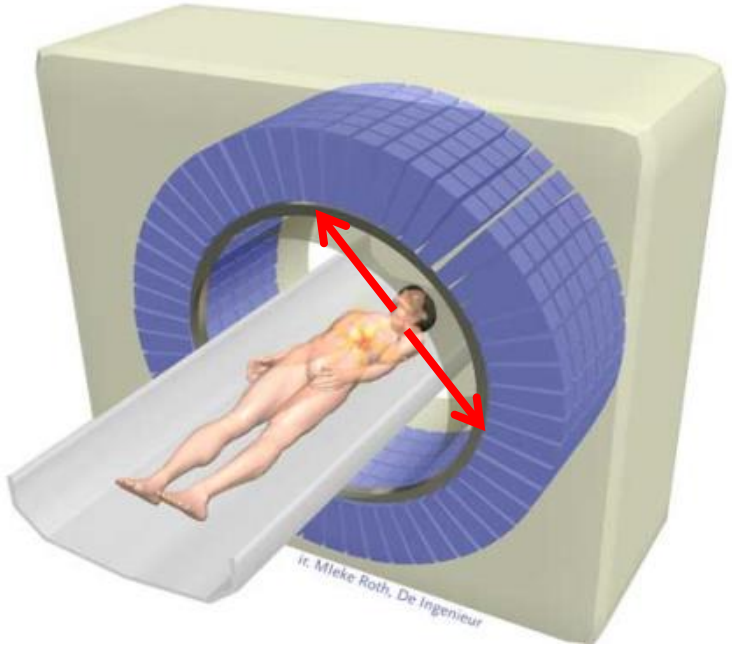
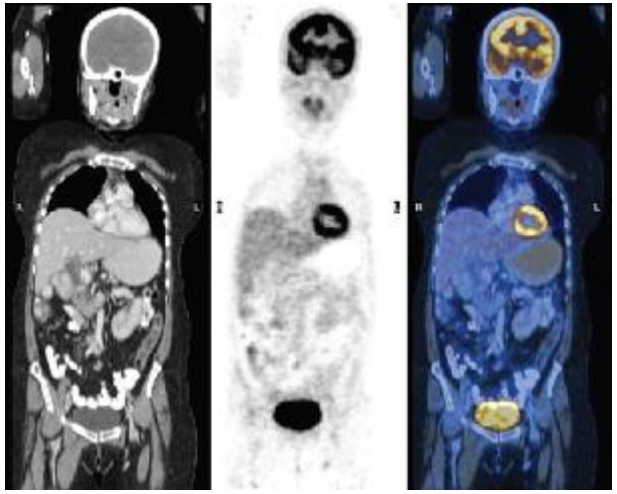




Siria Medici, PhD
Silvano Gnesin, PhD
Institute of Radiation physics (IRA)
UNIL - CHUV

Physics of Positron Emission Tomography (PET)

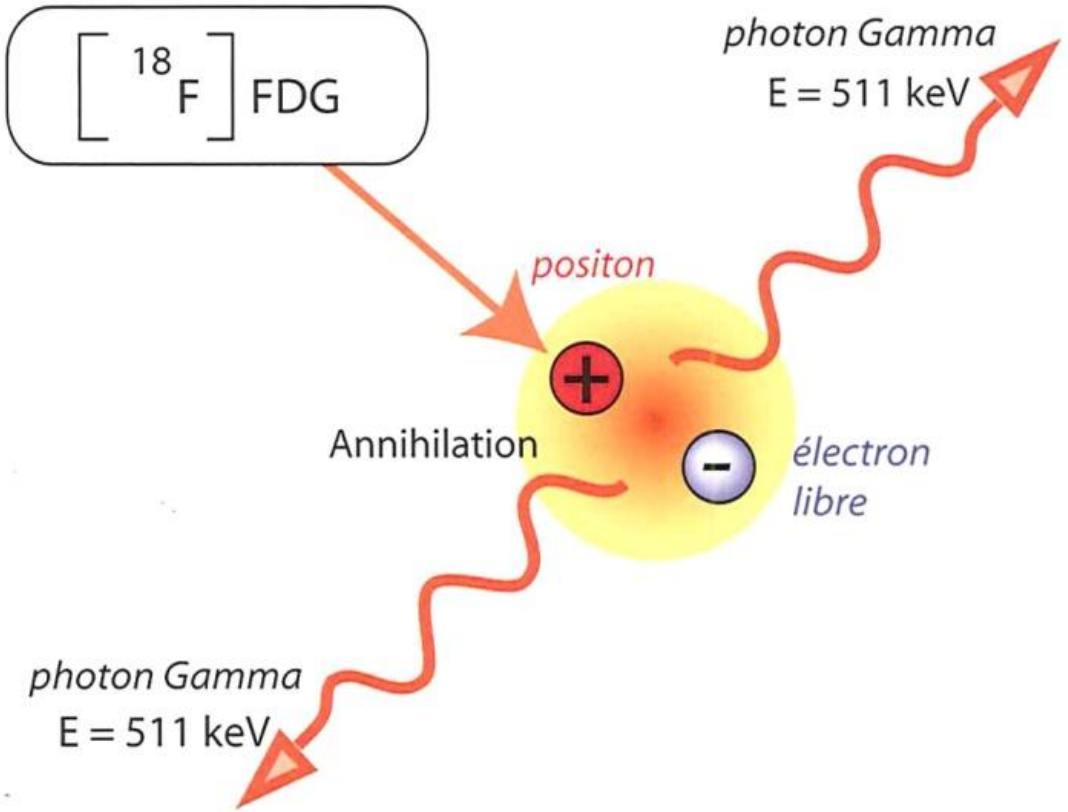
Master of Science EPF-ETH
Degree in Nuclear Engineering and Medical Radiation Physics

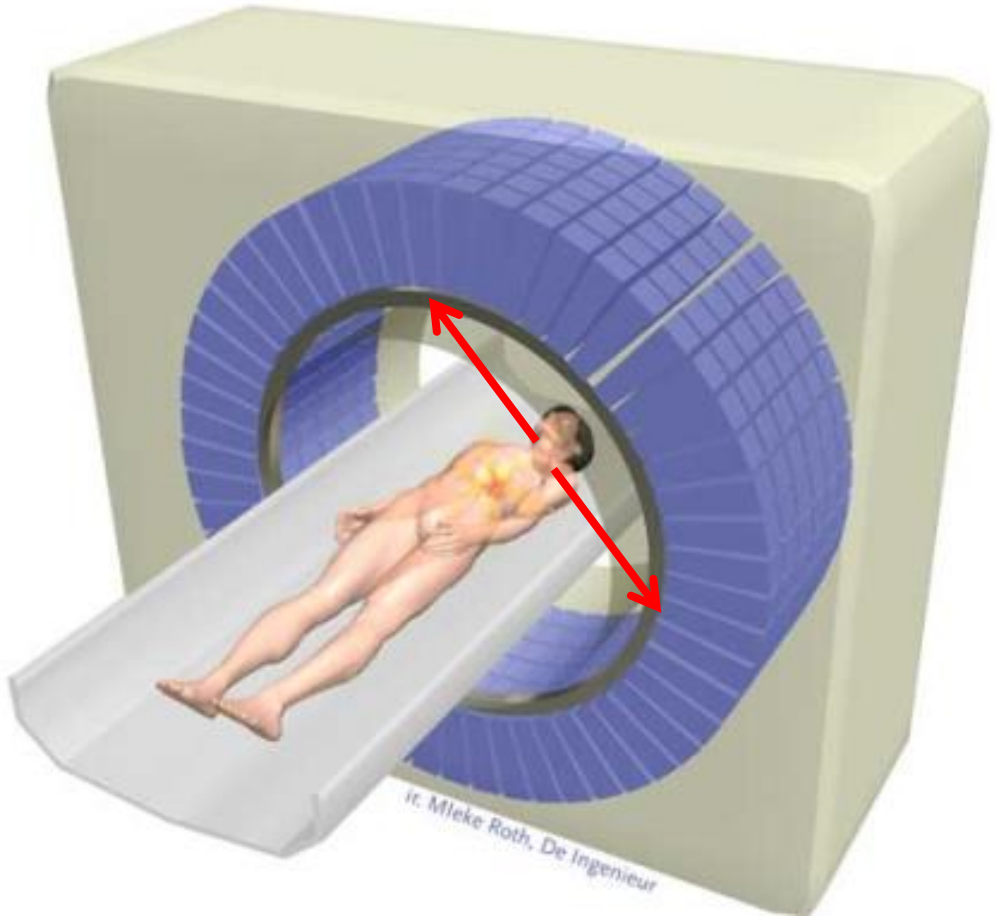
EPFL 20.12.2023

Goals

- Understand and describe **physical principles**, image acquisition modalities and reconstruction processes in **PET**.
- Explain the principles of **annihilation coincidence detection and time of flight**.
- Explain the main **components and design of a PET** scanner.
- Explain the **different types of events** that can be detected through PET and how to **discriminate / correct for the undesired ones** (attenuation, scattering, random coincidence, dead time).
- Introduce **quantification PET** and quantitative/semi quantitative metrics such as RC and SUV.
- Mention the parameters influencing **image quality** (noise, contrast, resolution)

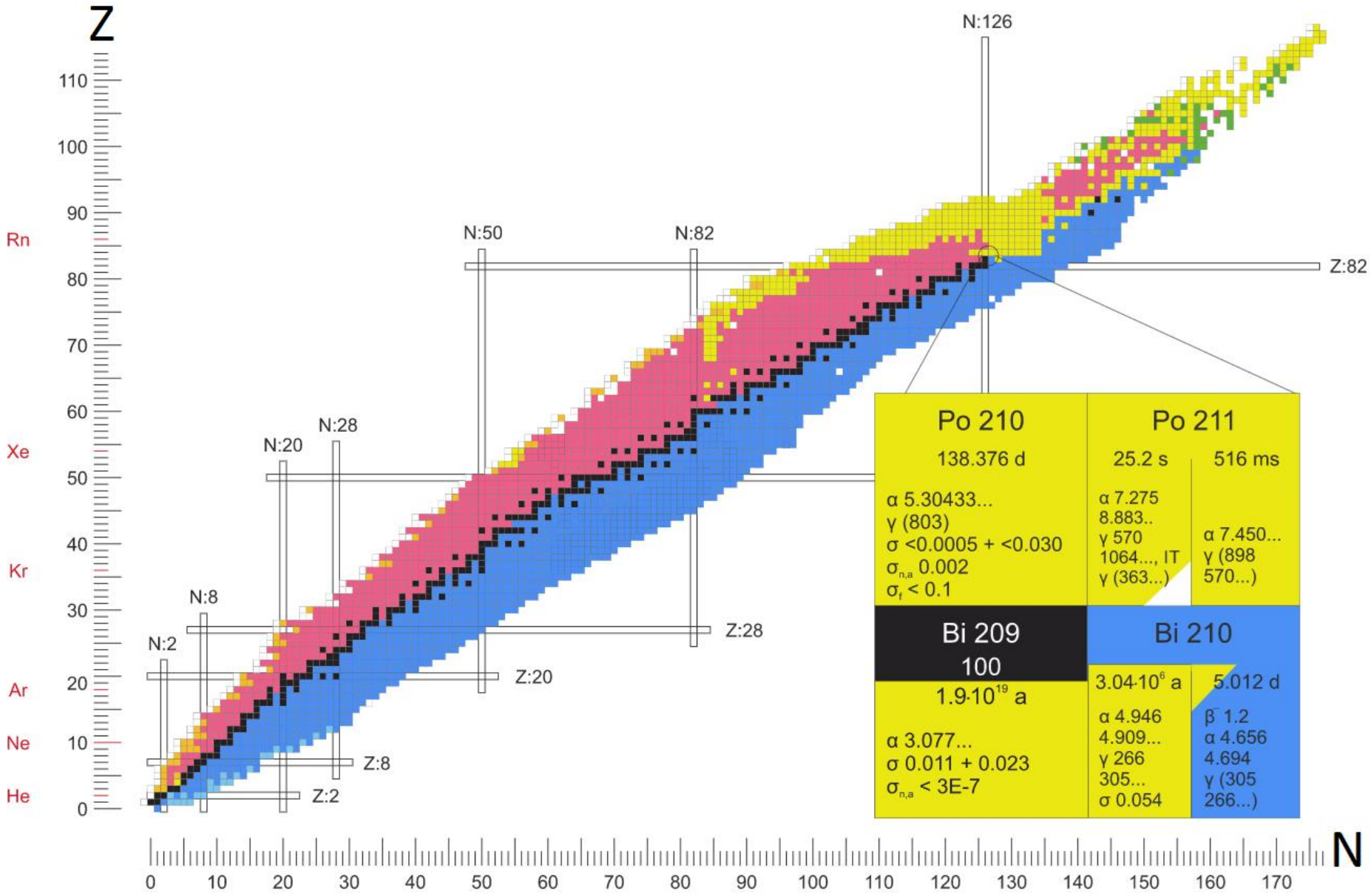
Basic principles of PET imaging : positron emission



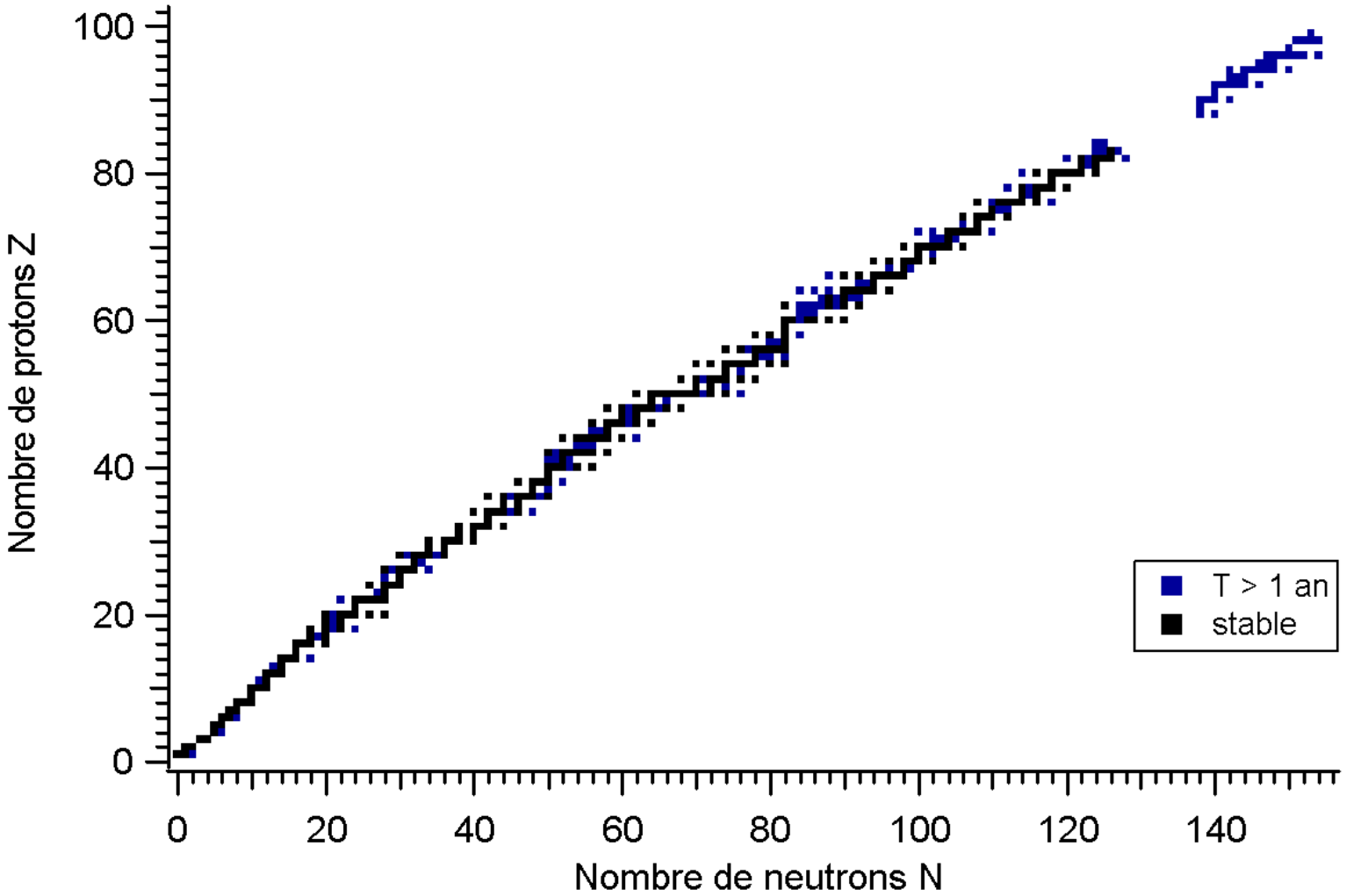


Some radionuclides used in PET : ^{11}C, ^{13}N, ^{15}O, $^{\mathbf{18}}\mathbf{F}$, ^{68}Ga, ^{82}Rb, ^{64}Cu, ^{44}Sc

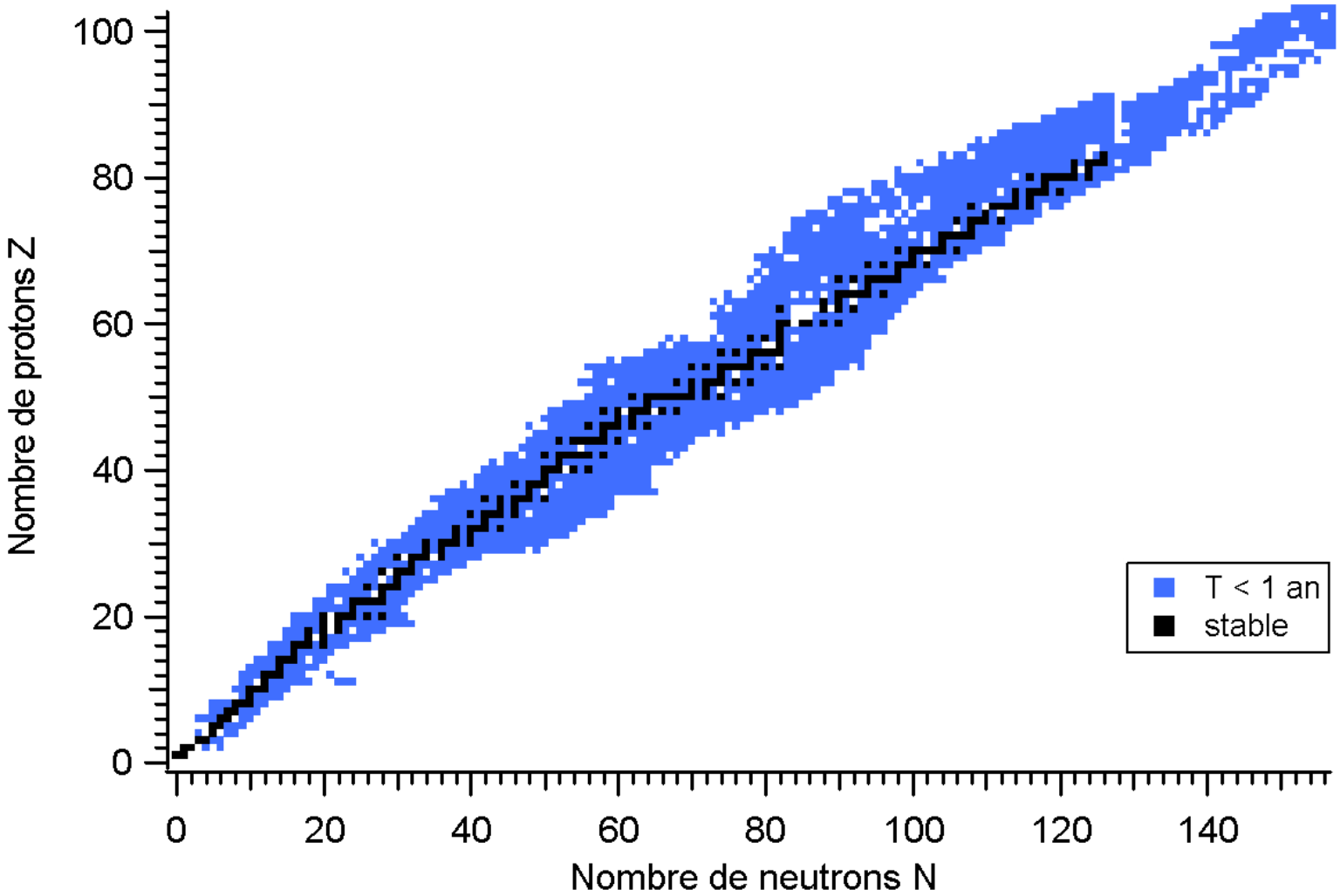
Basic principles of PET imaging : positron emission



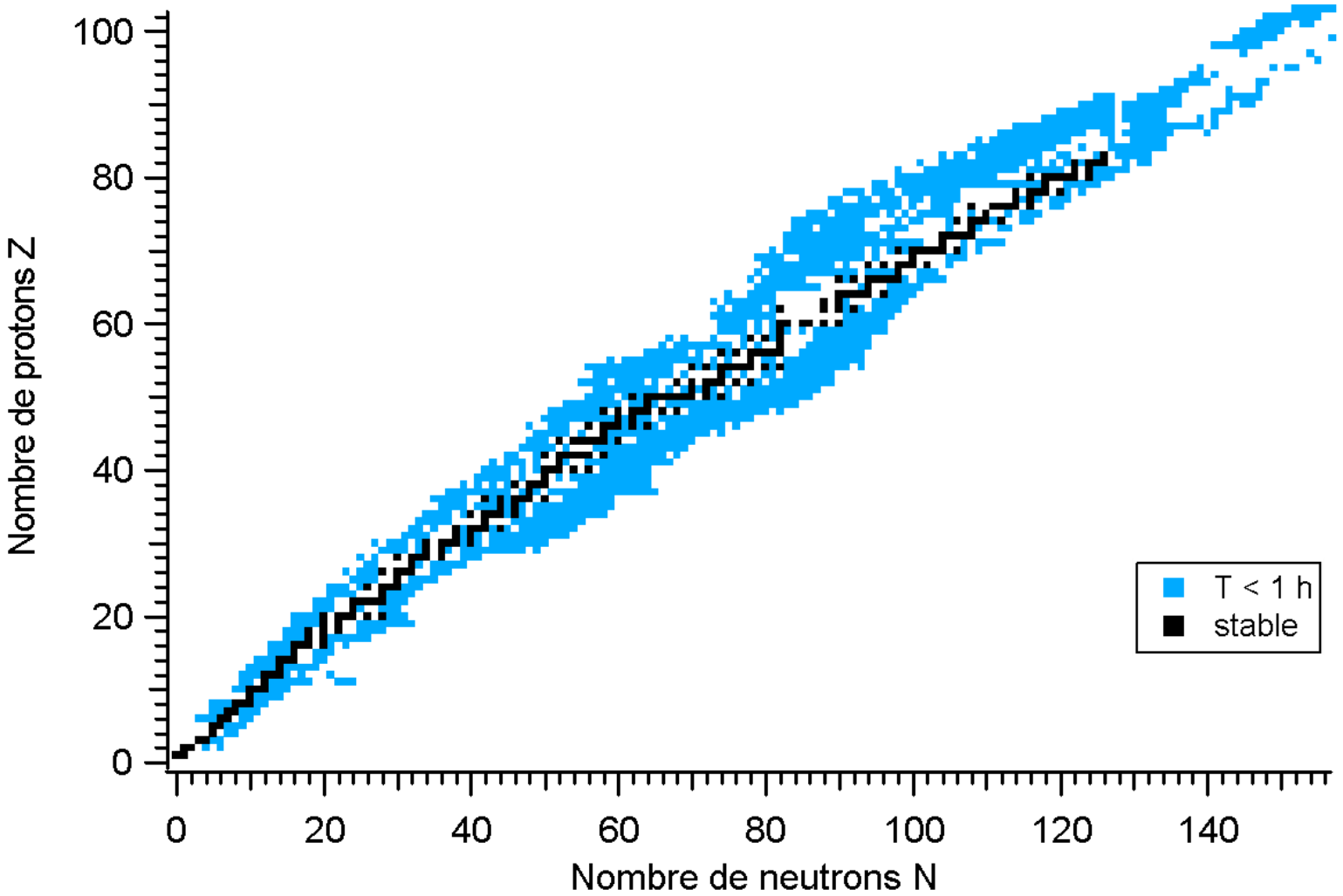
Basic principles of PET imaging : positron emission



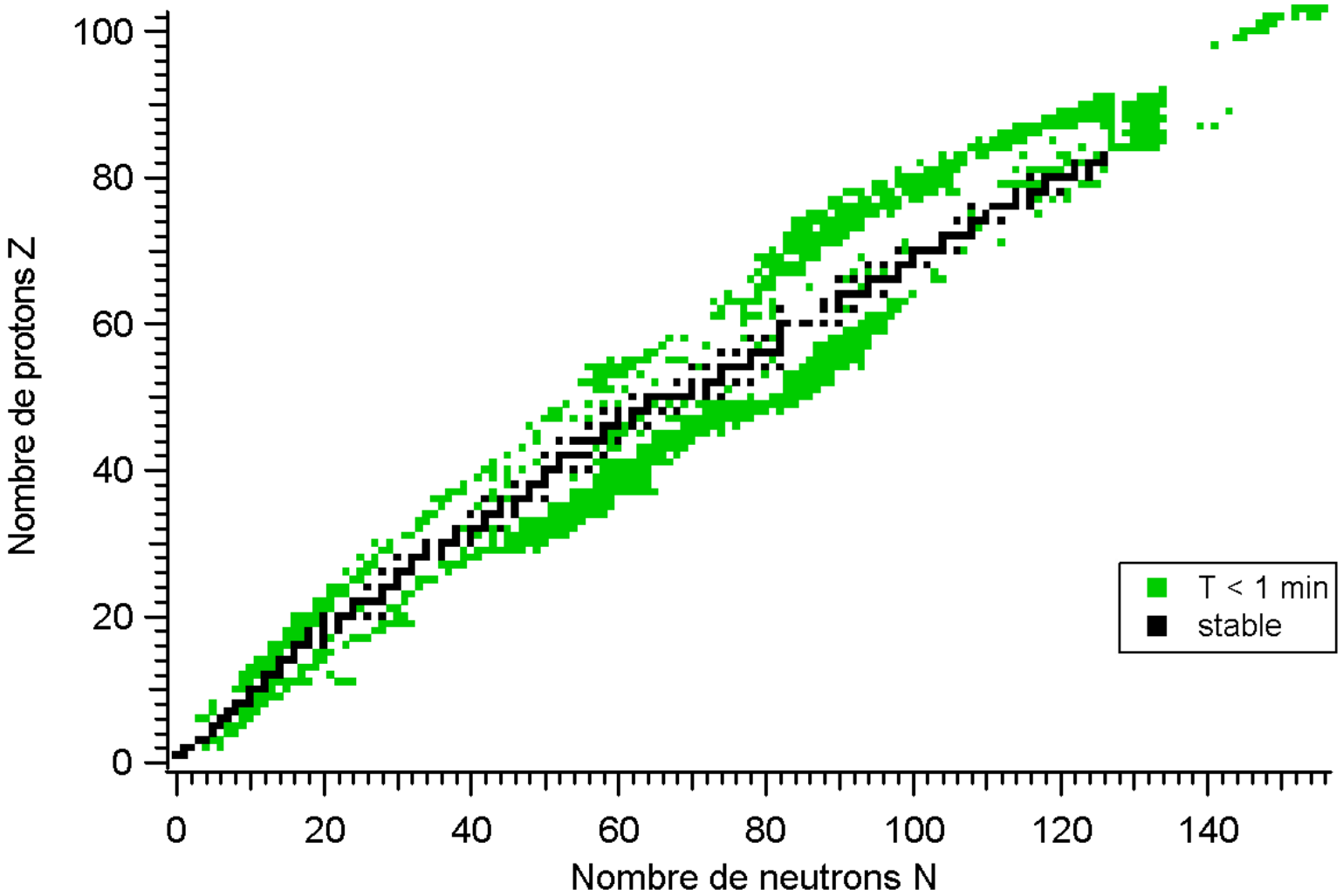
Basic principles of PET imaging : positron emission



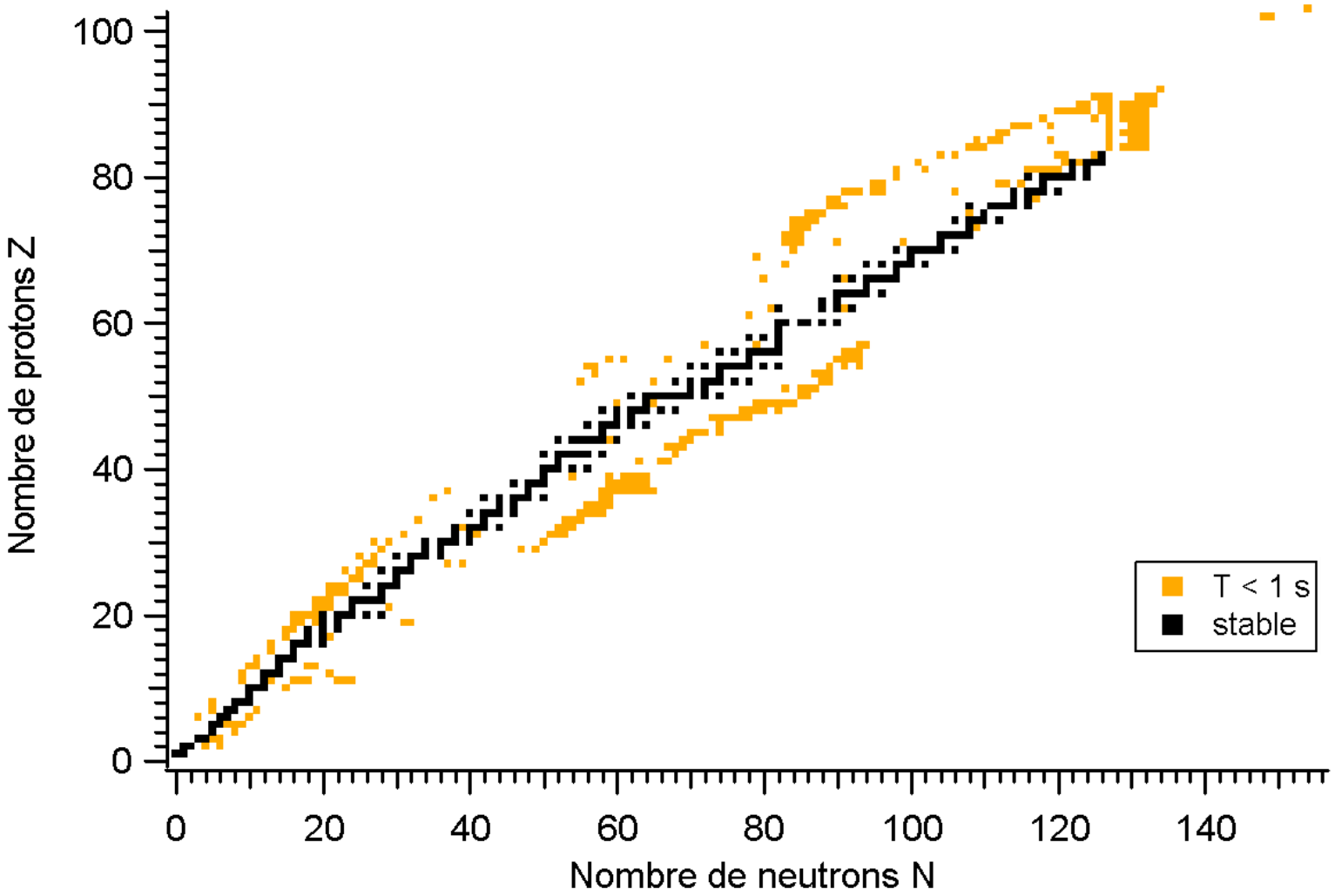
Basic principles of PET imaging : positron emission



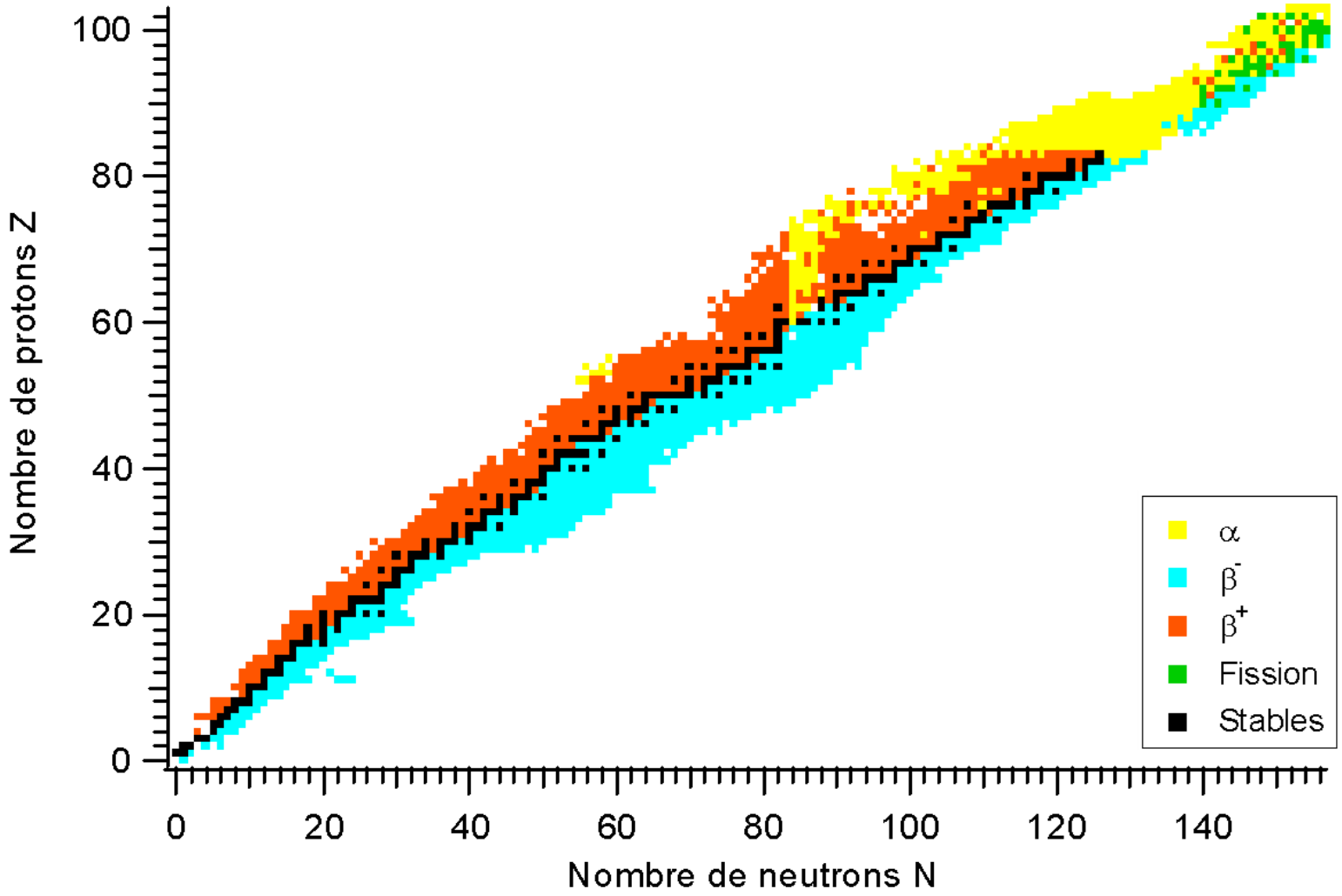
Basic principles of PET imaging : positron emission

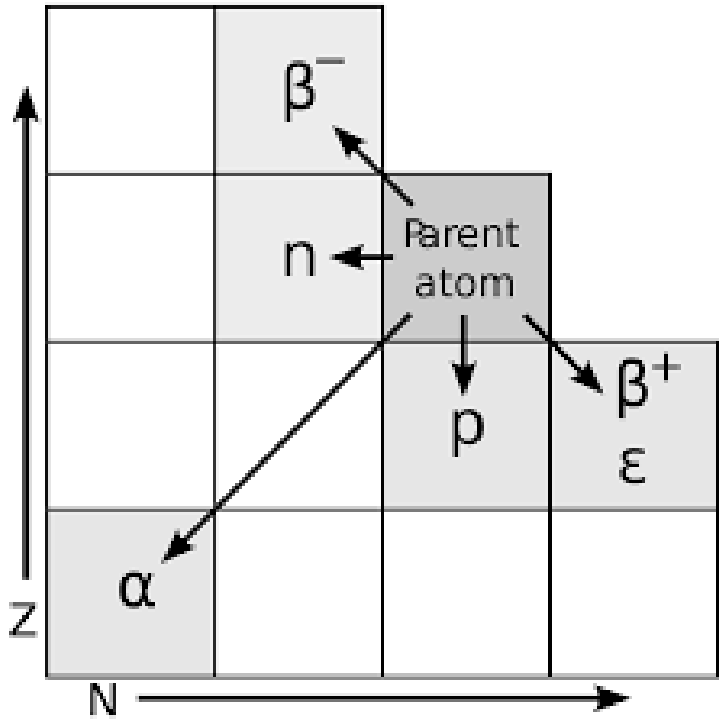


Basic principles of PET imaging : positron emission

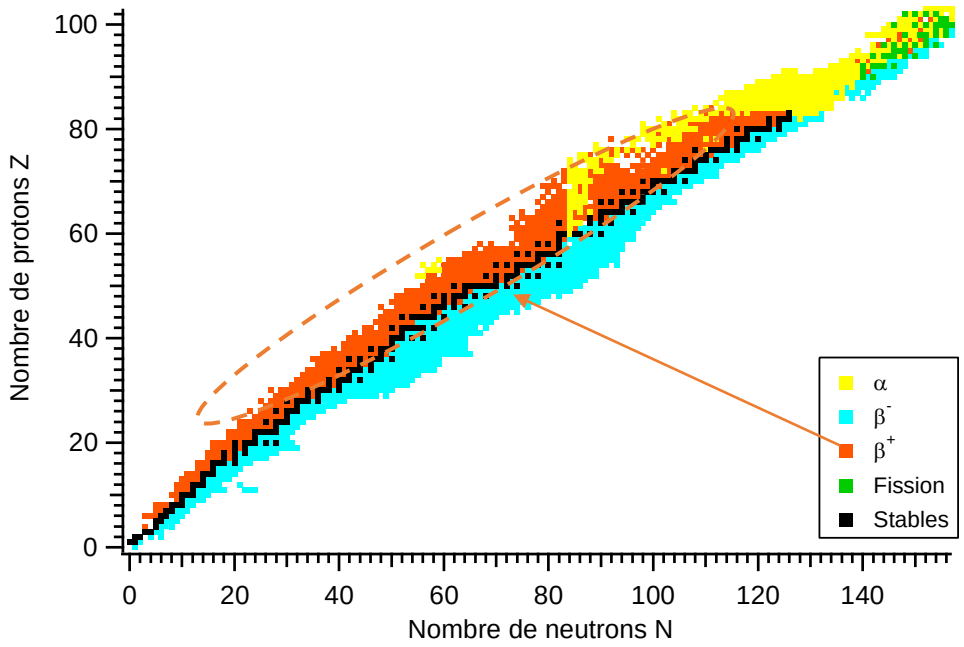


Basic principles of PET imaging : positron emission



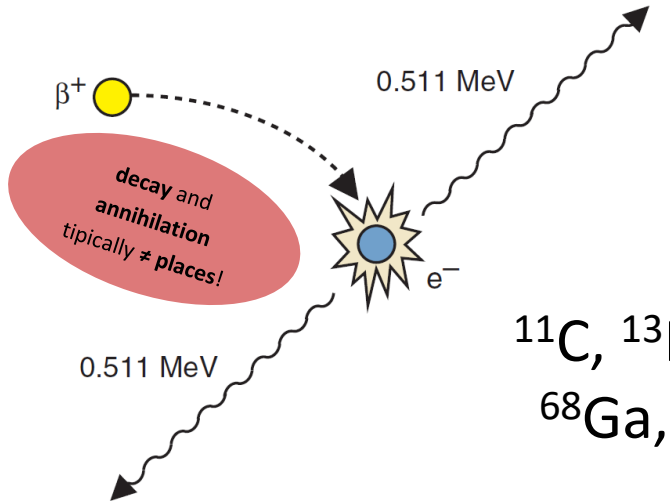


Basic principles of PET imaging : positron emission

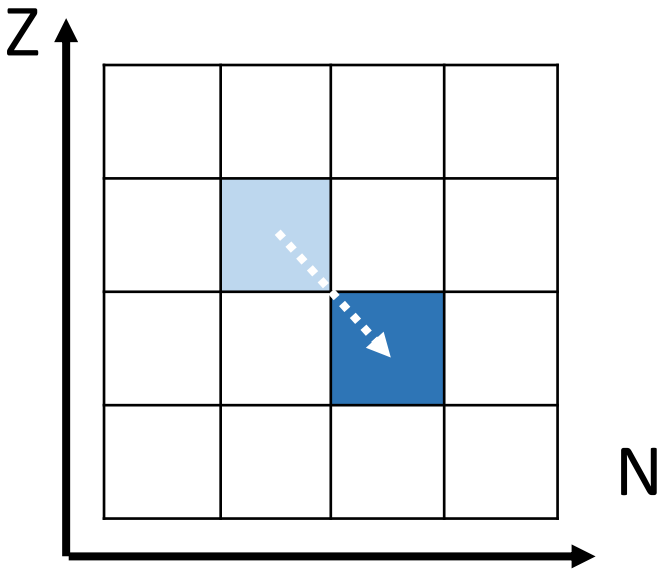


$$ {}^{A}_{Z}X_N \rightarrow {}^{A}_{Z-1}Y_{N+1} + \underbrace{\beta^+}_{\text{positron}} + \underbrace{\nu}_{\text{neutrino}} $$

