in sensitivity is ***not uniform*** (detailed in a later slide)

Note : *2D acquisition* mode still provides a full volume (*3D) of reconstructed images***!**

”2D” and ”3D”

– In 3D, there are extra LORs

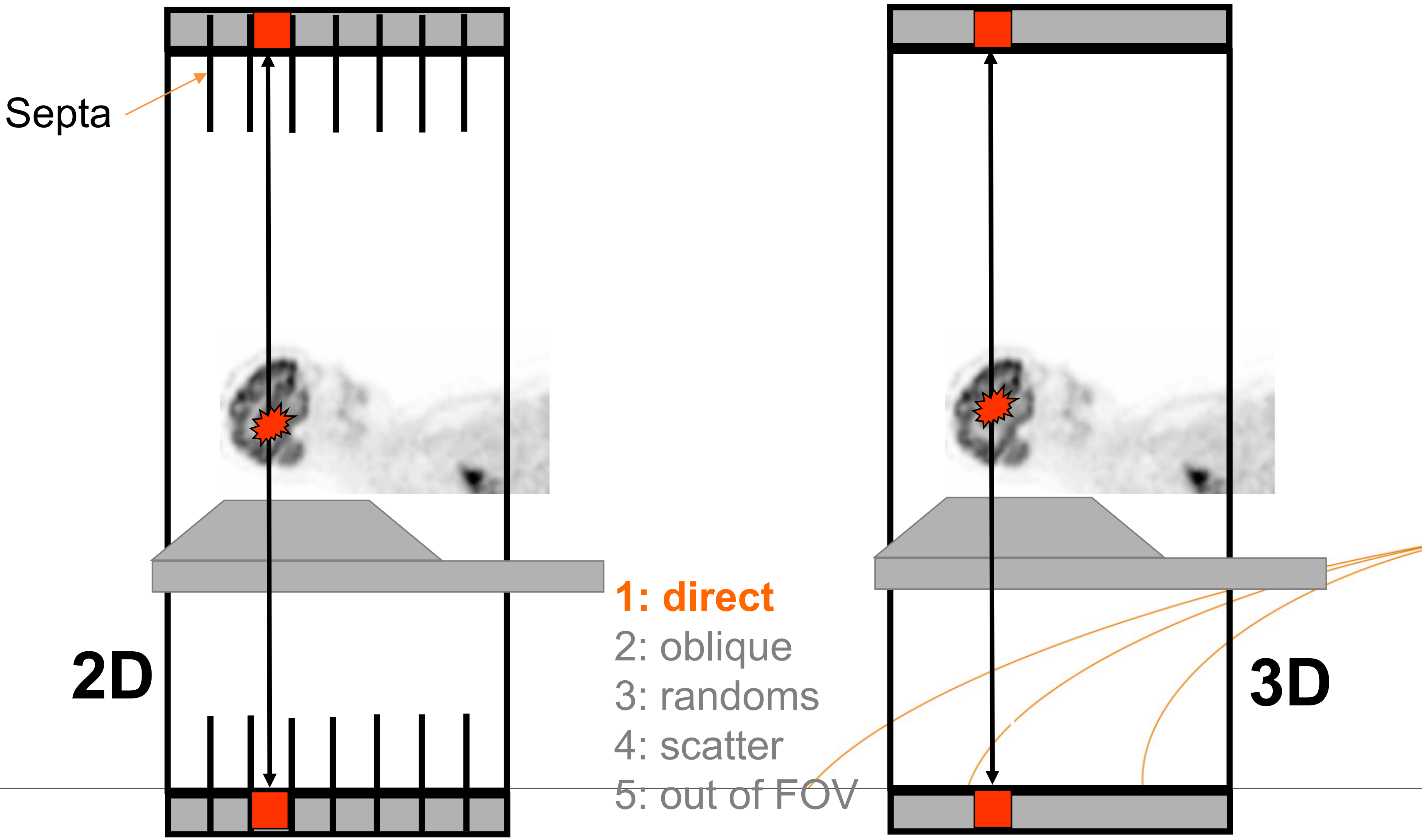


3D mode　　same planes as 2D　　+　　oblique planes

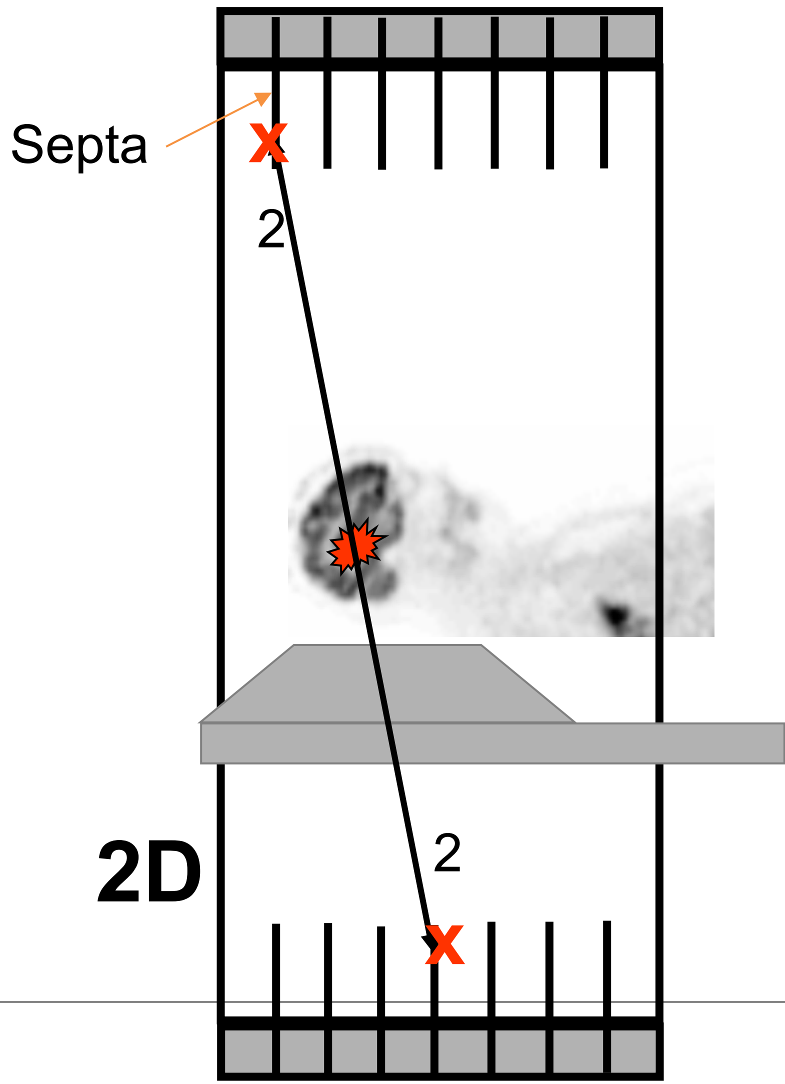
3D data takes up much more space than 2D

3D reconstruction is much more complex than 2D

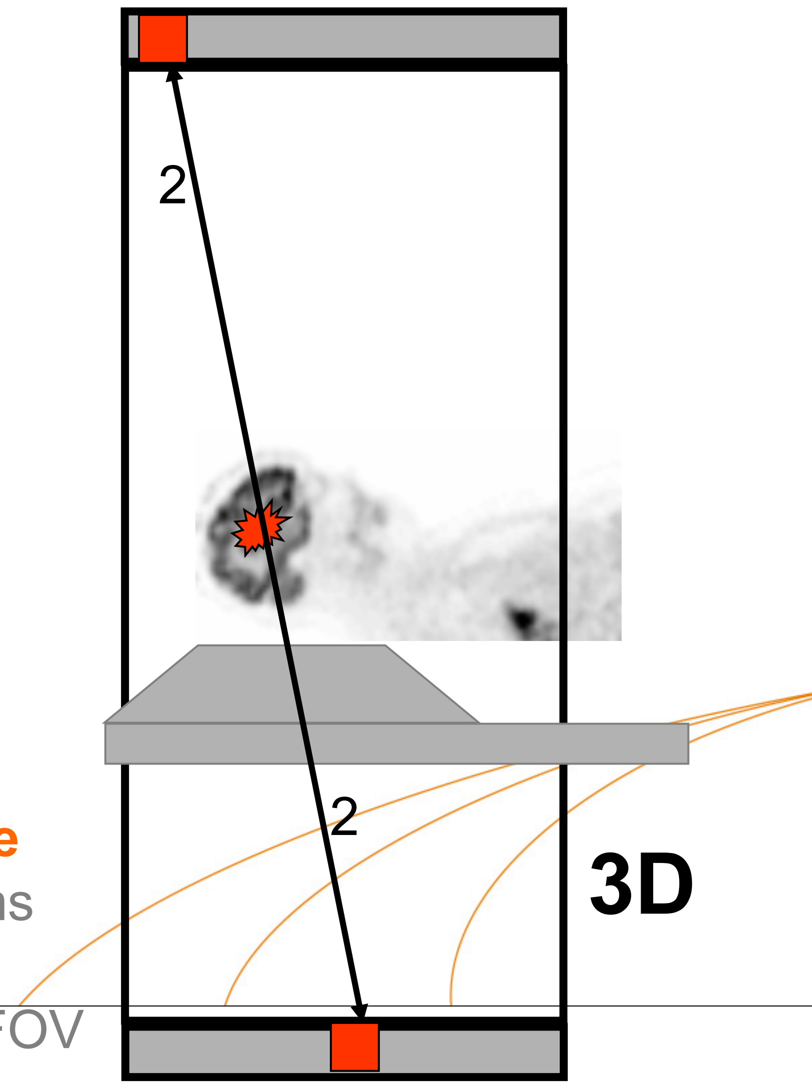
Types of “events”



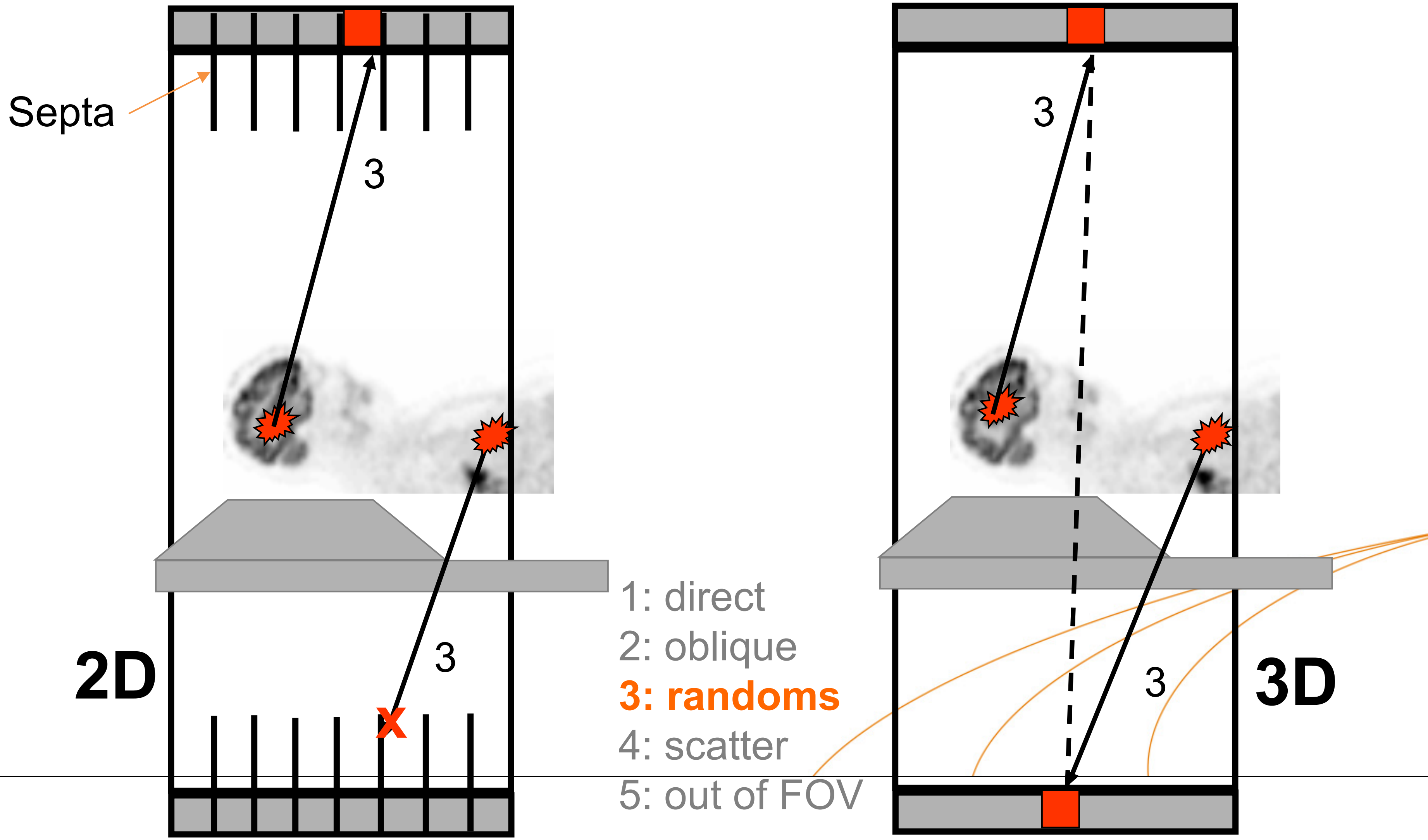
Types of “events”