Isobaric generation (A)



^{11}C, ^{13}N, ^{15}O, ^{18}F, ^{68}Ga, ^{82}Rb, ^{124}I



Two competitive processes: **beta plus decay vs electron capture**

$$ {}^{A}_{Z}X \rightarrow {}^{A}_{Z-1}Y + \beta^+ + \nu + energy $$

positron decay (transition energy ≥ 1.022 MeV), more frequent among lighter elements

$$ {}^{A}_{Z}X + e^- \rightarrow {}^{A}_{Z-1}Y + \nu + energy $$

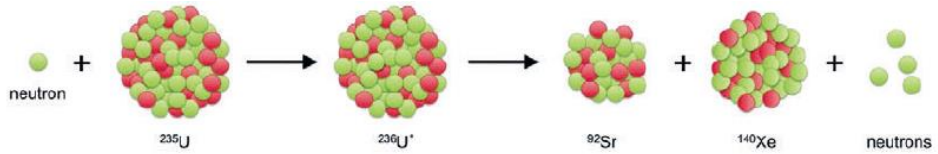
EC (+ characteristic X rays and Auger e-), more frequent among heavier elements

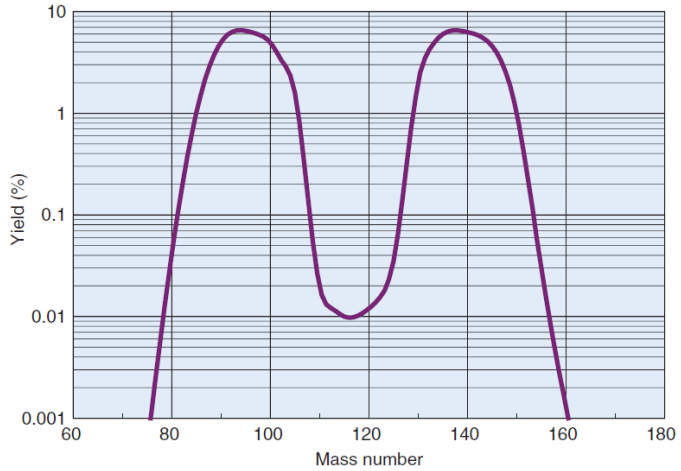
Both decay modes can coexist: F-18 (3% EC, 97% positron emission)

Basic principles of PET imaging : Radionuclide Production

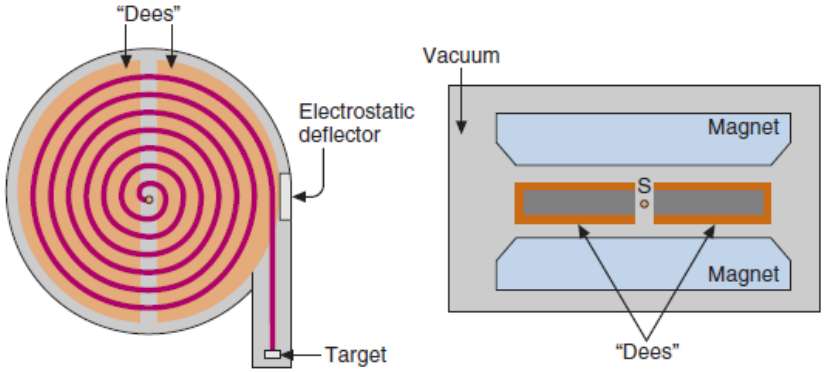
- Three main routes of production:

1. **Reactor**-produced (fission fragments / neutron activation)

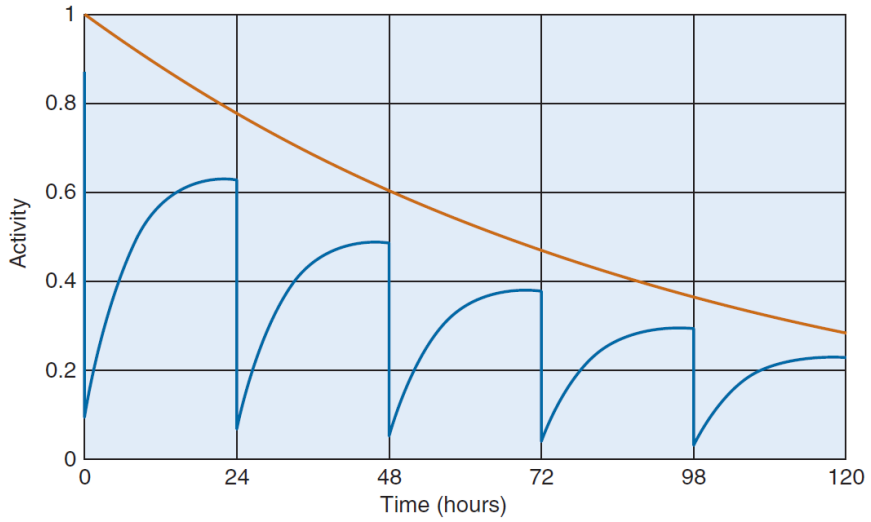




2. **Accelerator**-produced (F-18)



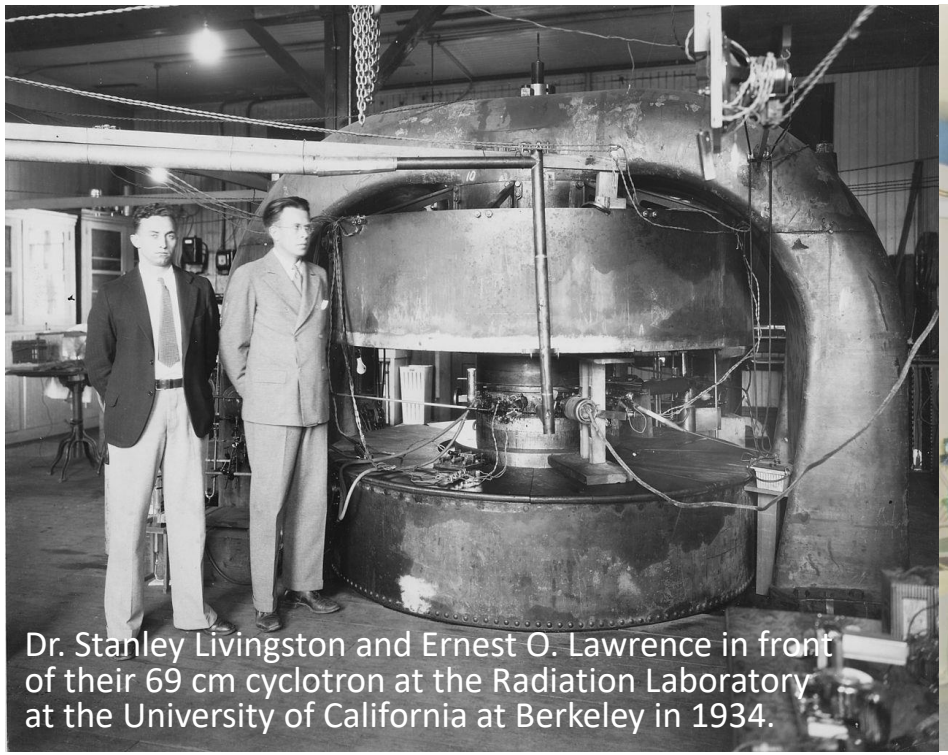
3. Radionuclide **generators** (Ga-68)



Basic principles of PET imaging : Radionuclide Production

Charged particle accelerators:

- Charged particles (such as *p*, *d*, *α*) accelerated by the electric field.
- 3 main types of accelerators: cyclotrons, synchrotrons, and linear accelerators (LINAC).
- Main difference with *n* activation: higher energies required (~10-20 MeV) → Coulomb forces!
- Cyclotrons are the most widely used for radionuclide production for medical applications.



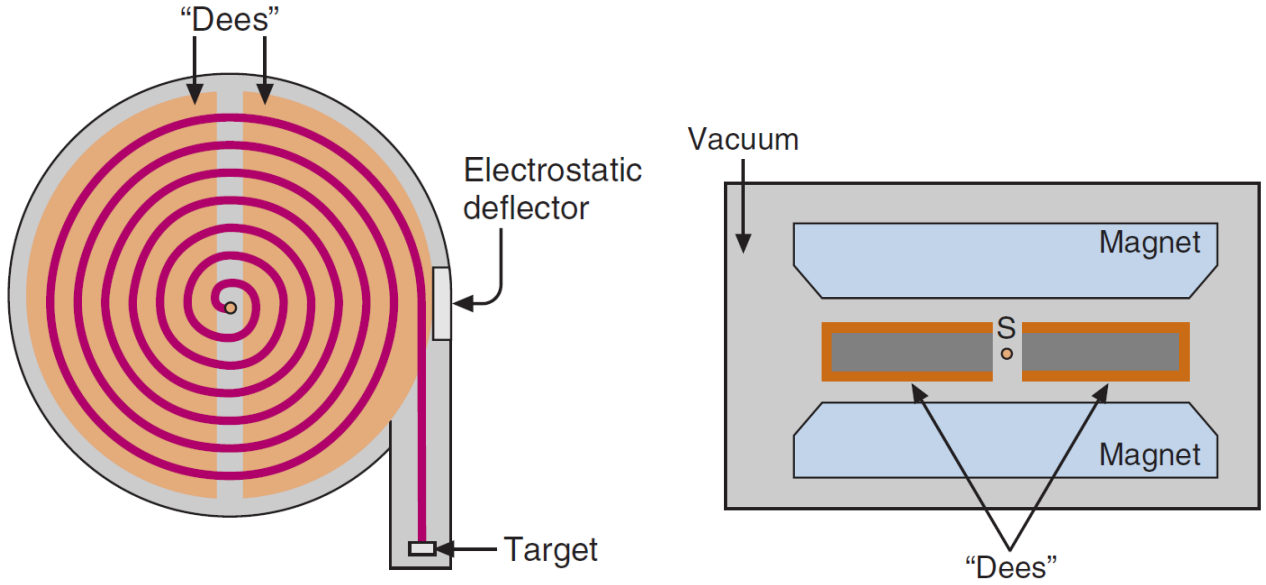
Dr. Stanley Livingston and Ernest O. Lawrence in front of their 69 cm cyclotron at the Radiation Laboratory at the University of California at Berkeley in 1934.

according to IAEA (in 2021):
1'500 cyclotron facilities worldwide

Cyclotron isotope production

Cyclotron:

- Pair of semicircular (D-Shaped) electrodes placed between poles of an electromagnet (vacuum).
- An ion source is placed at the centre of the electrodes.



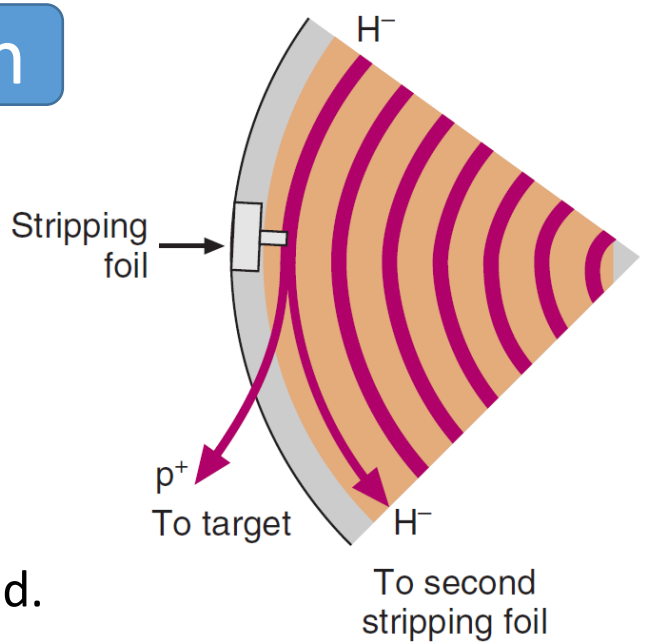
- High frequency oscillators generates alternate electric field applied across the D-shaped electrodes.
- Charged particles follow a circular path due to the B field (magnetic bending).
- Particles reach the gap between the electrodes when the voltage across them reaches its max value.
- Particles are accelerated across the gap and gain energy in the process (outward spiral path).
- Increasing speed compensates for increasing travel distance.
- Energy achievable: limited by B strength and electrodes size.
- Typical values: for B = 1.5 T, electrode diameter of 76 cm, *p* can be accelerated to ~15 MeV

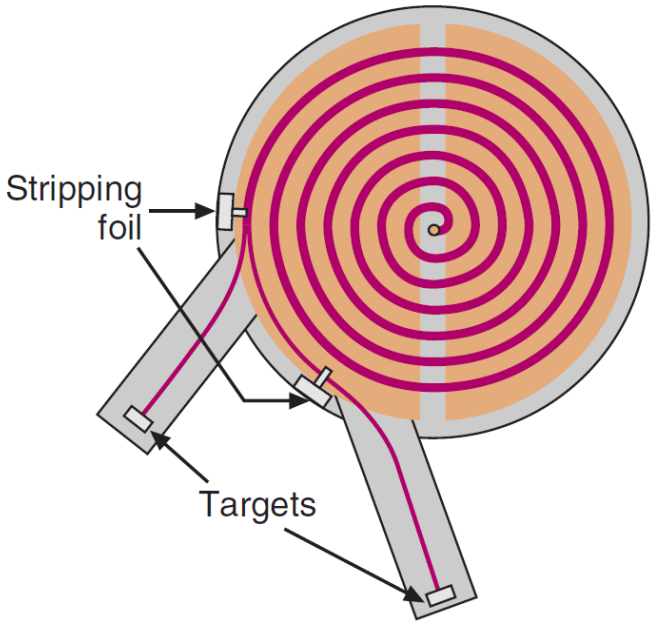
Cyclotron isotope production

Cyclotron:

- When max radius reached: beam is directed towards a target.

- For positive ion cyclotrons, the beam is deflected by a plate that is negatively-charged.





- But as much as 30% of the beam can be lost during extraction (inefficient electrostatic deflectors) → **activation!** RP is fundamental part of cyclotron operation and future disposal!

- For negative ion cyclotrons (H^-), the exiting beam is passed through a thin foil (carbon) → strips e- → beam becomes positively charged and is deflected → $\sim 100\%$ efficiency
  (low maintenance from RP, BUT higher vacuum requirements: 10^{-5} Pa vs 10^{-3} Pa due to unstable nature of H^-).

- Partial stripping is also possible (multiple targets).

Basic principles of PET imaging : Radionuclide Production

Accelerator-produced radionuclides

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

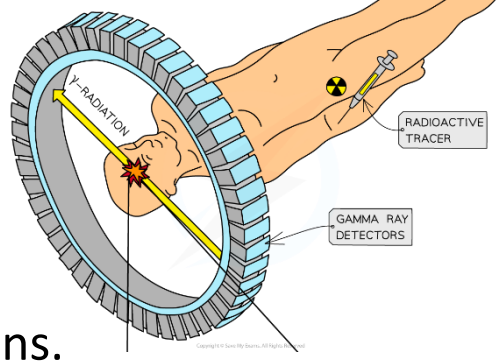
$$ {}^{18}O(p,n)^{18}F \qquad {}^{109}Ag(\alpha,2n)^{111}In \qquad {}^{122}Te(d,n)^{123}I $$

- In most activation processes, positive charge is added to the nucleus
  → β+ / EC decay
- Addition of positive charge changes to atomic number Z → generally different element, carrier-free.
- Smaller quantities of radioactivity when compared to reactor-produced radionuclides (due to generally higher activation cross-section for neutrons than for charged particles + lower beam intensities).

SOME CYCLOTRON-PRODUCED RADIONUCLIDES USED IN NUCLEAR MEDICINE

Product	Decay Mode	Common Production Reaction
^{11}C	β^+, EC	$^{14}N(p,\alpha)^{11}C$
		$^{10}B(d,n)^{11}C$
^{13}N	β^+	$^{16}O(p,\alpha)^{13}N$
		$^{12}C(d,n)^{13}N$
^{15}O	β^+	$^{14}N(d,n)^{15}O$
		$^{15}N(p,n)^{15}O$
^{18}F	β^+, EC	$^{18}O(p,n)^{18}F$
		$^{20}Ne(d,\alpha)^{18}F$
^{67}Ga	(EC,γ)	$^{68}Zn(p,2n)^{67}Ga$
^{111}In	(EC,γ)	$^{109}Ag(\alpha,2n)^{111}In$
		$^{111}Cd(p,n)^{111}In$
^{123}I	(EC,γ)	$^{122}Te(d,n)^{123}I$
		$^{124}Te(p,3n)^{123}I$
^{201}Tl	(EC,γ)	$^{201}Hg(d,2n)^{201}Tl$

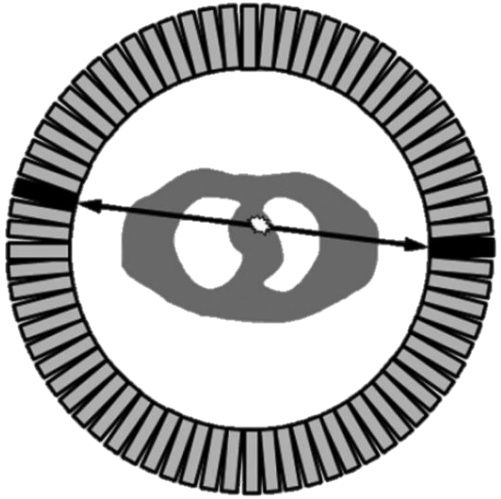
Basic principles of PET imaging : ACD

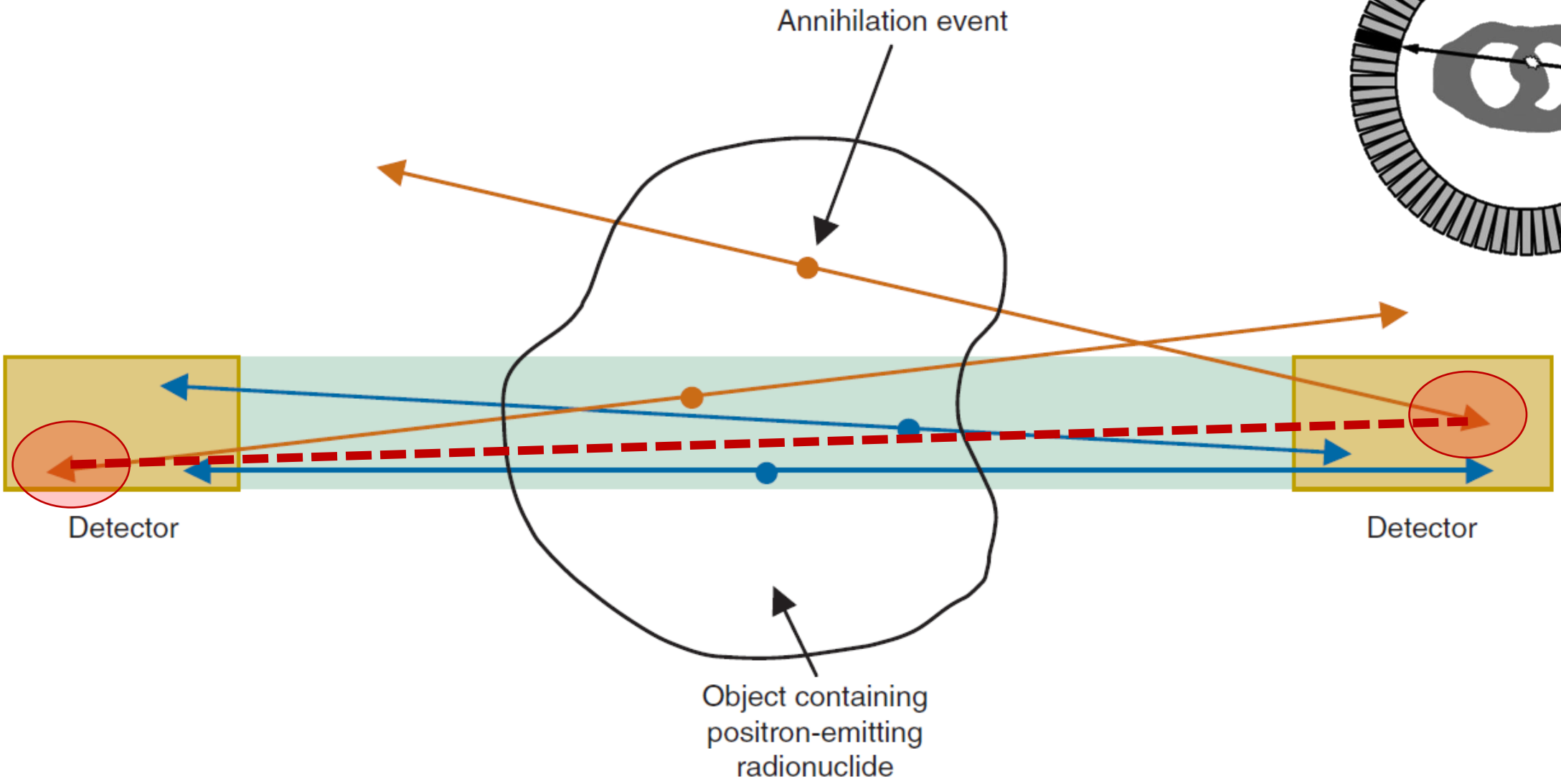


- Annihilation coincidence detection (ACD):
  - Positron and electron annihilation → rest masses converted into annihilation photons.
  - Annihilation photons emitted simultaneously, in ~180° degrees opposing direction.
  - Distance between positron emission and annihilation: few tens of mm – few mm.
  - ACD helps in localisation in PET, without the use of absorptive collimation → electronic collimation.
    - Collimator for spatial localisation not needed → sensitivity (efficiency) is much higher in PET than in SPECT !
    - Placing detector rings all around the patient → multiple projection angles acquired simultaneously

      → further increase in sensitivity → faster studies → less artifacts due to patient motion (or less injected activity).
  - Coincidence timing window: 5-10 ns.
  - Finite timing resolution needed: window should allow for signal transit time through cables/electronics and photon travel distance ≠ between the annihilation site and the detectors.

Basic principles of PET imaging : ACD





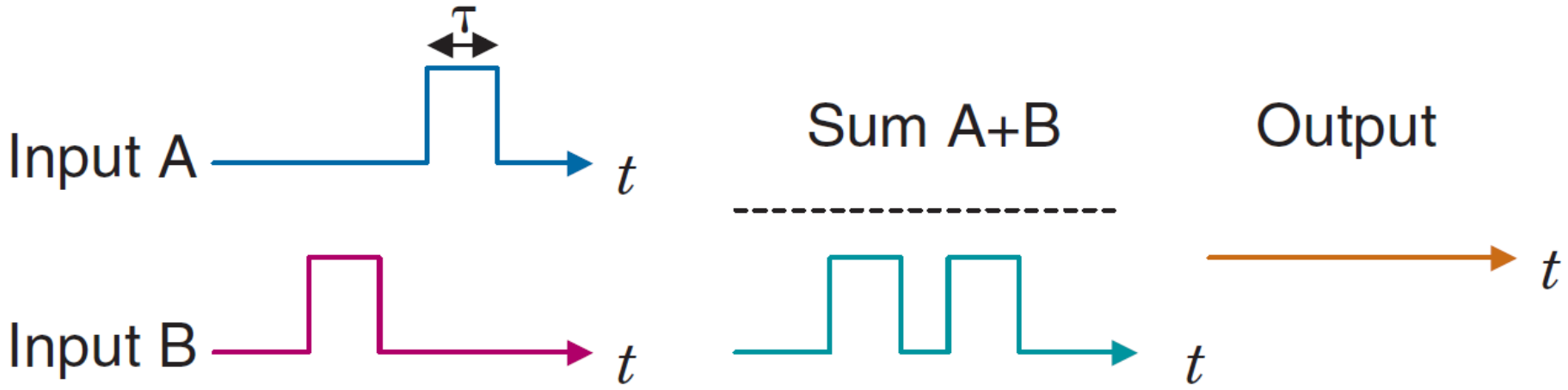
Basic principles of PET imaging : ACD

Based on the use of coincidence units:

- Produce a pulse only if multiple inputs occur in a defined coincidence timing window.
- Coincidence timing windows defines the maximum time interval between the two pulses for them to be counted as coincidence.

How to trigger coincidence?

- Compute the ∑ of two pulses that arrived within the window and feed them to a discriminator.
- Discriminator threshold set just below the amplitude that would be generated by the sum of two signals.



example with time window ~ 2x the input pulse width

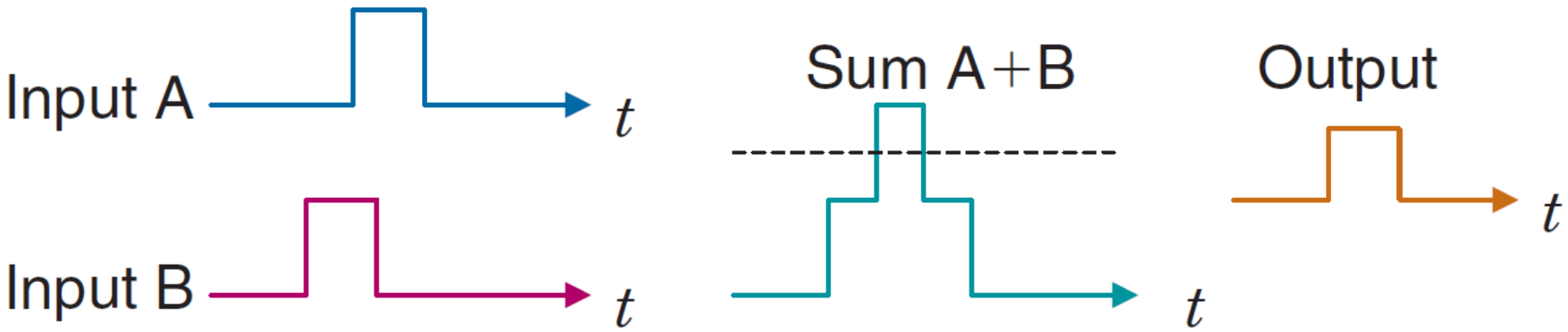
Basic principles of PET imaging : ACD

Based on the use of coincidence units:

- Produce a pulse only if multiple inputs occur in a defined coincidence timing window
- Coincidence timing windows defines the maximum time interval between the two pulses for them to be counted as coincidence.

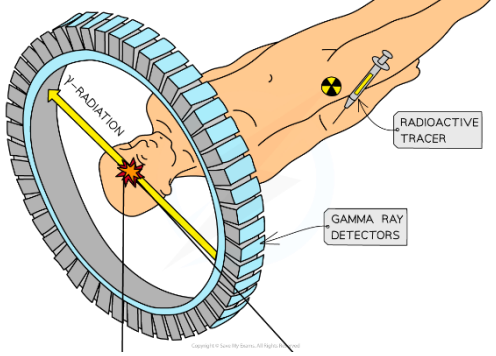
How to trigger coincidence?

- Compute the ∑ of two pulses that arrived within the window and feed them to a discriminator.
- Discriminator threshold set just below the amplitude that would be generated by the sum of two signals.

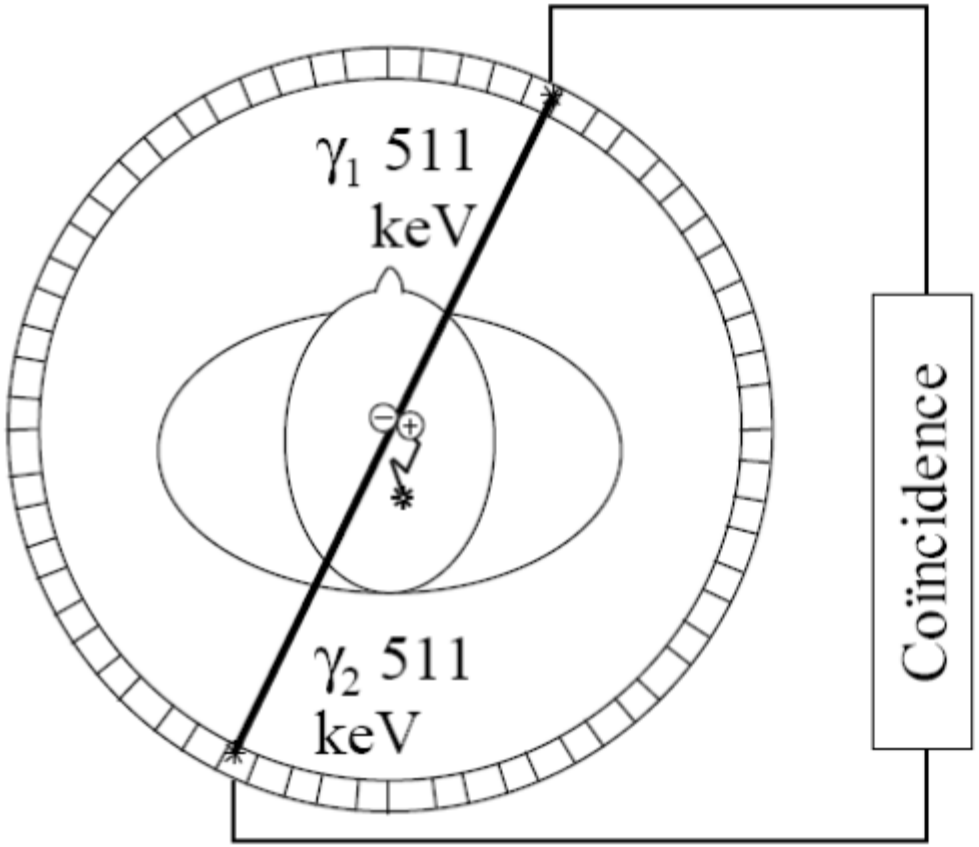


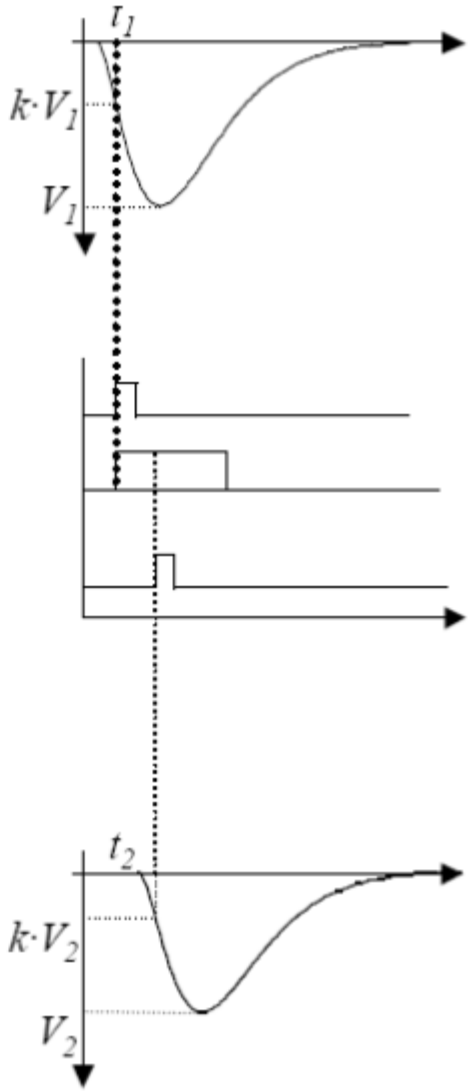
example with time window ~ 2x the input pulse width

Basic principles of PET imaging : ACD



detector ring with detector blocks





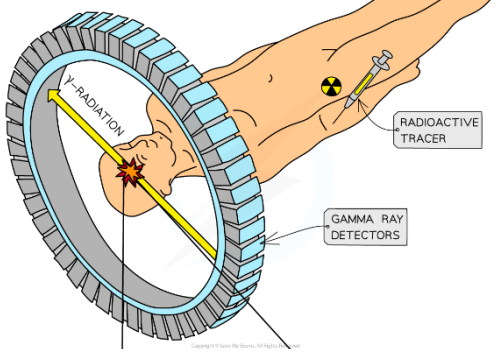
coincidence time window

time width: t ~ 5-10 ns

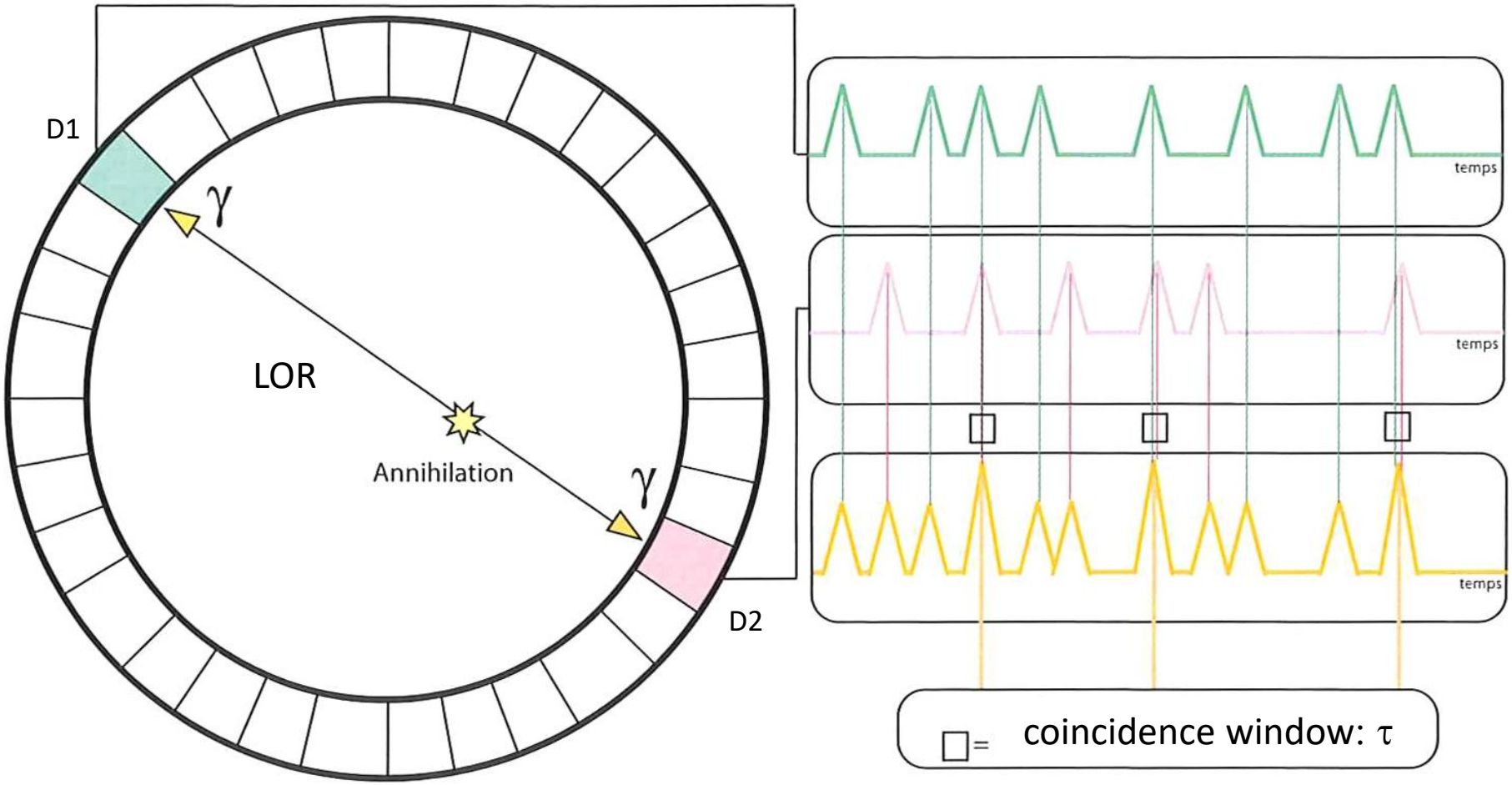
Coïncidence :

$$|t_1 - t_2| < \tau$$

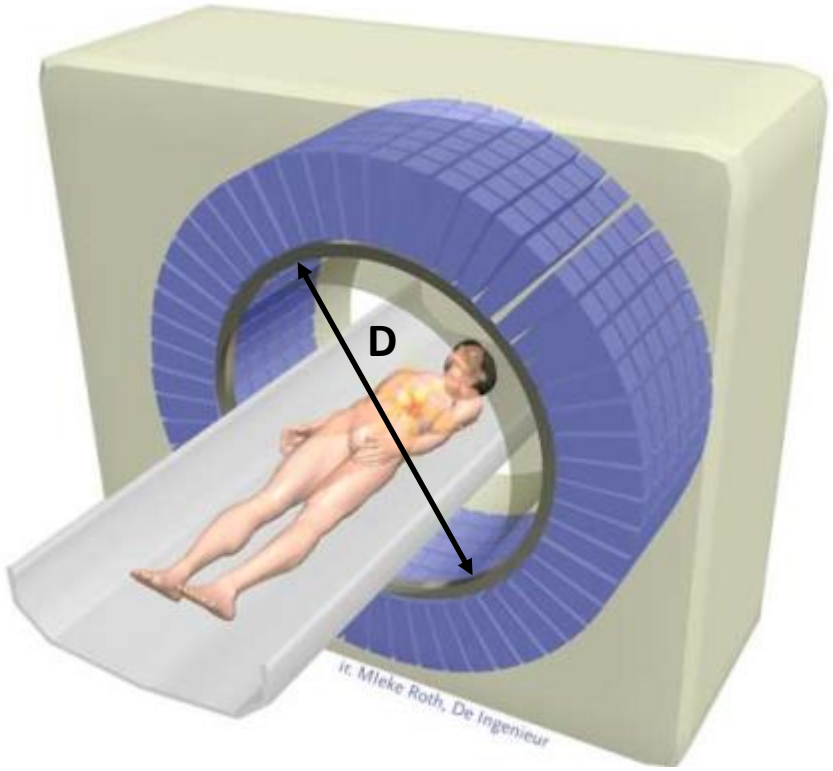
Basic principles of PET imaging : ACD



LOR: line of response



Basic principles of PET imaging : ACD



How to define the time coincidence window?