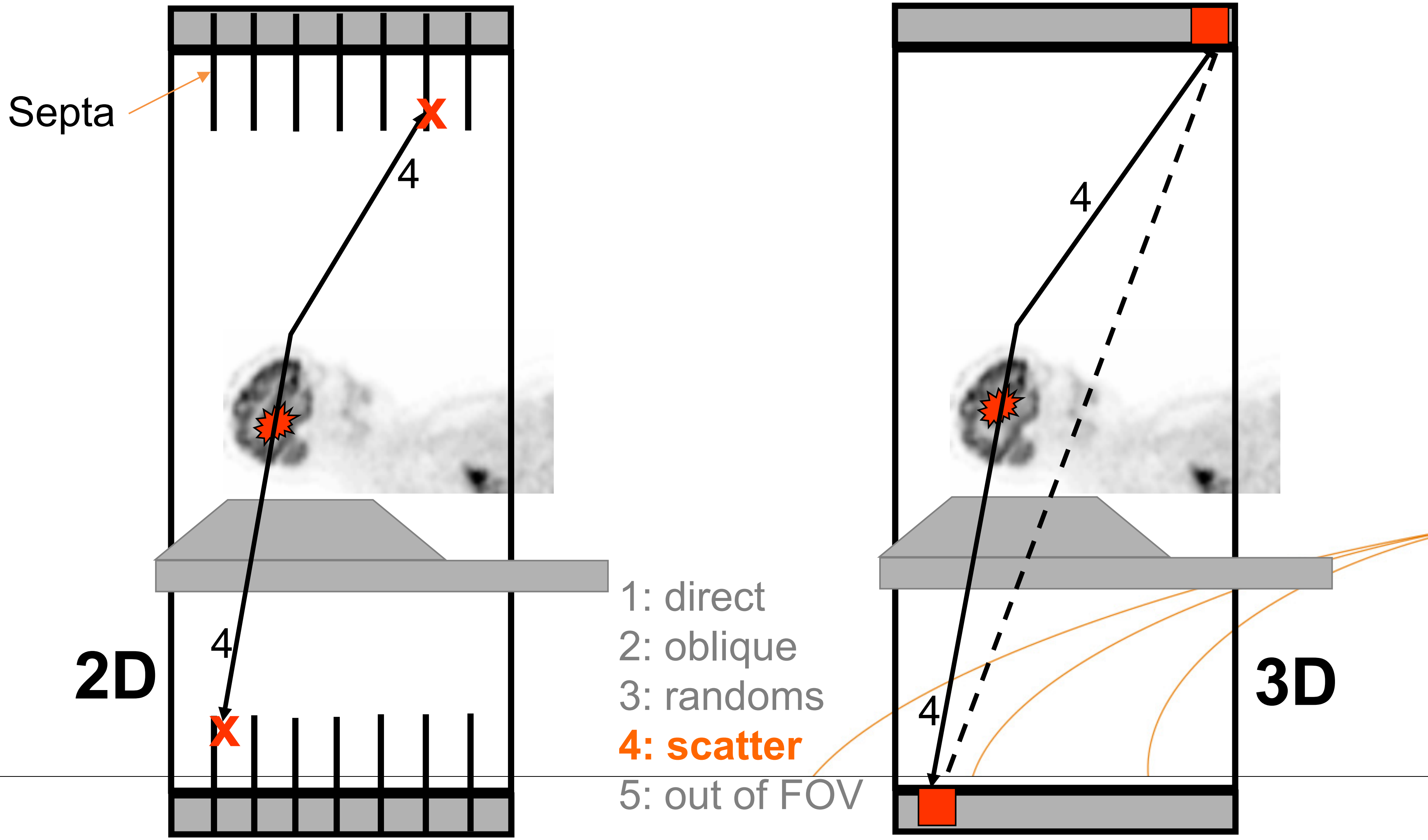
1: direct
2: oblique
3: randoms
4: scatter
5: out of FOV



Types of “events”

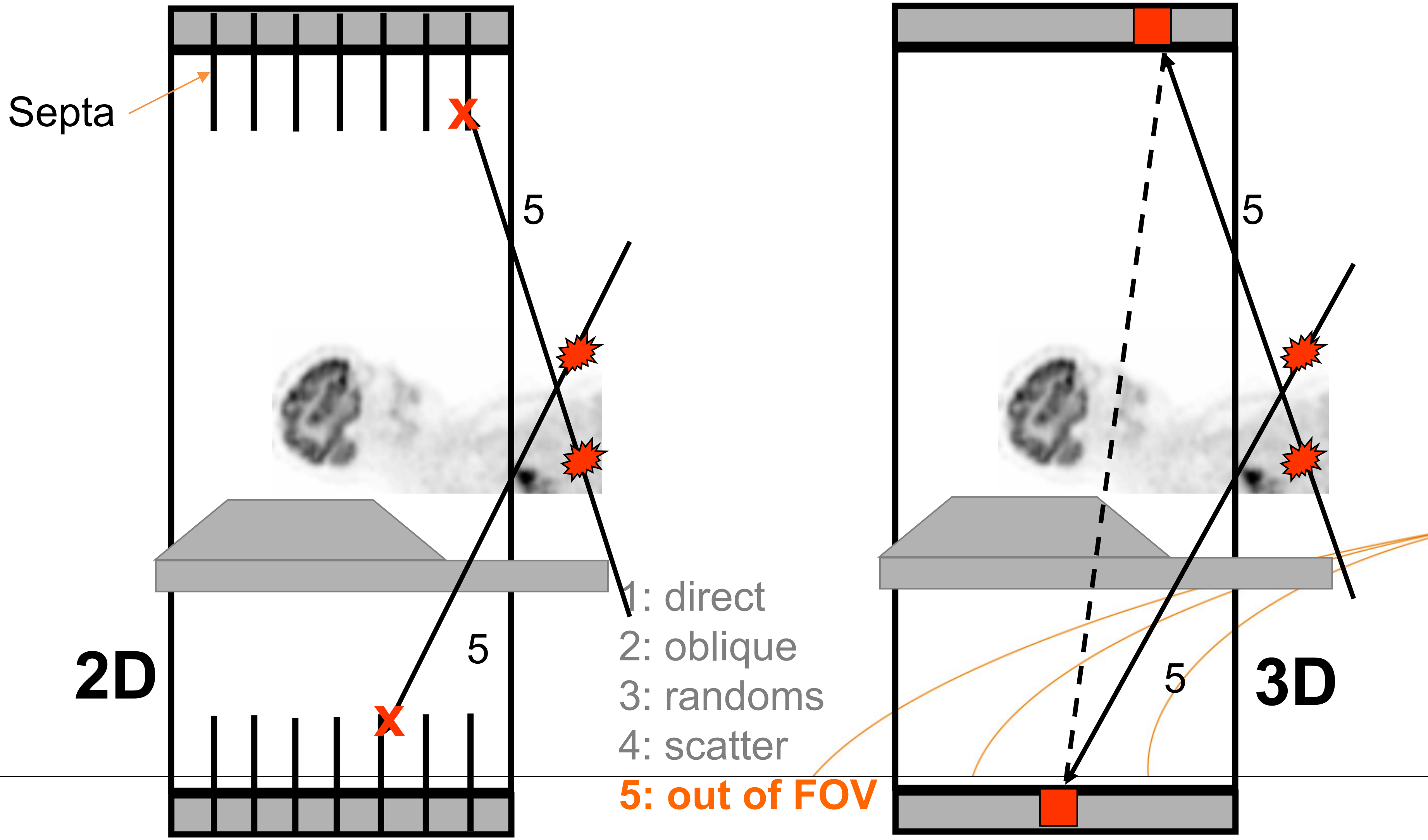


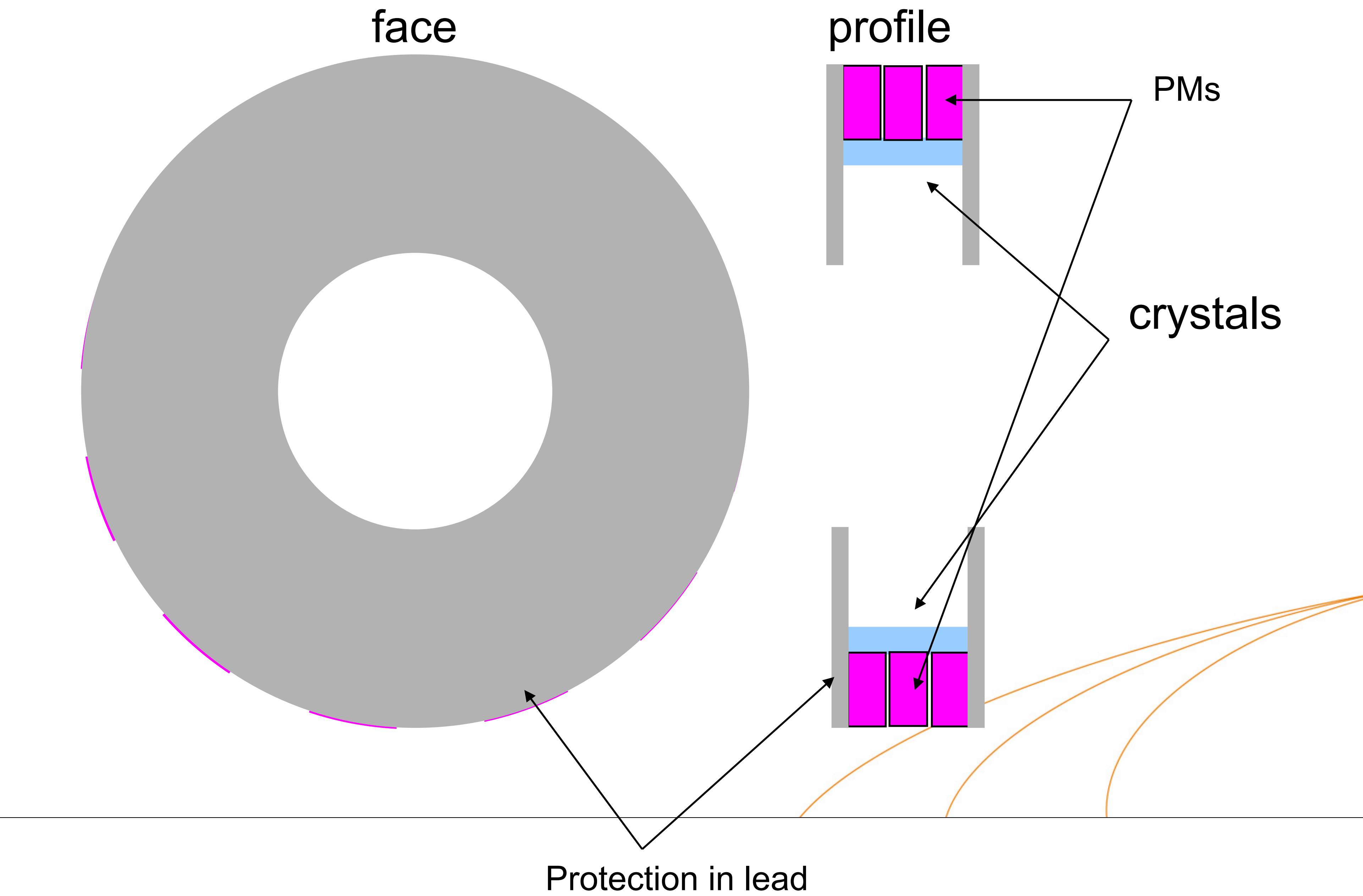
Types of "events"

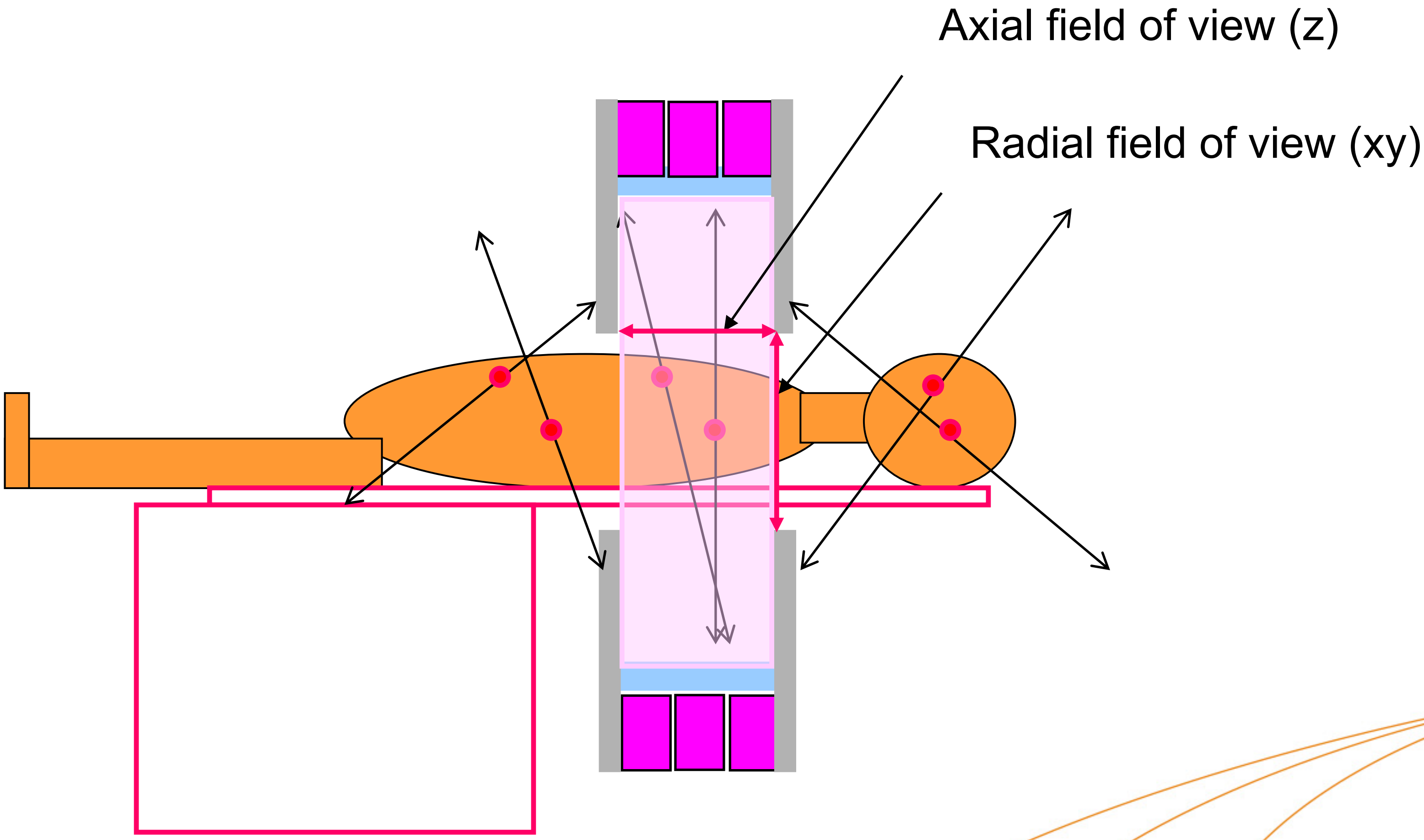


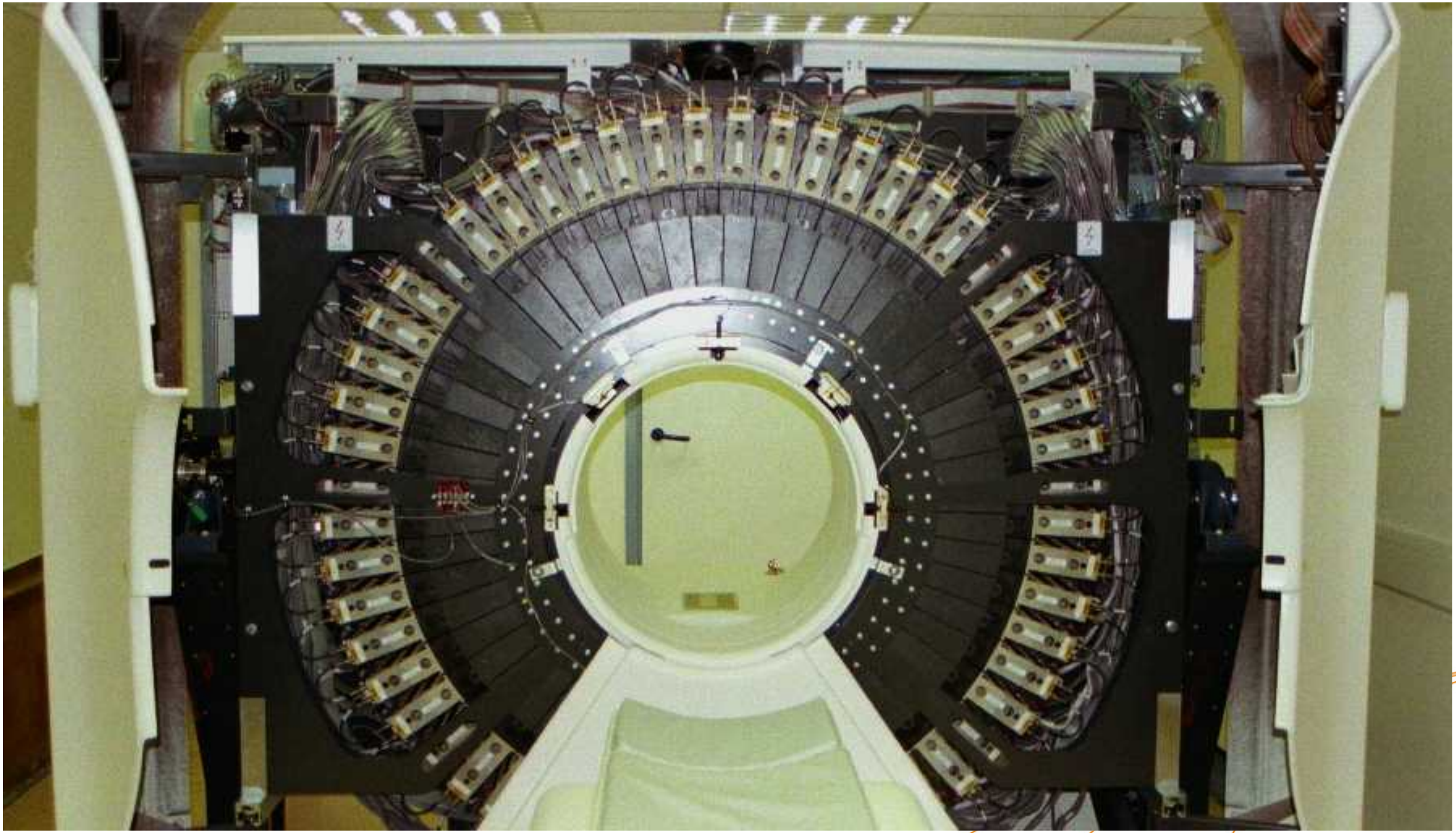
1: direct
2: oblique
3: randoms
4: scatter
5: out of FOV

Types of “events”

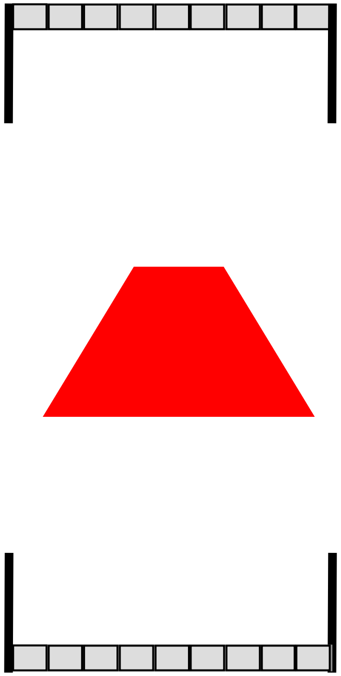



face
profile
PMs
crystals
Protection in lead


Axial field of view (z)
Radial field of view (xy)



Sensitivity in ”3D” is position dependent

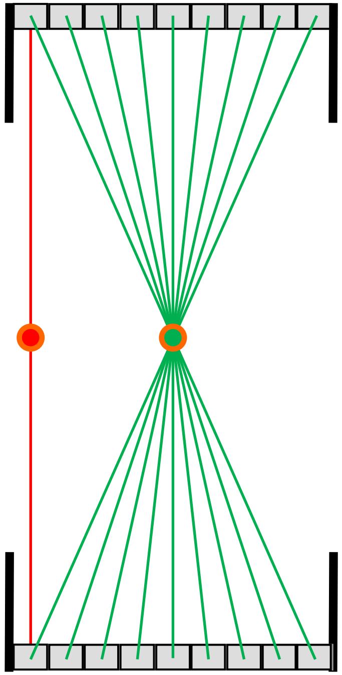


3D mode

There is a large difference between center and edge slices due to the number of LORs that contribute

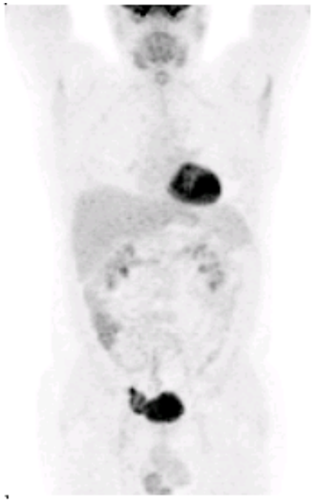
The ”ideal” triangle is most often truncated like this:

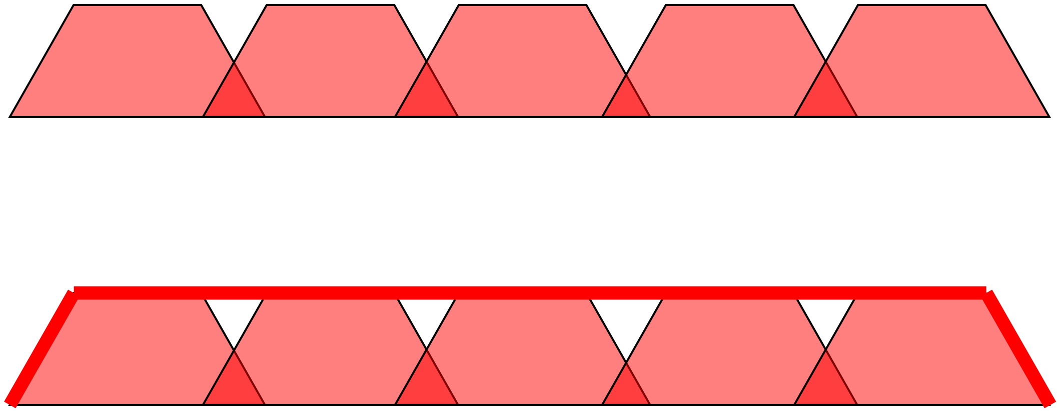
(we are not allowing all angles)



3D mode

- and therefore we need ”overlap” in whole-body scanning





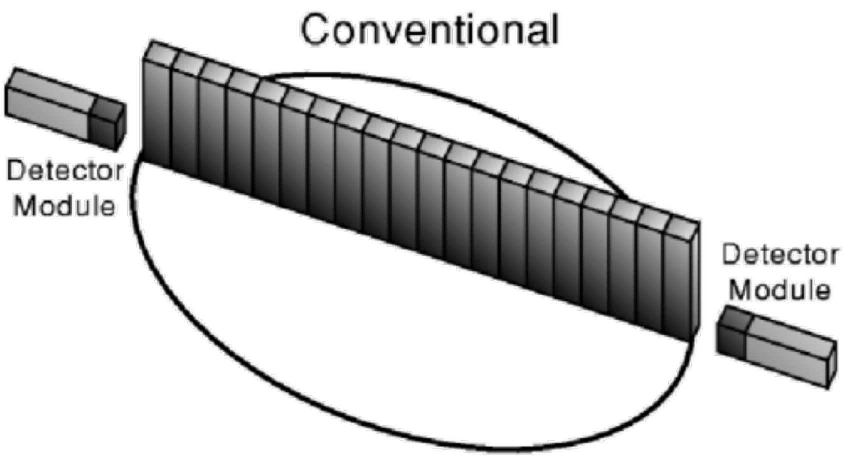
The overlapping scans add up to give a constant sensitivity and noise level (except for top and bottom)

Time of Flight (TOF) PET

– more than just a coincidence...

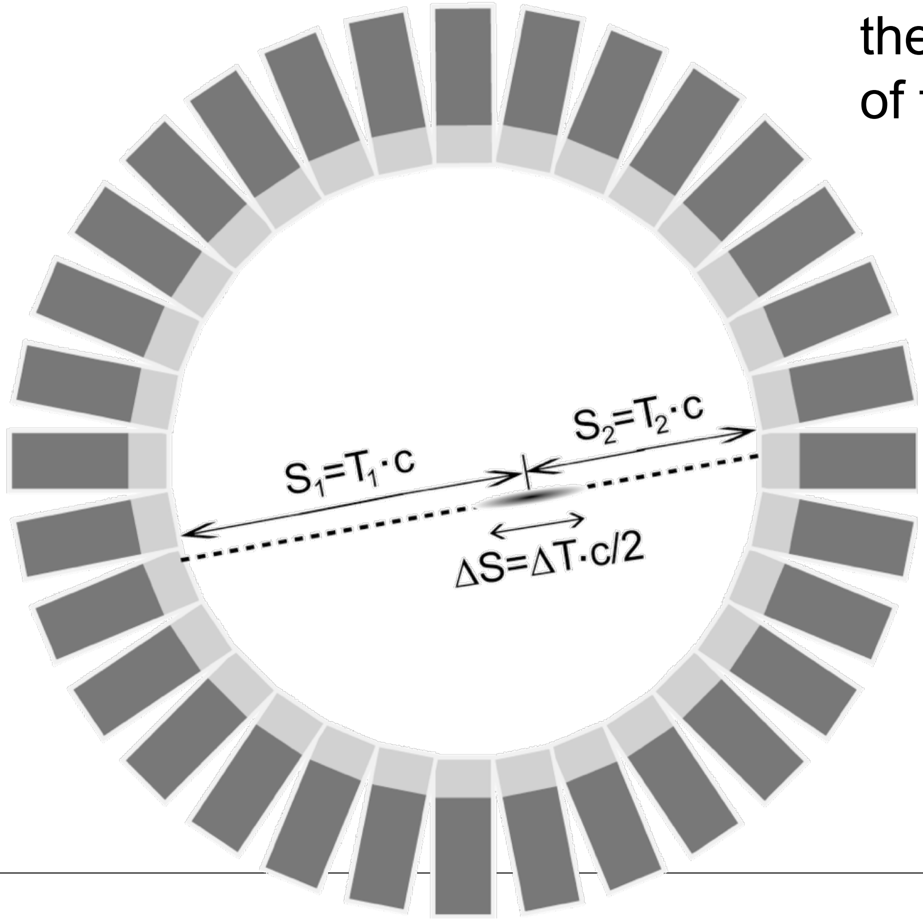
$$N_{\gamma-\gamma} = k \int_L \rho(x,y,z)\,dl$$

$\Delta t \approx$ 2-4ns



Time of Flight (TOF) PET

– more than just a coincidence...



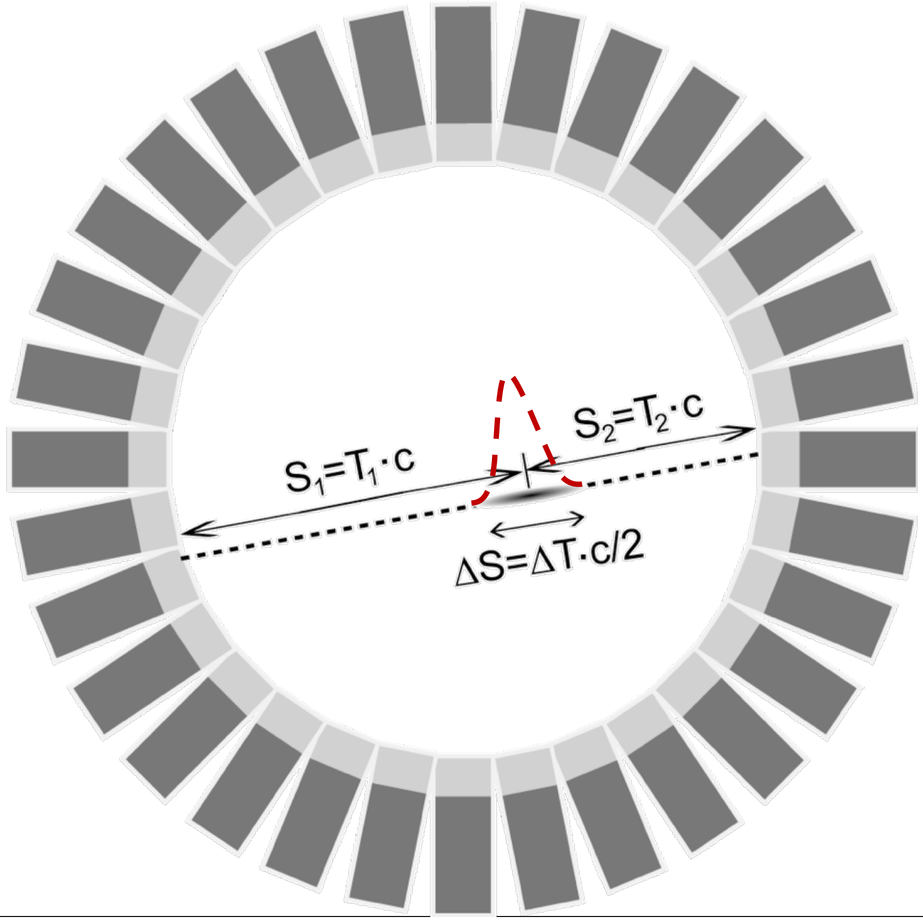
- A way to improve the noise is to limit the extent of the line integral measuring the time difference Δt of the arrival time of the to photons

→ The displacement of the annihilation point from the center can be estimated as:

$$\Delta S = \frac{c \cdot \Delta t}{2}$$

Time of Flight (TOF) PET

– more than just a coincidence...