- Maximum photon path along a line of response: D
- Time needed for a photon to travel a distance D:

$$T = D/c$$

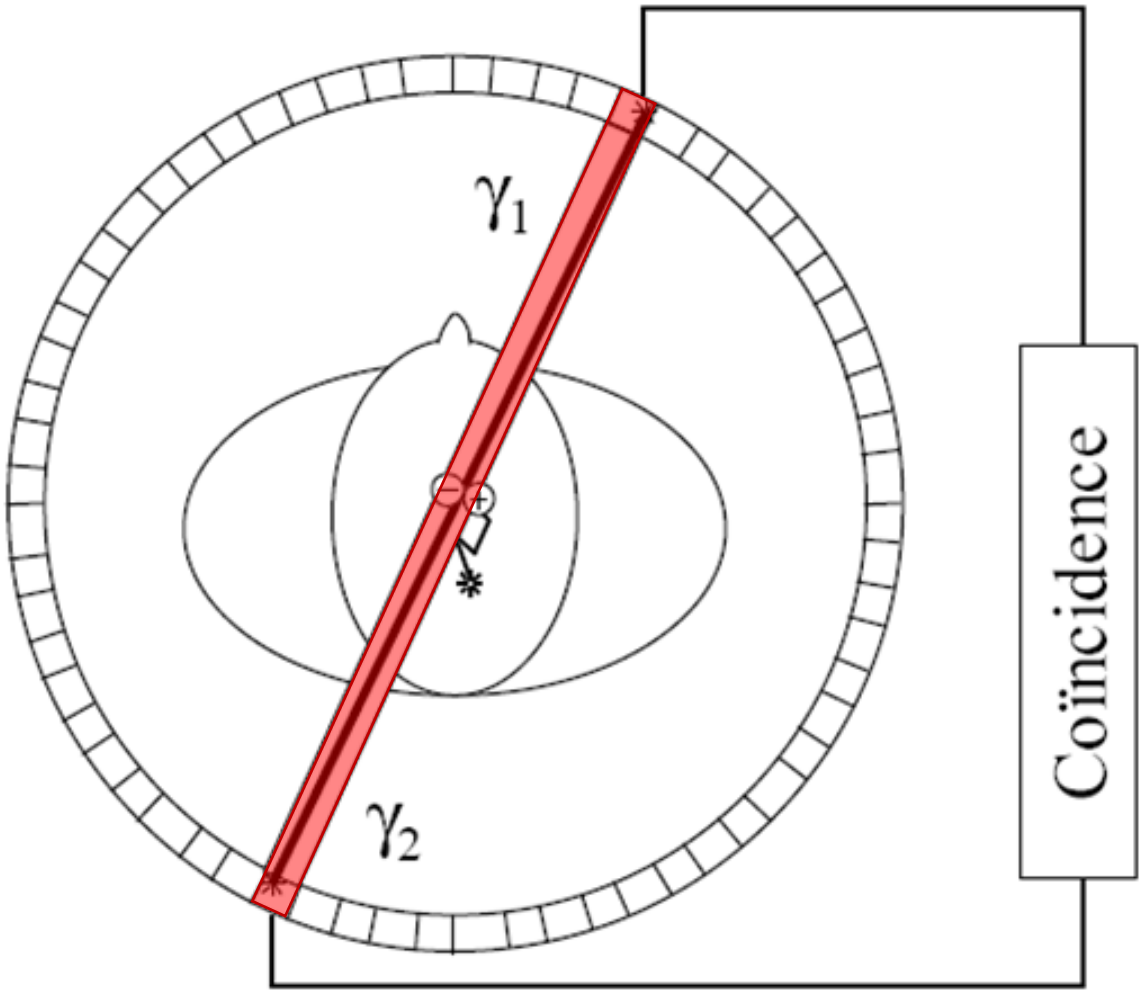
- **Practical example: D = 0.8m**

$$T = \frac{0.8\ m}{3 \cdot 10^8 m/s} = 2.7 \cdot 10^{-9} s \cong 3\ ns$$

- Taking into considerations for scintillation light propagation and electric signal collection :

$$\rightarrow \boldsymbol{T \sim 5\ ns}$$

Basic principles of PET imaging : ACD



Electronic collimation

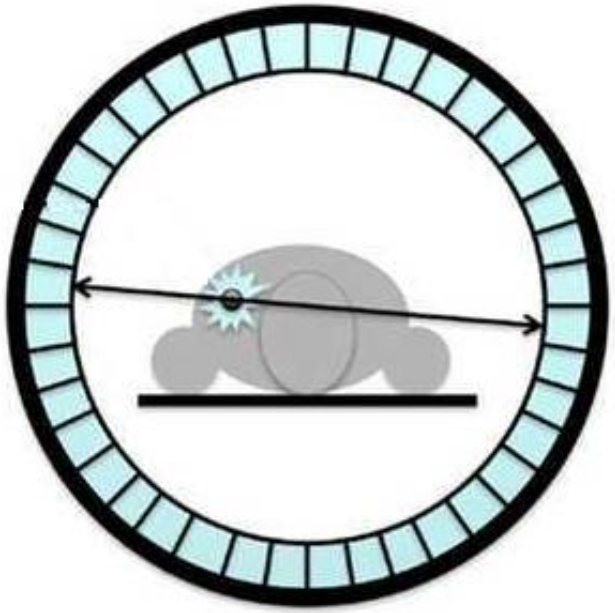
- Absence of physical collimation (no collimator)
- The LOR is defined by the “tube” connecting the two detectors elements responding in coincidence.

- **We only know the annihilation event happens somewhere along the LOR**

→ can we have more precise information?

Basic principles of PET imaging : TOF

- How to determine location along a LOR between ACD?
- ≠ of time between their detection → *time of flight (**TOF**)*
- Advantages:
  - Allows to determine approximate localisation of the annihilation event (hence positron emission*, hence radioactivity distribution).
  - Perfect TOF would theoretically allow for pure TOF image reconstruction → no need of tomographic reconstruction!



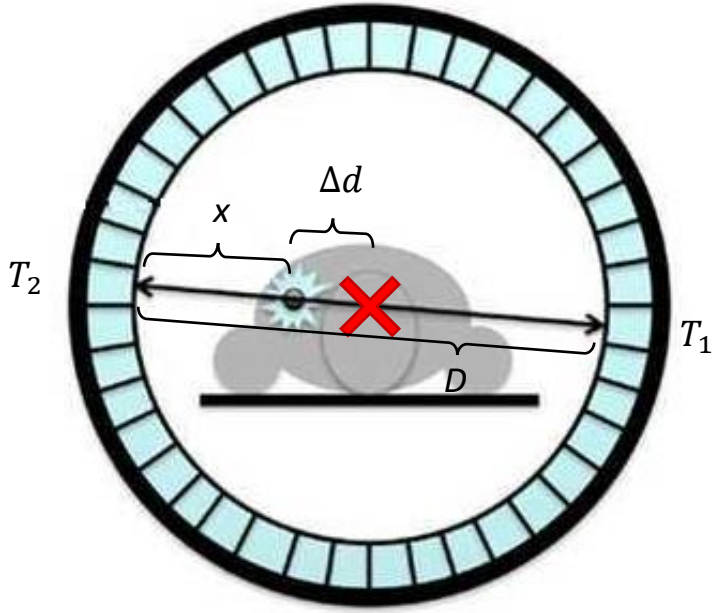
Basic principles of PET imaging : TOF

$$T_1 = \frac{D-x}{c}; \qquad T_2 = \frac{x}{c};$$

$$x + \Delta d = \frac{D}{2} \rightarrow D = 2x + 2\Delta d$$

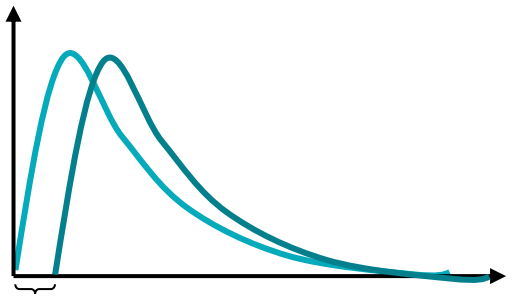
$$\Delta T = T_1 - T_2 = \frac{D-x}{c} - \frac{x}{c} = \frac{D-2x}{c} = \frac{2\Delta d}{c}$$

$$\Delta d = \frac{\Delta T \cdot c}{2}$$



Exercice 1: calculate the time needed to discriminate an event occuring at a distance of 1 cm wrt the midpoint between two PET detectors:

Basic principles of PET imaging : TOF



TOF time resolution shorter than coincidence window

- 66 ps : light output from scintillators are too slow to provide this timing resolution.

  → pure TOF image reconstruction not possible at present.

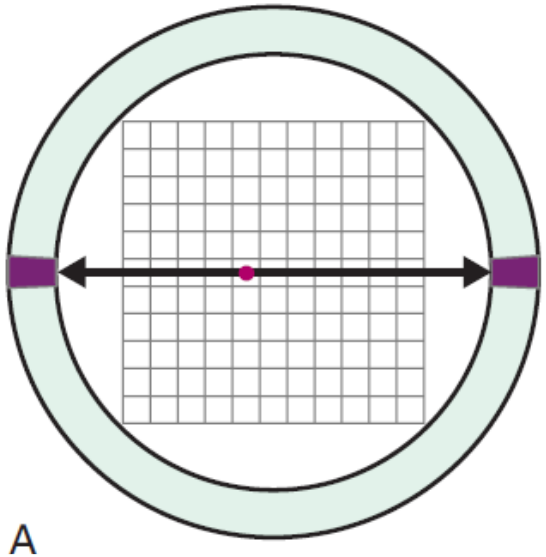
- With the fastest scintillators and electronic design: time resolution~ few hundreds of ps (typically **300 ps**).

- With a TOF time resolution of 300 ps → $\Delta d = \frac{\Delta t \cdot c}{2} \cong \mathbf{4.5}\ \boldsymbol{cm}$.

- Images reconstructed with TOF information have better (i.e. high) SNR.

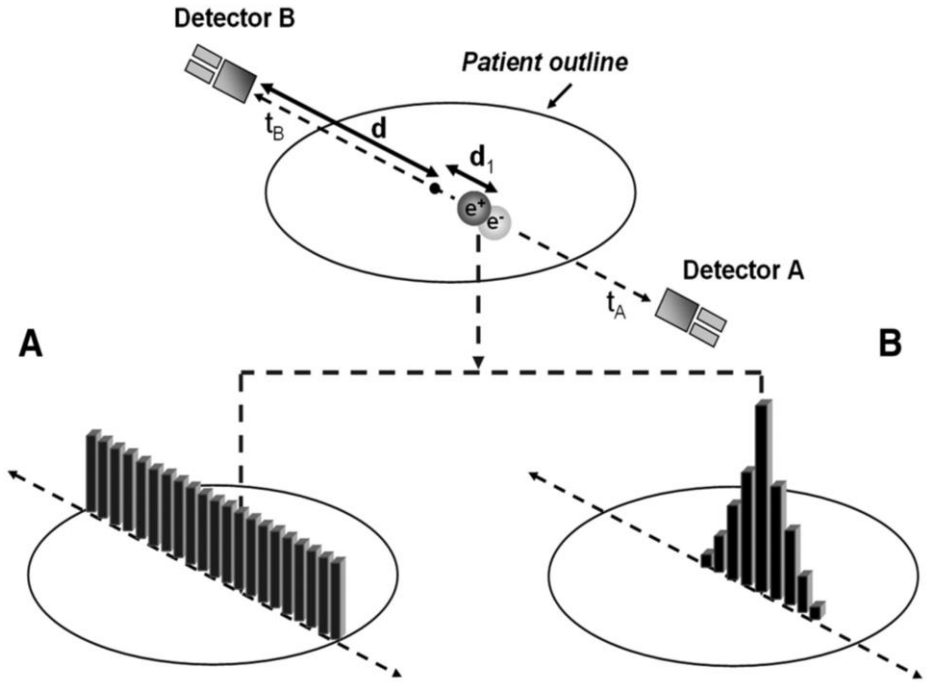
- Why? → With TOF, individual events can be constrained to a limited volume during the reconstruction process (unnecessary information is not used!).

Basic principles of PET imaging : TOF



A

- In the absence of TOF info: during reconstruction, the event is back-projected with equal probability of having occurred in all pixels along the LOR.
- With TOF, some (limited) info on the event localisation along the LOR is available. Events are back-projected with probabilities following a Gaussian centred on pixel Δd and FWHM = TOF timing resolution of the detector pair.

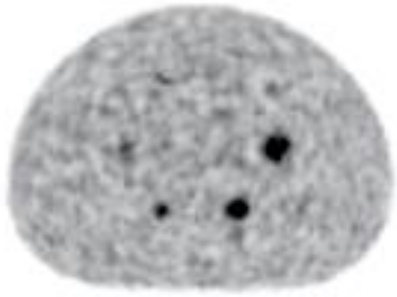


Basic principles of PET imaging : TOF

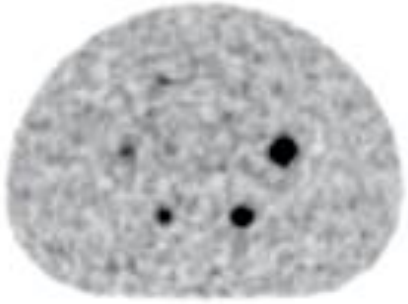
IQ vs. TOF time resolution

8 cm
segment response

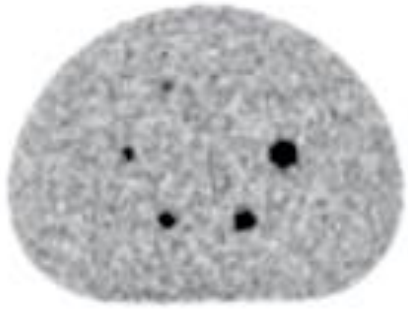
3.7 cm
segment response



No TOF



540ps TOF

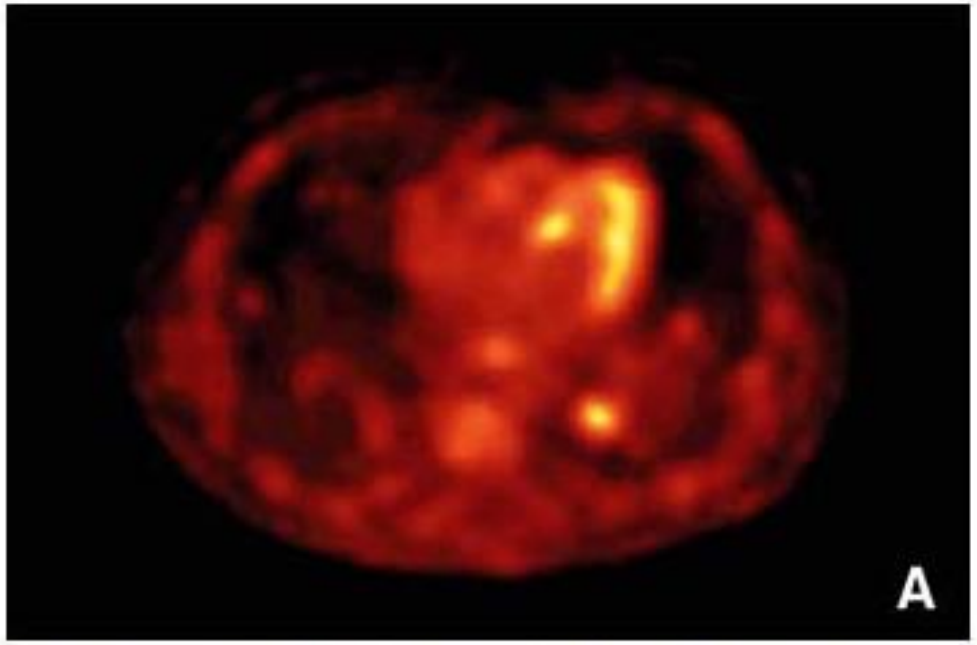


250ps TOF

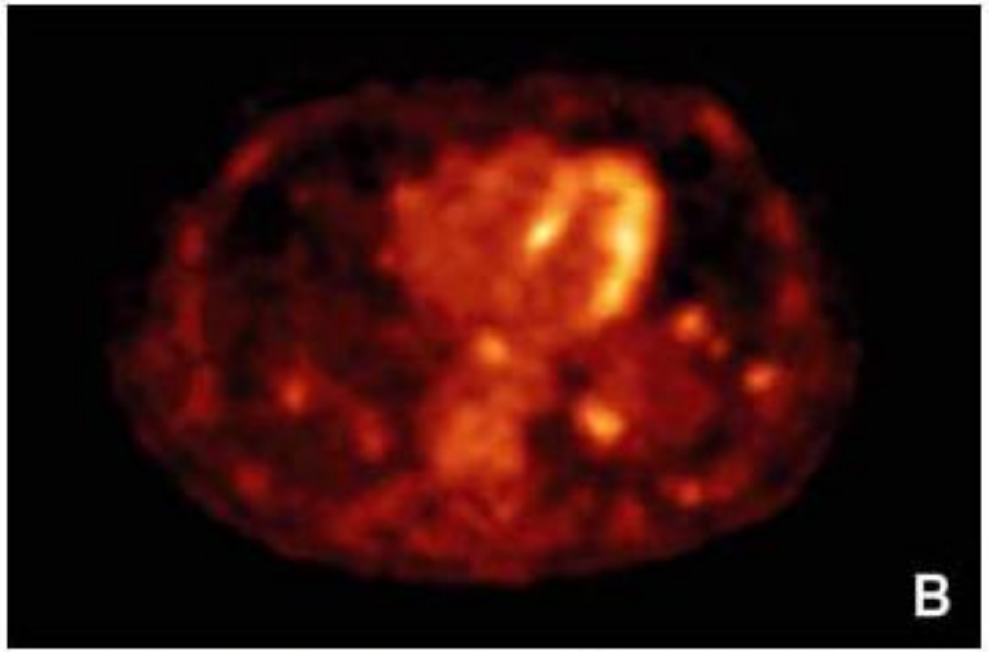
- Improved image contrast
- Improved lesion detectability

Basic principles of PET imaging : TOF

TOF improves in image quality (SNR) and quantification

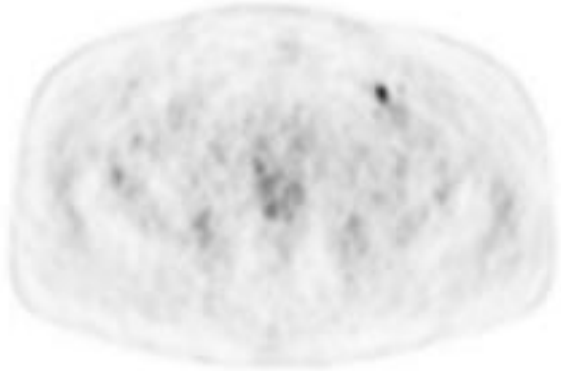


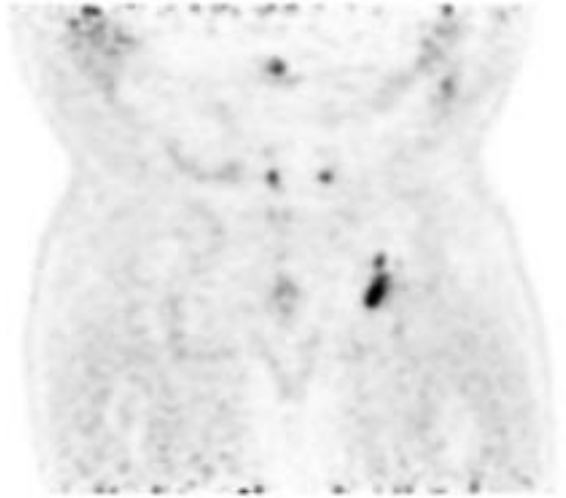
PET reconstruction <u>without</u> TOF



PET reconstruction <u>with</u> TOF

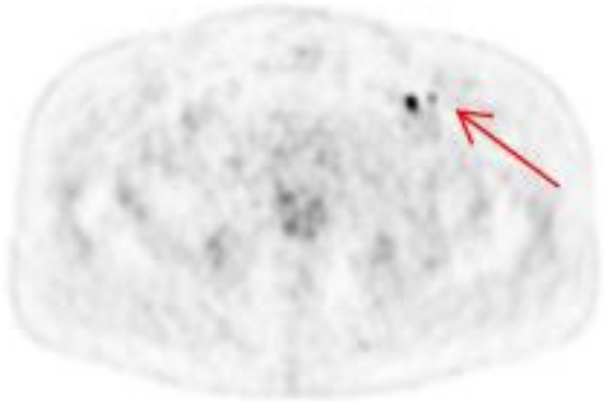
Basic principles of PET imaging : TOF

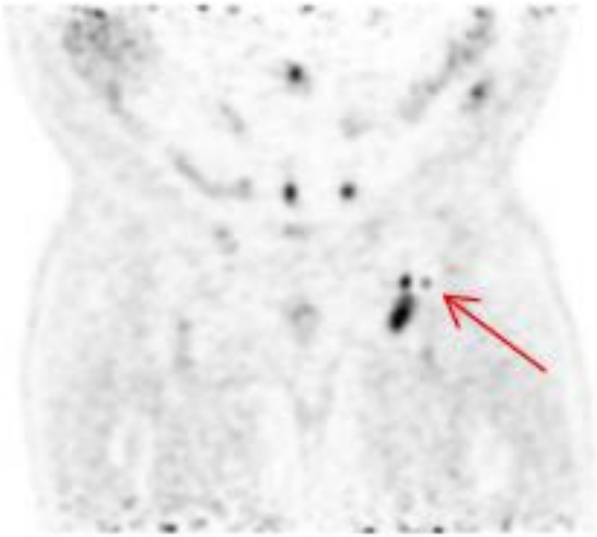


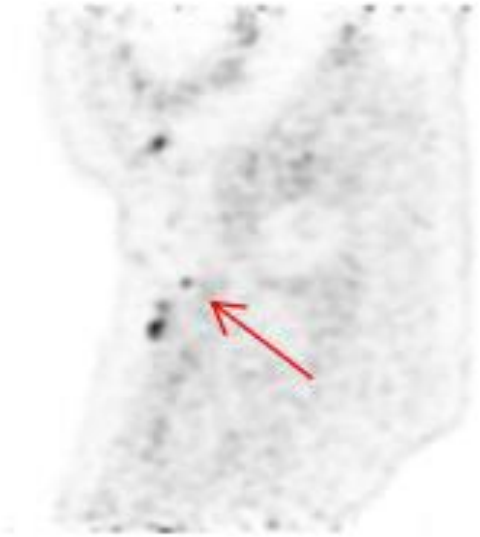


example: TOF-improved pelvic nodule visualization

without TOF







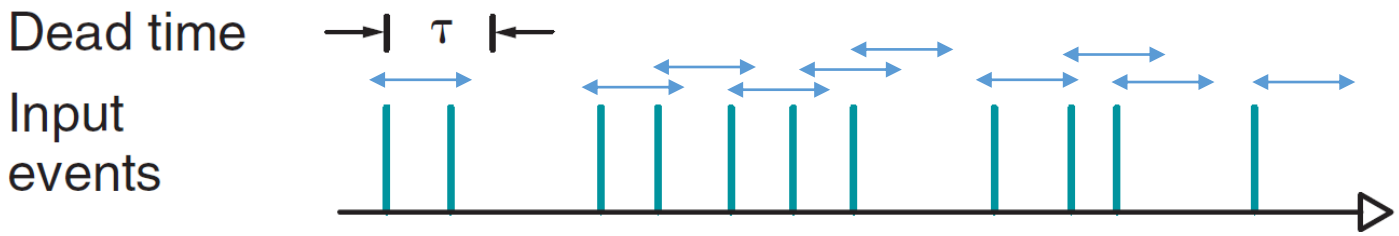
with TOF

Basic principles of PET imaging : dead time and pile-up

Dead time:

← *both dead time and pile-up occur at high counting rates*

- Dead time (or pulse resolving time τ) : time required to process individual detected events.
- Pulses in radiation detectors have finite duration → if a second pulse occurs while the first is still detected, the two pulses will overlap and form a single distorted pulse.
- Detectors can behave either as paralyzable or non-paralyzable
  - Non-paralizable: if event occurs during dead time → simply ignored, no effect on subsequent events
  - Paralyzable: if event occurs during dead time → not counted, but will introduce its own dead time, extending it



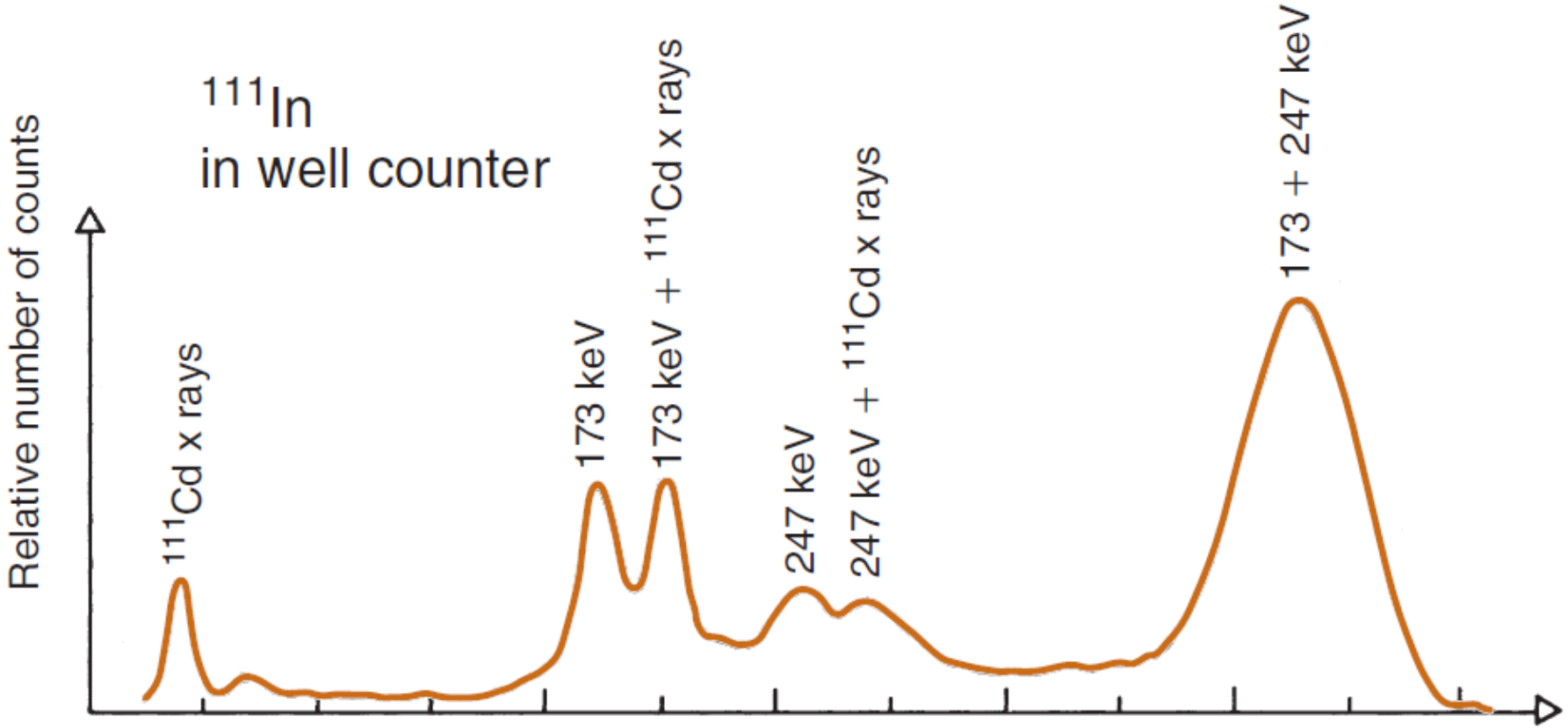
for extremely high count rates → counter paralysis

Basic principles of PET imaging : dead time and pile-up

Pile-up:

← *both dead time and pile-up occur at high counting rates*

- Amplifier pulses can occur very close and are not distinguished as separated → pulse pile-up.
- Pulses are summed together, and information is lost: resulting amplitude (and thus energy) is not representative for neither of them + contributes to dead time.

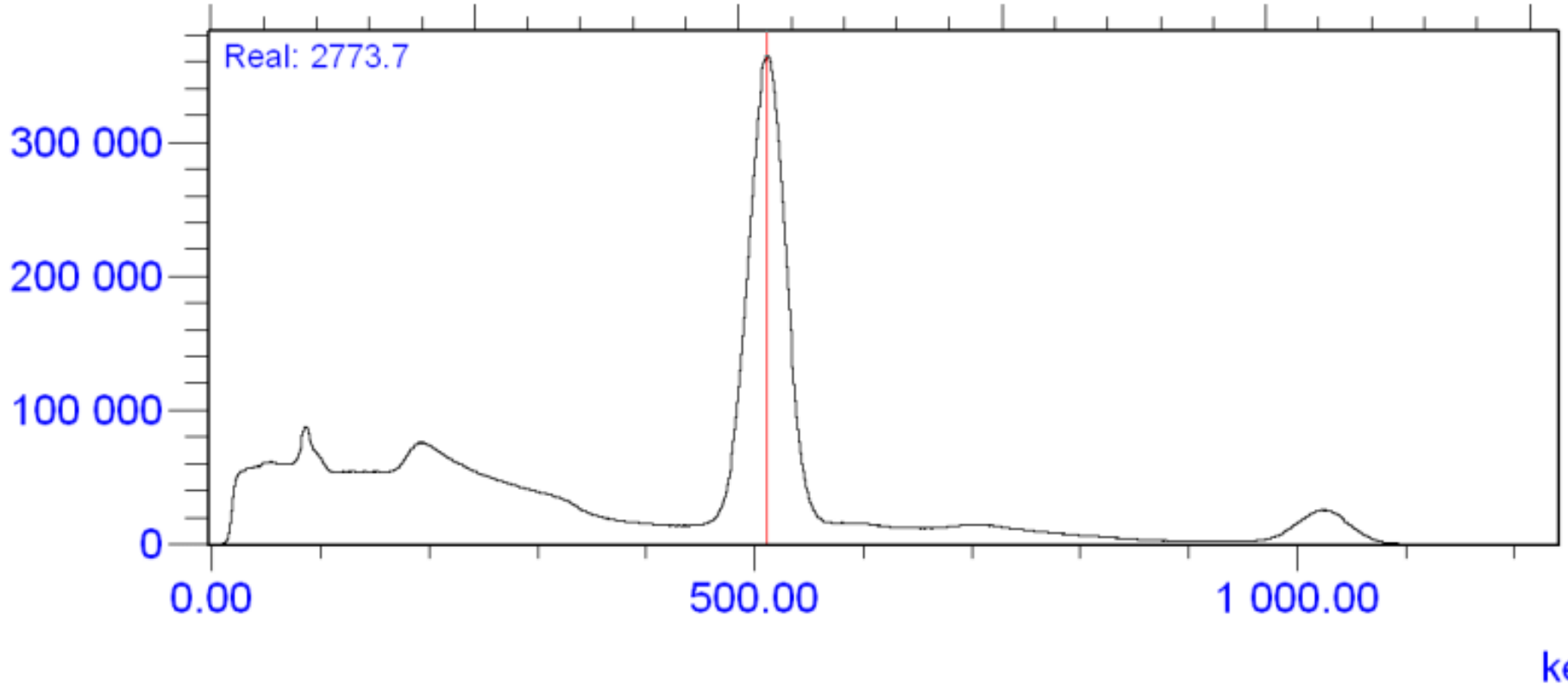


Basic principles of PET imaging : dead time and pile-up

Pile-up:

← *both dead time and pile-up occur at high counting rates*

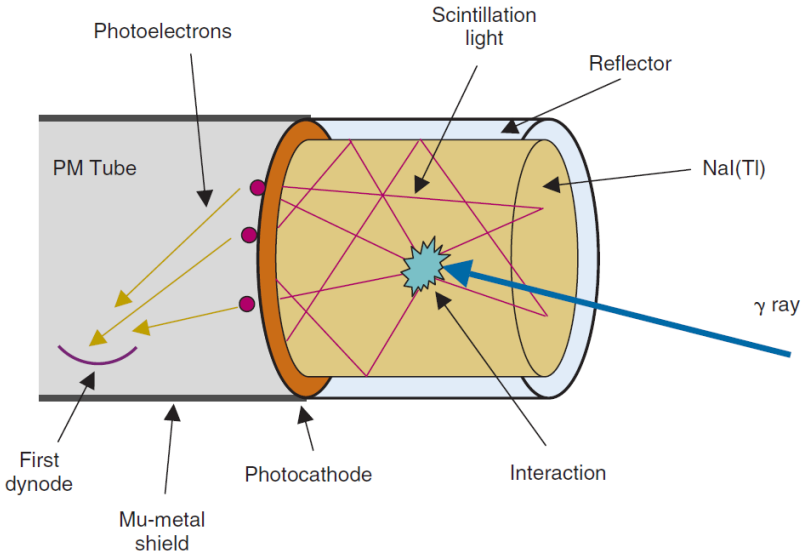
- Amplifier pulses can occur very close and are not distinguished as separated → pulse pile-up
- Pulses are summed together and information is lost : resulting amplitude (and thus energy) is not representative for neither of them + contributes to dead time.

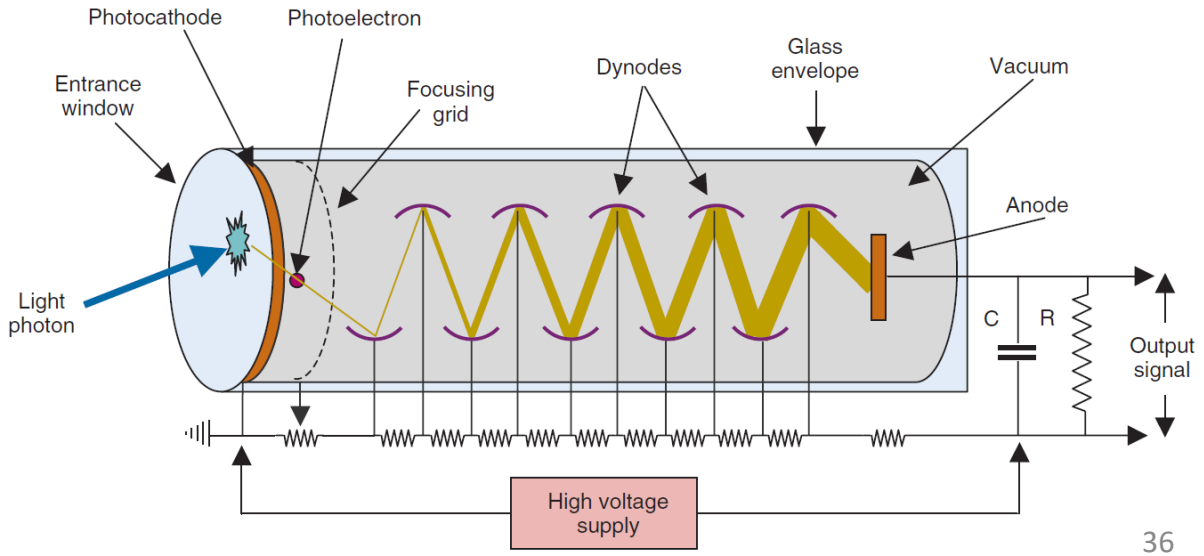


for PET, pile-up results in a peak having a total energy of 511x2 = 1'022 keV

Basic principles of PET imaging : detectors

	NaI (T1)	BGO	BaF_2	GSO	LSO	LuAp
Density (g/cm^3)	3,67	7,13	4,9	6,71	7,35	8,34
Zeff	50	73	53	58	65	65
μ at 511 keV	0,38	0,90	0,45	0,67	0,80	0,91
Photofraction (%)	18	42	19	26	33	32
Decay time (ns)	230	300	0,8	60	40	18





Basic principles of PET imaging : detectors

Characteristic for PET detectors:

- **Stopping power:** inverse of the mean free path, depends on Z

  (should be short, to favour interactions within the crystal element).

- **Decay time:** duration of the scintillation light flash (shorter is preferred → more responsive detector and less prone to dead-time).

- **Energy resolution:** finer energy resolutions allows to distinguish scattered from unscattered 511 keV photons (depends on crystal type).

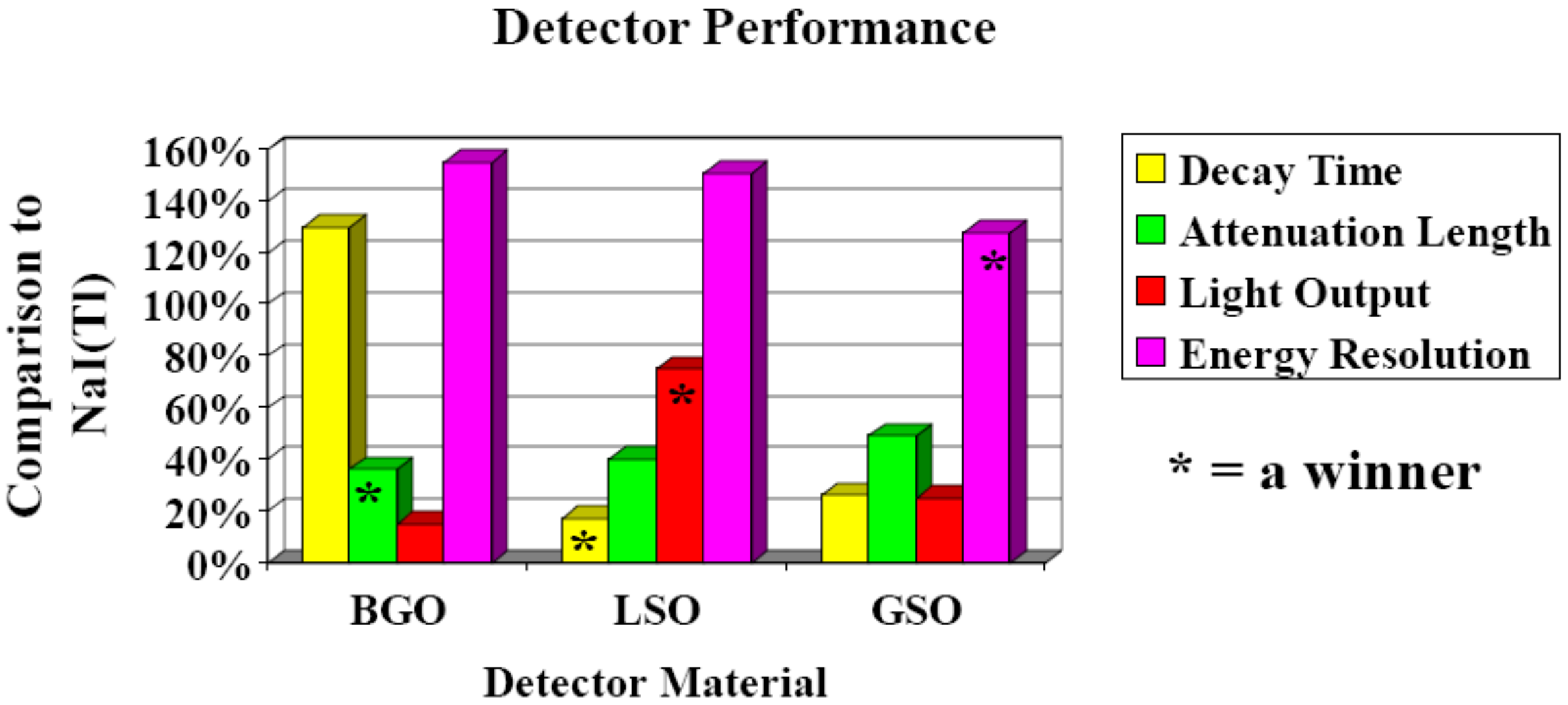
- **Light output (photon yield):** # of scintillation photons produced (should be high).