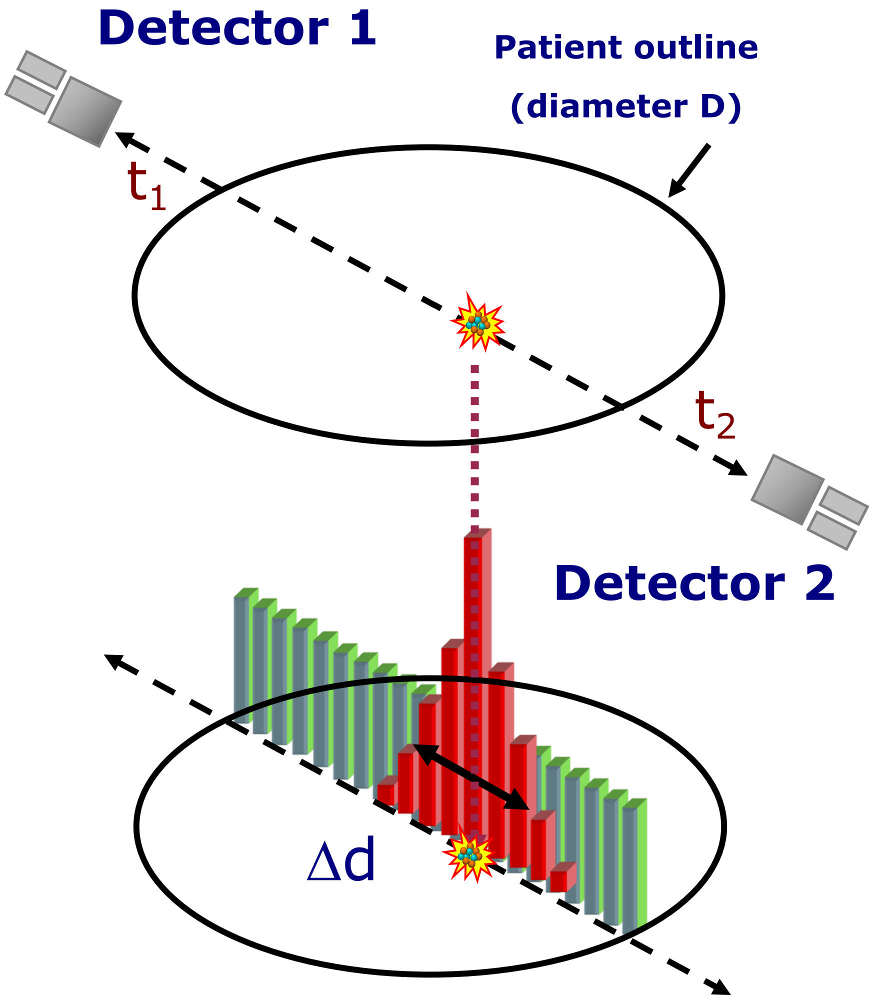
Example: Time resolution 500ps
→ possible to measure the point of annihilation with a accuracy of 75mm FWHM:

$$\Delta S = \frac{3 \cdot 10^{8} m \cdot 5 \cdot 10^{-10} s}{2\ s}$$
$$= 7{,}5 \cdot 10^{-2} m = 75 mm$$

- Improved energy resolution
  → reduce scatter
- Small coincidence Window
  → reduce randoms
- Time of Flight feature
  → Improvement of image quality

Time of Flight (TOF) PET

– more than just a coincidence...



- tried and abandoned in ancient PET times (~1985)
- idea commercially relaunched in 2006 by Philips

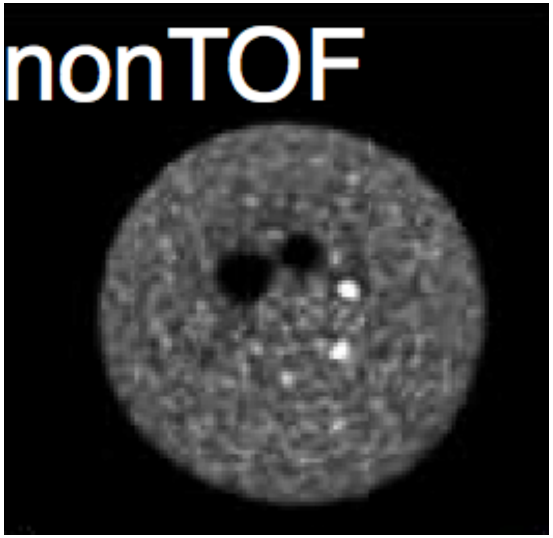
Δt (ps)	Δd (cm)
100	1.5
300	4.5
500	7.5
600	9.0

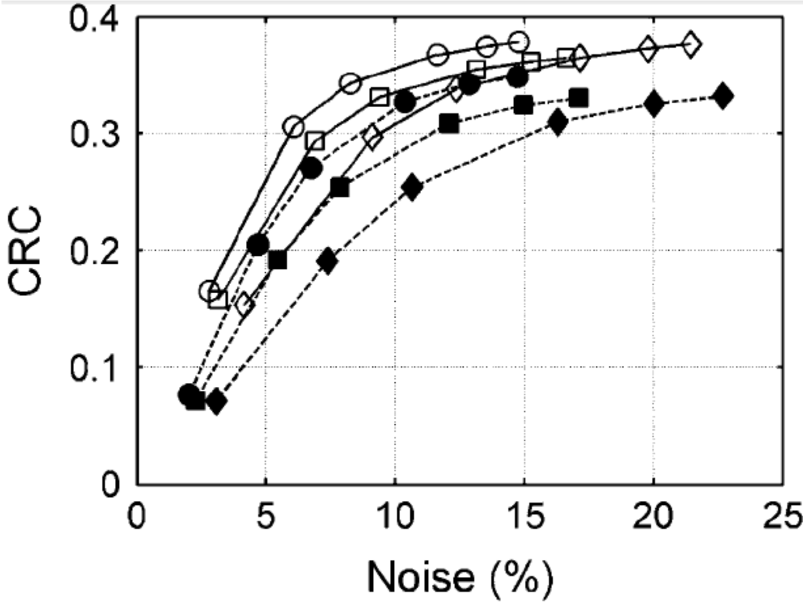
1 ps = 10^{-12} s

- More information available for image formation
- Hypothesis: better image quality, or shorter scanning time, or less injected activity

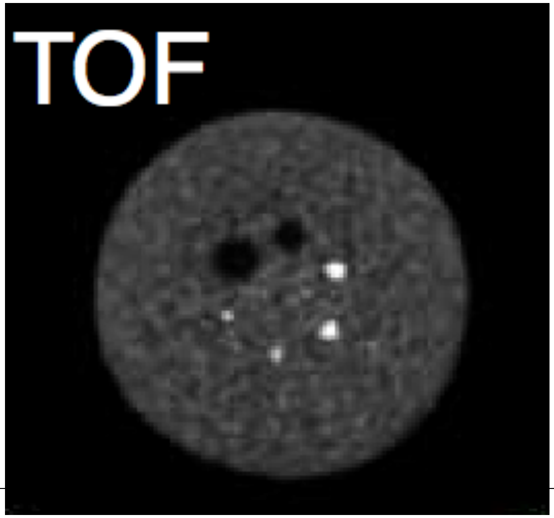
Time of Flight (TOF) PET

13 mm hot spheres

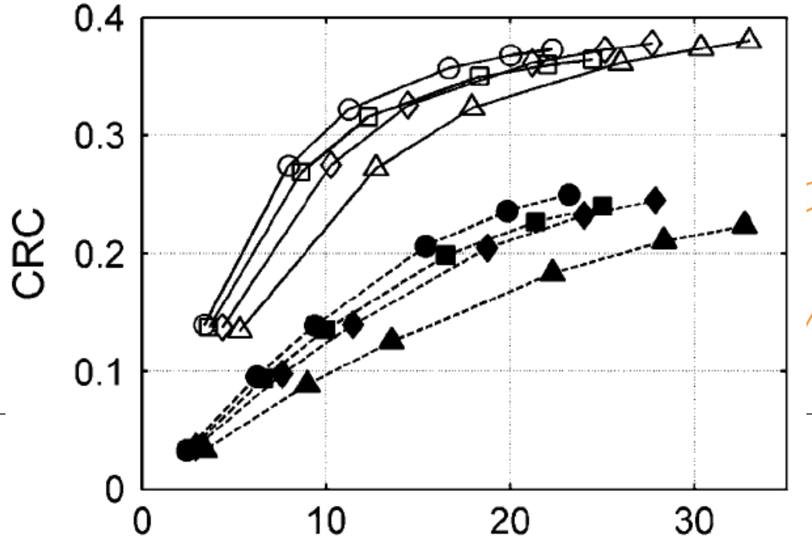




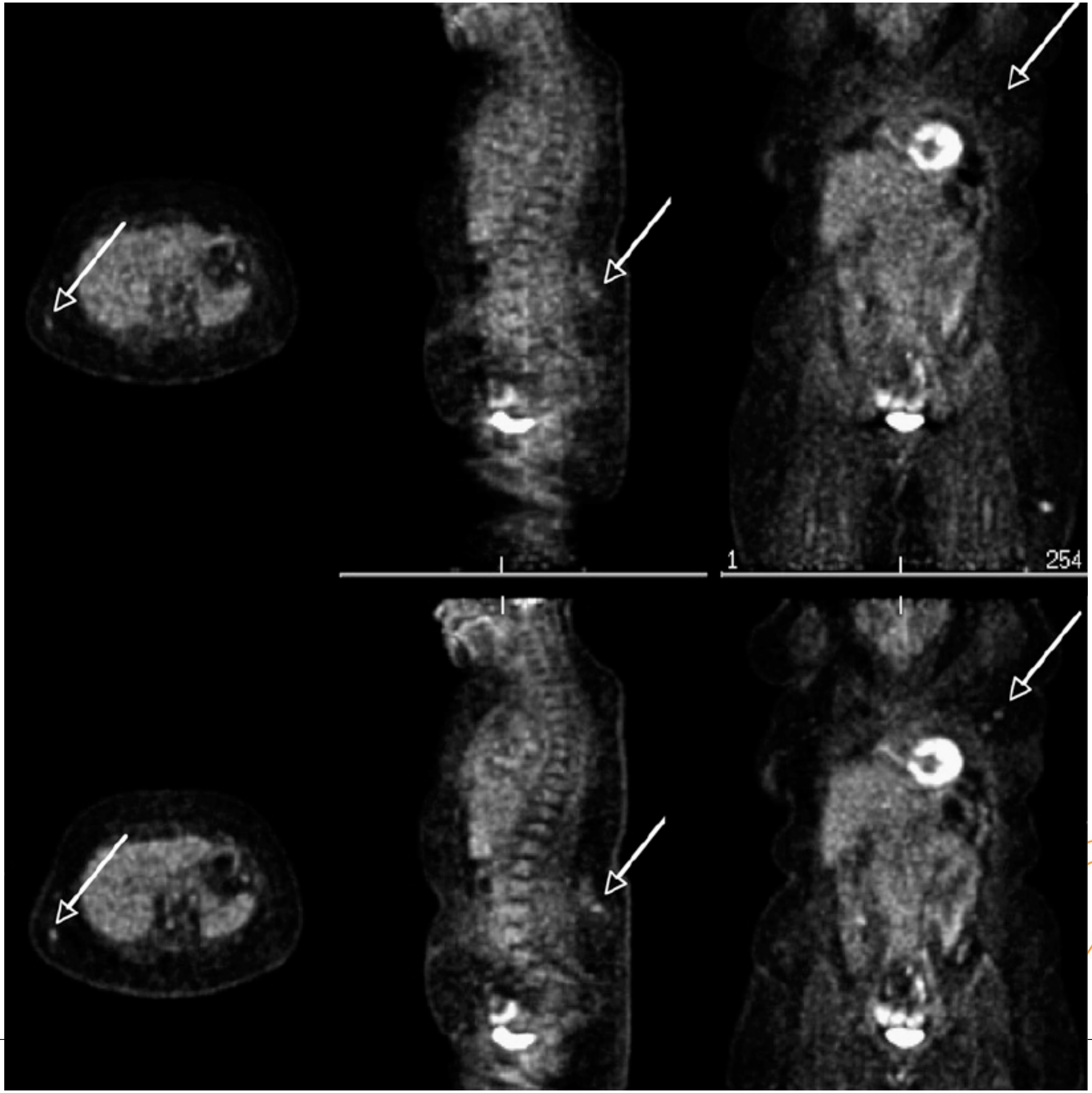
27-cm cylinder



5 min scan , 35-cm cylinder



35 cm cylinder

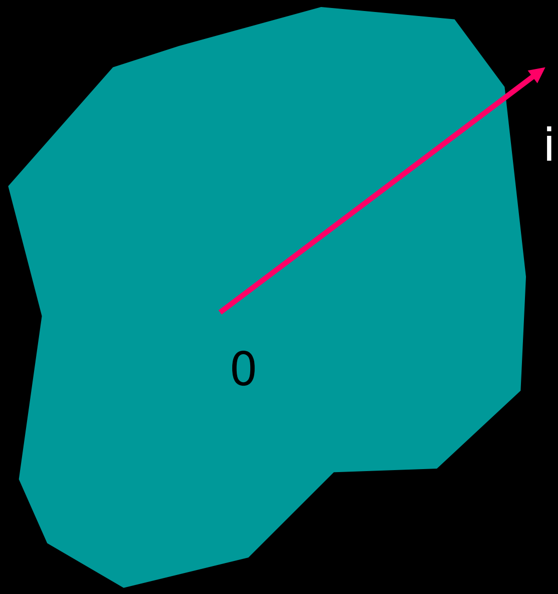

1
254

Photon attenuation in PET

- Attenuation of a single γ:

$$A_i = \tau_i A_0$$

$$\tau_i = e^{\int_0^i -\mu(x)dx}$$

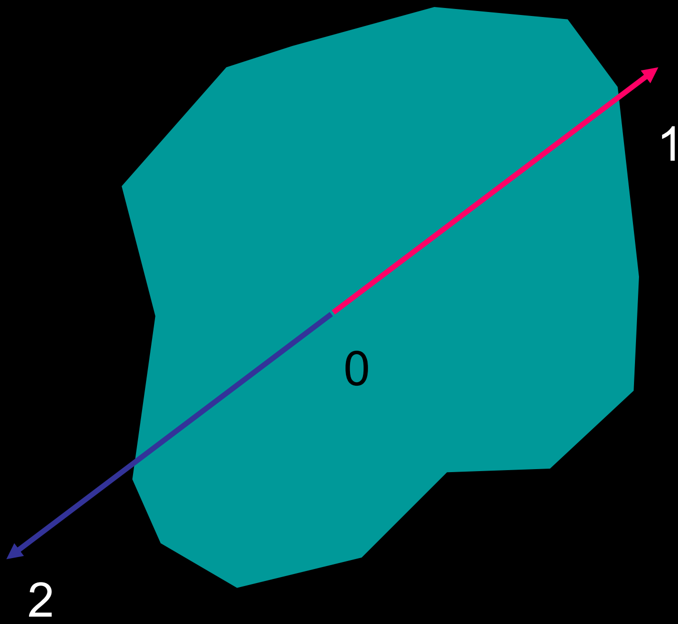


τ_i: probability of the photon transmission from 0 to i
μ: linear attenuation coefficient (cm^{-1})