Basic principles of PET imaging : detectors

Material	Cost	Light Output	Effective Density	Light Decay Time
NaI(Tl)	cheap (relatively)	highest	lowest	long
BGO	expensive	lowest	highest	long
LSO (or LYSO)	more expensive	high	high	very short
GSO	more expensive	very high	somewhat lower than LSO	very short

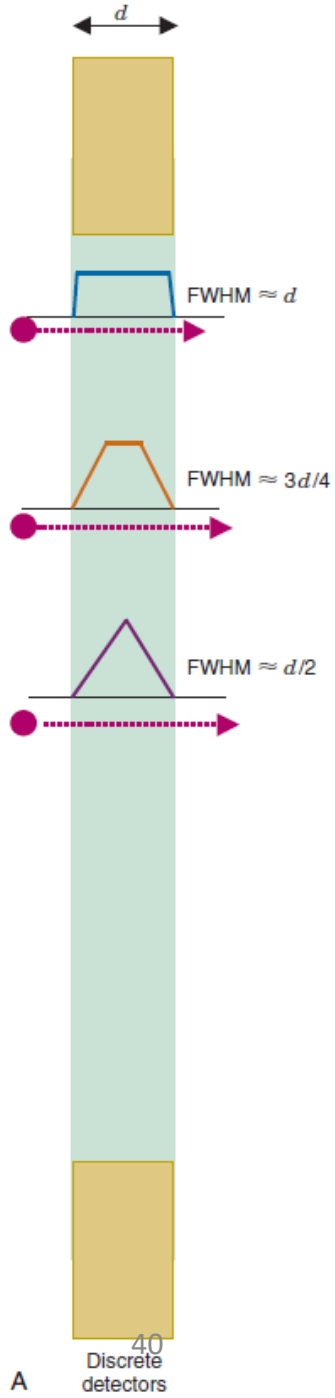
https://depts.washington.edu/imreslab/education/Physics%20of%20PET.pdf

Basic principles of PET imaging : detectors



Basic principles of PET imaging : detector spatial resolution

- Spatial resolution is mainly determined by the size of the individual detector elements.
- Response profile depends on the distance from the centre of the detectors.
- Spatial resolution in ACD is determined by detector size and its intrinsic resolution ($\boldsymbol{R_{det}}$).
- ≠ from SPECT (resolution mainly determined by the collimator)

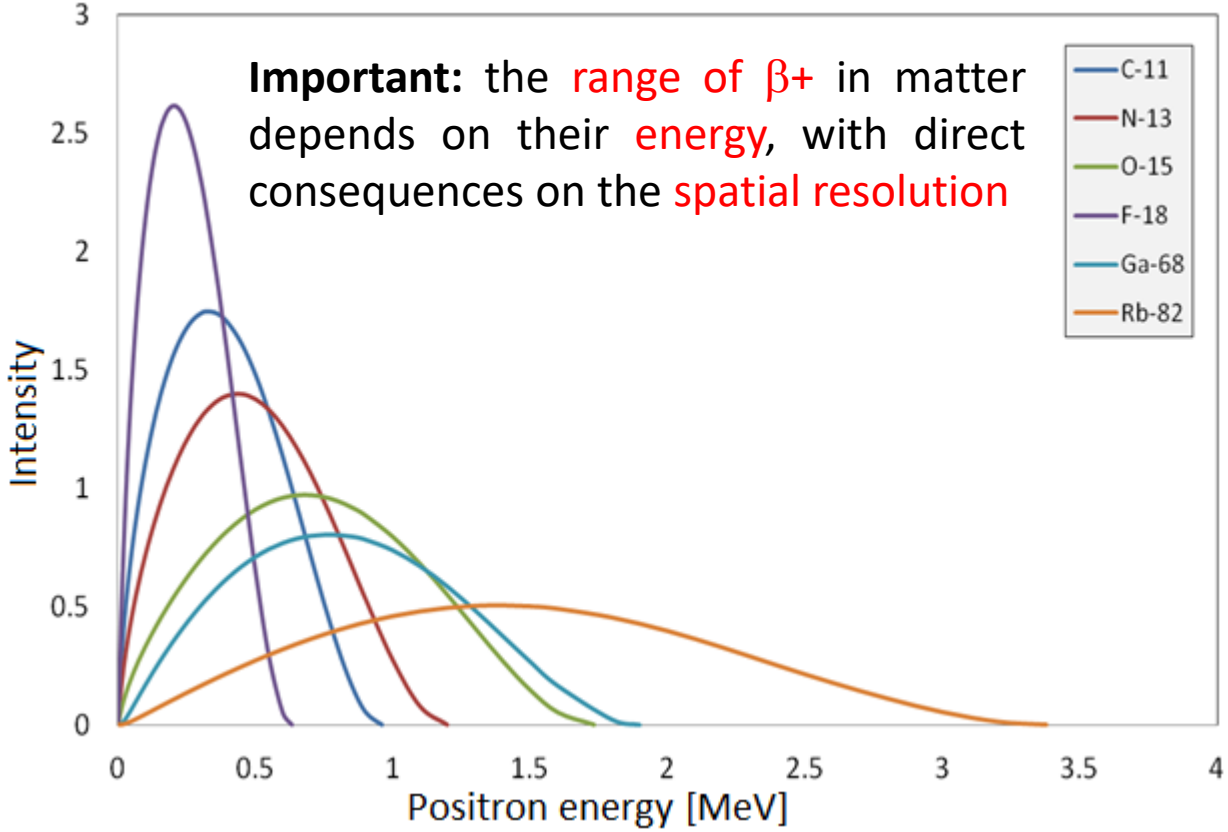


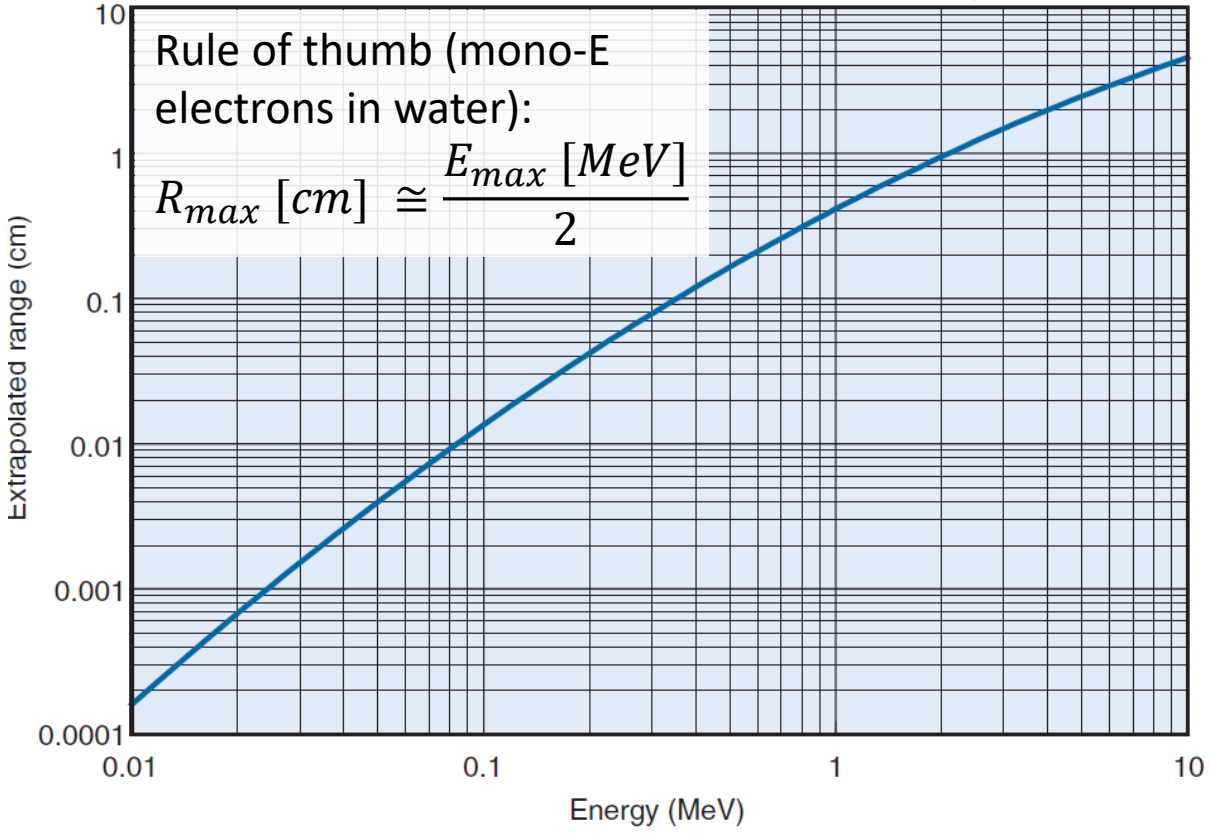
Basic principles of PET imaging : positron-dependent spatial resolution

Spatial ACD resolution is degraded by 2 physics properties of β^+ decay:

1. **Finite positron range (R_{range})** : positron *annihilation* location may not directly reflect the positron *emission* location, due to their range in matter.

   Range of positron is the same for an electron and depends on its energy.

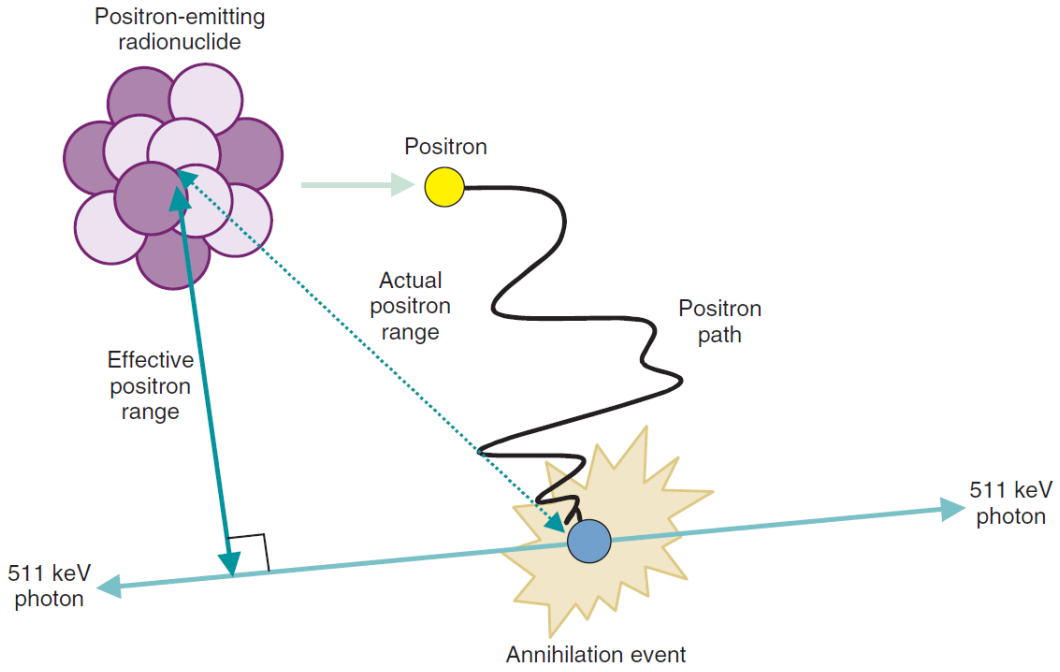




Basic principles of PET imaging : positron-dependent spatial resolution

Spatial ACD resolution is degraded by 2 physics properties of β^+ decay:

1. **Finite positron range (R_{range})** : positron *annihilation* location may not directly reflect the positron *emission* location, due to their range in matter.
   - Max. positron energies used in NM : 0,5 - 5 MeV.
   - Average range : 0,5 - 4 mm.



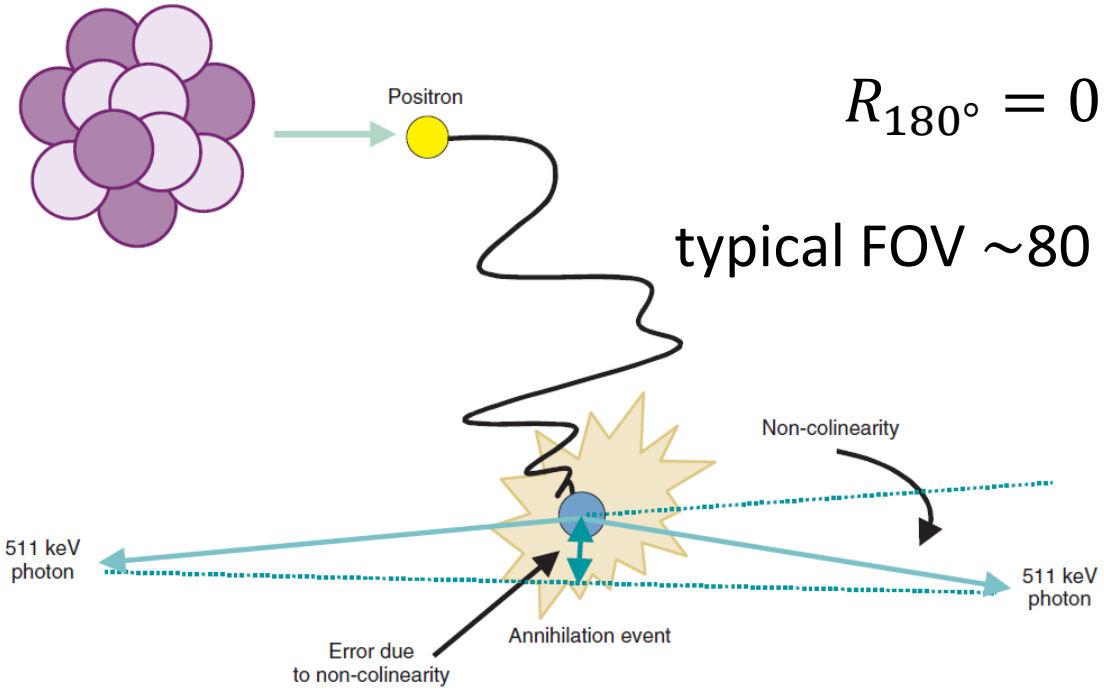
Isotopes	Mode de production	Périodes (en min)	Énergie du positon	Libre parcours moyen du positon dans l'eau (en mm)
^{18}F	$^{18}O(p,n)^{18}F$	109,8	634 keV	0,6
^{11}C	$^{14}N(p,\alpha)^{11}C$	20,4	960 keV	1,12
^{13}N	$^{16}O(p,\alpha)^{13}N$	10	1 200 keV	1,44
^{15}O	$^{14}N(d,n)^{15}O$	2	1 730 keV	2,22
^{68}Ga	Générateur ^{68}Ge	68	1 899 keV	2,4
^{82}Rb	Générateur ^{82}Sr	1,3	3 350 keV	4,7

Basic principles of PET imaging : positron-dependent spatial resolution

Spatial ACD resolution is degraded by 2 physics properties of β^+ decay:

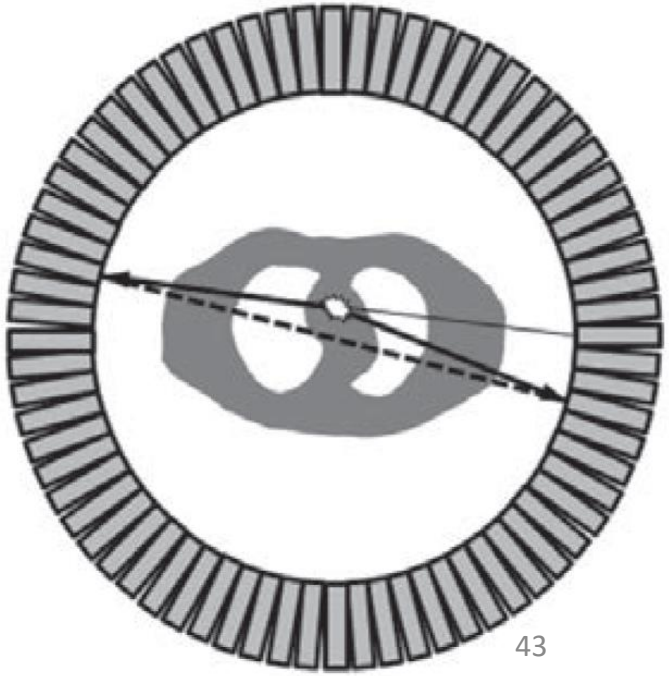
2. **Noncollinearity of annihilation photon emission ($R_{180°}$)** : 511 keV photons not emitted at exactly 180° → residual positron momentum at the end of its range (not at rest).

   - Angular distribution is a Gaussian with FWHM of ~0.5°
   - This effect is dependent on the distance D between the ACD detectors:



$$R_{180°} = 0.0022 \cdot D$$

typical FOV ~80 cm → 2 mm (FWHM)



Basic principles of PET imaging : system resolution

$$R_{sys} \approx \sqrt{R_{det}^2 + R_{range}^2 + R_{180°}^2}$$

***Exercice 2**:*

Consider a PET system with detector ring $\emptyset = 80\ cm$ and detectors with side $d\ = 6\ mm$ and ^{18}F as radiotracer.

- Compute the system resolution at the center of the PET.

Basic principles of PET imaging : system resolution

$$R_{sys} \approx \sqrt{R_{det}^2 + R_{range}^2 + R_{180°}^2}$$

R_{range} $R_{180°}$ intrinsic limitation of PET imaging, cannot be (physically) improved

***Exercice 2**:*

Consider a PET system with detector ring $\emptyset = 80\ cm$ and detectors with side $d = 6\ mm$ and ^{18}F as radiotracer.

- Compute the system resolution at the center of the PET.

$$R_{det} = d/2 = 3\ mm$$

$$R_{range\ F-18} \approx 0.6\ mm$$

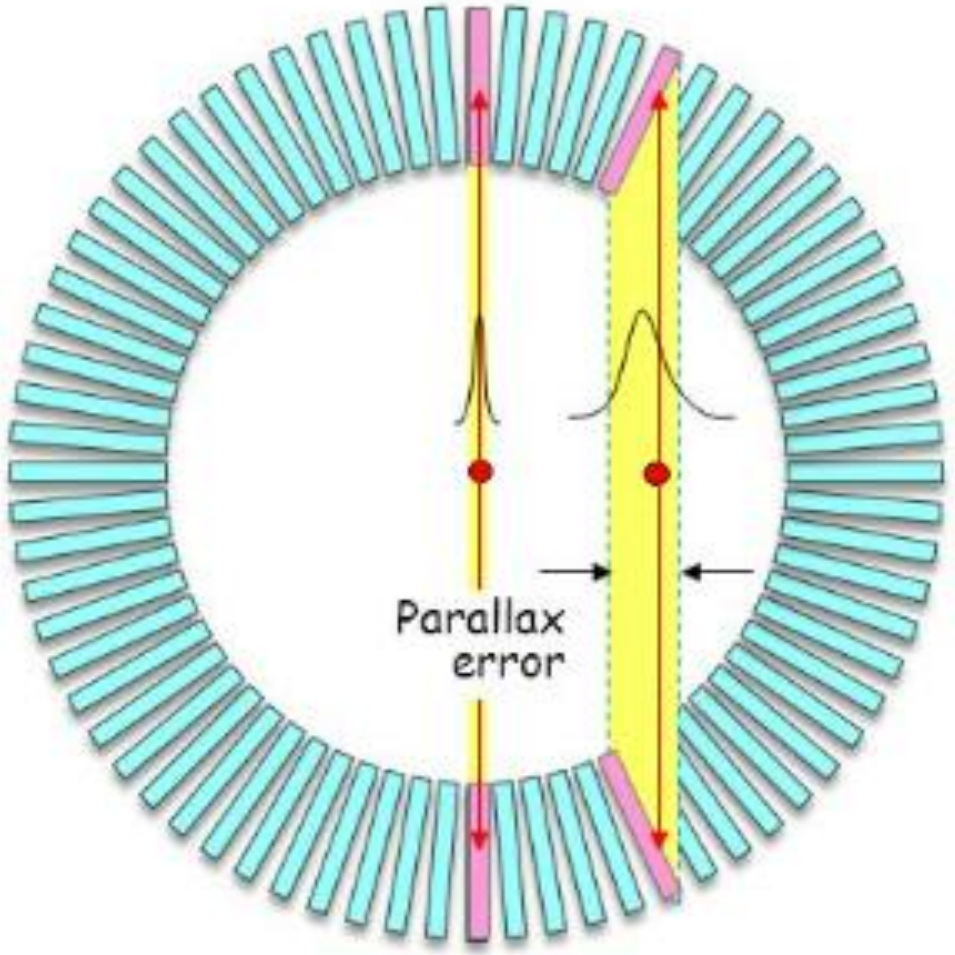
$$R_{180°} = 0.0022 \cdot 80\ cm = 1.76\ mm$$

…but this is not all. Other factors contribute in degrading PET resolution!

$$R_{sys} \approx \sqrt{R_{det}^2 + R_{range}^2 + R_{180°}^2} = \sqrt{3^2 + 0.6^2 + 1.76^2} \approx 3.5\ mm$$

Basic principles of PET imaging : depth of interaction resolution

- SPECT vs PET: ≠ photon range (100-350 keV) vs 511 keV.
- SPECT → NaI with thickness less than 1.25 cm.
- PET → scintillators (BGO, LSO) with thickness of 2-3 cm.
- Depth of interaction (DOI) effect results in resolution degradation.
- Depth of interaction within the detector is unknown!
- The apparent width d' of a detector element in a detector ring is always ≥ than the real side d of the detector element (with thickness x):
- $d' = d\cos\theta + x\sin\theta$
- $R'_{det} \approx d'/2 = d/2\,(\cos\theta + x/d\sin\theta) \approx R_{det}\,(\cos\theta$



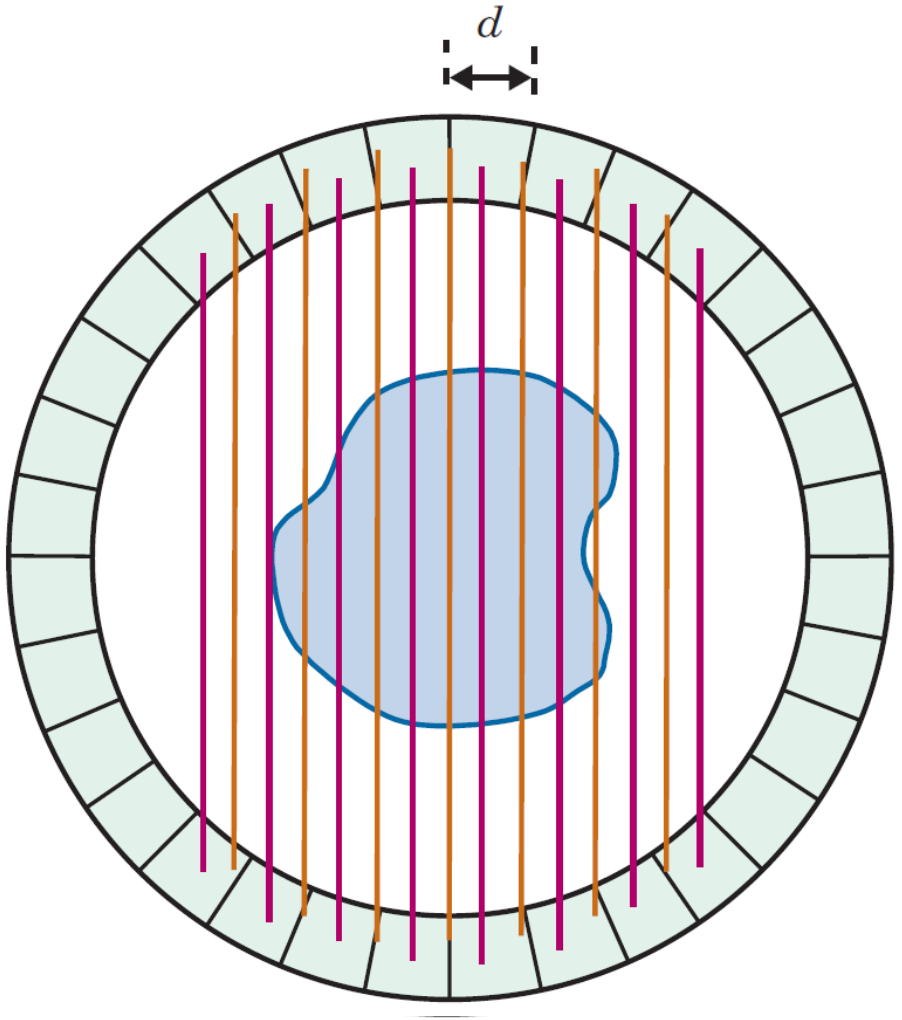
Typically: $d \sim$ 0.3- 0.6 cm, $x \sim 2 - 3$ cm

Basic principles of PET imaging : sampling resolution and reconstruction filters

Other effects contributing to the spatial resolution are the sampling resolution and reconstruction parameters:

- Sampling resolution
  - If only the detector resolution is considered for sampling →undersampling issues *(Nyquist–Shannon sampling theorem)*, resulting in missing high-frequency components.
  - Nowadays PET use coincidence events in adjacent detectors, creating additional samples between detector elements.
  - For image reconstruction purposes, these are treated as if they were parallel.

- Reconstruction
  - Using iterative reconstruction algorithms (cf. SPECT lecture).
  - Filters (high-pass or low-pass) are applied to the recorded projection (compromise between noise and spatial resolution).
  - The reconstruction can thus greatly influence the final image resolution (filters depend on the type of study).



Basic principles of PET imaging : resolution summary

$$R_{tot} = K \cdot \sqrt{R_{det}^2 + R_{range}^2 + R_{180°}^2 + R_{DOI}^2}$$

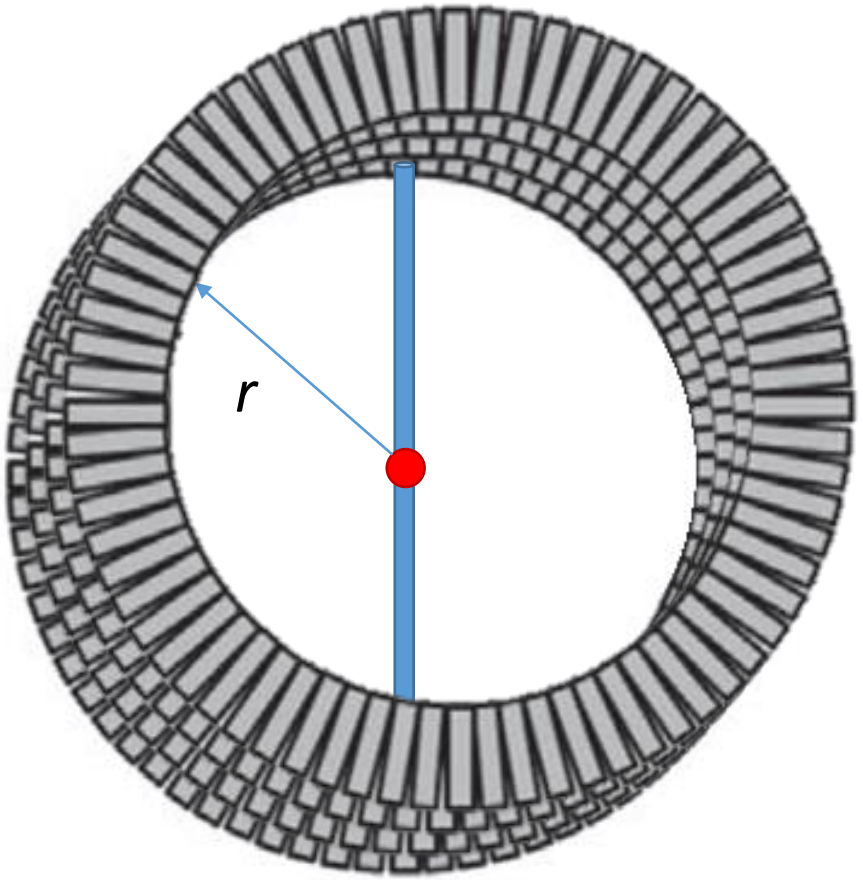
- R_{det} is related to the detector side (d)
  - from d/2 (center) to d (detector), 2 – 4 mm
- R_{range} is related to the positron range
  - 0.2 mm for ^{18}F and 2.6 mm for ^{82}Rb
- $R_{180°}$ is related to the γ non-collinearity
  - $\pm$ 0.25° deviation from 180°
  - ~1.8 mm for a 80-cm PET scanners
- R_{DOI} is related to the depth of interaction in the detector
  - depends on the crystal thickness
- K is a factor related to sampling and reconstruction techniques (1.2 to 1.5)

R_{tot} for F-18 at the centre of the FOV ≈ 5 mm

…do you remember SPECT ? ≈ 10 mm

Basic principles of PET imaging : sensitivity

- $S = \frac{A}{4\pi r^2}\varepsilon^2$ *[cps/Bq]*



- A: detector area seen by a point-source to be imaged.
- ε : detector's efficiency ($\varepsilon = 1 - e^{-\mu x}$), where μ is the linear attenuation coefficient of 511 keV and x is the detector thickness
- r: radius of the detector ring.

For a small volume source near the centre of the FOV (2D):

$$S \approx 0.2 - 0.5\%$$

For a small volume source near the centre of the FOV (3D):

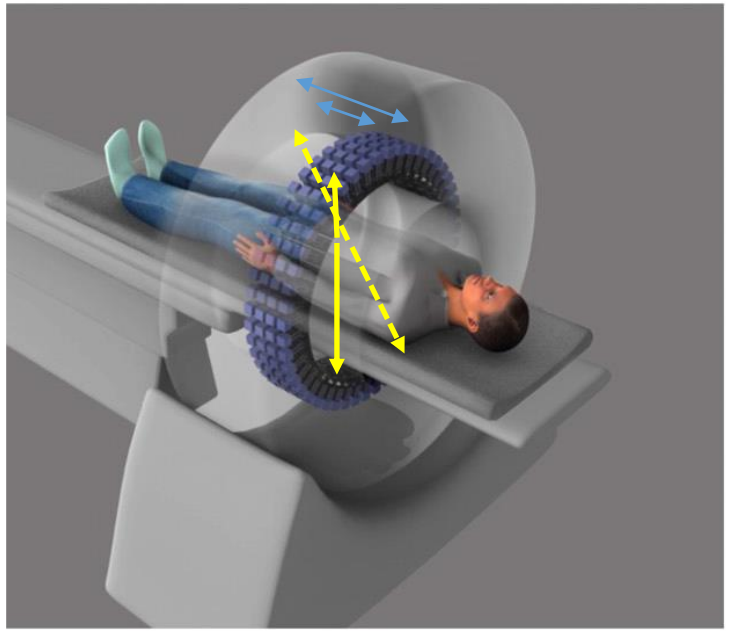
$$S \approx 2 - 10\%$$

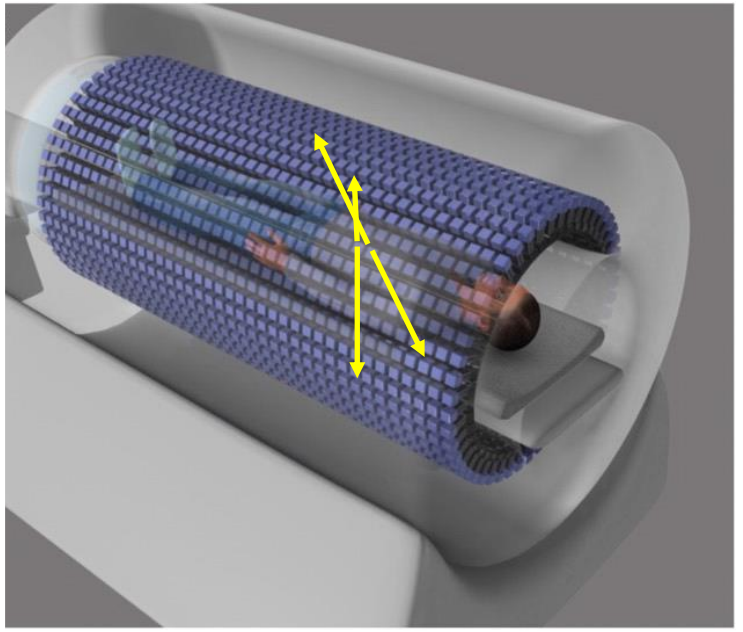
… do you remember SPECT?

$\sim 10^{-4} = 0.0001 \rightarrow 0.01\%$

- … and what about latest advances in PET in terms of sensitivity? → *long-axial FOV*

Basic principles of PET imaging : sensitivity





EXPLORER Total Body PET S.R.Cherry et al. J Nucl Med 2018; 59:3–12

- Increasing PET ring coverage (solid angle) — Costs
- Increase crystal thickness (increase probability of interaction) — Light collection efficiency; Depth of interaction
- Increase energy windows width around the 511 keV peak — Scatter and prompt gamma pollution

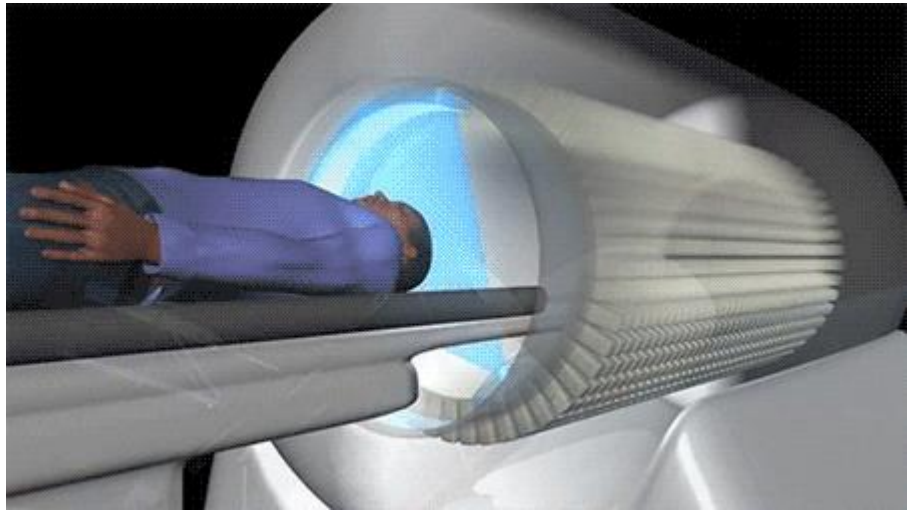
1. Margin for **reducing patient administered activity** and thus patient dose.
2. Margin for **reducing exam duration** with consequent improved patient comfort.

Basic principles of PET imaging : sensitivity

Biograph Vision Quadra
by Siemens Healthineers

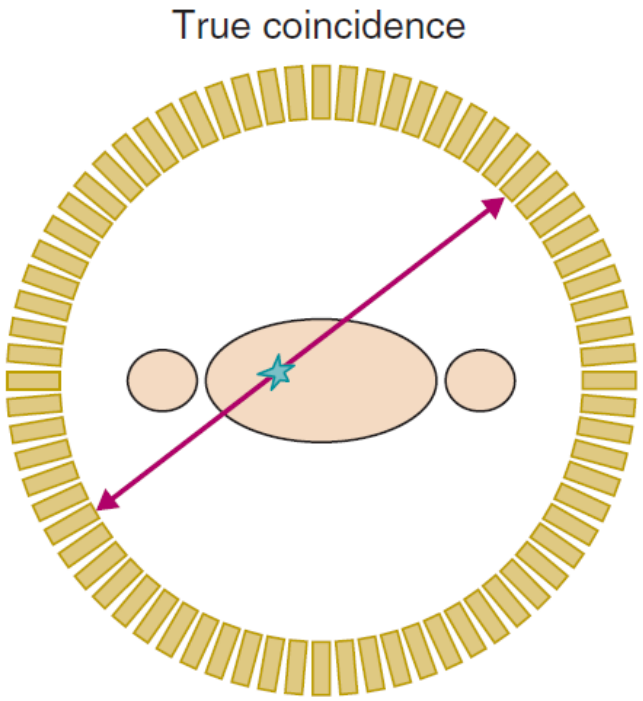
Omni Legend
by GE

uEXPLORER
by UNITED

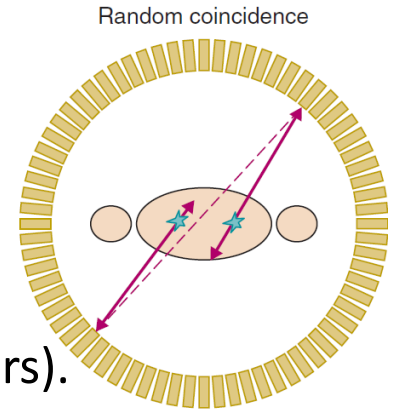


ACD: types of events

- ACD records coincidences that fall within a given timing window.
- But, such as for SPECT, not all the detected events are useful :
  - True coincidences (correct localisation, useful for image reconstruction)
  - Scatter coincidences (mislocation, contrast reduction, quantitative bias)
  - Random coincidences (mislocation, contrast reduction, quantitative bias, count rate saturation)



ACD: types of events



Random coincidences

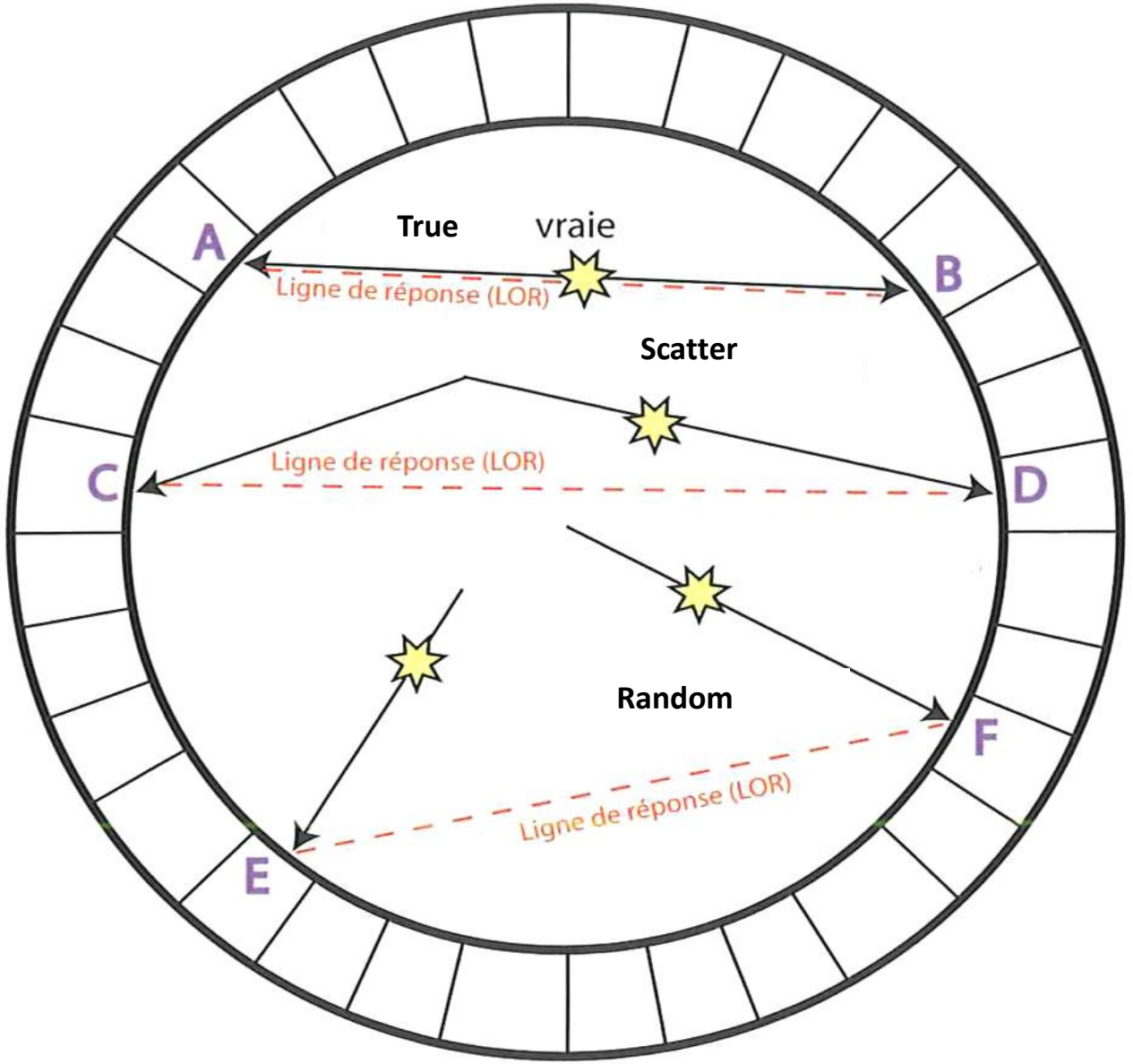
- $R_{random} = \Delta t \cdot R_{s,1} \cdot R_{s,2}$ (Δt: counting window, R single counting rate in the two detectors).
- Depend on both source and detector geometry.
- The greater the activity, the greater the ratio of random vs true coincidence ratios.
- Random increase as the square of the activity, while true coincidences only scale linearly with activity.
- Random vs true coincidence ratios can be reduced by reducing Δt (but limitations).
- Septa could be used on individual detectors to restrict their FOV (but efficiency loss).
- Random vs true coincidence ratios: 0.1 for brain vs >1 for abdomen. How is this possible? e.g. abdominal images where radionuclides is excreted and concentrated in the bladder (that stays outside the FOV).
- Random coincidences occur homogeneously across the FOV → loss of contrast and activity mislocation.

ACD: types of events

Scatter coincidences

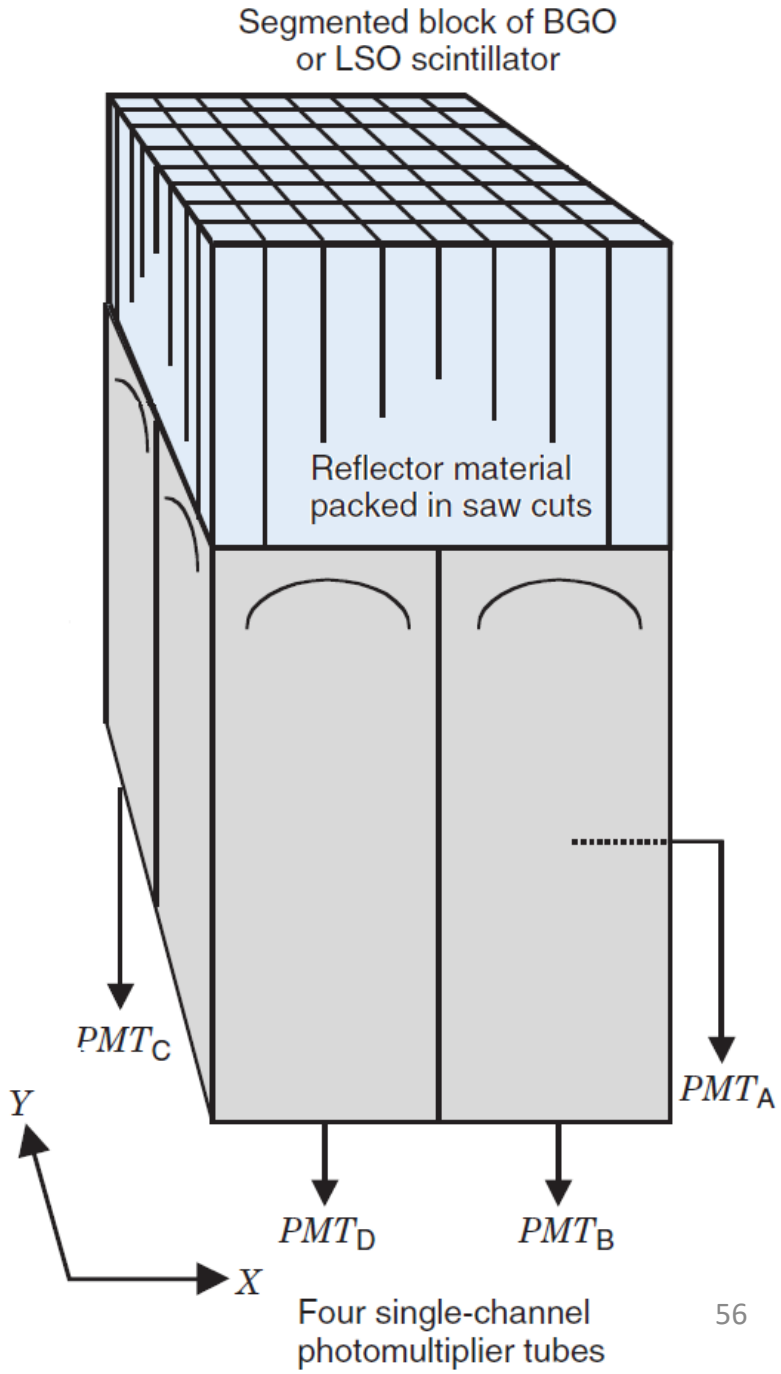
- They also depend on both source and detector geometry.
- Use of septa may help reduce them.
- Unlike random coincidences, they are not dependent on source activity, as both true and scatter coincidences increase linearly with it.
- They also arise from the same annihilation event → no impact of Δt
- Scatter vs true coincidence ratios: 0.2-0.5 for brain vs. 0.4-2 for abdomen imaging.
- Scatter coincidences lead to mislocation of activity distribution.

ACD: types of events



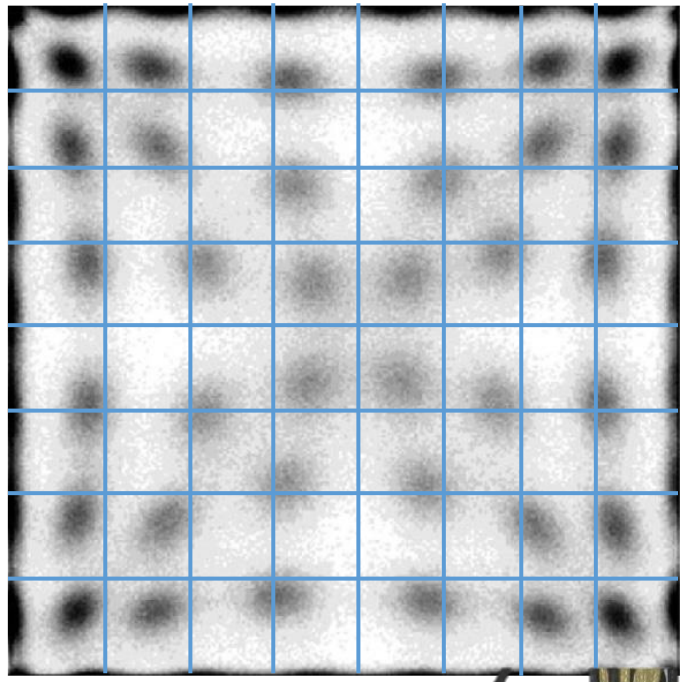
PET design: detectors and scanner

- Most PETs = blocks of detectors arranged around the object.
- Early PET detectors used individual detectors:
  - Piece of scintillator coupled to its own PMT, then arranged in a ring.
  - To improve spatial resolution, detector element should be small.
  - But design is costly if each detector element has its own PMT!
- Block detectors :
  - Still allows for small detector elements to be used (maintain resolution), but reducing the number of needed PMT.
  - Large piece of scintillator material (BGO, LSO, LYSO) is finely cut into many element arrays, separated by opaque reflective material.
  - The crystal array is connected by a set of 4 PMT.
  - Signal origin within the element is obtained similarly as done in SPECT (weighted PMT response)

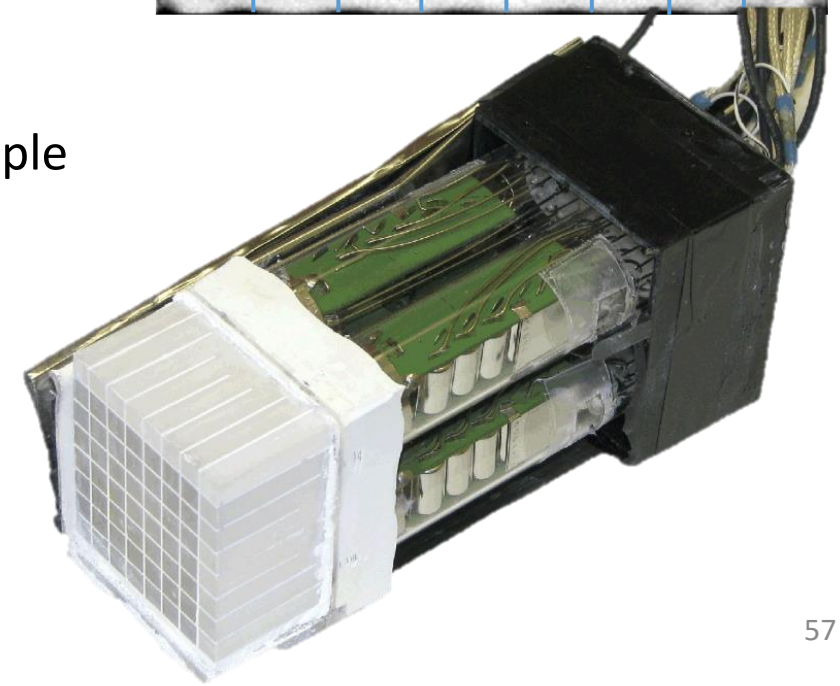


PET design: detectors and scanner

- When detectors are exposed to a homogeneous source:
  - Recorded events are clustered in areas corresponding to the individual detector locations.
  - The patterns is not linear, but the locations are clearly separated
    → "mapping" the detector elements response to allow for the reattribution of specific activity distributions in the image.



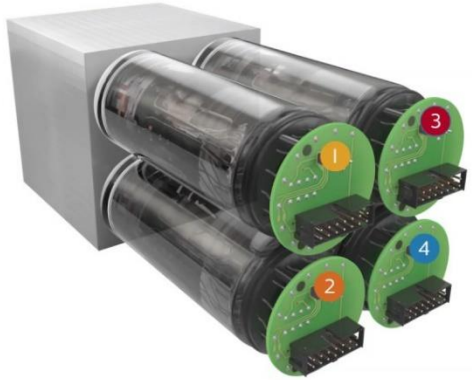
- Main advantage of block detectors :
  - Allows to use only 4 PMT to decode the signal coming from multiple detector elements (typically 8x8=64).
  - Typically 20-30 mm thick blocks, detector sides: 4-6 mm
  - Contained cost.
  - High spatial resolution.

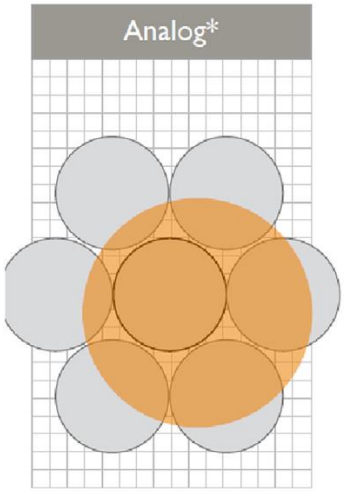


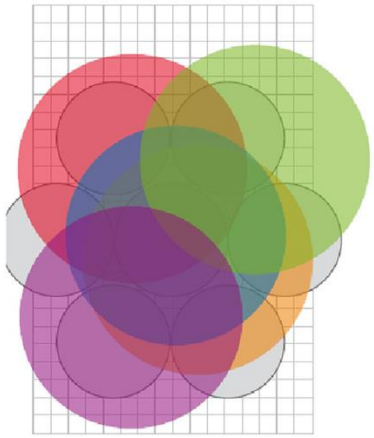
PET design: detectors and scanner

Digital vs. Analog PET technology

LSO or LYSO scintillator

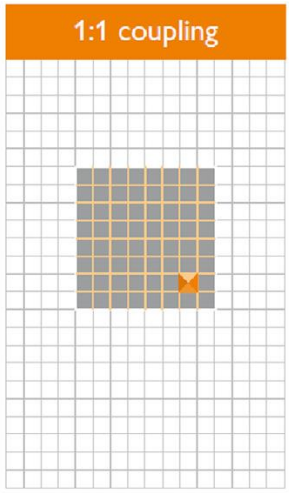


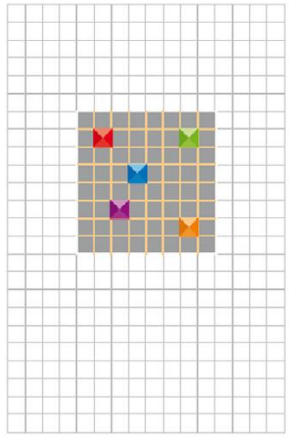




Digital:
still based on scintillator technology
(indirect conversion),
but PMT replaced by photodiodes

digital SiPM





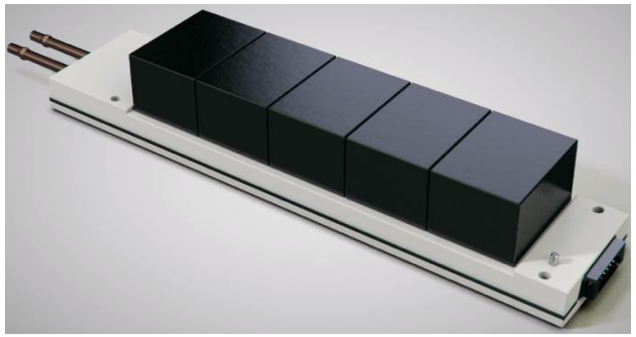
- Improved space resolution
- Improved signal localization
- Reduced signal Pile-up
- Higher count rate achievable

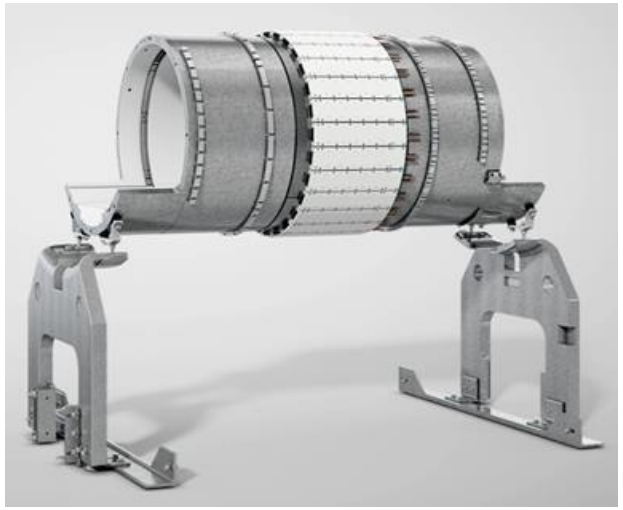
Source: Ge and Philips

PET design: detectors and scanner

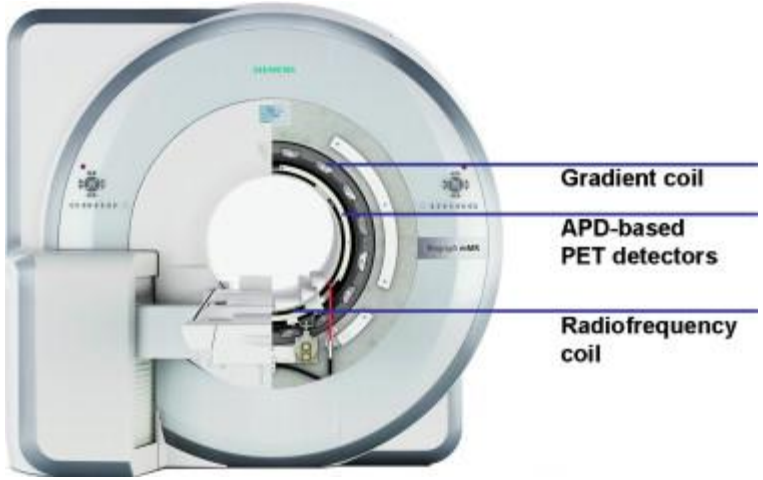
Digital vs. Analog PET technology

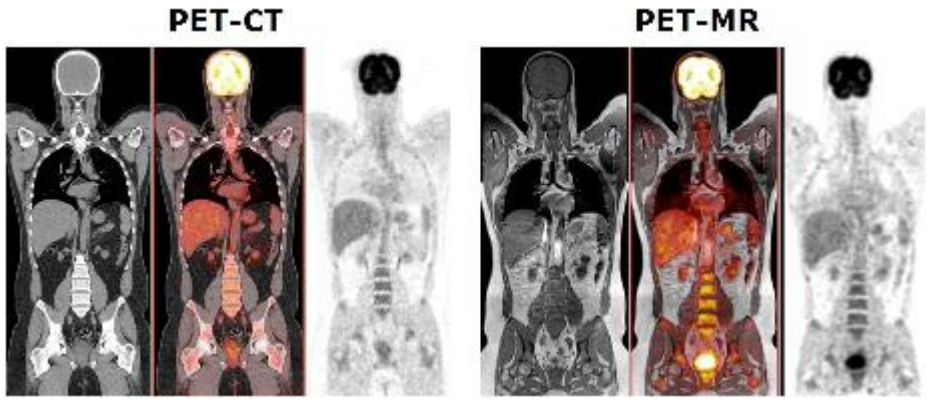
digital PET technology is compatible with strong magnetic fields → PET / MR scanners





Source: GE and Siemens





PET design: detectors and scanner

Digital vs. Analog PET technology

Table – Comparison of the Philips Ingenuity TF, GE Discovery 710, Biograph mCT Flow and the new Philips digital PET/CT Vereos.

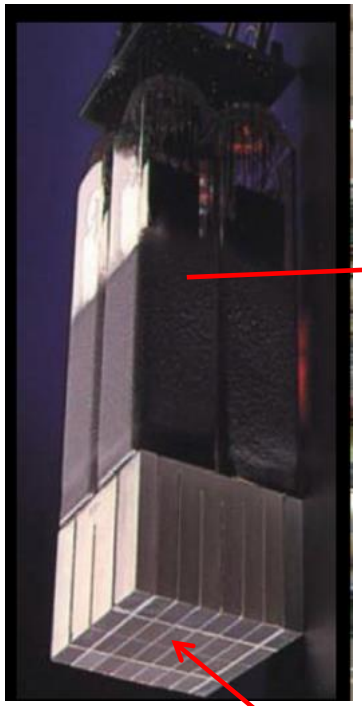
Model Product Name	Ingenuity TF	Discovery 710	Biograph mCT Flow	Vereos
Patient port [cm]	70 OpenView	70	78	70
Patient scan range [cm]	190	200	195	190
Maximum patient weight [kg (lb)]	195 (430)	226 (500)	226 (500)	195 (430)
Acquisition modes	3D S&S	3D S&S	3D S&S, continuous	3D S&S
Number of image planes	45 or 90	47	109	72
Plane spacing [mm]	2 or 4	3.27	2	1, 2, or 4
Crystal size [mm]	4 × 4 × 22	4.2 × 6.3 × 25	4 × 4 × 20	4 × 4 × 22
Number of crystals	28,336	13,824	32,448	23,040
Number of PMTs	420	256	768	23,040 SiPMs
Physical axial FOV [cm]	18	15.7	21.8	16.3
Detector material	LYSO	LYSO	LSO	LYSO
System sensitivity 3D, [%]*	0.74	0.75	0.95	>1.0
Trans axial resolution @ 1 cm [mm]*	4.7	4.9	4.4	4.0
Trans axial resolution @ 10 cm [mm]*	5.2	5.5	4.9	4.5
Axial resolution @ 1 cm [mm]*	4.7	5.6	4.5	4.0
Axial resolution @ 10 cm [mm]*	5.2	6.3	5.9	4.5
Peak NECR [kcps]	120 @19 kBq/ml	130 @29.5 kBq/ml	175 @28 kBq/ml	400 @30 kBq/ml
Time-of-flight resolution [picoseconds]	591	544	540	307
Time-of-flight localization [cm]	8.9	8.2	8.1	4.6
Coincidence window [nanoseconds]	4.5	4.9	4.1	1.5

The sensitivity, NECR (noise equivalent count rate), coincidence window and TOF resolution are higher for the digital PET/CT digital PET/CT.
Abbreviations: FOV, field-of-view; PMT, photomultiplier tubes; NECR, noise equivalent count rate; kcps, kilocounts per second; kBq/ml, kiloBecquerel/milliliter; S&S, step and shoot.
* NEMA 2001.

PET design: detectors and scanner

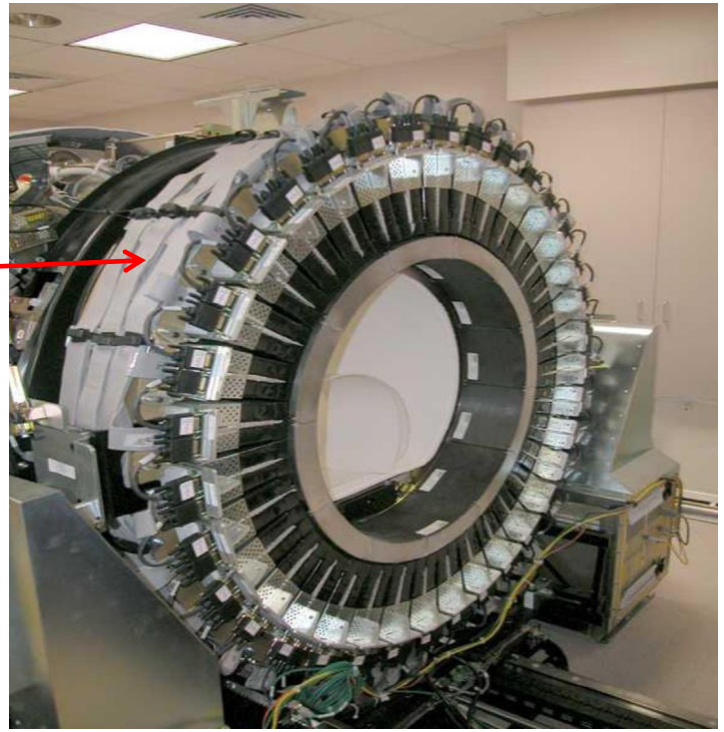
PET detector design

Module



Block

PET ring

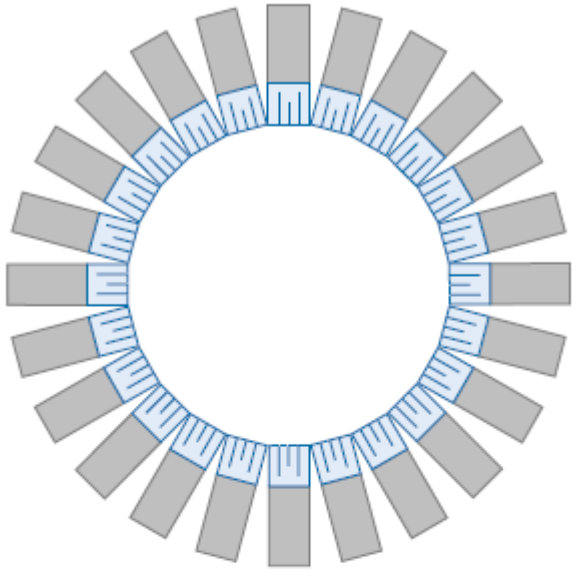


Detector elements (scintillators)

PET design: detectors and scanner

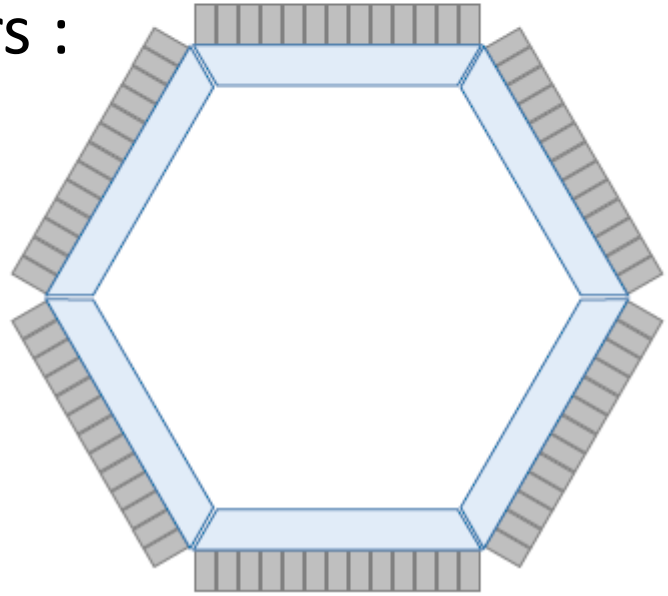
Different whole-body (WB) designs have been used:

→ blocks of discrete detectors & continuous gamma camera plates



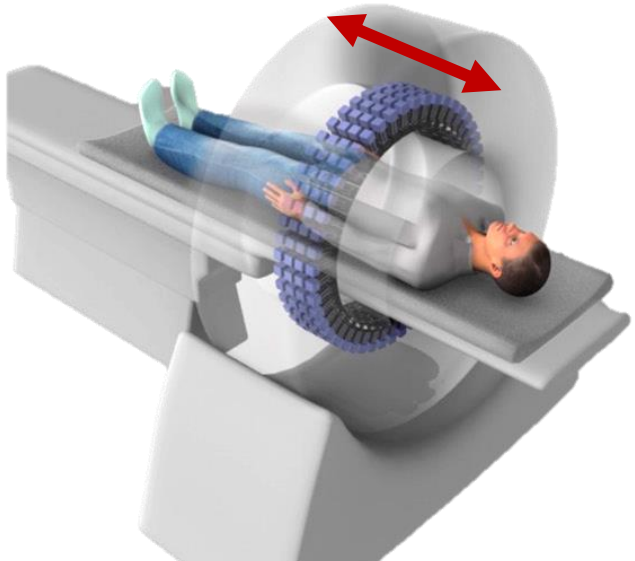
Typical PET diameter : 80-90 cm

After inserting shielding to reduce scatter + detector covers : 55-60 cm



FOV in axial view greatly varies:

typically from 15-40 cm (but up to 194 cm)



PET design: whole-body systems

Nowadays trends:

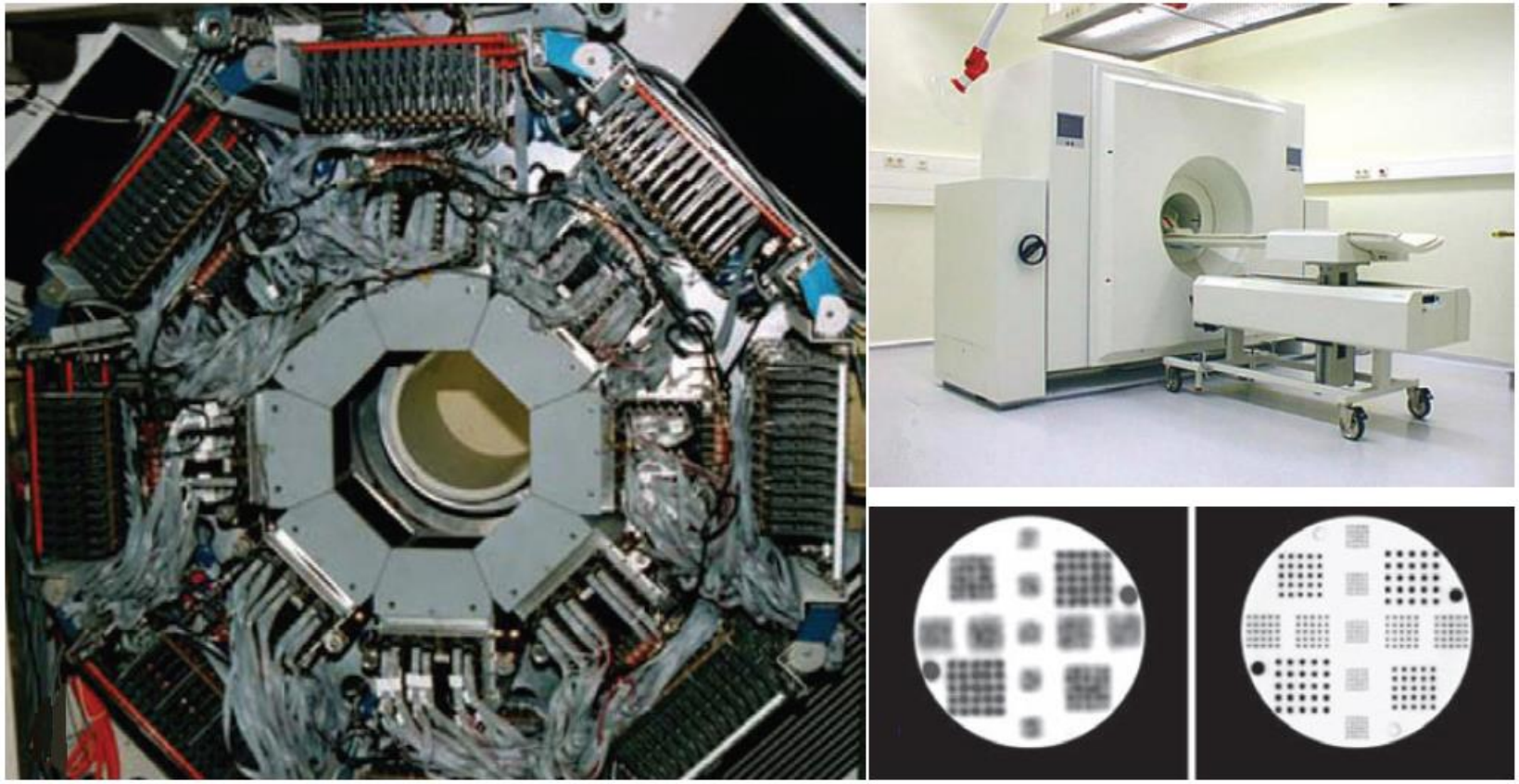
- Improve spatial resolution by decreasing element dimension
- Increase number of detector along the axial view to have long-axial FOV (LAFOV)
- Improve detectors and electronics to improve TOF

PET design: special designs

Special designs of PET are available, e.g. for brain imaging and preclinical studies (small animals)

- Small ring diameter: 47 cm
  - Improves geometric efficiency
  - Reduces non-collinearity effects
- Small detector elements: 2.1x2.1 mm^2
- 8 detector panels arranged around the head of the patient.
- Reconstructed (final) spatial resolution: ~2.5 mm (vs. 4–6 mm of clinical PET).

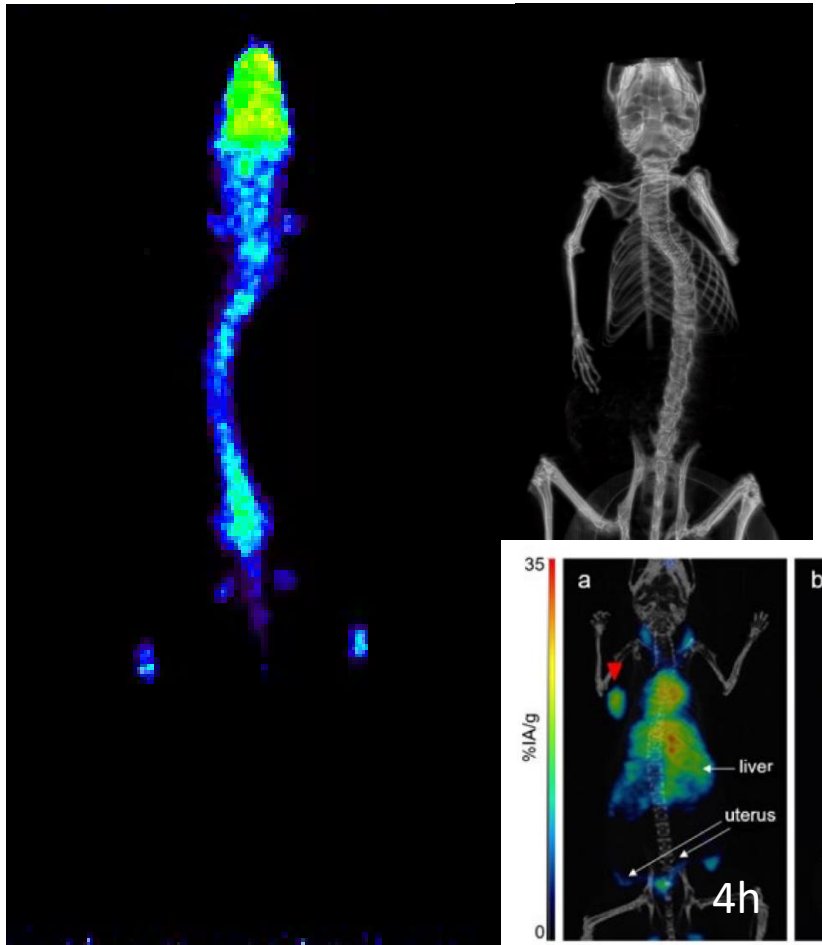
Brain imaging example

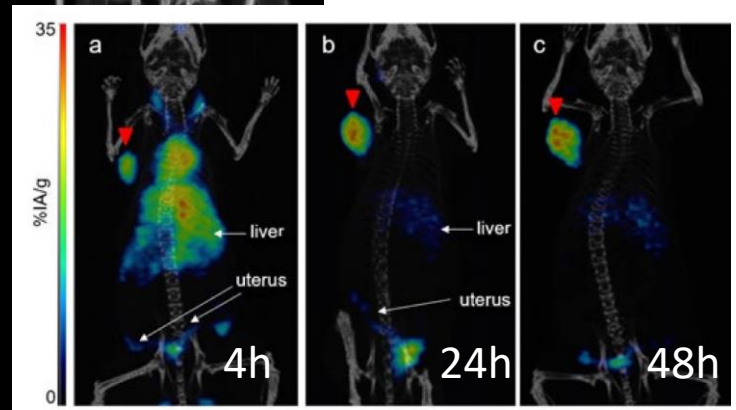


PET design: special designs

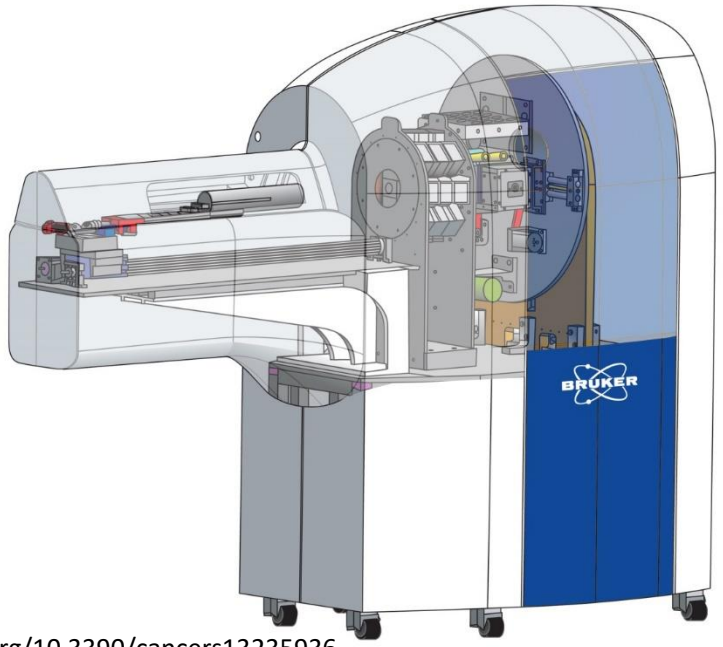
Special designs of PET are available, e.g. for brain imaging and preclinical studies (small animals)

Small animal PET (+ SPECT + CT)





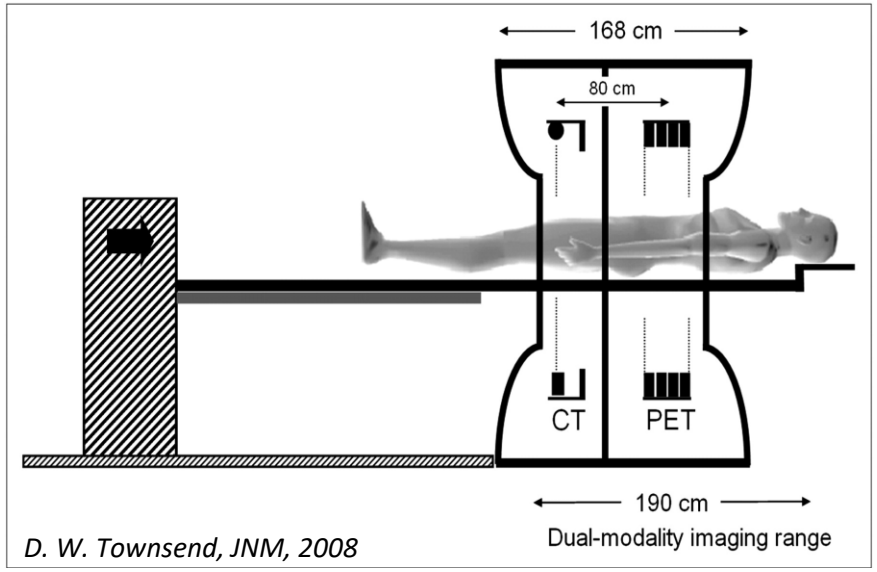
- PET spatial resolution ~ 1.5 mm
- Reduced impact of non-collinearity
- Very small detector elements (1-2 mm) and also thin (10-15 mm) to reduce DOI



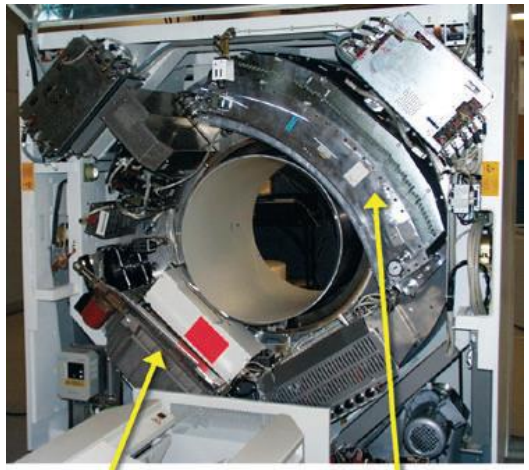
From Delage et al. https://doi.org/10.3390/cancers13235936

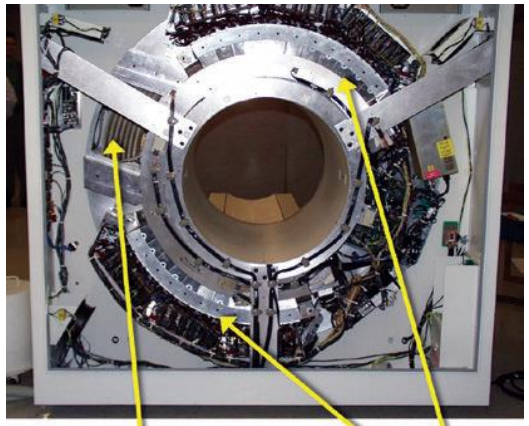
PET design: PET/CT

- **Goal** : improve activity localization and implement attenuation correction (auto-registration of anatomic CT and functional PET)

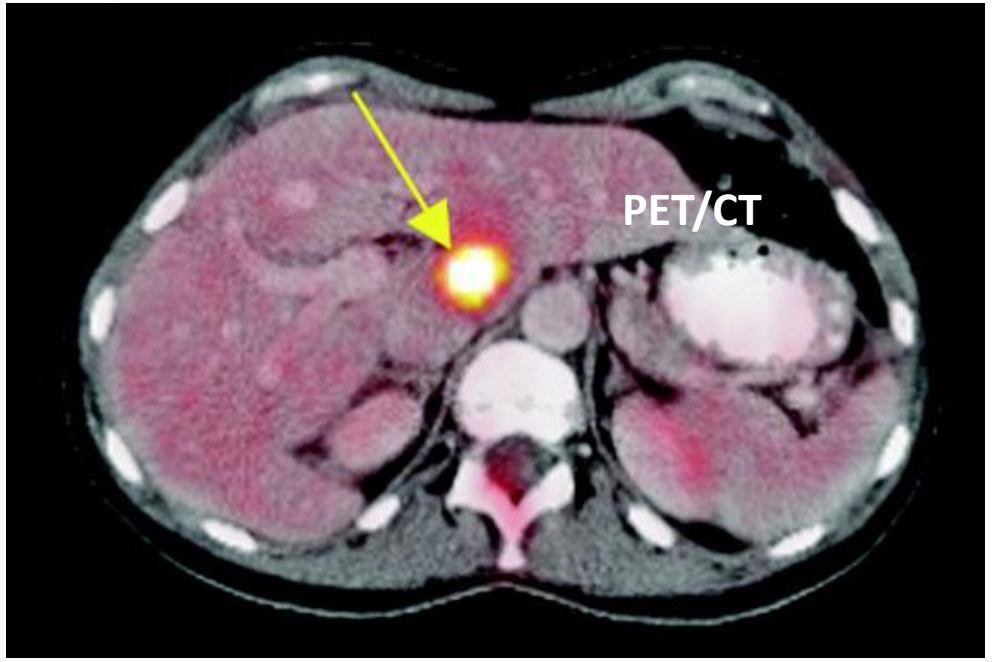


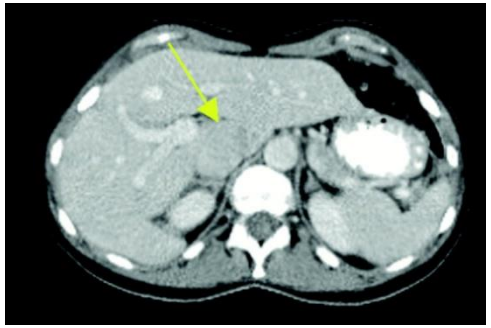
D. W. Townsend, JNM, 2008

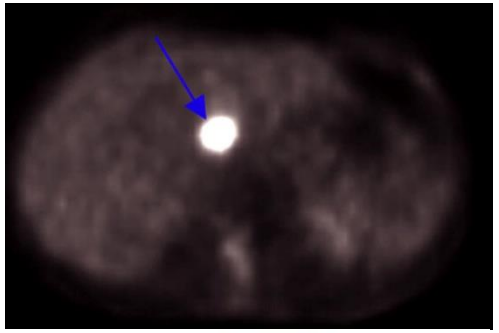


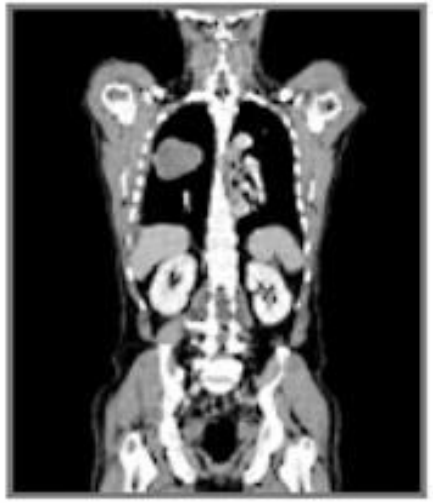


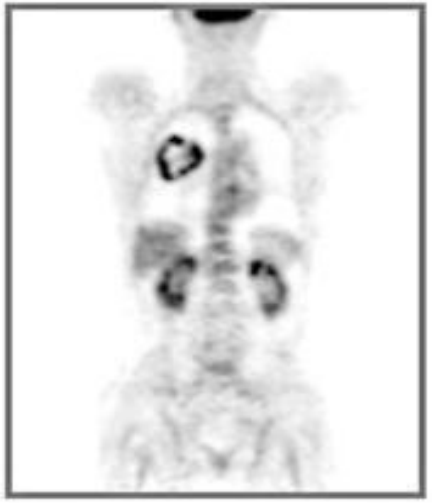
PET design: PET/CT

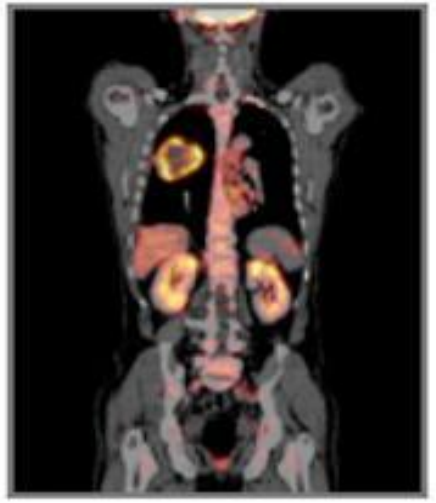












PET design: analog vs digital

Some commercially available devices

Digital:

Philips Vereos

TOF : 310 ps
Axial extension :164 mm
NEMA sensitivity : 5.7 kcps/MBq
TOF eff. sensitivity : 22 kcps/MBq

GE Discovery MI

TOF : 370 ps
Axial ring extension: 200mm
NEMA sensitivity : 13.5 kps/MBq
TOF eff. sensitivity : 48 kcps/MBq

Siemens Biograph Vision

TOF : 250 ps
Axial ring extension: 248mm
NEMA sensitivity : 15 kcps/MBq
TOF eff. sensitivity : 84 kcps/MBq

Analog:

GE Discovery 690

TOF : 540 ps
Axial ring extension: 153 mm
NEMA sensitivity : 7.5 kcps/MBq
TOF eff. sensitivity : 19 kcps/MBq

Spatial resolution (F-18) ~4 mm

- For most diagnostic examinations, activity administered to patient in NM depends on the patient mass.
- Activity can be ≠ depending on the system performances and particular situations, but some reference values are provided by the **Diagnostic Reference Levels (DRL).**
- Defined by the Federal Office of Public Health.
- DLR: 75 percentile of the dose indicator distribution for a given examination (e.g. CT) or median value (injected activity).