Photon attenuation in PET

$$A_1 = \tau_1 A_0 = e^{\int_0^1 -\mu(x)dx} A_0$$

$$A_2 = \tau_2 A_0 = e^{\int_0^2 -\mu(x)dx} A_0$$

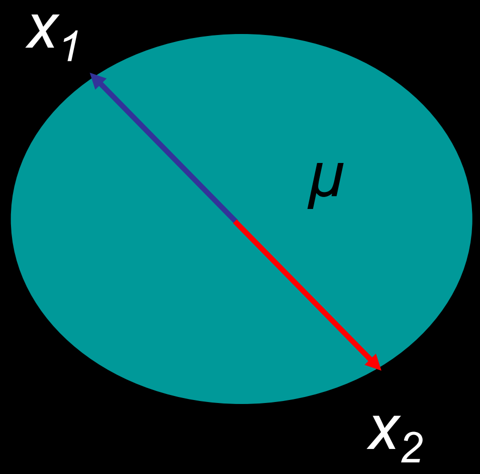


$$A_c = \tau_1 \tau_2 A_0 \Rightarrow A_c = e^{\int_1^2 -\mu(x)dx} A_0 \Rightarrow \frac{A_0}{A_c} = e^{\int_1^2 \mu(x)dx}$$

Photon attenuation in PET

$$\frac{A_0}{A_c} = e^{\int_1^2 \mu(x)dx} \Rightarrow \frac{A_0}{A_c} = e^{\mu \int_1^2 dx} \Rightarrow \frac{A_0}{A_c} = e^{\mu(x_2 - x_1)}$$

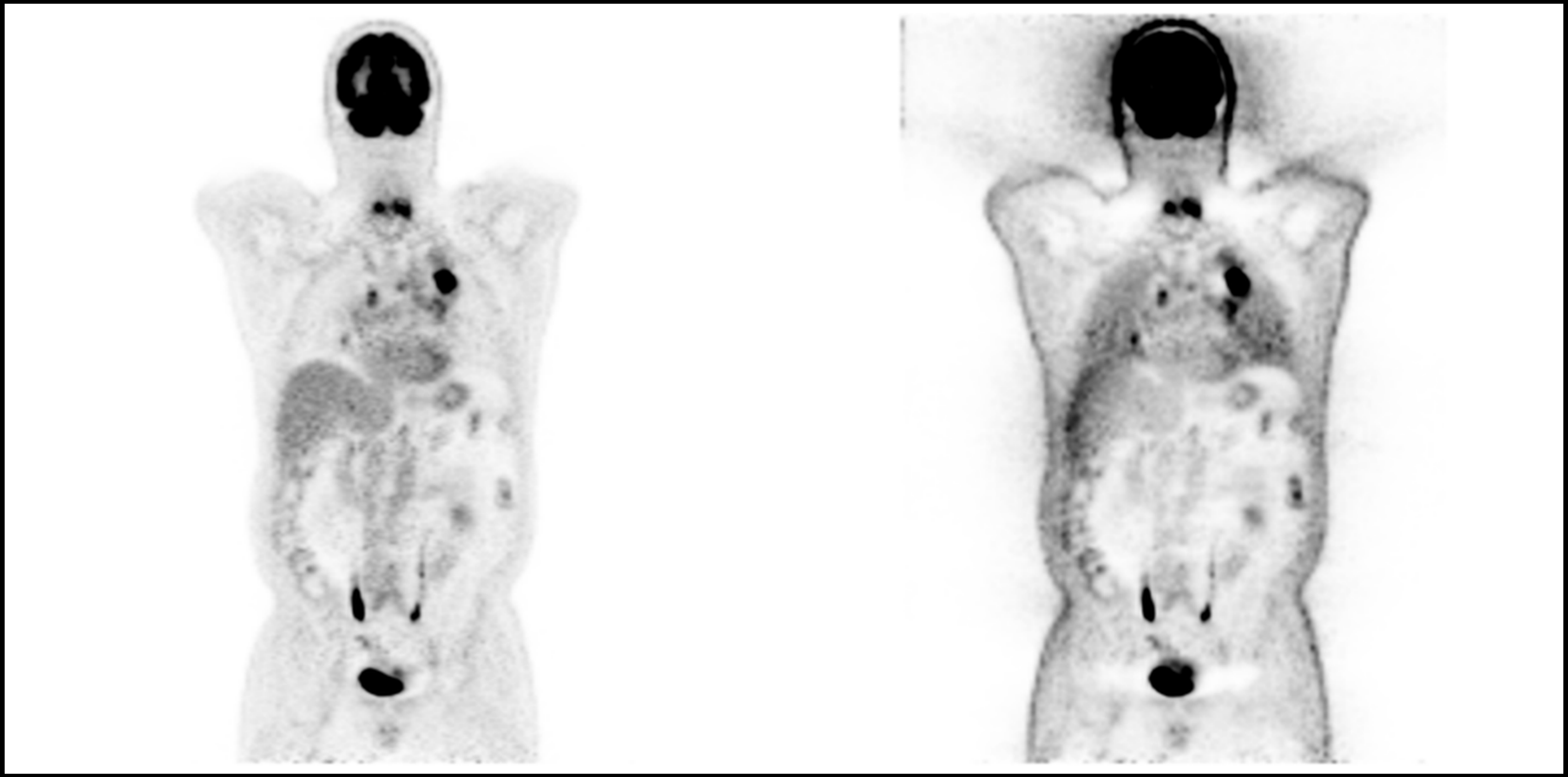
- ✓ it does not depend on the location of the annihilation along the line of response
- ✓ depends on the integral attenuation distance x = $(x_2 - x_1)$
- ✓ μ is constant for all positron emitters since the emission energy is 511keV
- ✓ need to know the density of the object



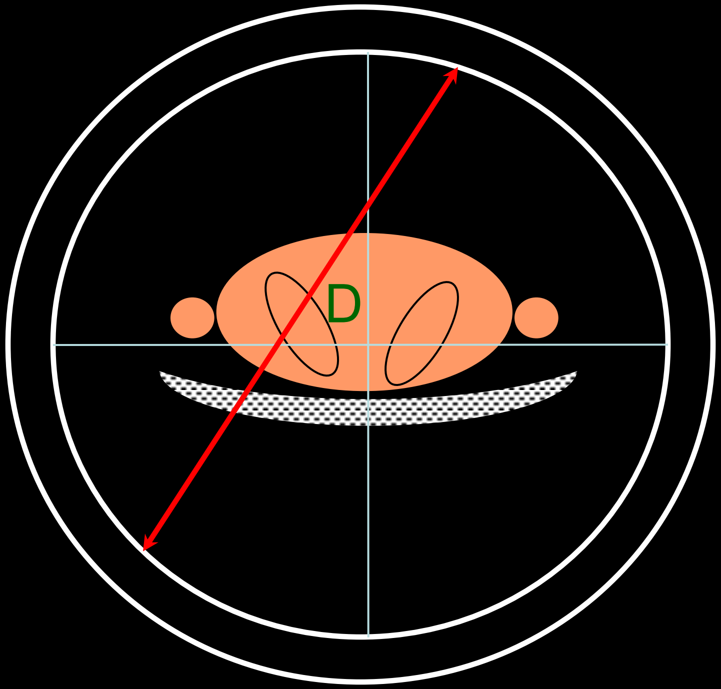
Attenuation effects in PET

- More significant in PET compared to SPECT since there are two photons involved
- Significant loss in sensitivity (a factor of 5 and 20 for brain and whole body imaging respectively)
- Quantitative accuracy
- Potentially higher impact for deep located lesions? (it has never been established in reality)

Attenuation effects in PET

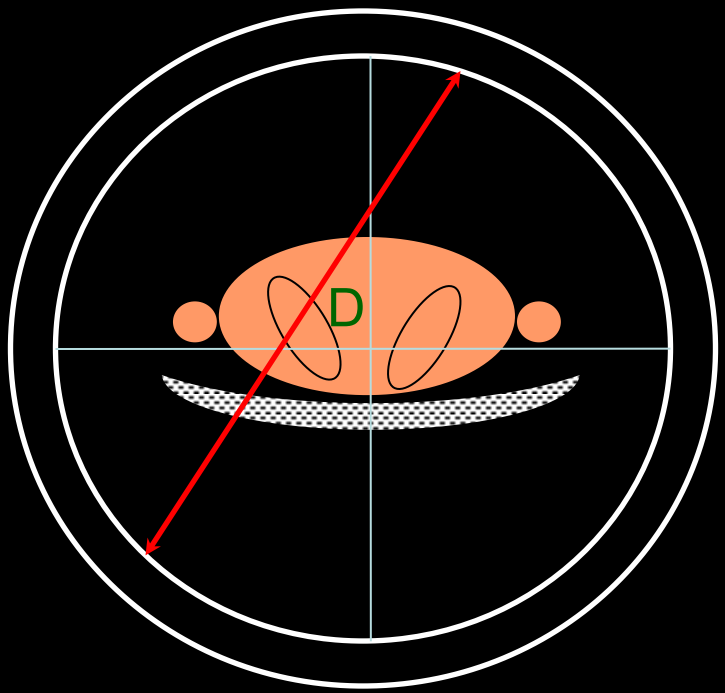


Attenuation correction in PET



- ✓ Attenuation independent of the position of the annihilation along the line of response
- ✓ Need to know the distribution of the attenuation coefficients.
- ✓ No need to know the activity distribution for the calculation of attenuation as it is the case in SPECT

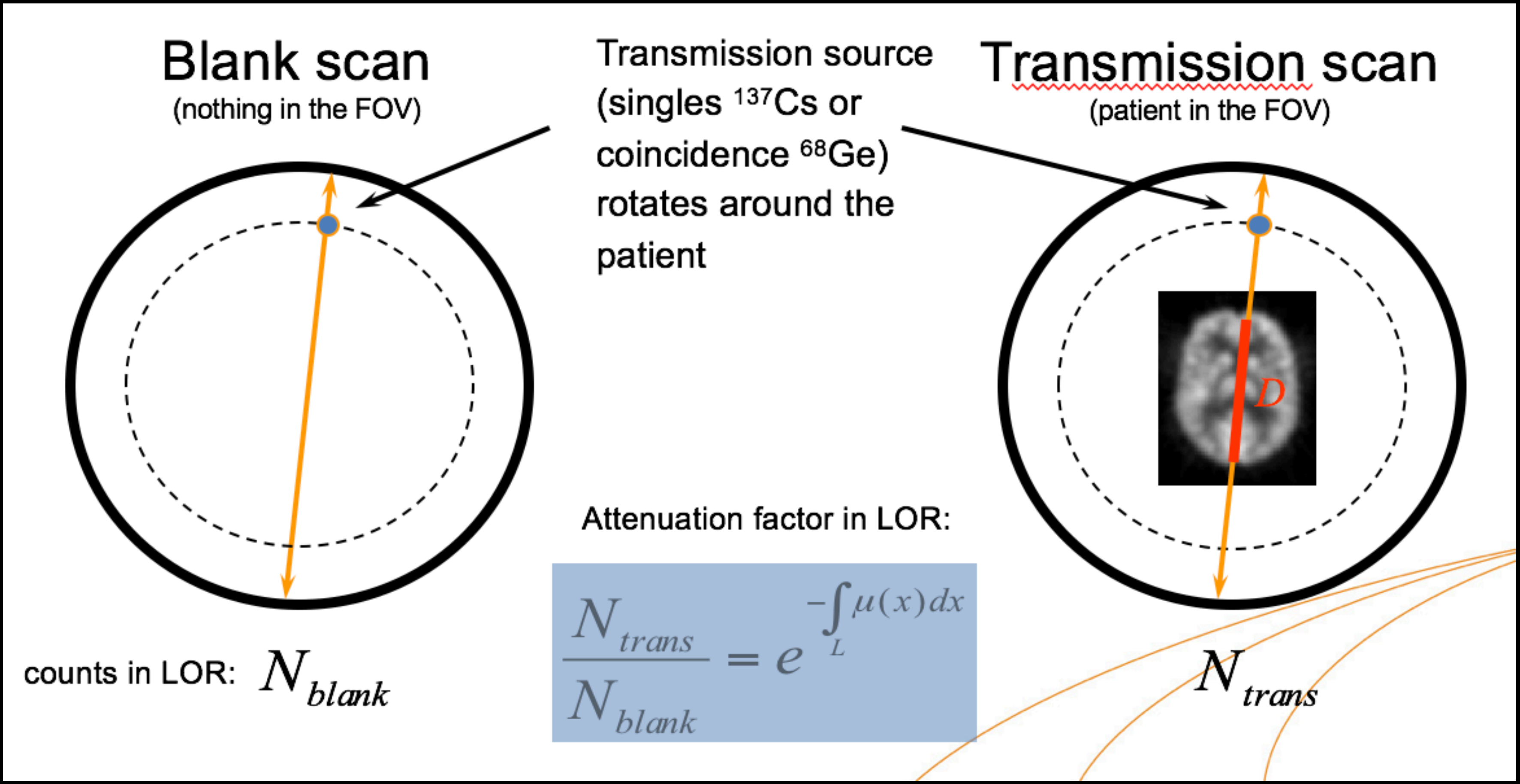
Attenuation correction in PET



How to obtain the distribution of attenuation coeffs:

- ✓ some sort of transmission scanning
- ✓ need the attenuation coeffs at 511keV

Attenuation correction in PET



Attenuation factor in LOR:

$$\frac{N_{trans}}{N_{blank}} = e^{-\int_L \mu(x)\,dx}$$

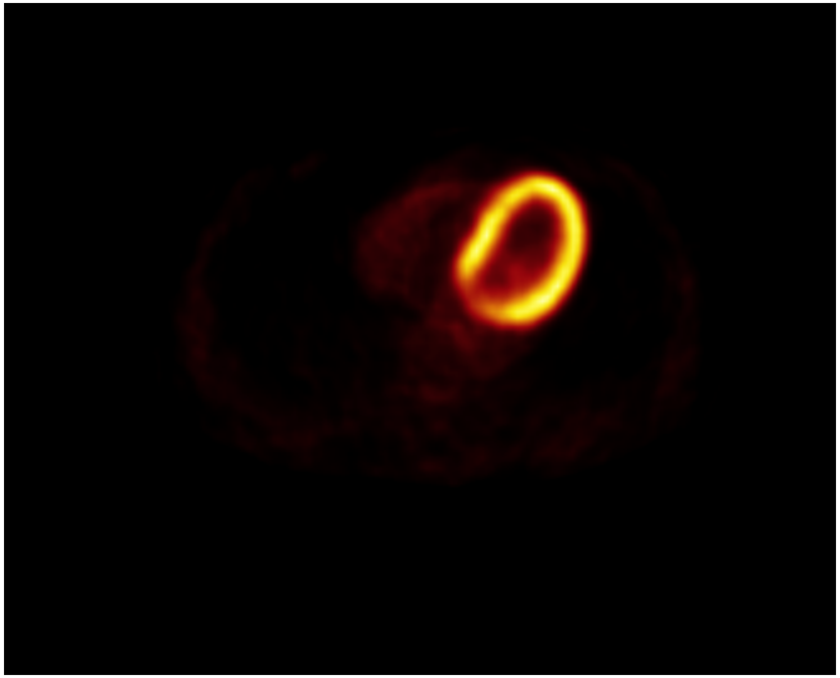
Radionuclide based AC

CT

attenuation of photons

structure / anatomy

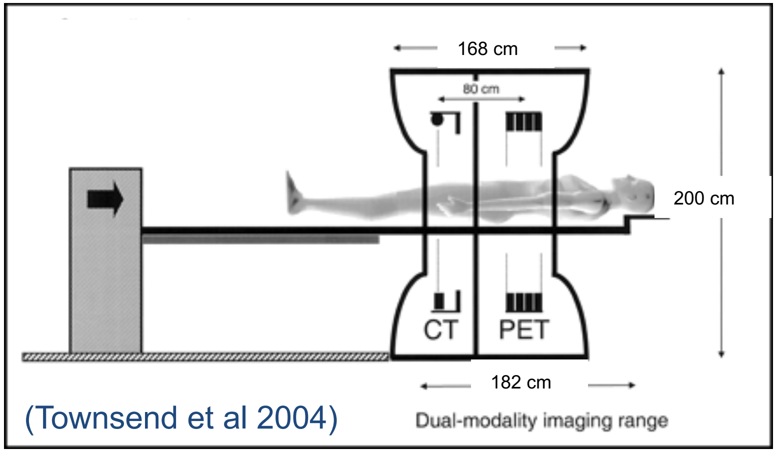
PET



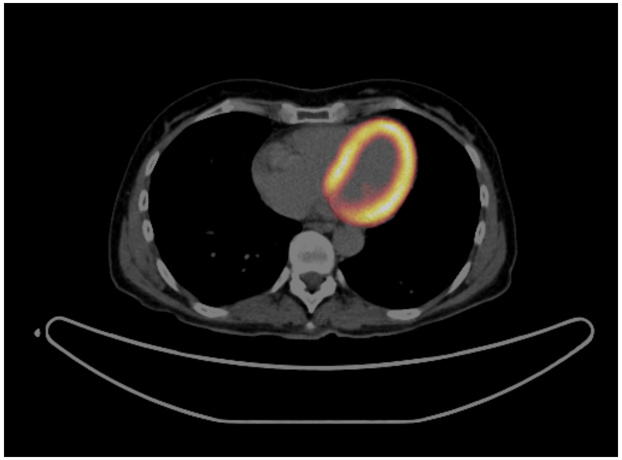
distribution of tracer

function / physiology

PET/CT scanner:



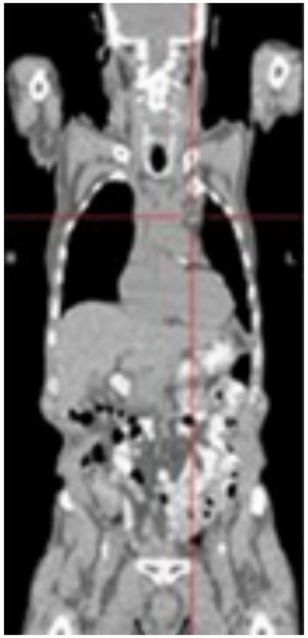
(Townsend et al 2004)



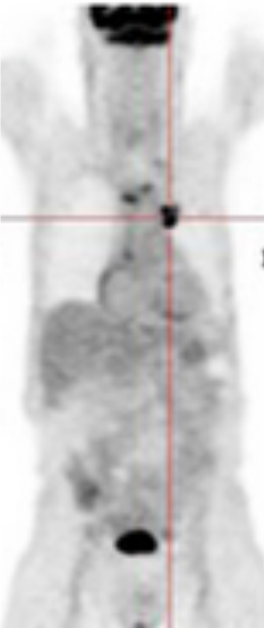
- combines two modalities in one gantry, common axis, common bed
- allows precise fusion of images
- provides structure + function in the same image
- can use CT for attenuation correction of PET /SPECT

Anatomical localisation of tracer – Attenuation correction

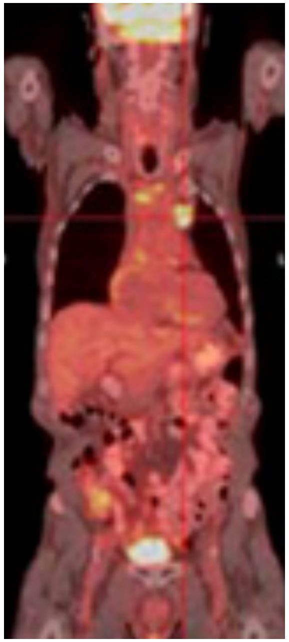
CT



PET



PET/CT



CT based PET Attenuation Correction

- Attenuation coefficient scaling method

~70-80keV → 511keV

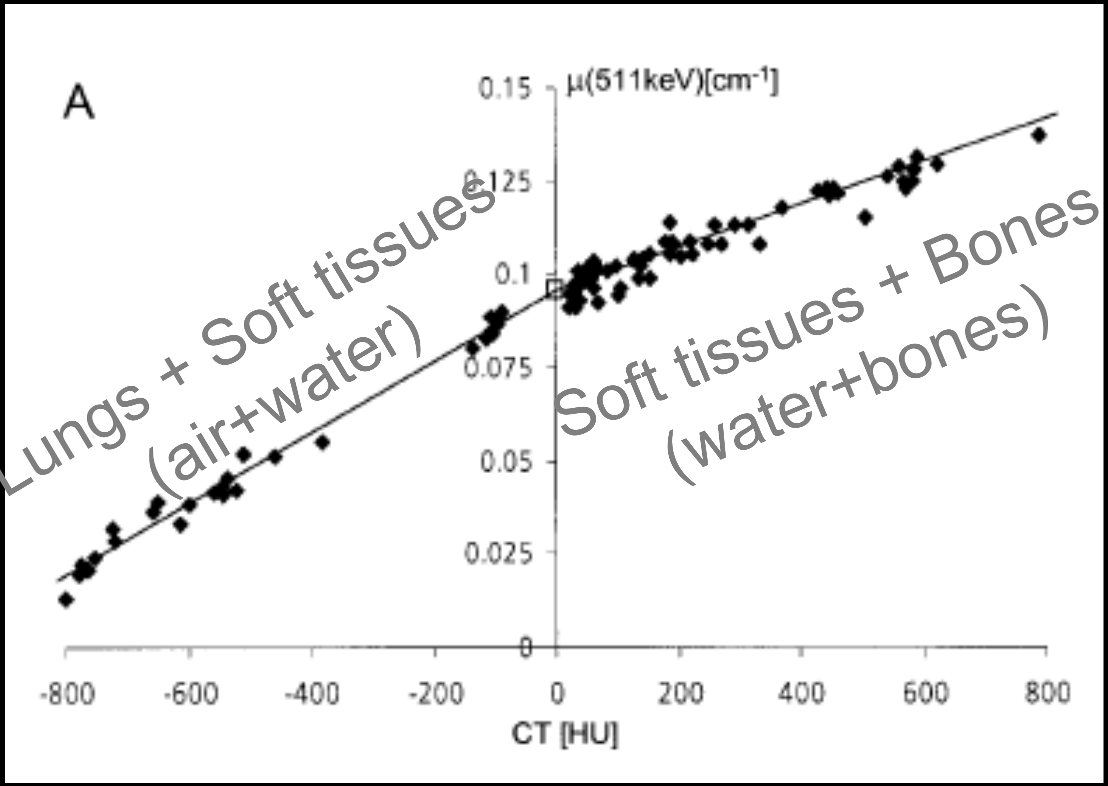
- Potential of misclassification of tissue types

contrast agents metallic implants

- Differences in the conditions of acquisition for PET and CT

D Visvikis, DC Costa, I Croasdale, et al; *"CT based attenuation correction in the calculation of semi-quantitative indices of 18FDG uptake in PET"* Eur J Nucl Med Mol Imag 2003, 30(3), 344-353, Nuclear Medicine Book of the Year 2003, ed. I Zubal, Elsevier

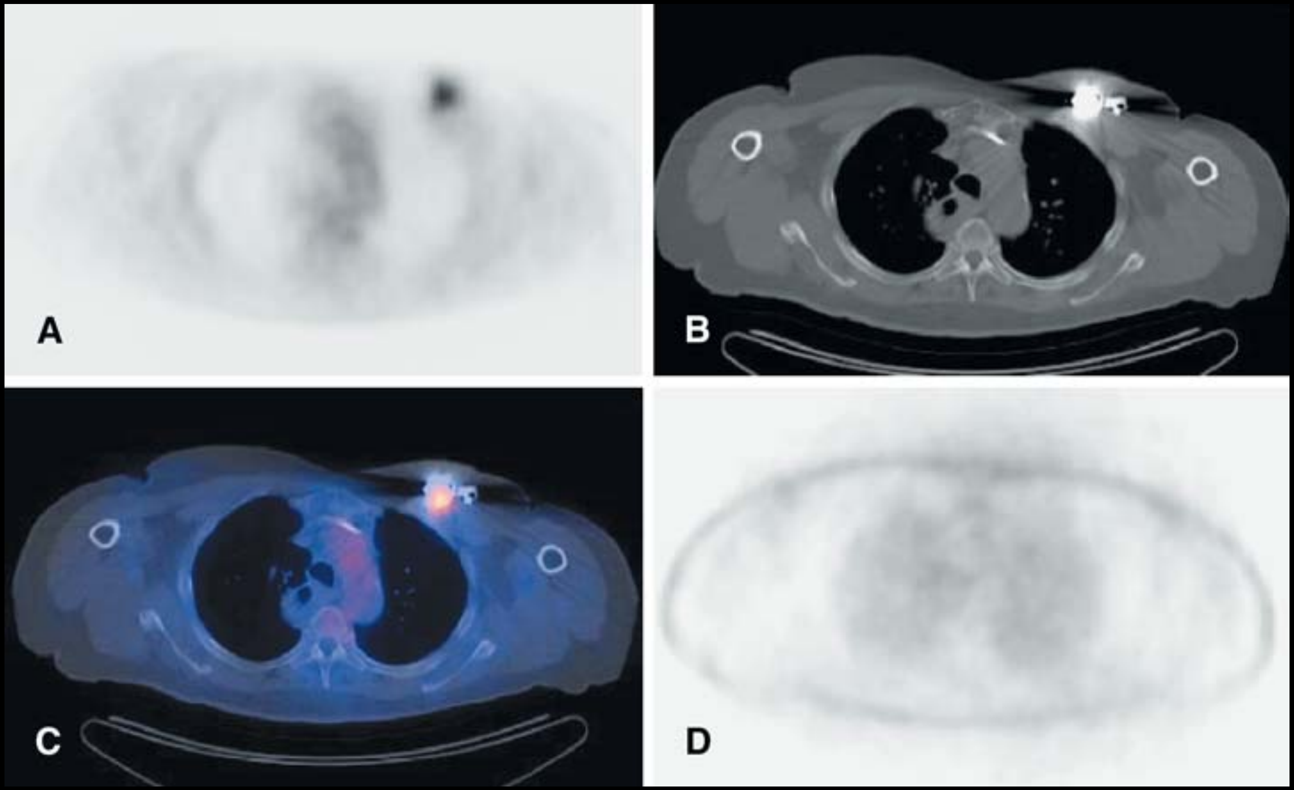
CT based PET Attenuation Correction



$$\mu = \mu_{H2O} \frac{(HU + 1000)}{1000}$$

$$\mu = \mu_{H2O}^{PET} + HU \frac{\mu_{H2O}^{CT}(\mu_{bone}^{PET} - \mu_{H2O}^{PET})}{1000(\mu_{bone}^{CT} - \mu_{H2O}^{CT})}$$