Tableau 1.1 Niveaux de référence diagnostiques lors d'examens de médecine nucléaire chez les adultes

Examen	Nucléide	Produit radiopharmaceutique	NRD (activite) (median)		CT Absorption/Localisation NRD (75e percentile)		Dose effective E_{50} due au produit radiopharmaceutique
			pour 70 kg [MBq]	par poids [MBq/kg]	$CTDI_{vol}$ [mGy]	DLP [mGy·cm]	[mSv]
Système osseux	Tc-99m	DPD (Teceos), MDP (Lenoscint), HDP	700	10,0	10 (bassin) 5 (CV) 5 (extr.)	410 (bassin) 190 (CV) 160 (extr)	4,0
Thyroïde	I-123	Iodure	10		4	160	2,2[1]
Tumeur (TEP)	F-18	FDG (2D)	350	5,0	5 (corps entier) 6 (tronc)	760 (corps entier) 620 (tronc)	
	F-18	FDG (3D)	250	3,5			4,8

Figure 7 : Représentation schématique visant à déterminer les niveaux de référence diagnostiques

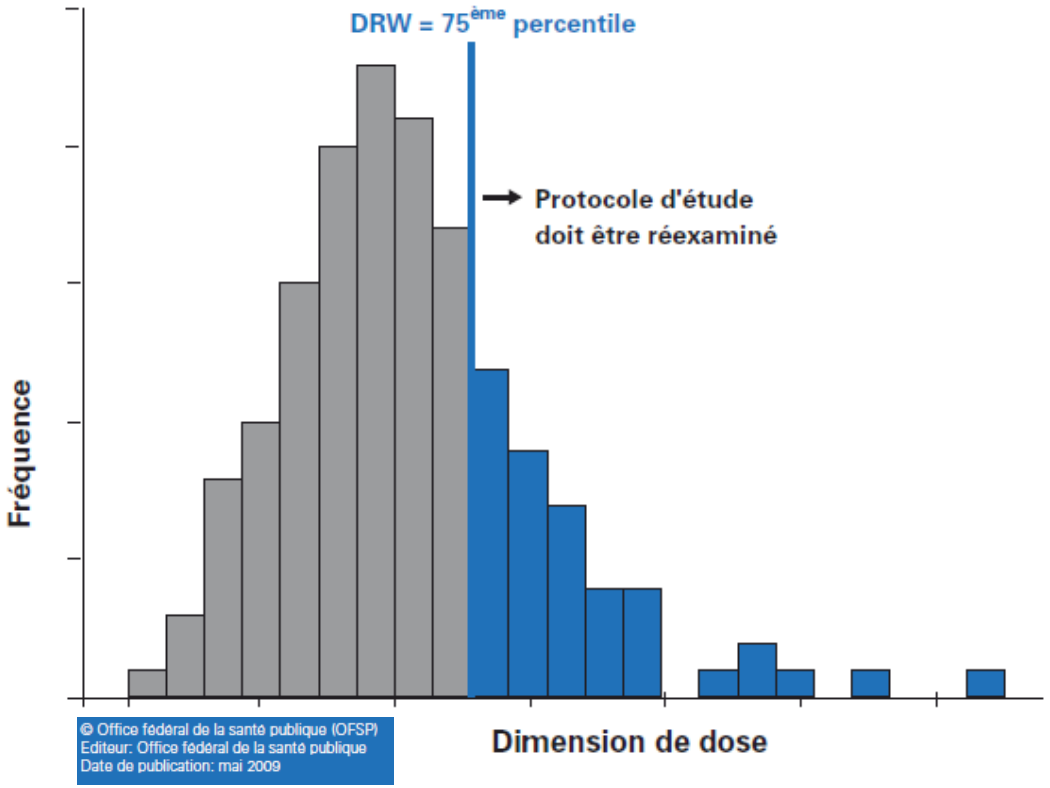


Image quality in NM also depends on the image statistics, hence the product of the acquisition time and the patient administered activity:

Time x mass-activity product (TAP)

PET design: analog vs digital

Some commercially available devices

clinical acquisition / reconstruction parameters

$$SNR \propto \sqrt{N_{photons}}$$

$$N_{photons} \propto \mathbf{duration}_{acquisition} \cdot \mathbf{activity}_{injected}$$

Philips Vereos

Admin. A : 2 MBq/kg
Time per bed position: 90 s
TAP = 3 min.MBq/kg
OSEM param: 3it × 15ss TOF+PSF
Image smoothing: NONE
Image matrix: 288×288
Pixel size: 2×2×2 mm

GE Discovery MI

Admin. A : 2.5 MBq/kg
Time per bed position: 90 s
TAP = 3.75 min.MBq/kg
OSEM param: 3it × 16ss TOF+PSF
Image smoothing: Gaussian 6.4mm
Image matrix: 256×256
Pixel size: 2.73×2.73×2.79 mm

Siemens Biograph Vision

Admin. A : 2 MBq/kg
Time per bed position: 120 s
TAP = 4 min.MBq/kg
OSEM param: 3it × 5ss TOF+PSF
Image smoothing: NONE
Image matrix: 440×440
Pixel size: 1.65×1.65×2 mm

GE Discovery 690

Admin. A : 3.5 MBq/kg
Time per bed position: 90 s
TAP = 5.25 min.MBq/kg
OSEM param: 3it × 16ss TOF+PSF
Image smoothing: Gaussian 5mm
Image matrix: 256×256
Pixel size: 2.73×2.73×3.27 mm

TAP =
time activity product

PET data acquisition: 2D vs 3D

2D = old design

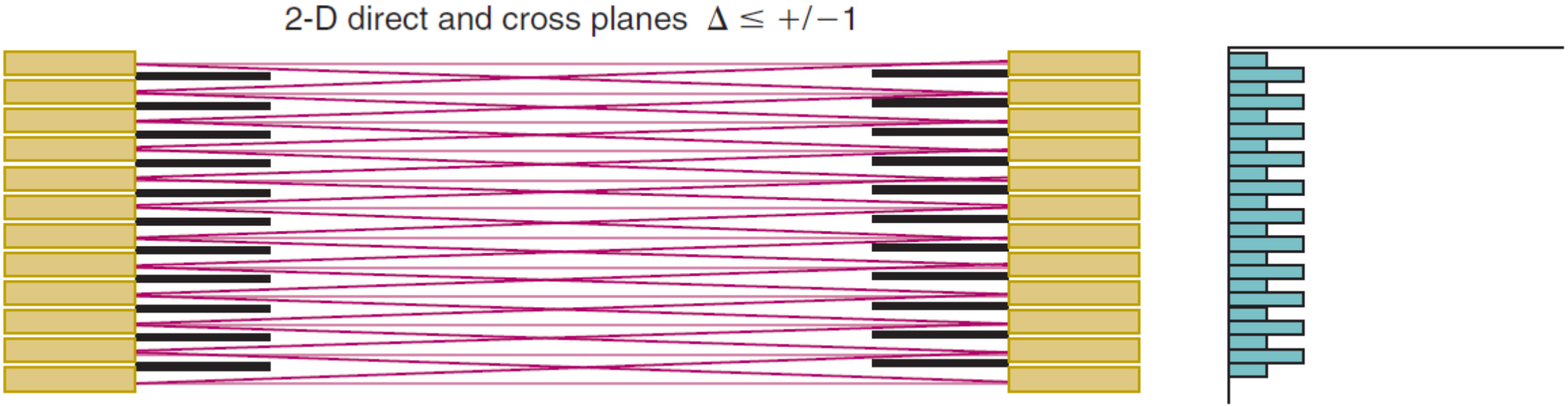
2D data acquisition (direct planes):

- Each ring of detectors is «isolated» from the others, thanks to the presence of septa.
- Septa allow to efficiently reject photons that scattered within the body.
- Septa reduce single-channel count rate, thus reducing random coincidence rate and dead time losses.
- Each detector crystal only sees events coming from a single slice → ~ to SPECT γ camera → tomographic reconstruction techniques apply *(cf. previous courses)*
- By using multiple (separated) rings and moving transaxially the patient within the scanner → 3D images

PET data acquisition: 2D vs 3D

2D data acquisition (cross planes):

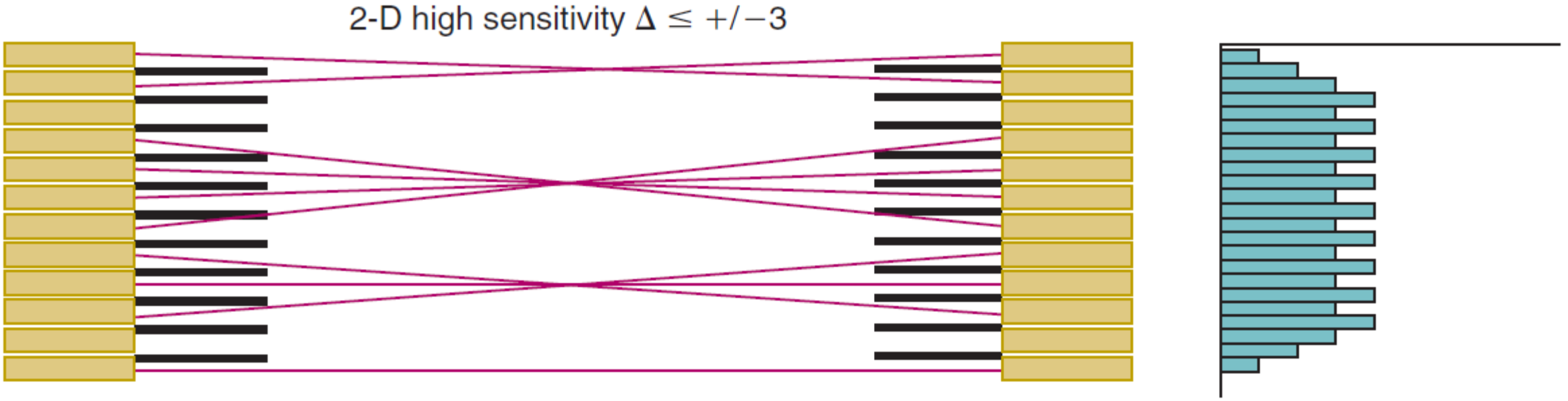
- Ring scanner (even with septa) can also acquire data from adjacent rings. So, in addition to direct planes, each crystal element can see more events than the ones allowed only by direct planes.
- Cross planes receive data from two lines of response → increased sensitivity wrt direct planes only.
- Coincidence events between adjacent rings are combined into a sinogram, as if the cross-plane data were acquired by a virtual ring shifted by half the detector width.
- The cross plane is considered to be parallel to the direct planes, even if the LORs are slightly oblique.
- Inclusion of cross planes ↑ axial sampling and sensitivity, but ↓ spatial resolution in the axial direction.



PET data acquisition: 2D vs 3D

2D data acquisition (cross planes):

- Ring scanner (even with septa) can also acquire data from adjacent rings. So, in addition to direct planes, each crystal element can see more events than the ones allowed only by direct planes.
- Cross planes receive data from two lines of response → increased sensitivity wrt direct planes only.
- Coincidence events between adjacent rings are combined into a sinogram, as if the cross-plane data were acquired by a virtual ring shifted by half the detector width.
- The cross plane is considered to be parallel to the direct planes, even if the LORs are slightly oblique.
- Inclusion of cross planes ↑ axial sampling and sensitivity, but ↓ spatial resolution in the axial direction.

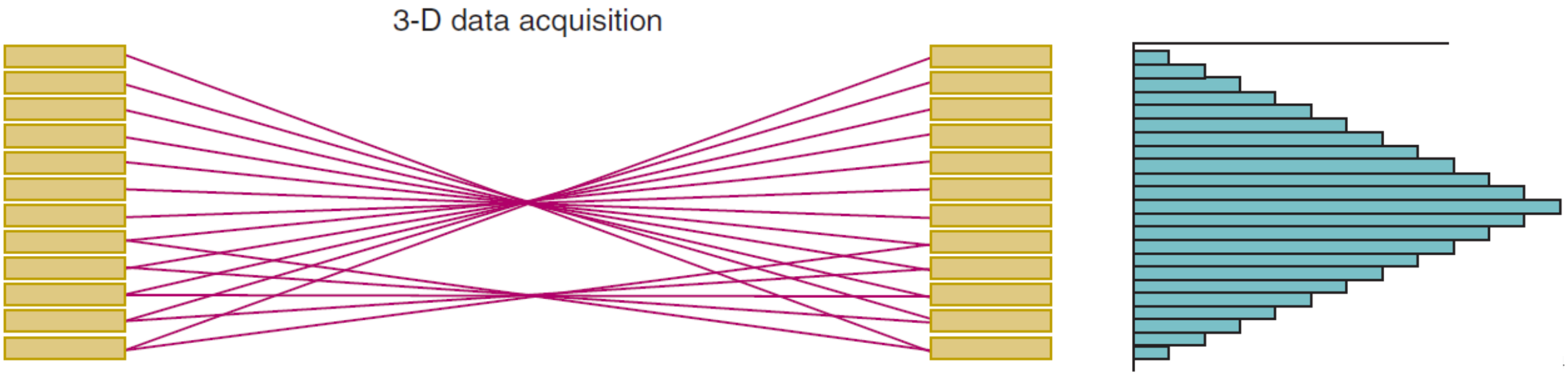


PET data acquisition: 2D vs 3D

3D = current design

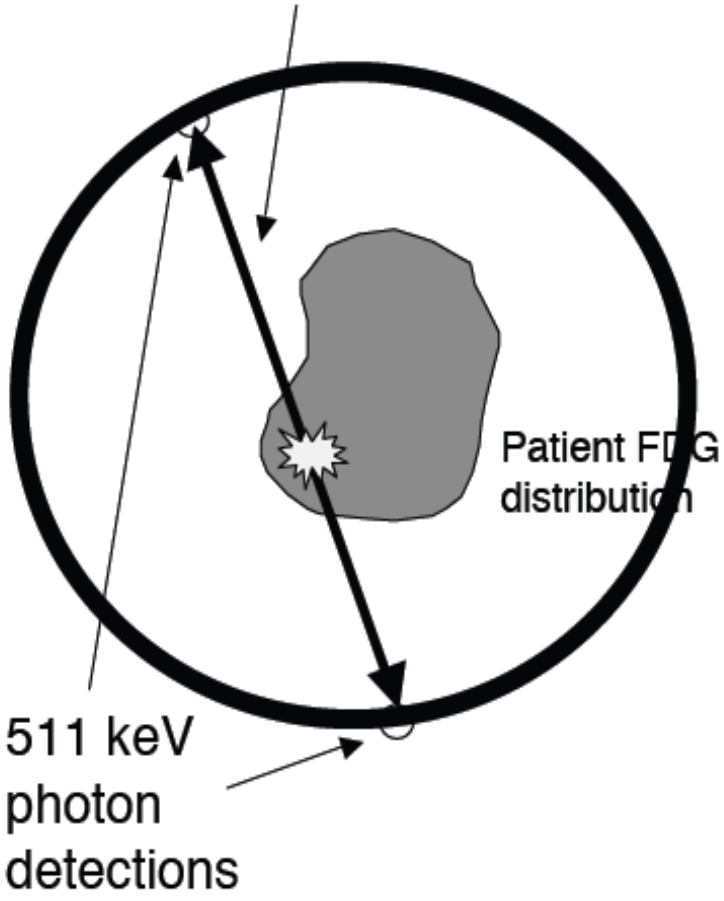
3D data acquisition:

- Multi 2D slices reject photons that cross multiple rings (2 or 3).
- Waste of signal, since true coincidences can be absorbed by the septa and thus missed.
- In 3D acquisition, intersepta are removed : coincidences coming from all LOR are accepted.
- Massive increase in sensitivity (x4-x8), but scattered coincidences ↑ along with true counting rates.
- Important to place the structure of interest as close as possible to the centre of the axial FOV.



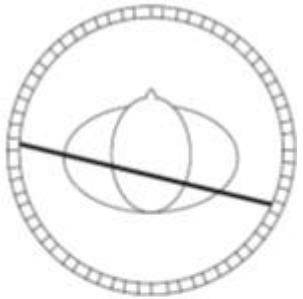
PET data acquisition & reconstruction

The number of events detected along an (LOR) is proportional to the integral of activity (i.e. FDG concentration) along that line.

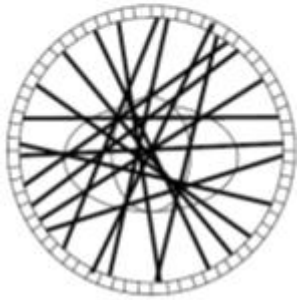


PET data acquisition & reconstruction

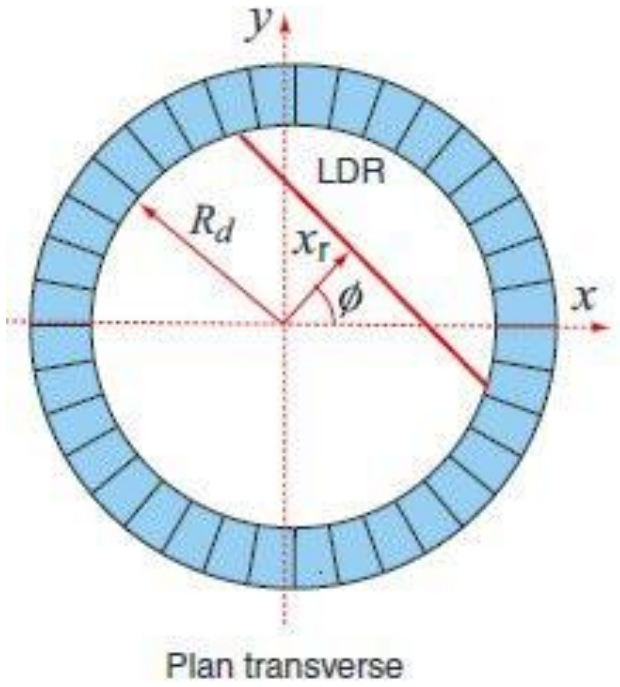
- Sinograms are constructed from collections of parallel LOR.
- x_r is the perpendicular distance of the LOR from the centre of the FOV.
- ϕ is the angle subtended by x_r.
- Sinograms are acquired also at different angles θ (adjacent rings).

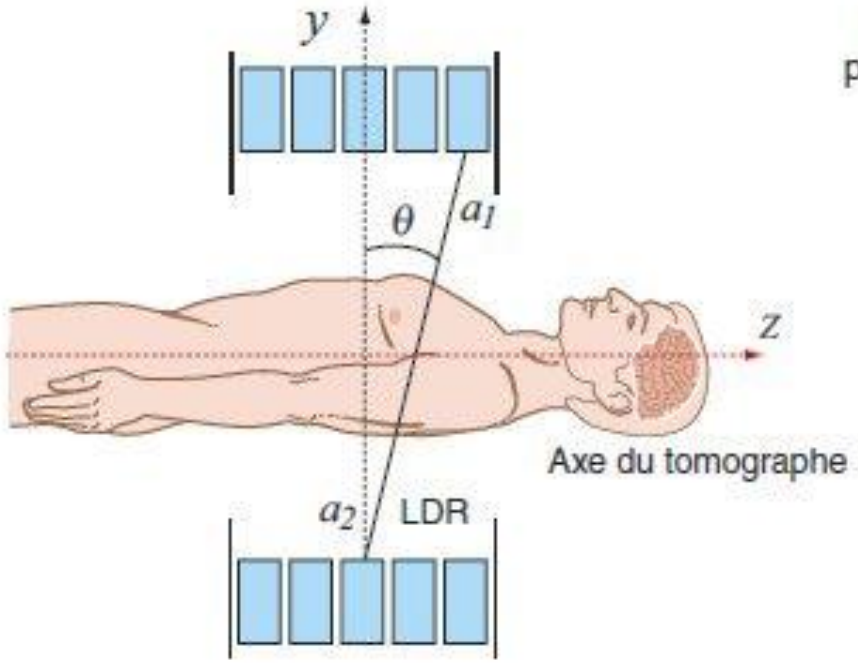


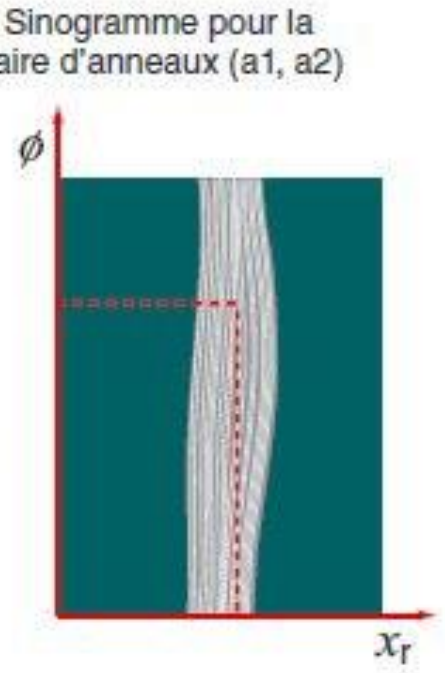
- 1 LOR (one detected coincidence)
  - The annihilation happened somewhere along the LOR.
  - No direct localisation (in absence of TOF).



- Many LORs
  - The activity distribution can be obtained from tomographic reconstruction techniques.

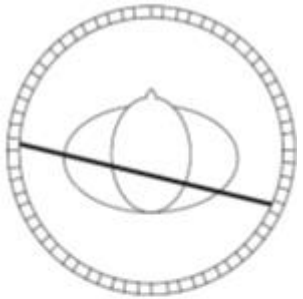




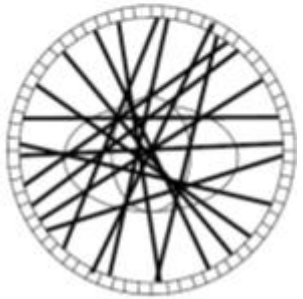


PET data acquisition & reconstruction

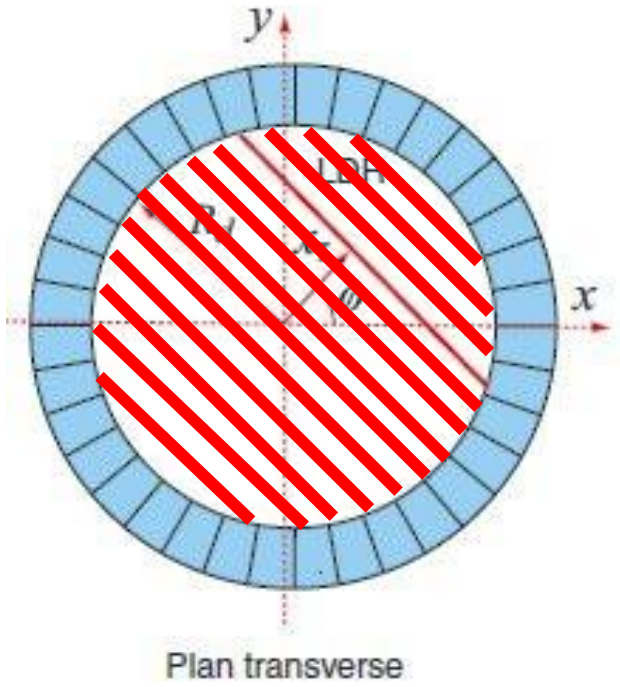
- Sinograms are constructed from collections of parallel LOR.
- x_r is the perpendicular distance of the LOR from the centre of the FOV.
- ϕ is the angle subtended by x_r.
- Sinograms are acquired also at different angles θ (adjacent rings).

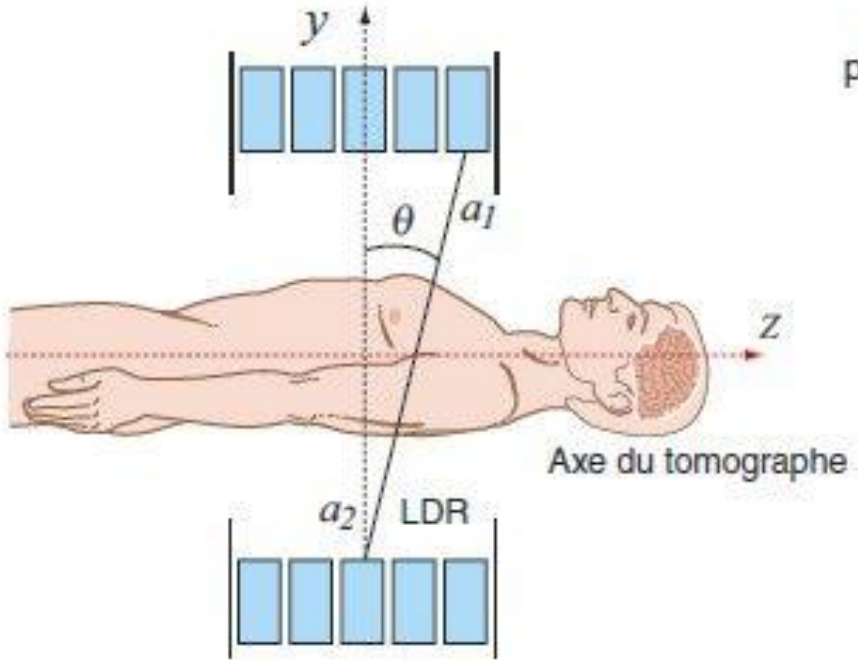


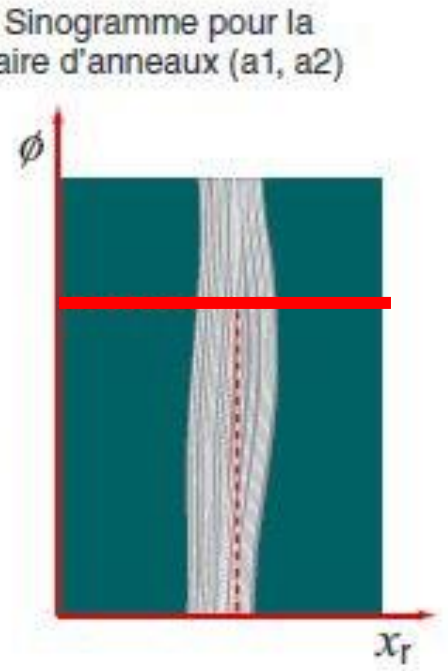
- 1 LOR (one detected coincidence)
  - The annihilation happened somewhere along the LOR.
  - No direct localisation (in absence of TOF).



- Many LORs
  - The activity distribution can be obtained from tomographic reconstruction techniques.

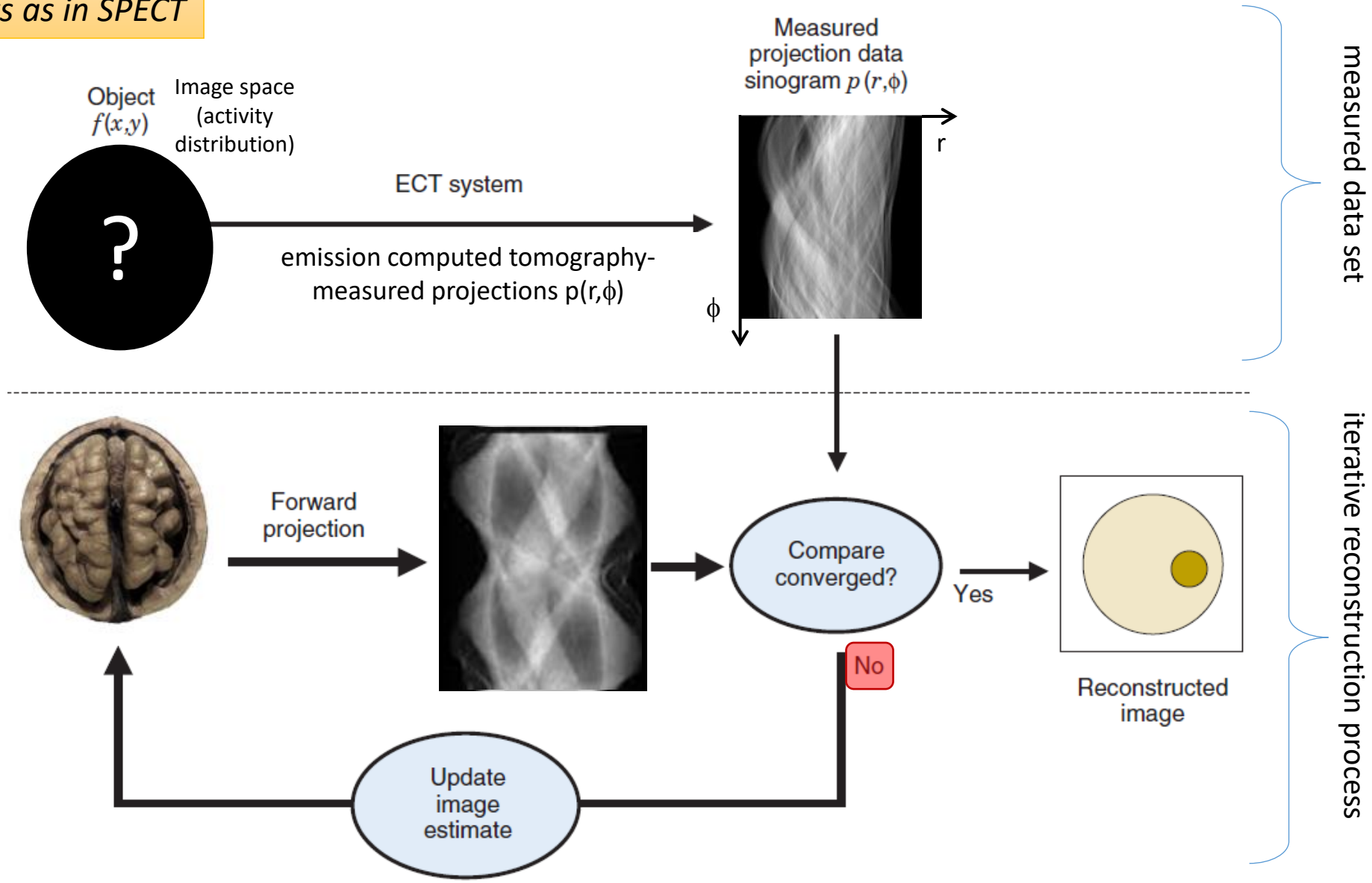






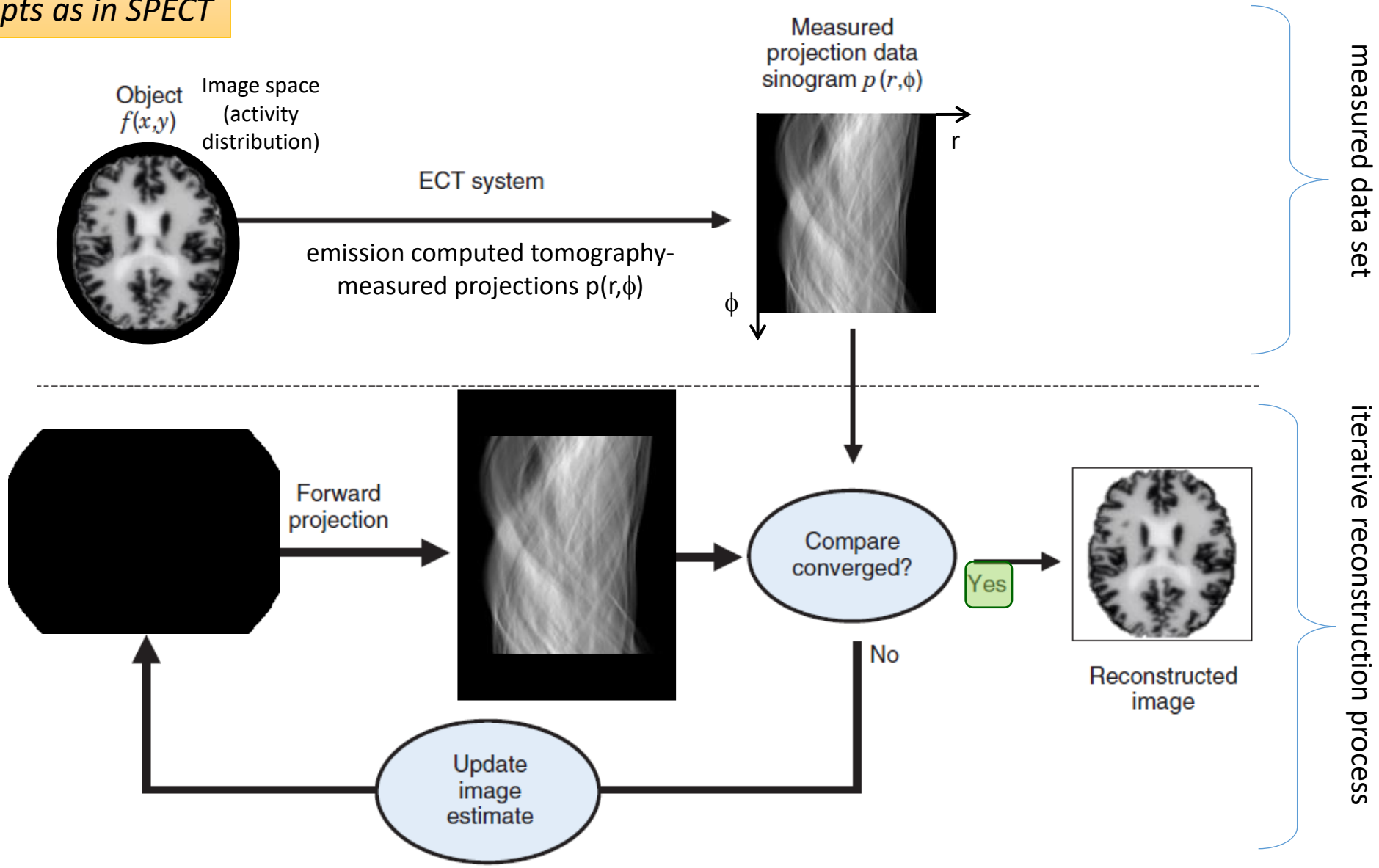
PET data acquisition & reconstruction

same concepts as in SPECT



PET data acquisition & reconstruction

same concepts as in SPECT



Animations from:
Floris HP van Velden, PhD

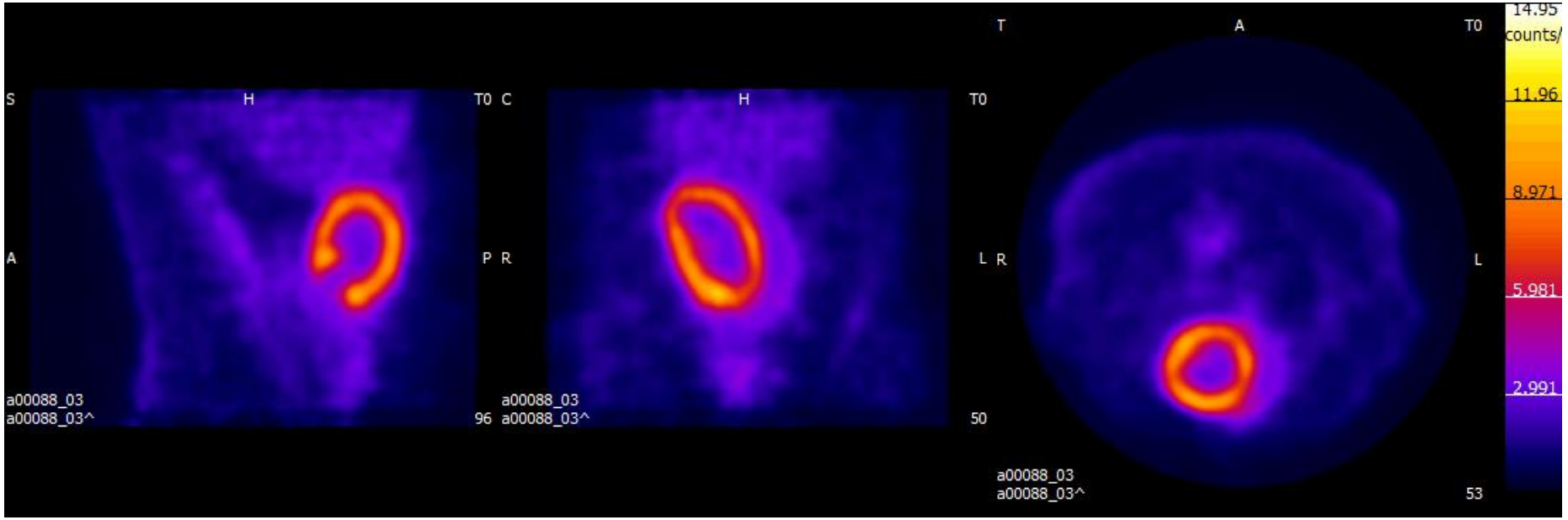
PET data acquisition : dynamic studies

- 3D PET can acquire projection data simultaneously for all the projection angles used for reconstruction.
- In comparison with whole-body SPECT examinations, PET are way quicker!
- Dynamic studies (i.e. follow the radiotracer distribution according to time) can be performed more quickly.
- Frame times of only few seconds are achievable!
- For some examinations (e.g. myocardial perfusion with ^{82}Rb, $T_{1/2}$= 75 s), the scan starts at injection.
- WB studies are acquired by translating the patient into the scanner.
- To improve sensitivity and reduce errors during reconstruction, bed positions are generally overlapped and the different bed positions are then put together again to form a WB image.