Metallic inserts: Pacemakers



H Schoder, et al, Eur J Nucl Med Mol Imag 2003, 1419

Respiratory motion effects

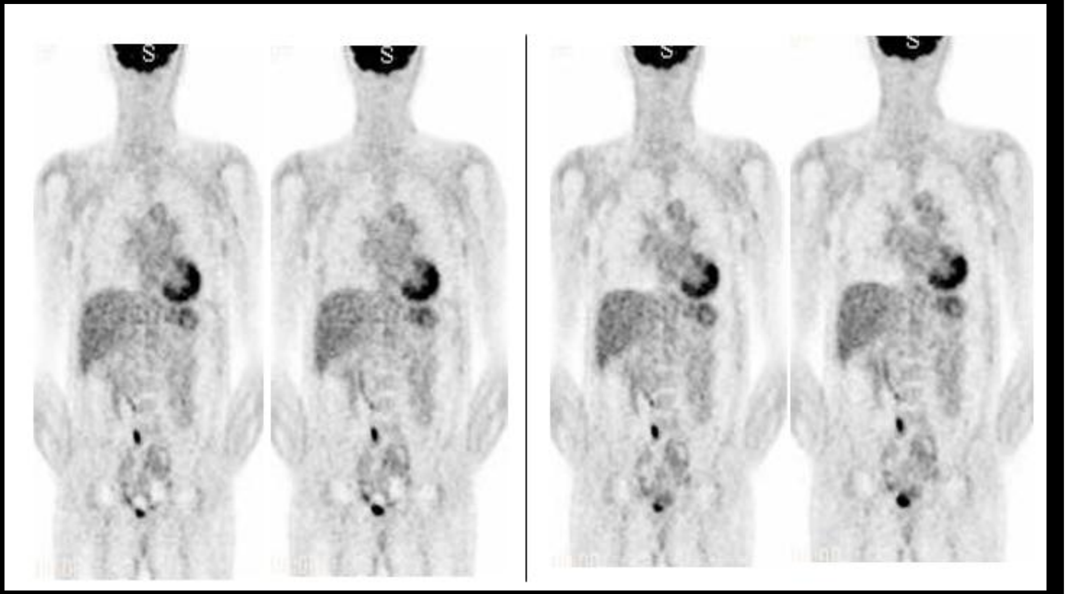
Rod sources

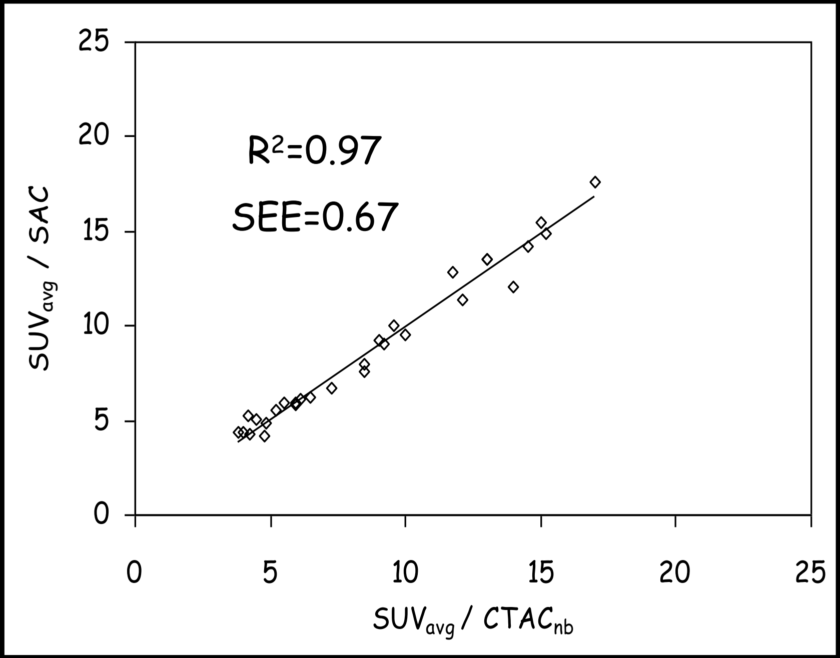
CT insp

CT exp

D Visvikis, DC Costa, I Croasdale, et al; *"CT based attenuation correction in the calculation of semi-quantitative indices of 18FDG uptake in PET"* Eur J Nucl Med Mol Imag 2003, 30(3), 344-353, Nuclear Medicine Book of the Year 2003, ed. I Zubal, Elsevier

CT based PET Attenuation Correction





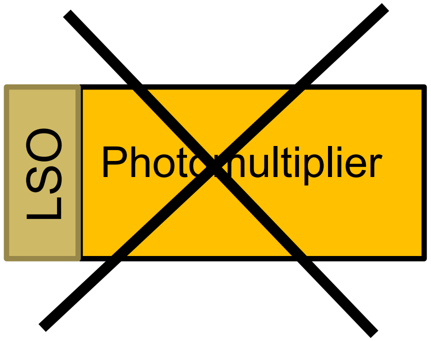
SAC

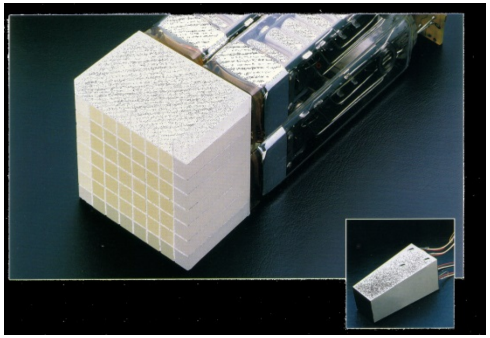
$CTAC_{nb}$

- An improvement of >20% in image contrast

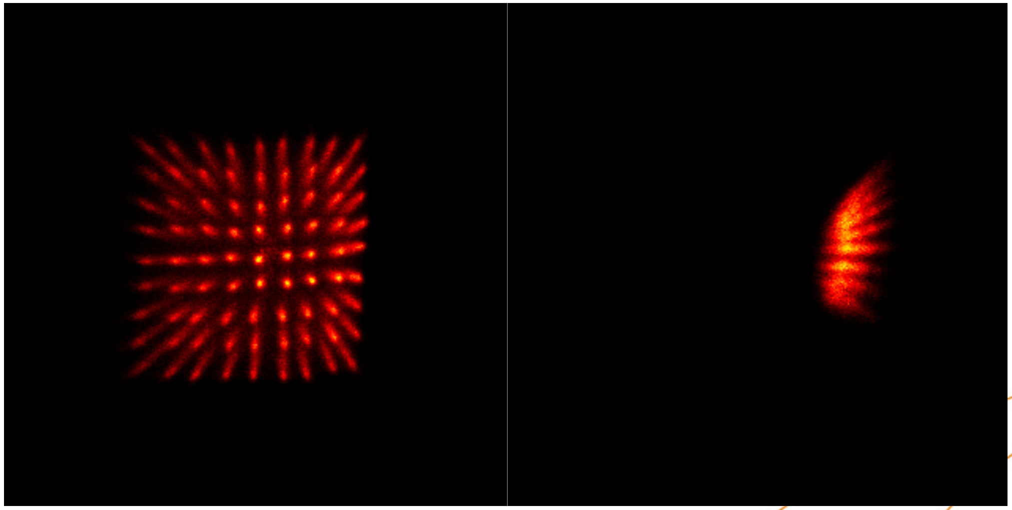
D Visvikis, DC Costa, I Croasdale, et al; *"CT based attenuation correction in the calculation of semi-quantitative indices of 18FDG uptake in PET"* Eur J Nucl Med Mol Imag 2003, 30(3), 344-353, Nuclear Medicine Book of the Year 2003, ed. I Zubal, Elsevier

PET Detector technology



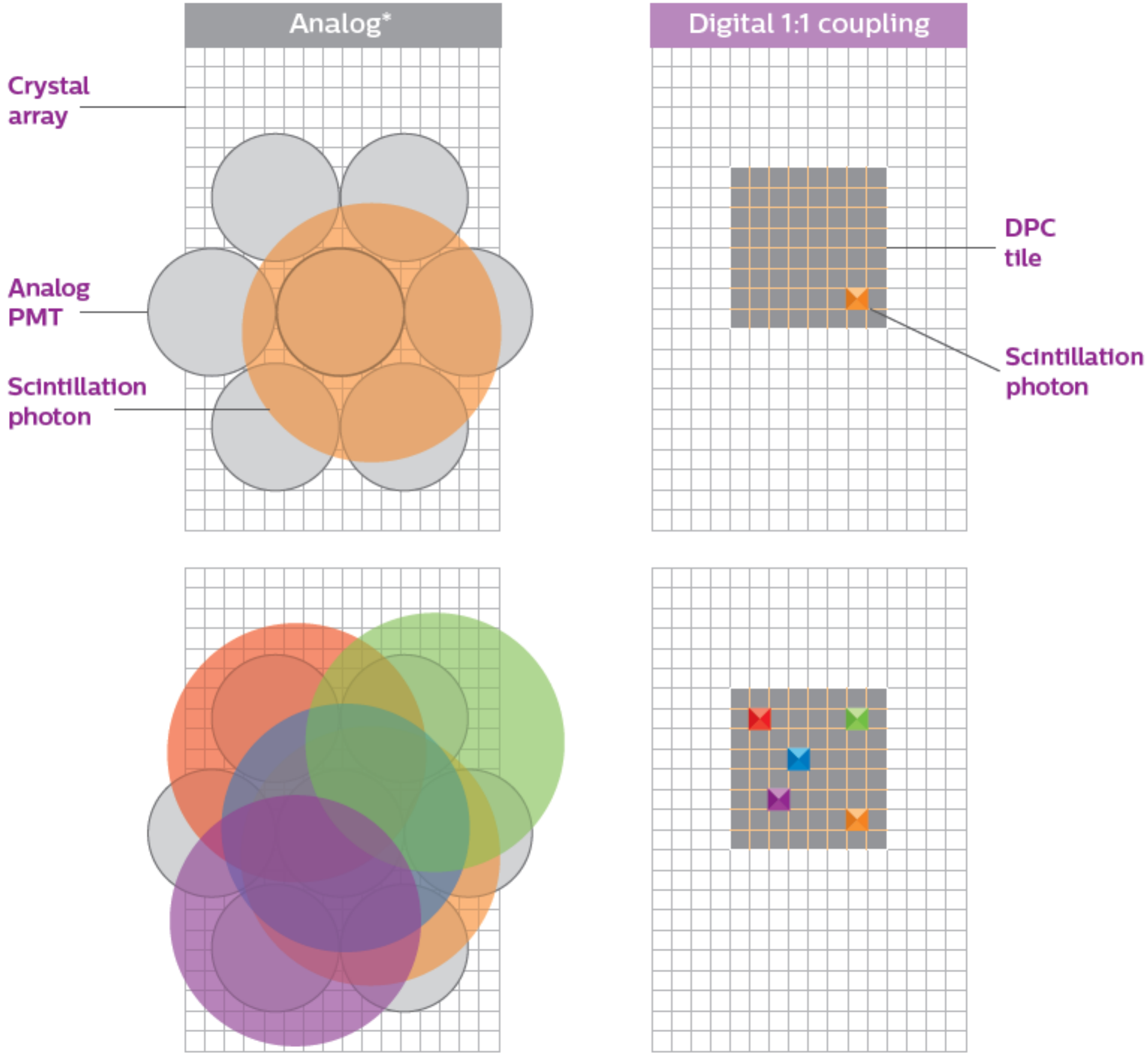


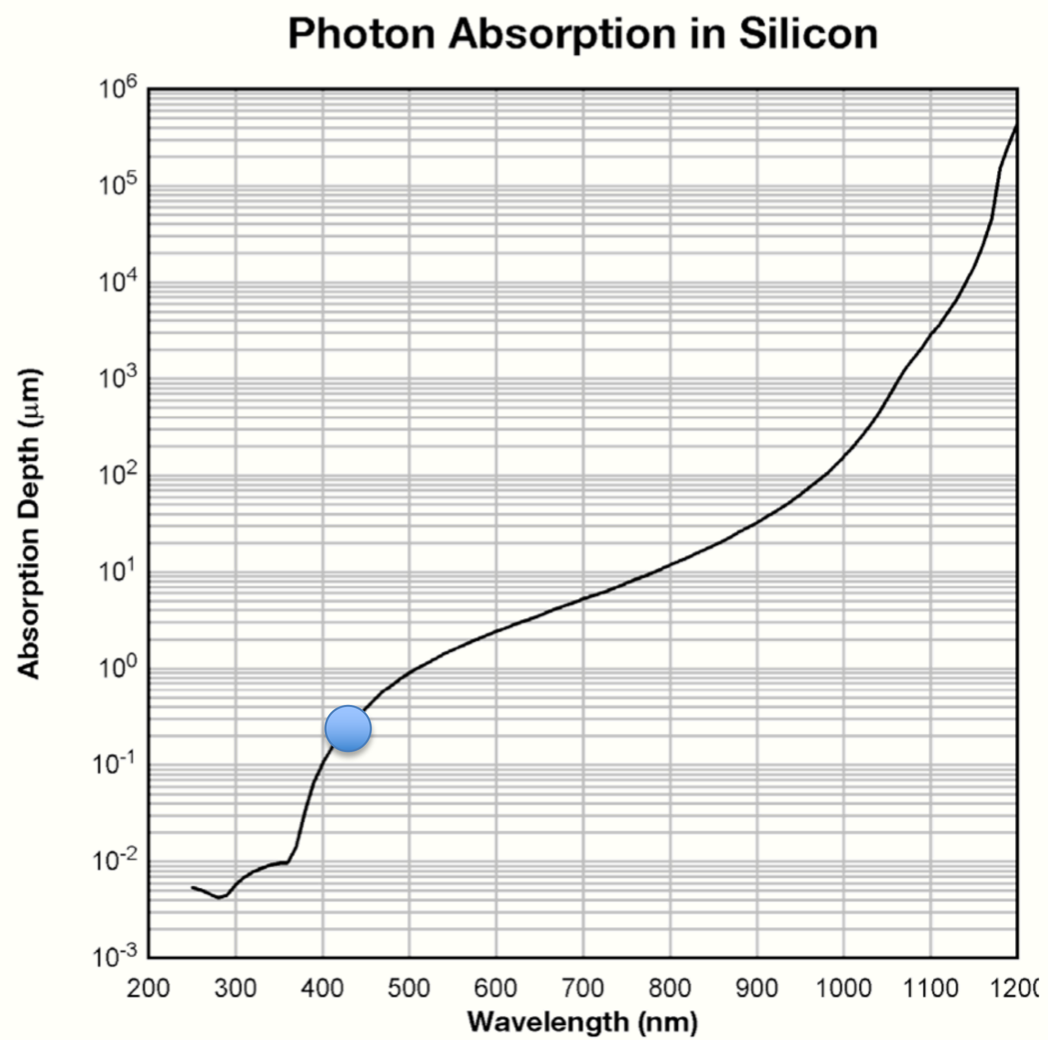
PMT:
Size:10-50 mm
Gain: up to 10^6
Rise time: 1 ns
QE: 20 %