PET data acquisition : dynamic studies

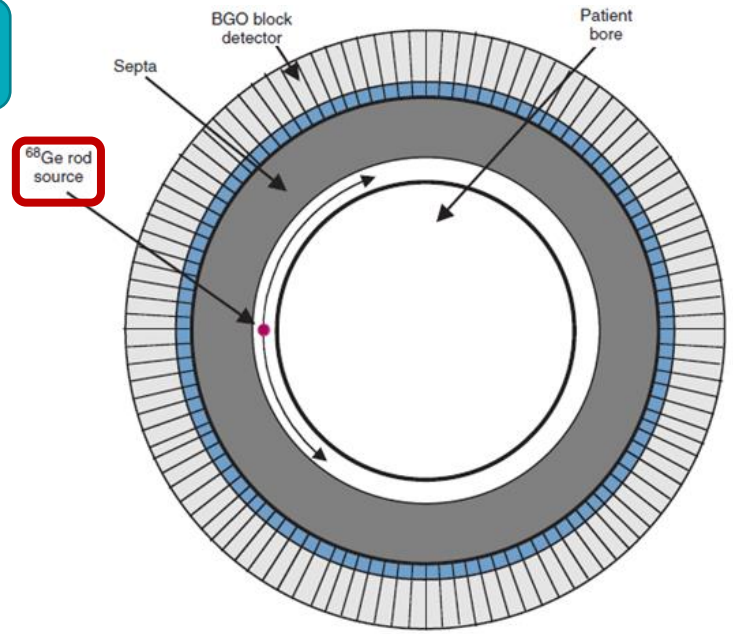
For some systems, an acquisition approach called *list-mode acquisition* is available:

- Each coincidence event and its time stamp are recorded sequentially.
- Information on each single event and the time where it occurred are thus available.
- After the scan is over, this allows to integrate events only during a selected time interval:
  - Gating (e.g. for cardiac imaging : only select time points corresponding to a particular moment in the cardiac cycle).
  - Selective removal of time points (e.g. if an unwanted patient movement occurred).
  - Reconstruction of the PET images with reduced events (less statistics) to study the performances of the imaging system (e.g. study the possibility to inject less radiotracer / perform shorter scans).



PET corrections : normalisation

Remember: *corrections are fundamental to achieve absolute activity quantification! (cf. SPECT course)*



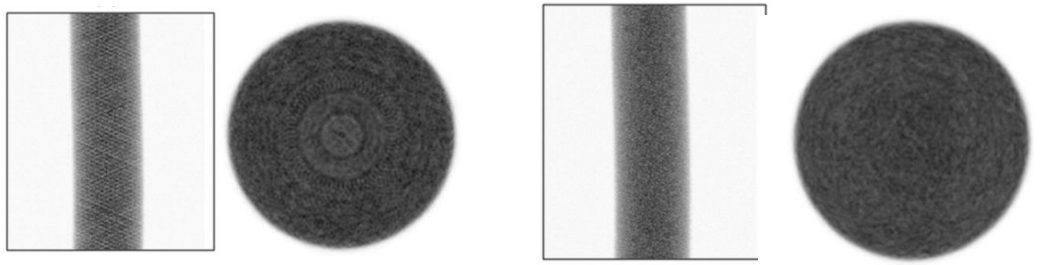
Quantification:

- Ability to correlate the intensity of the reconstructed signal to the activity (in Bq) contained in the considered volume.
- Necessary for comparing activity levels of different structures and essential for the clinical outcome of some studies.

Normalisation:

- PET scanners require corrections for non-linearity and non-uniformity *(cf. SPECT lecture)*, to prevent artefact formation → normalisation correction.
- In a typical PET: 10'000-20'000 individual detector elements: differences in size, thickness, in the coupling to the PMT, etc.
- Approach for normalisation correction: expose all detectors to the same radiation source (e.g. Ge rod source) and record their response.
- In a perfect scanner, all detectors will respond in the same fashion.
- In practice, some detector pairs will record more, some less due to efficiency ≠.

PET corrections : normalisation



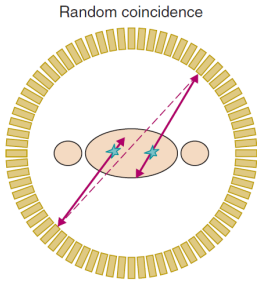
Normalisation:

- Compute a normalisation factor for detector pair *i,j* : $Norm_{i,j} = N_{i,j}/\bar{N}$
- The normalisation factor for each detector pair is then used to correct the counts acquired during a patient scan. Correction is applied to the sinogram (projection representation) prior to reconstruction.
- Normalisation should be very precise as it directly impacts the intensity in the sinogram and thus pixel values in the reconstructed image.
- Normalisation scan should have high counts to reduce statistical uncertainties, but at the same time limited count rates to mitigate dead time and pileup effects:

  → very long scans are required (several days!).

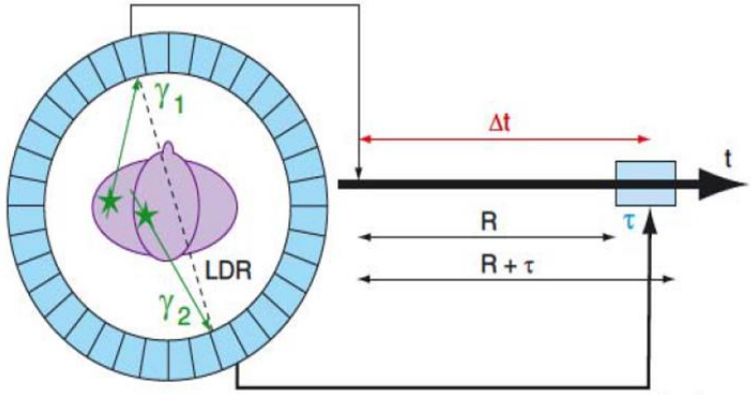
  → alternative methods exist (compute efficiency of single detector elements and then combine them to find the response of all possible detector pairs).

PET corrections : random coincidences



Correction for random coincidences:

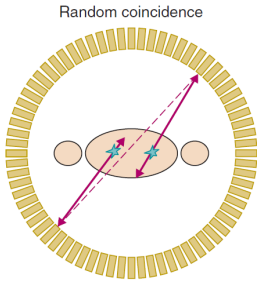
- They contribute uniformly to loss of contrast and thus bias the relation between pixel intensity and activity.
- Two methods to take them into account:

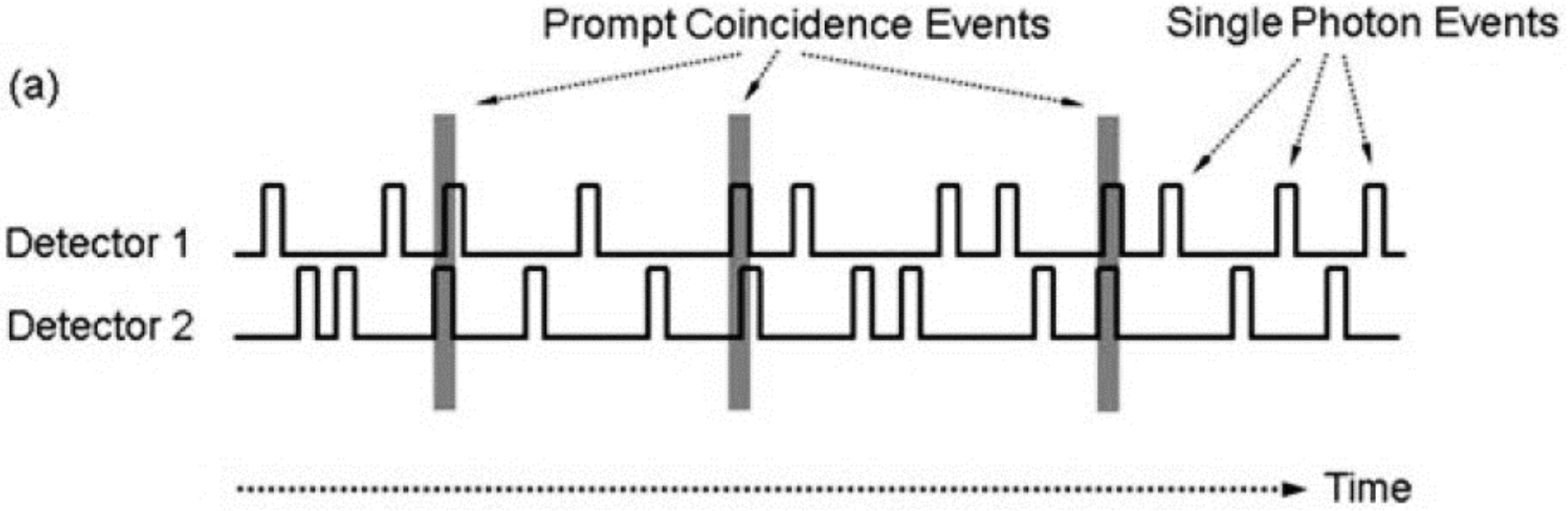


1. Delayed window method

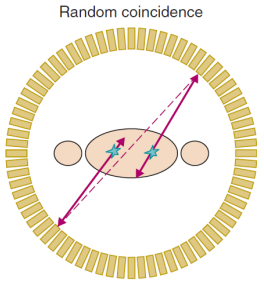
- In most scanners, each photon is recorded with an accuracy of ~2 ns.
- The system checks if any other events occurred within the coincidence timing window (~4-12 ns). If so, they are recorded as valid for the given detector pair.
- Secondary coincidence circuit: the coincidence window is *delayed* by a time that is greater than its width → no true or scattered prompt coincidences will be detected → however, random coincidences will still be detected at the same rate as for the primary circuit!
- Secondary coincidence circuit gives an idea of the *frequency of random events happening in the first* (if enough statistics if acquired).

PET corrections : random coincidences





PET corrections : random coincidences



2. Singles method:

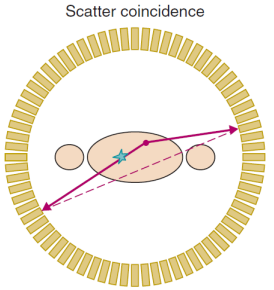
- Based on the measurement of single (not coincidence) events:
- $R_{random} = \Delta t \cdot R_{single,1} \cdot R_{single,2}$

Advantage of this method: singles count rate are higher (>1 order of magnitude) than coincidence count rates.

→ lead to random estimated with better statistics than the one provided by the delayed method.

In every case, subtraction of random counts results in increased noise in the image!

PET corrections : scatter events



Two methods:

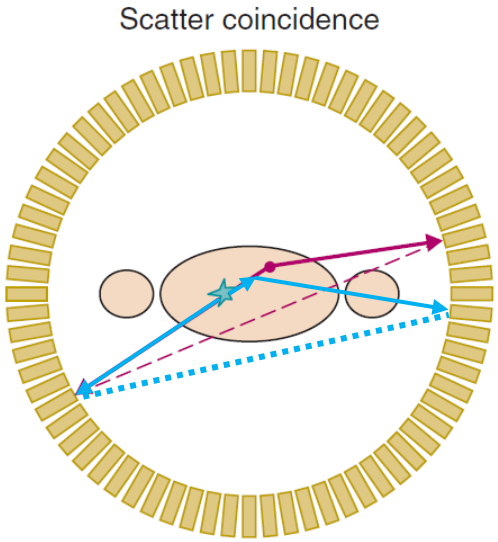
Narrowing the coincidence energy window is also possible, but usually not sufficient!

1. Use of transmission data

- Use emission image (radionuclide concentration) and transmission image (e.g. CT, reflects the attenuation coefficient of the tissue).
- Attenuation at 511 keV can be attributed to Compton scatter.
- Especially important for 3D acquisition modes.
- Possible to model physics interaction using the transmission image and estimate the contribution of scattered events (e.g. through MC simulations).
- These are removed form the projection profiles prior reconstruction.

→ Computationally expensive.

PET corrections : scatter events

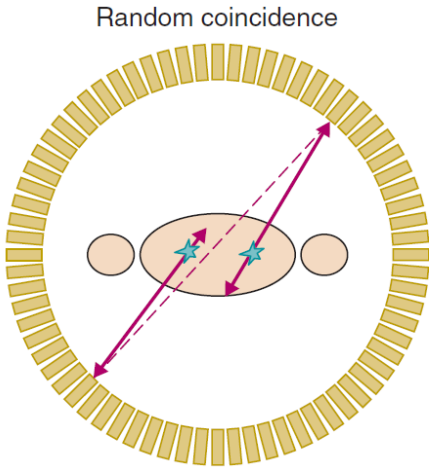


Two methods:

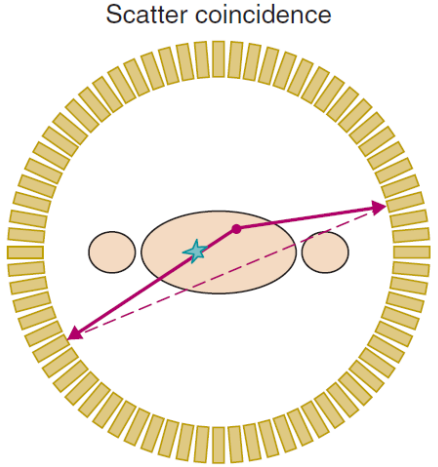
2. **Use of projection profiles just outside the object** (projection profiles that lead to activity localisation outside the patient).

- After random coincidence subtraction, such unphysical activity localisations can only be attributed to scattering.
- Analyse these profiles and derive an extrapolated scatter distribution to be applied to the totality of the projection profiles.

→ Not very precise for complex scatter distribution or when the object to be imaged covers the whole FOV, without leaving space for evident scattered projections to be acquired (e.g. prone to errors for lung images).



PET corrections: random & scatter

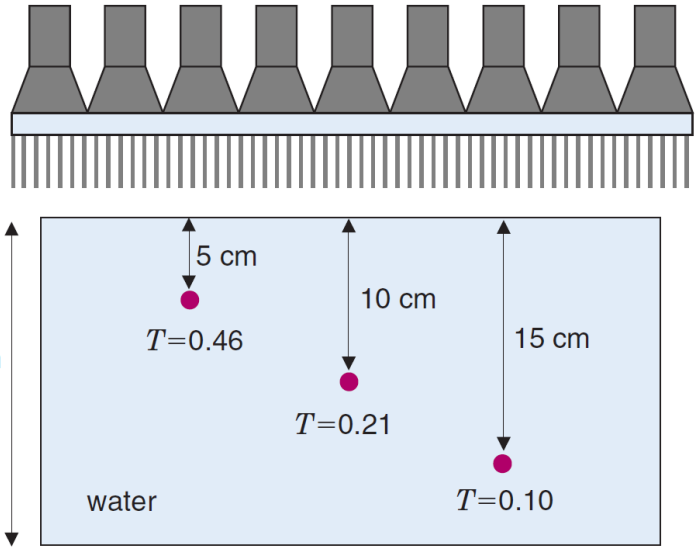


Random coincidences	Scatter coincidences
Depend on source and detector geomety	
Increase with square of activity $R_{random} = \Delta t \cdot R_{s,1} \cdot R_{s,2}$ (Δt: counting window, R: singles count rate).	Increase linearly with activity (similar to true coincidences)
Ratio between random and true coincidences can be reduced by reducing Δt (but limitations!) → influenced by temporal resolution	Come from same annihilation event (no impact on Δt) but can be discriminated (also) according to their energy → influenced by energy resolution
Ratio between unwanted and true coincidences : < 1 for brain imaging vs. >1 for abdomen. Why? Signal comining from regions outside the FOV (e.g. the bladder in the case of abdomen imaging)	
Lead to errors in localisation and in activity quantification.	

PET corrections : attenuation correction

Remember : *this also applies for SPECT !*

- **Tissue attenuation** results in depleted signal from deeper location in patient (signal recorded not proportional to total activity along the line of response!)
- $\frac{I}{I_0} = T = e^{-\mu x}$ (Beer–Lambert law)



Transmission $T = e^{-\mu x}$
for 140-keV γ rays in water, μ=0.155 cm^{-1}

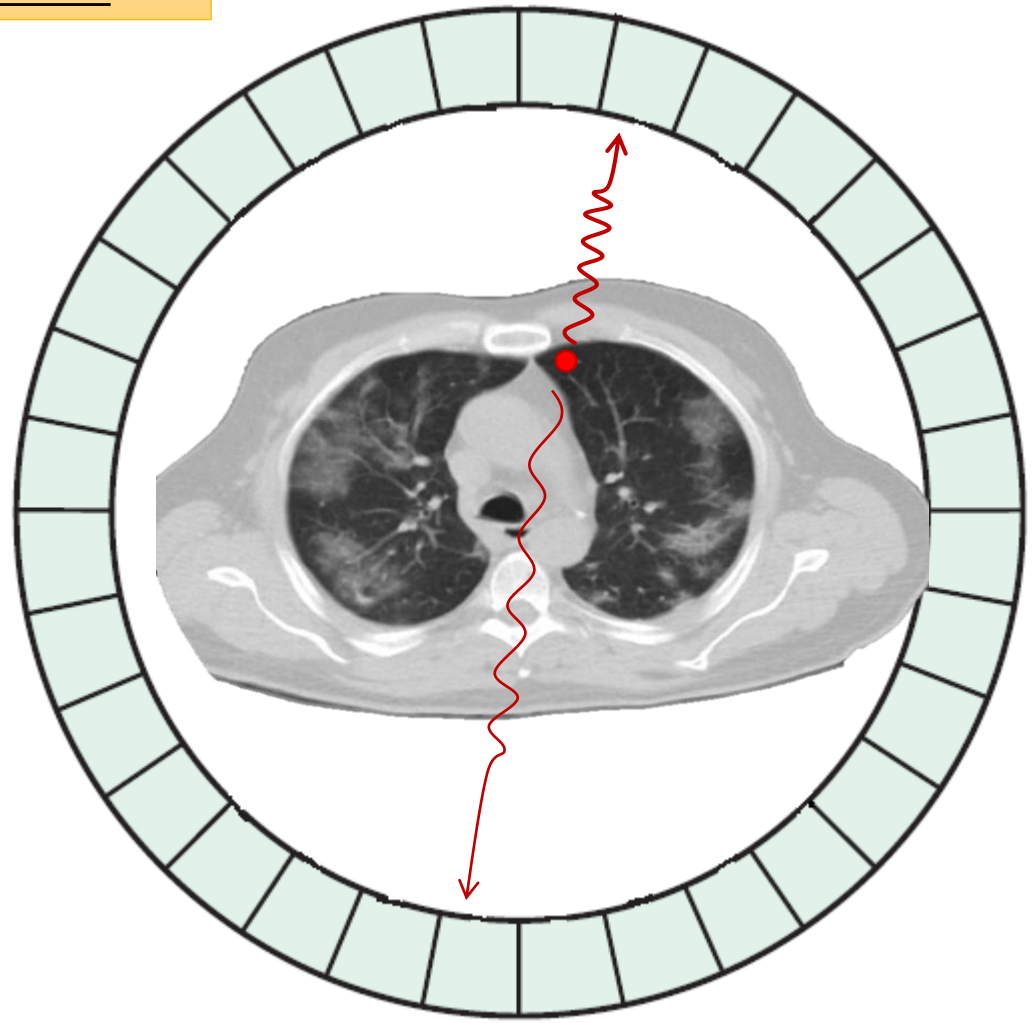
↑ gamma camera example

μ: linear attenuation coefficient **for 511 keV** (in cm^{-1})

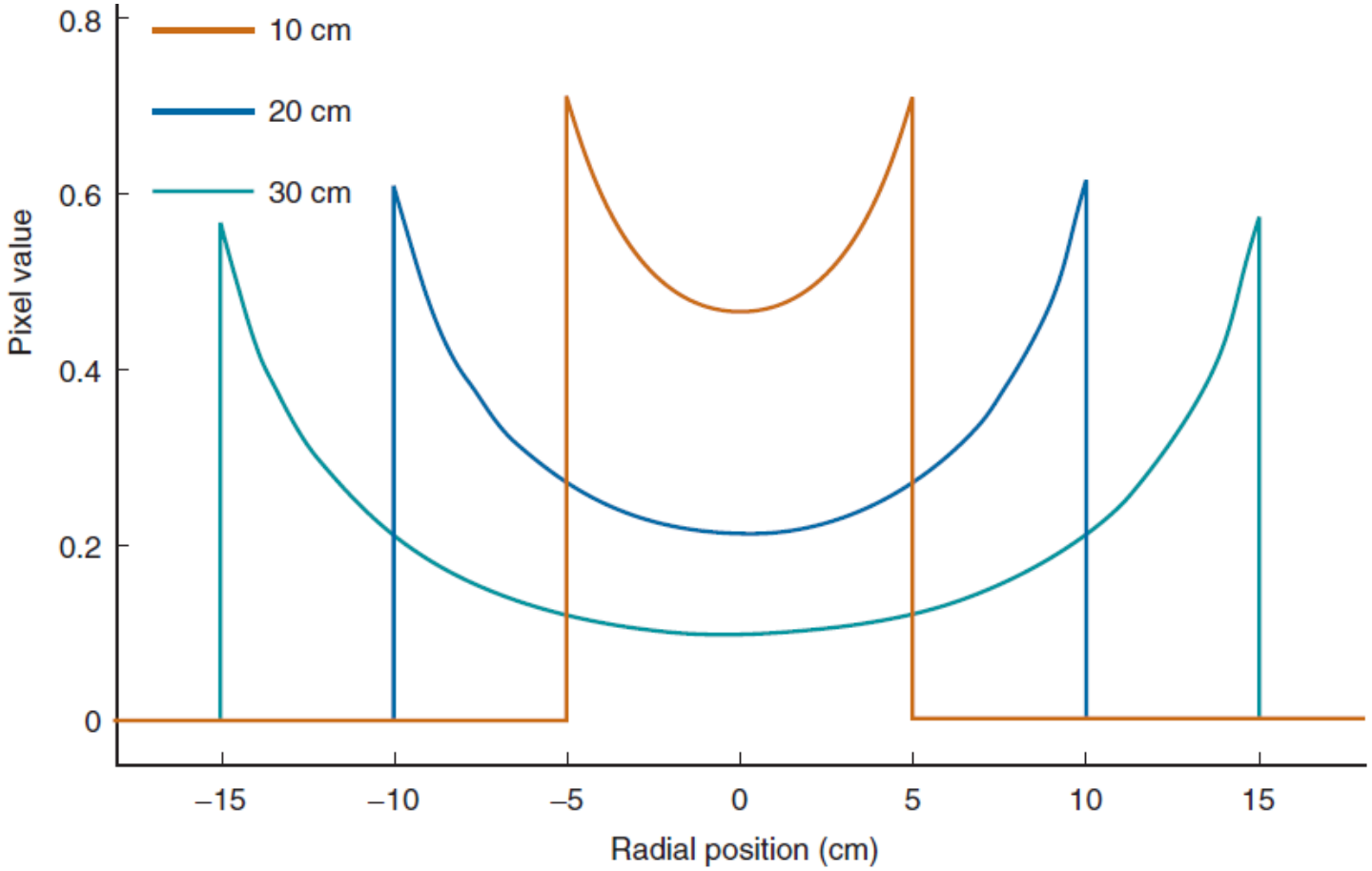
$\mu_{tissue}(511\ keV) = 0.095\ cm^{-1}$

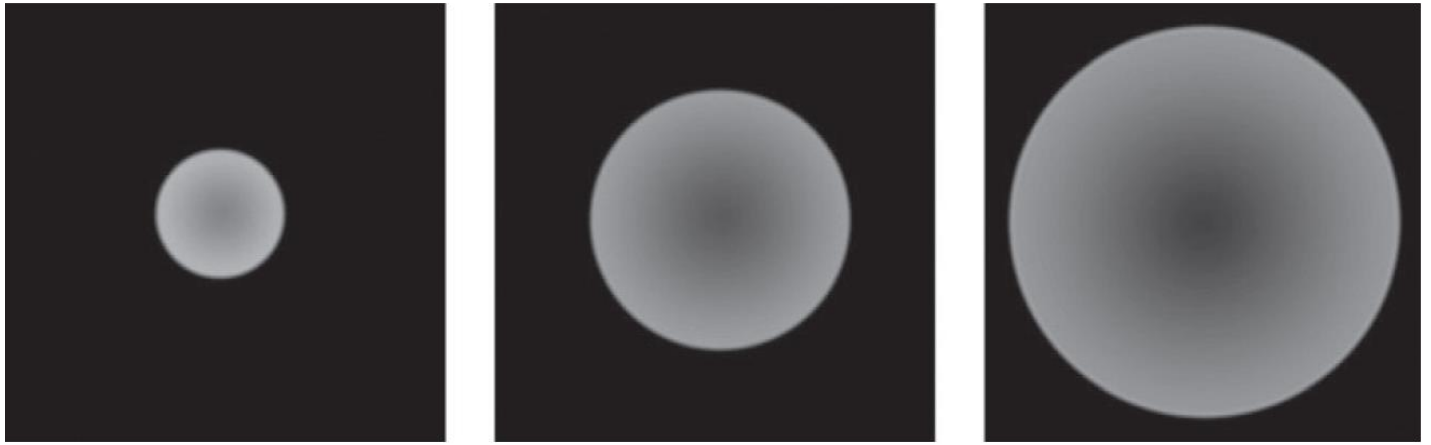
$\mu_{bone}(511\ keV) = 0.130\ cm^{-1}$

$\mu_{lung}(511\ keV) = 0.035\ cm^{-1}$



Valid for both SPECT and PET



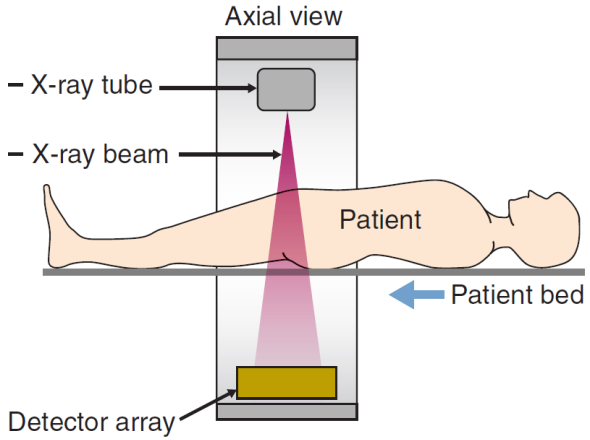


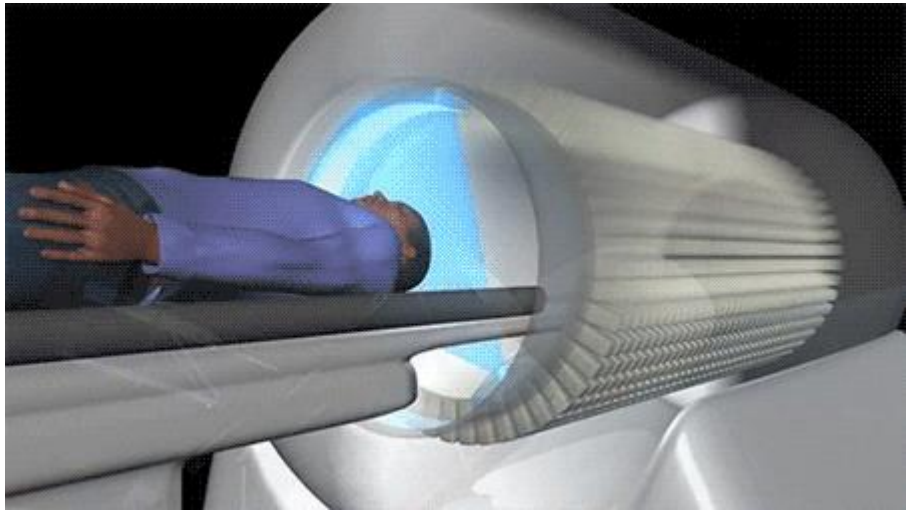
PET attenuation correction

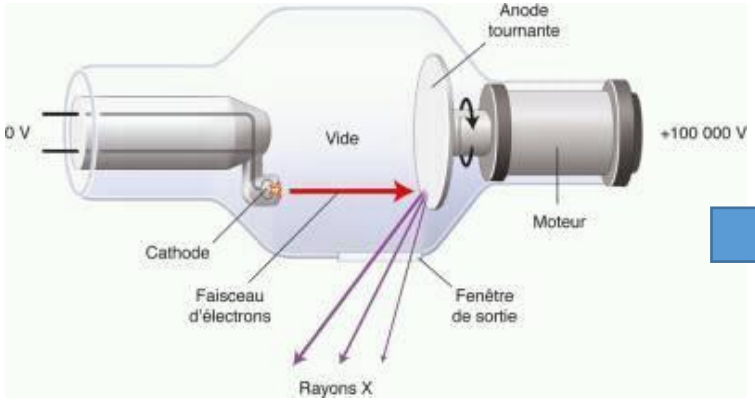
Concept : use attenuation map from CT (transmission) to apply attenuation correction (AC) on emission imaging (SPECT or PET).

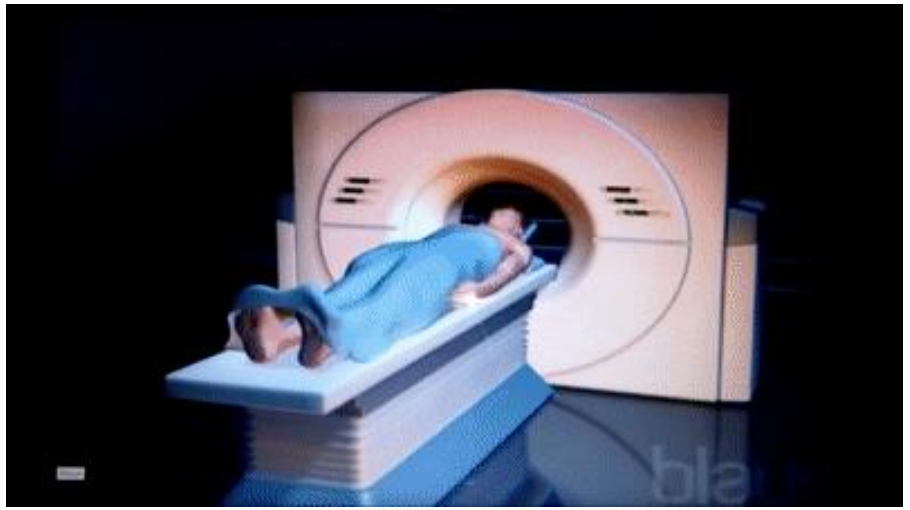
Measure attenuation from a transmission scan (hybrid systems → CT)

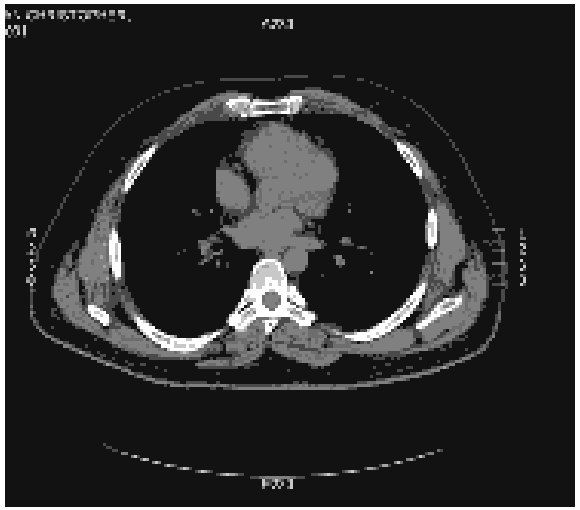
⚠ CT scans for AC are low dose ! ☢









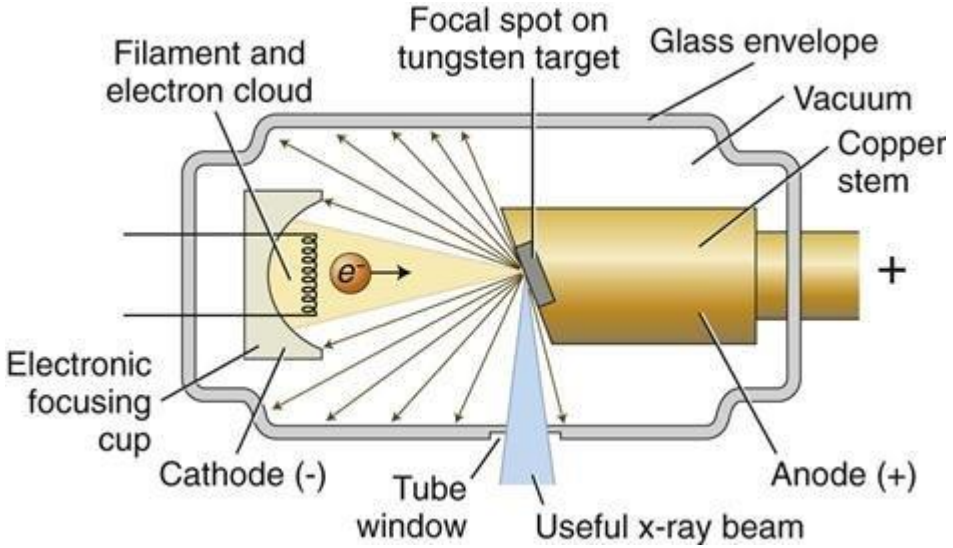


CT-AC is standard in modern hybrid system (SPECT/CT & PET/CT)

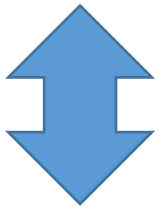
PET attenuation correction

(← little reminder, but cf. lecture on CT for more detailed infos on this imaging modality)

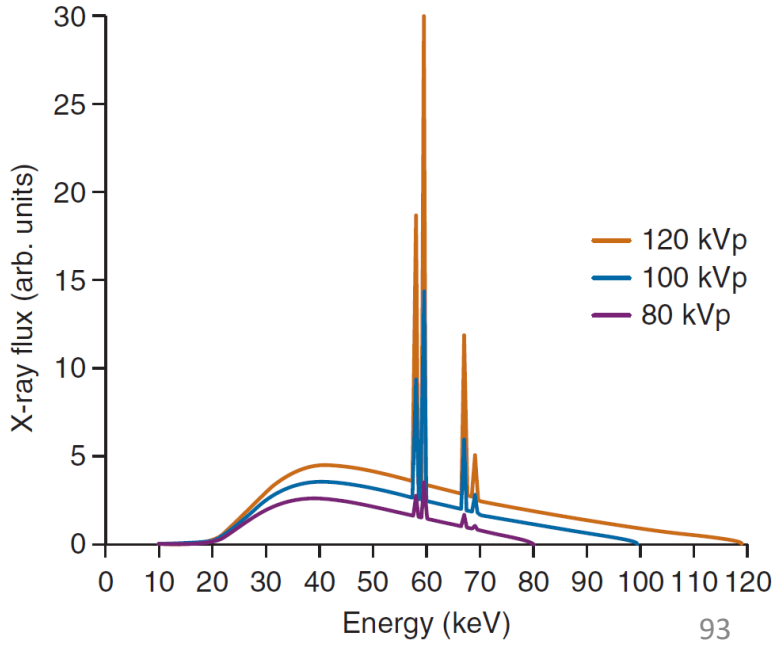
- Vacuum tube with cathode (filament heated through an electrical current).
- e- are liberated and accelerated by a bias voltage towards the anode (rotating tungsten plate).
- Production of continuous Bremmstrahlung radiation + discrete characteristic X-rays (anode material).
- Tube current → # of emitted e-



- Voltage → energy spectrum of X-rays (max =kVp) and intensity
- X-ray beam collimated and filtered.
- CT provide a map of μ



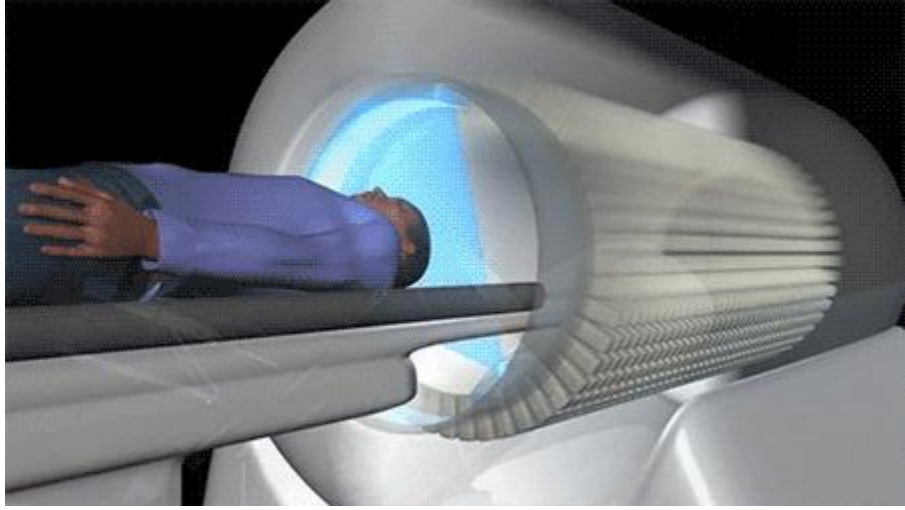
- Conversion between the map of μ acquired with the CT transmission to the energy used for emission imagining.