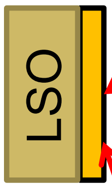
No magnetic field In magnetic field

Shared PMTs versus 1 to 1 coupling




Photon Absorption in Silicon
Absorption Depth (μm)
10^6
10^5
10^4
10^3
10^2
10^1
10^0
10^-1
10^-2
10^-3
200
300
400
500
600
700
800
900
1000
1100
Wavelength (nm)

PET Detector technology



APD: (Avalanche Photo Diode)

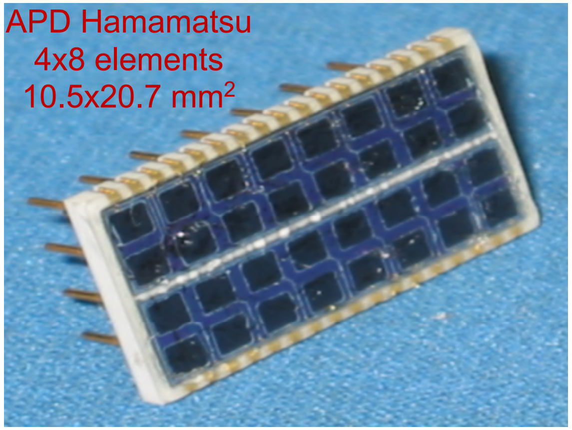
Compact, no impact of magnetic fields

Size:5x5 mm^2

Gain: up to 10^3

Rise time: 5 ns

QE: 60 %



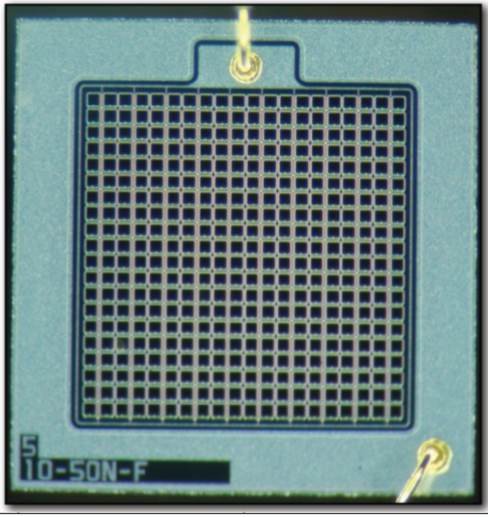
SiPM: (Silicon Photomultiplier)

Size:5x5 mm^2

Gain: 10^5-10^6

Rise time: 1 ns

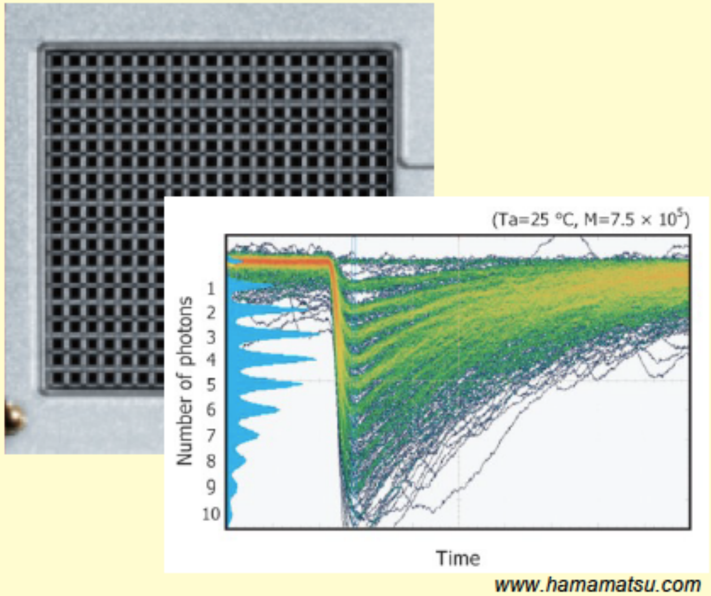
QE: 30%



Matrix of n elements connected in parallel
10.5x20.7 mm^2

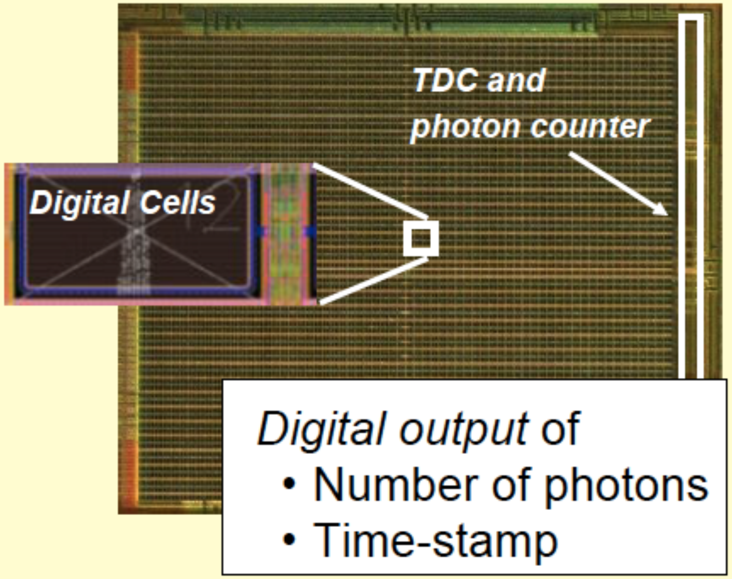
PET Detector technology

Analog SiPM



- Cells connected to common readout
- Analog sum of charge pulses
- Analog output signal

Digital SiPM

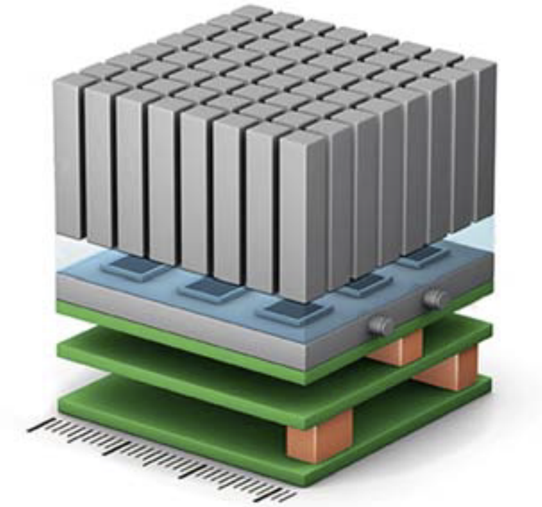


- Each diode is a digital switch
- Digital sum of detected photons
- Digital data output

PET Detector technology

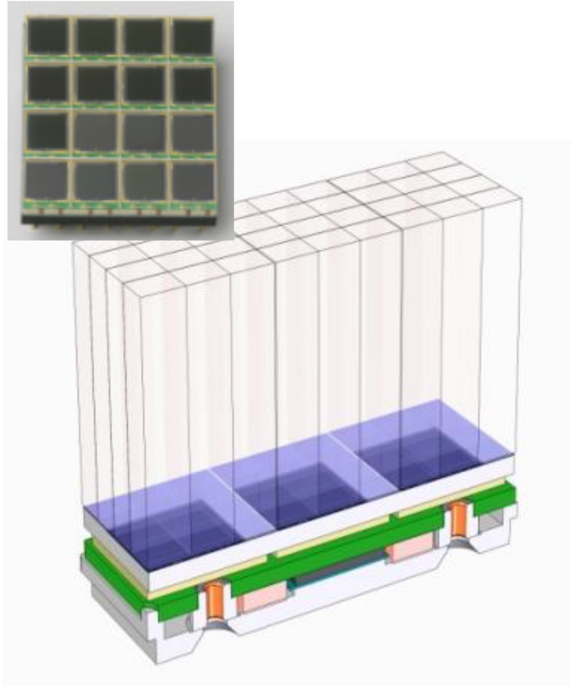
	Photomultiplier-tubes (PMT)	Avalanche-photodiodes (APD)	Silicon-photomultiplier (SiPM)
Sensitive to magnetic fields	y	n	n
Quantum efficiency	20%	70%	70% (PDE 25% - 65%)
Signal rise time	~1 ns	~5 ns	<1 ns
Gain	up to10^6	up to10^3	up to10^6
Bias voltage	>1000 V	300-1000V	30-80V
Temperature dependence	<<1% per K	~ 3% per K	~ 3% per K
Size	Ø10 - 52 mm	5x5 mm^2	1x1mm^2

PET detector technology



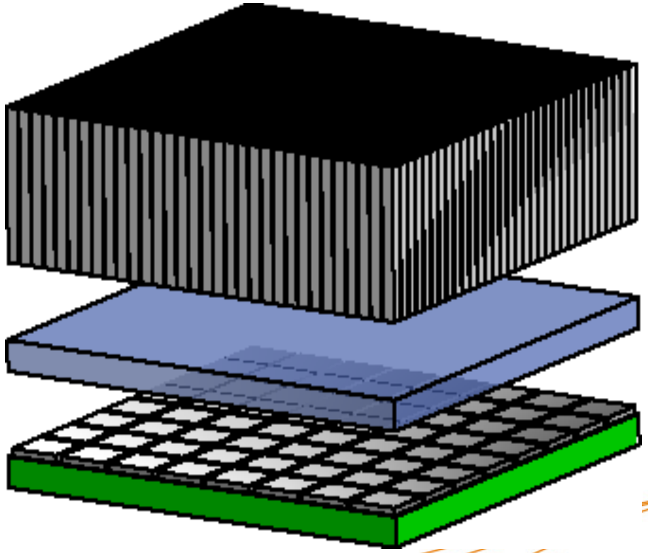
3x3 Hamamatsu-APD based detector for mMR (Siemens)

no Time of Flight (TOF)



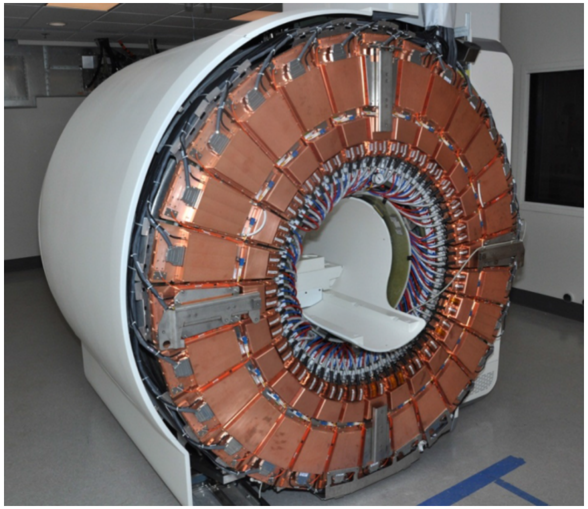
Hamamatsu SiPM based detector (GE)

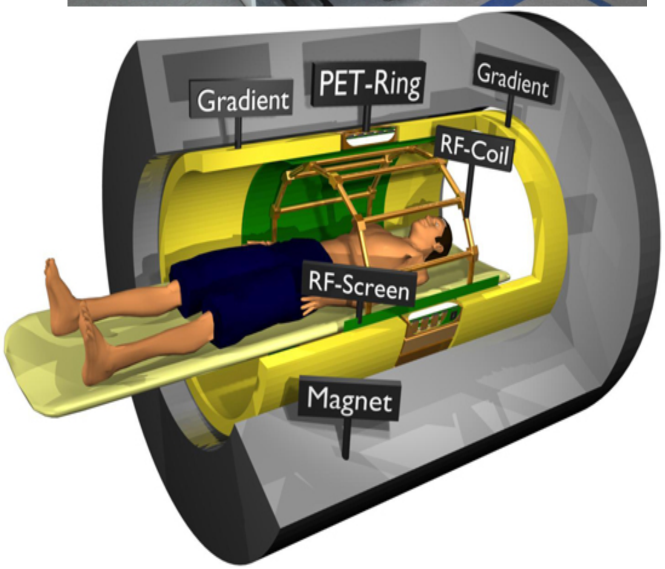
TOF
Higher Sensitivity
Comparable spatial resolution

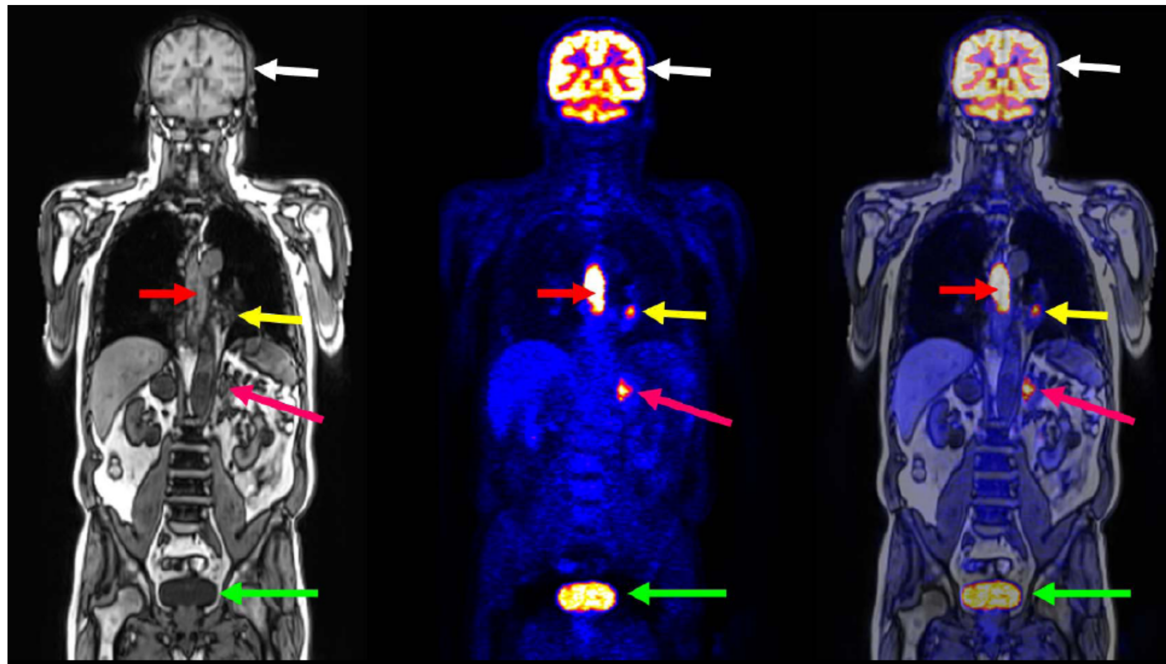


Digital SiPM based detector (Philips)

TOF
Even higher sensitivity
Superior spatial resolution




Gradient
PET-Ring
Gradient
RF-Coil
RF-Screen
Magnet




time for questions

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