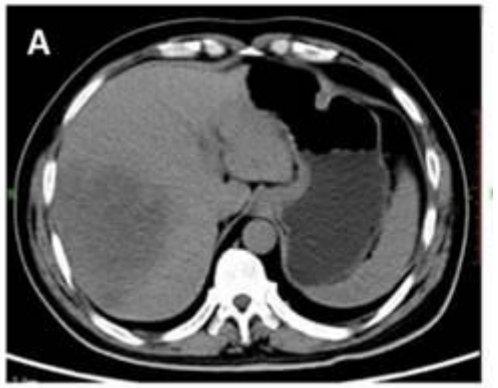


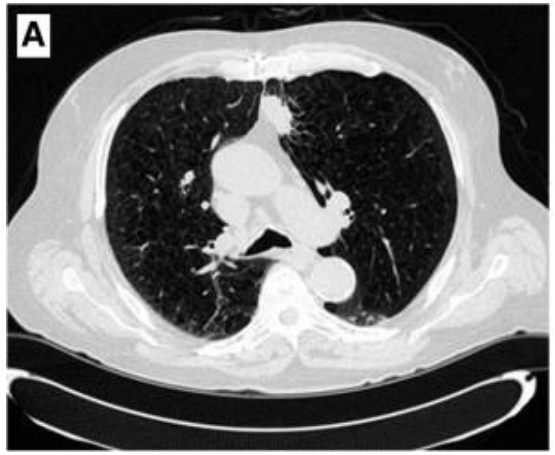
PET corrections : attenuation correction

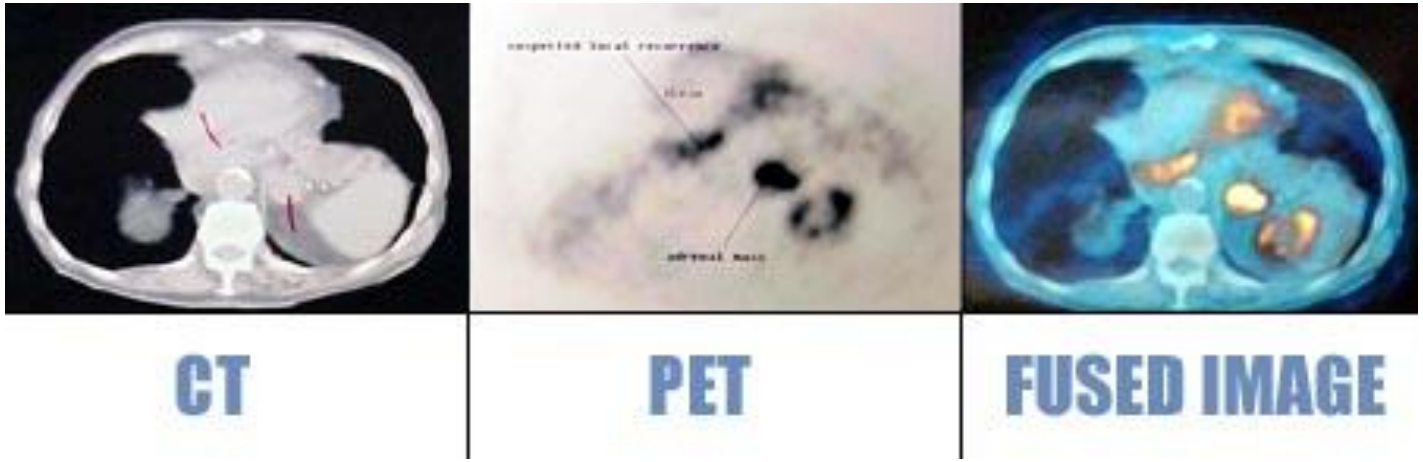
- Hybrid systems ensure good spatial and termporal correlation between tranmsission and emission imaging.

- Image fusion : merge anatomical and metabolical information !





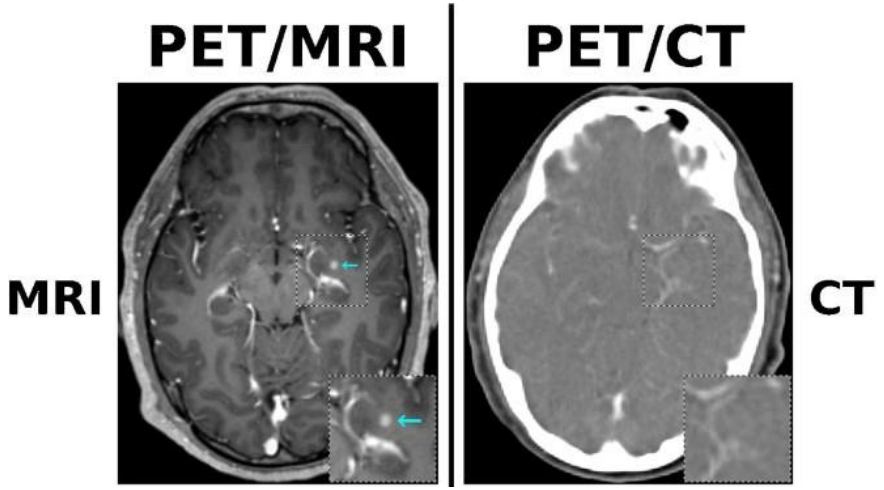


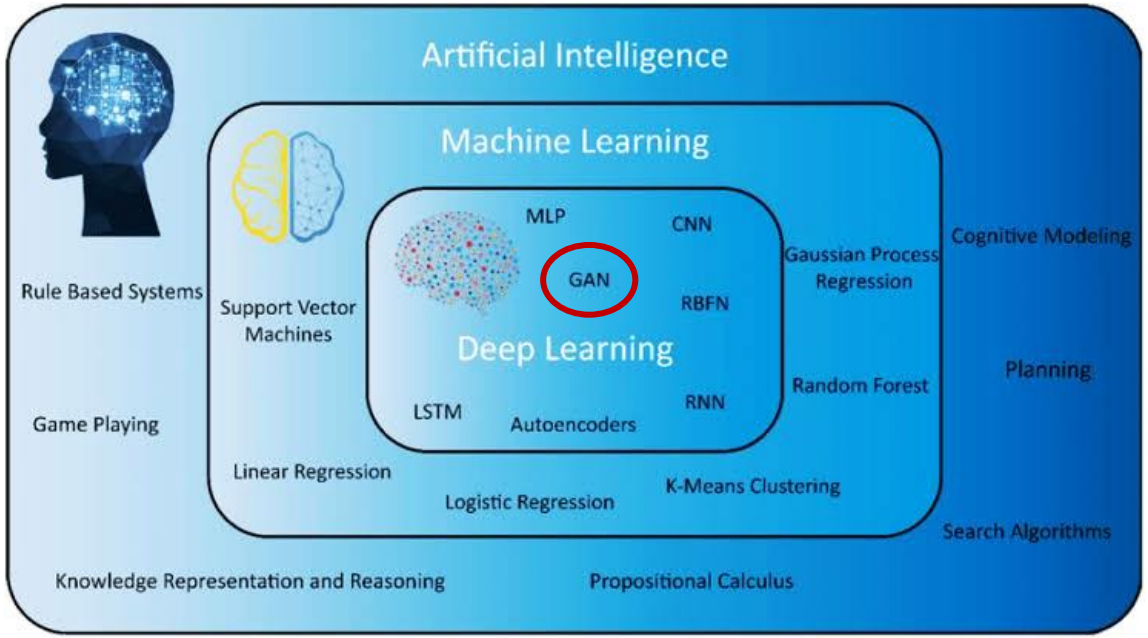


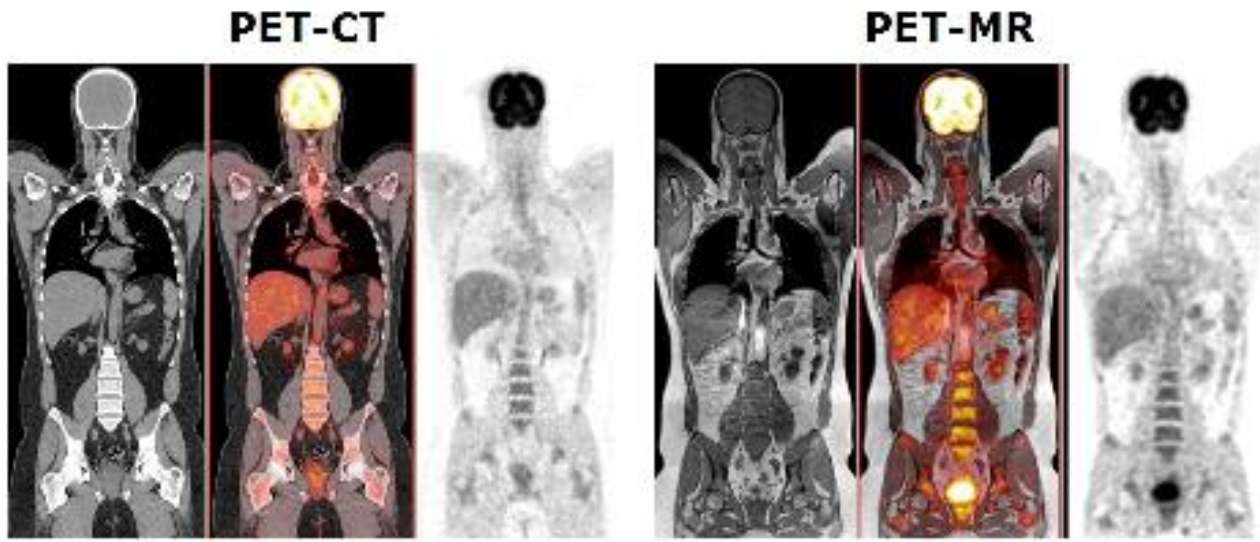
PET attenuation correction

→ *what about PET/MRI?*

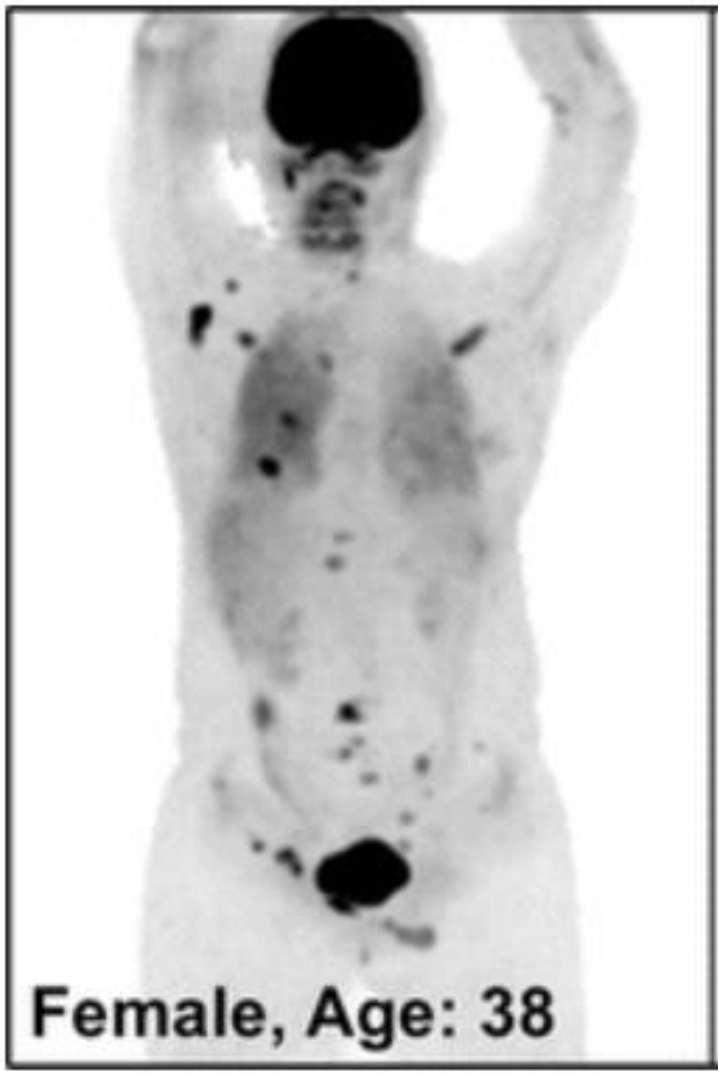
- Digital PET technology compatible with strong B fields → PET / MRI scanners.
- MRI provides excellent soft tissue contrast when compared to CT.
- However, MRI provides information on proton density, not electron density (necessary for AC).
- Nowadays, synthetic (virtual) CT scans can be generated starting from MRI acquisitions and then used for attenuation correction (through artificial intelligence)
  (GAN: generative adversarial networks)







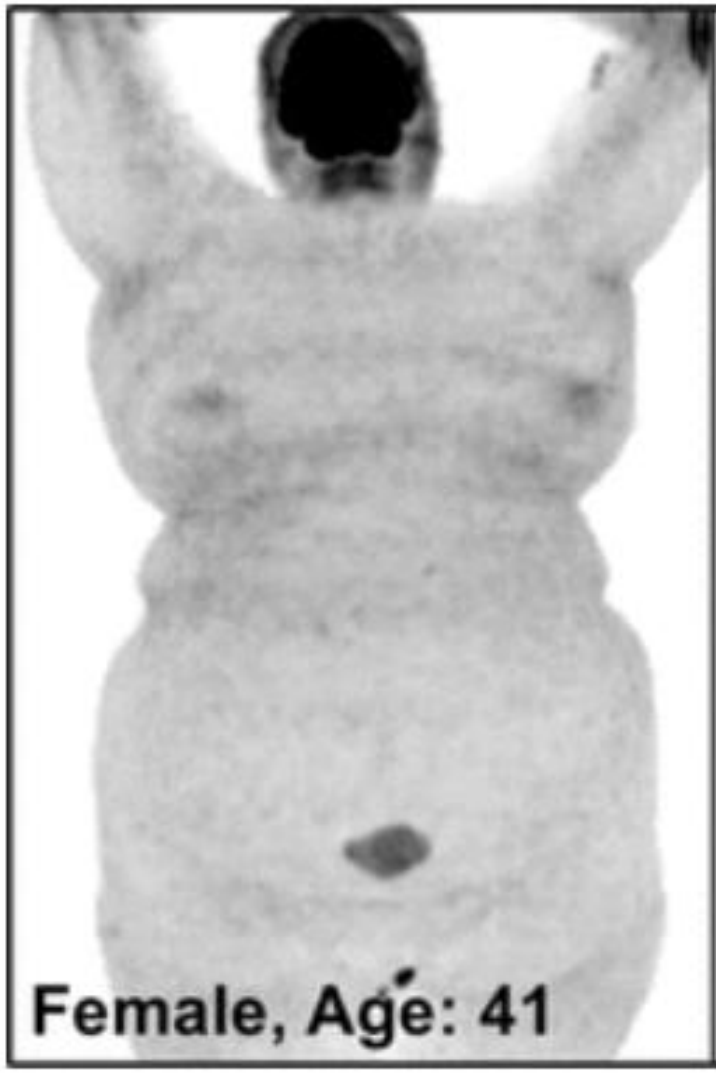
PET corrections : attenuation correction



Non corrected image

https://pubs.rsna.org/doi/full/10.1148/ryai.2020200137

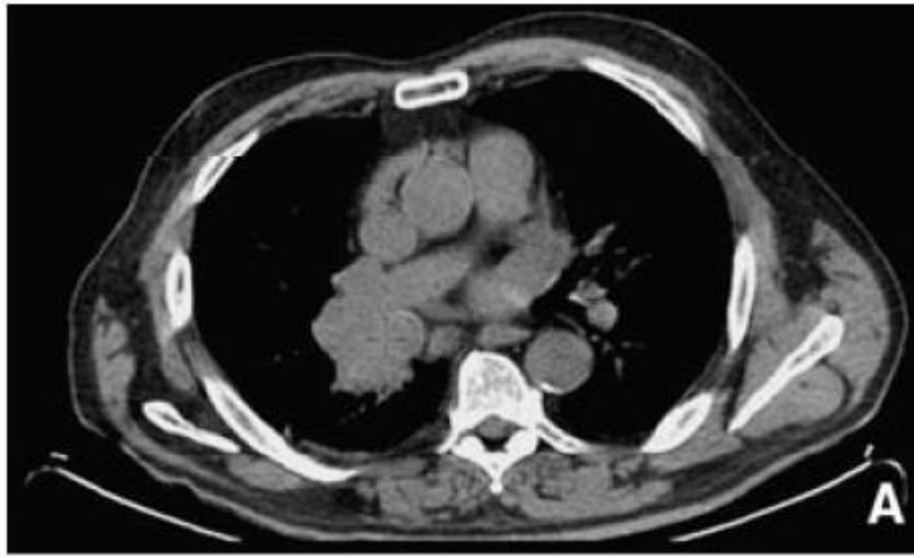
PET corrections : attenuation correction

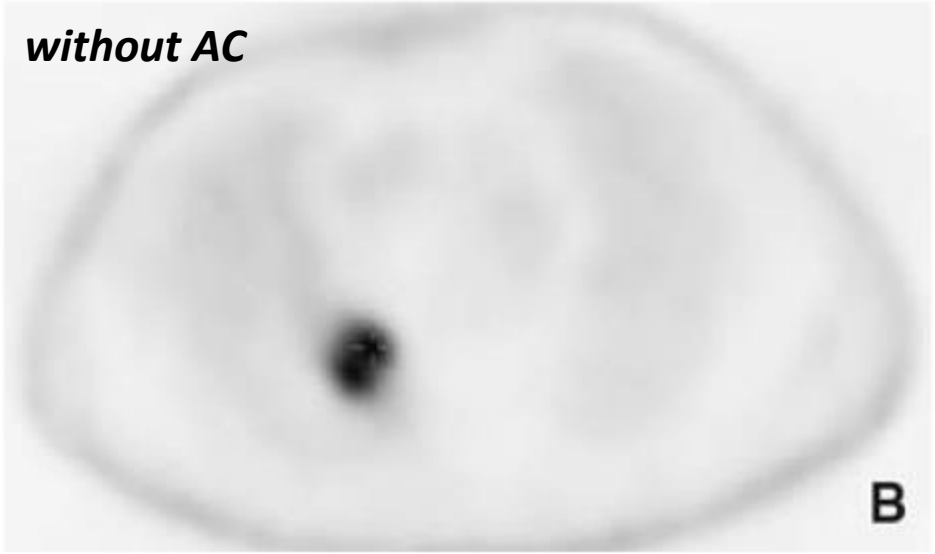


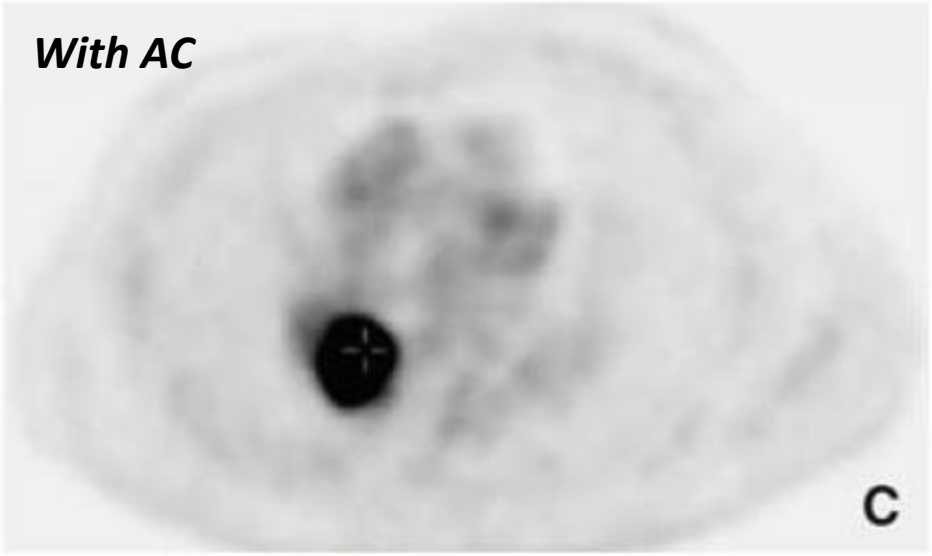
Non corrected image

https://pubs.rsna.org/doi/full/10.1148/ryai.2020200137

PET corrections : attenuation correction





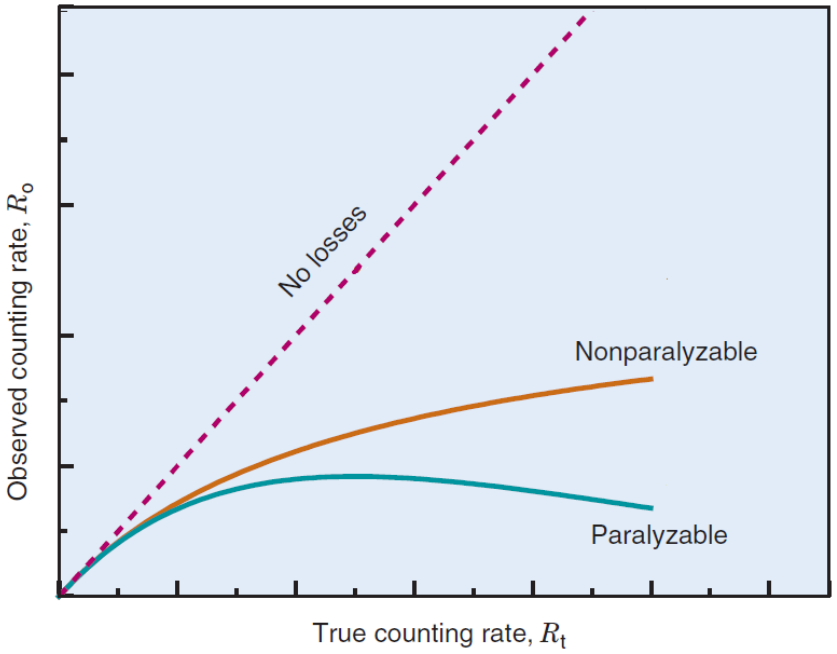


PET corrections : dead time

At high counting rates: dead time and pile-up effects.

Dead time : leads to underestimation of activity concentration.

Empirical dead time models are used : record counting rate according to radioactivity concentration for different objects.



→ Fit those data to a model to take into account for dead time.

Examples of high count rate studies were dead time corrections are paramount:

- imaging with very short-lived radionuclides (high activity to start with!)
- imaging of structures near high uptake regions (e.g. the bladder)

PET corrections : all corrections → towards quantitative PET !

Raw Sinogram Data (Trues + Scatters + Randoms)

Remove Randoms

Normalize Detector Responses

Correct for Deadtime

Correct for Scatter

Correct for Attenuation

Sinogram
Ready for Reconstruction

corrections (e.g. scatter and attenuation) can be directly integrated in the iterative reconstruction process!

It's not exactly like this, and it's not necessarily as linear as this !

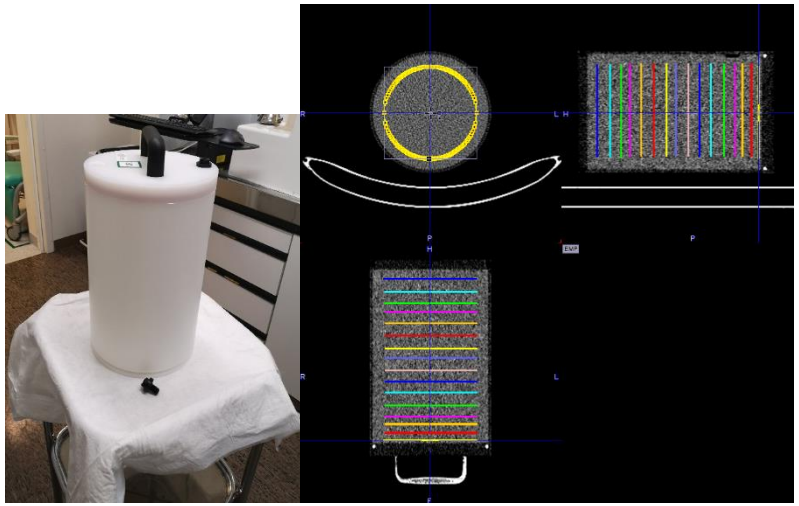
PET corrections → absolute quantification

- Relative quantification:
  - Signal in a certain region compared to others (e.g. tumor to healthy tissue ratios).

- Aim of **absolute** quantification :
  - To obtain a quantitative estimate of the activity concentration (in a given region, organ, tissue) expressed in kBq/mL (with no reference to other regions).

- Goals :
  - Comparison between patients.
  - Perform 3D dosimetry.
  - Therapy follow-up (response to therapy).
  - Dose/response relation in radionuclide therapy.

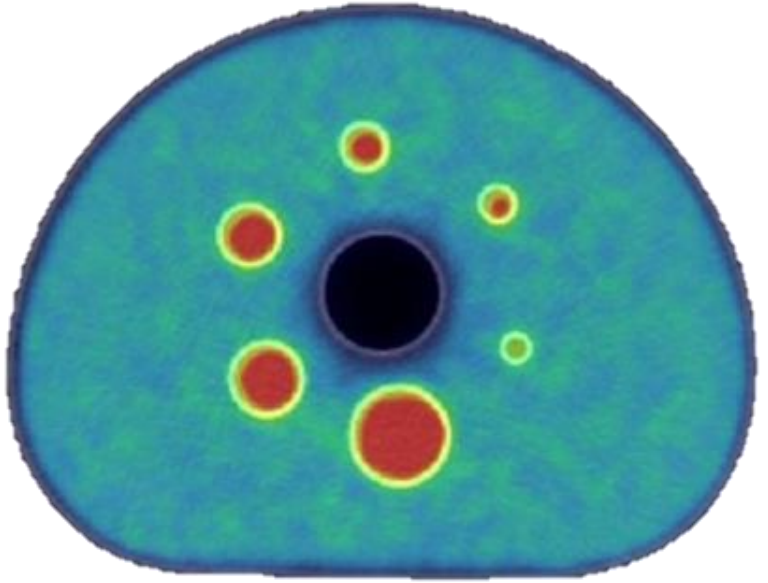
- Calibration factor : $CF \quad in \quad \frac{Bq/mL}{cps/voxel}$



e.g. using simple phantom configurations

PET corrections → absolute quantification

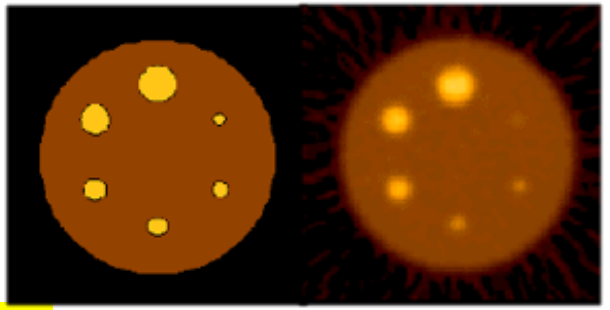
- Can be achieved only if *all* the corrections are applied.
- They are generally applied before reconstruction (and can be for instance taken into account in the *M* matrix in iterative reconstruction techniques).
- Hopefully, the voxel intensity will be then representative of the activity distribution.



- Absolution quantification allows to apply a conversion between acquired counts [cps/voxel] and activity concentration [kBq/cc].
- This can be verified with test objects.
- ⚠ PET imaging is also subjected to partial volume effects *(cf. SPECT lecture)*.

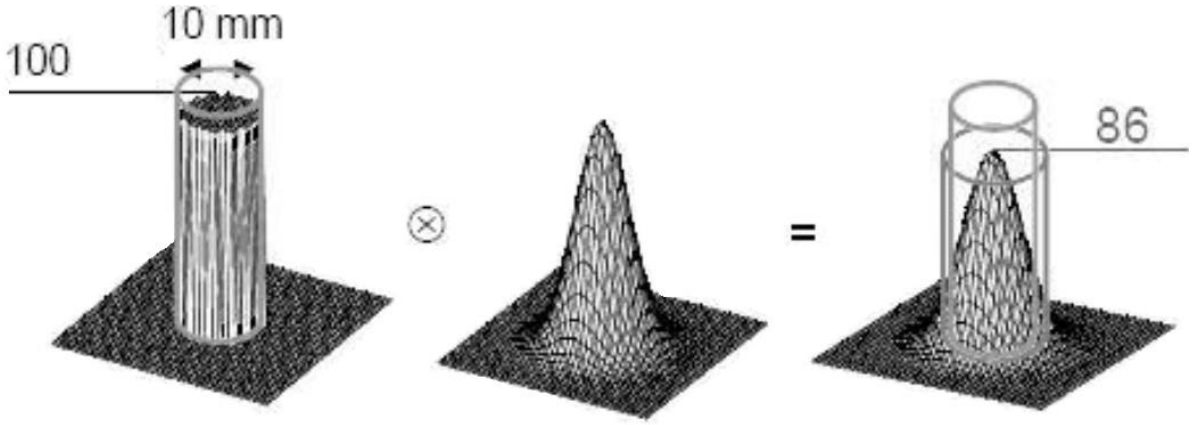
Useful quantities in PET : RC

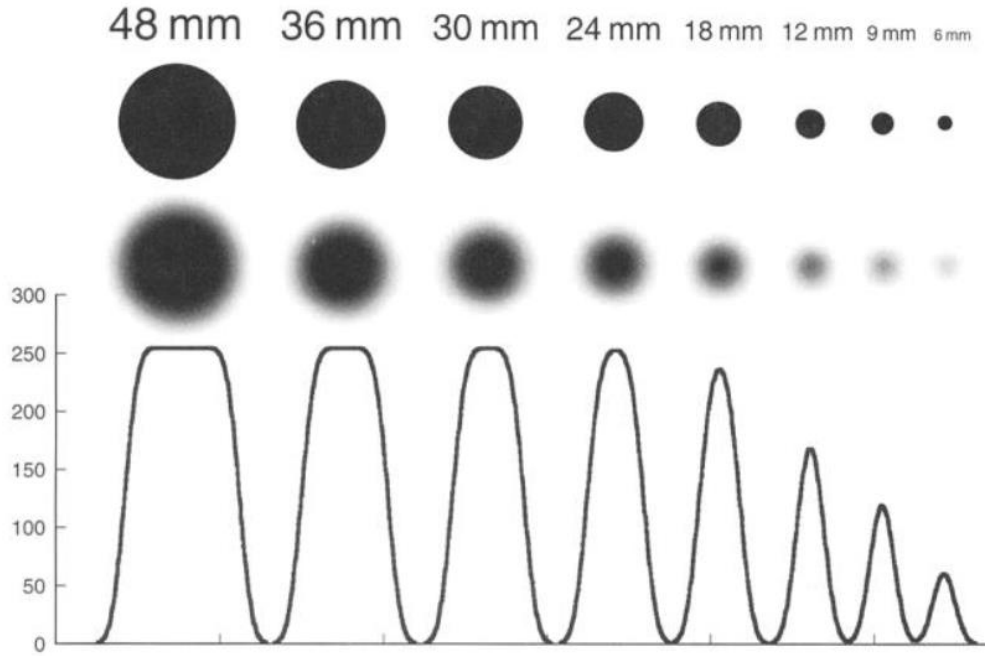
+ SPECT !



- **Recovery coefficient (RC)**

→ allows to quantify and compensate for **partial volume effects (PVE):**





Activity concentration underestimation occurs when the lesion size is ~2-3 times the system spatial resolution.

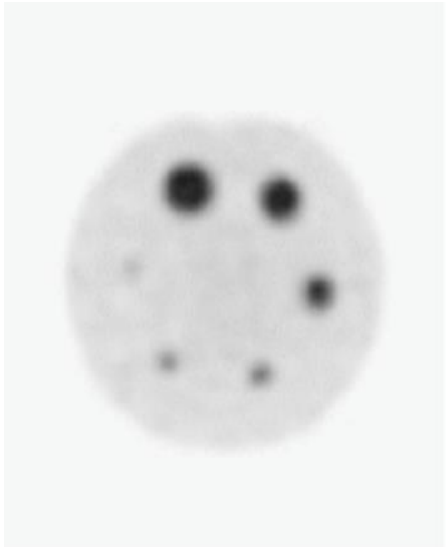
PVE is stronger as the lesion size is smaller.

Useful quantities in PET : RC

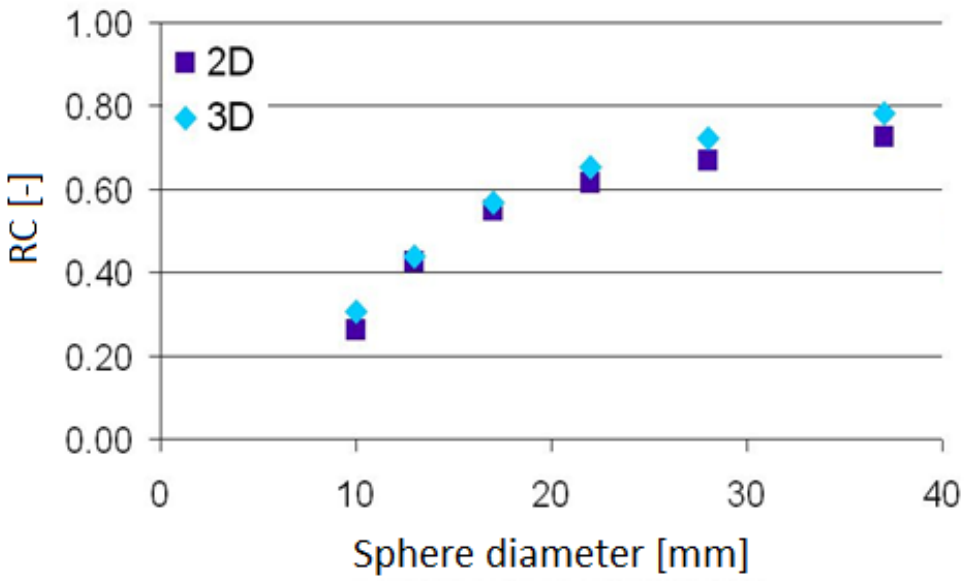
+ SPECT !

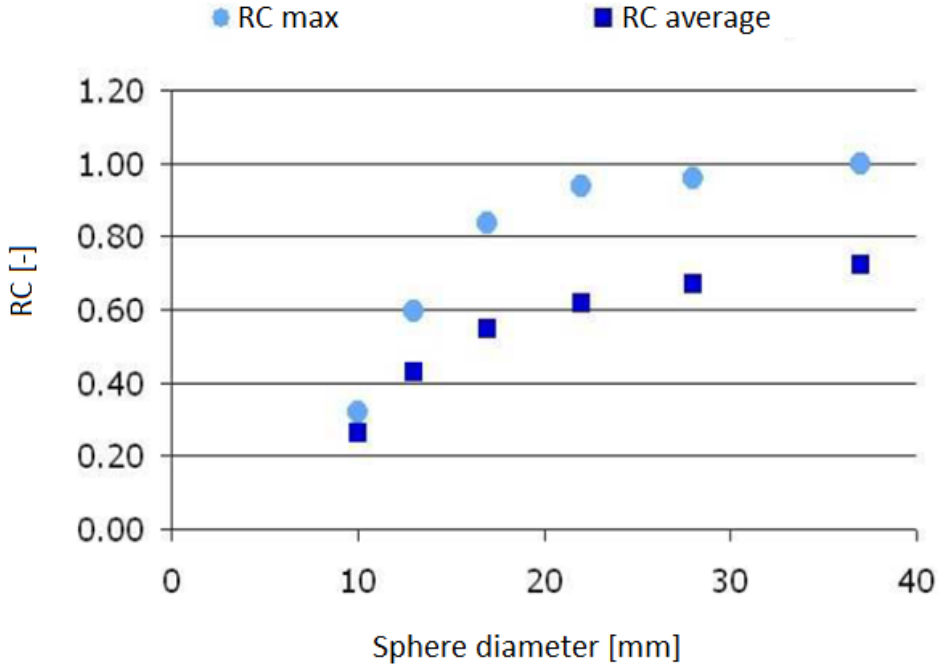
- **Recovery coefficient (RC) :**

$$RC = \frac{measured\ activity\ concentration}{true\ activity\ concentration} \Rightarrow A_{corrected} = \frac{A_{measured}}{RC}$$



^{18}F (GE Discovery LS)





Useful quantities in PET : SUV

+ SPECT !

- **Standardised uptake value (SUV):**
  - semi-quantitative metric of radiotracer (e.g. FDG) accumulation in a region of interest.
    → makes possible the comparisons between exams performed on ≠ patients

$$SUV\ [g/cc] = \frac{A_{volumetric\ in\ region}\ [kBq/cc]}{A_{total\ administered}\ \cdot [kBq]} \cdot M_{patient}\ [g]$$

→ideally, it allows to eliminate variability introduced by differences in patient size and the amount of radiotracer.

→allows to distinguish between “normal” and “abnormal” levels of uptake.

It depends on :

- time between injection and acquisition,
- patient’s weight,
- patient’s blood sugar level (FDG),
- quantification quality,
- partial volume effects,
- correction + reconstruction parameters, etc.

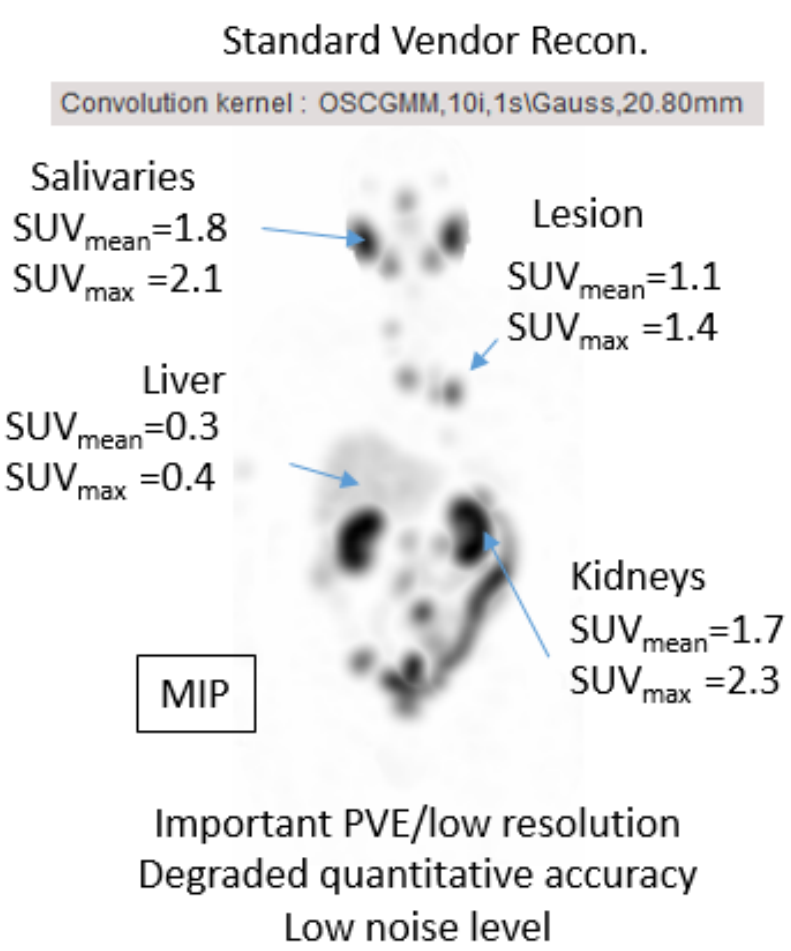
} patient dependent

} machine-dependent

Useful quantities in PET : SUV

+ SPECT !

Example of Lu-177 PSMA quantitative SPECT/CT (metastatic prostate cancer)



Important PVE/low resolution
Degraded quantitative accuracy
Low noise level

MIP : maximum intensity projection

Useful quantities in PET : NECR

PET only !

Noise Equivalent Count Rate (NECR):

- Performance parameter specific of PET.
- Accounts for the statistical noise introduced by random and scatter coincidence corrections.

$$NECR = \frac{R_{true}^2}{R_{true} + R_{scatter} + R_{random}}$$

- It corresponds to the coincidence count rate that would have the same statistical noise level as the measured trues rate after correcting for scattered and random events.

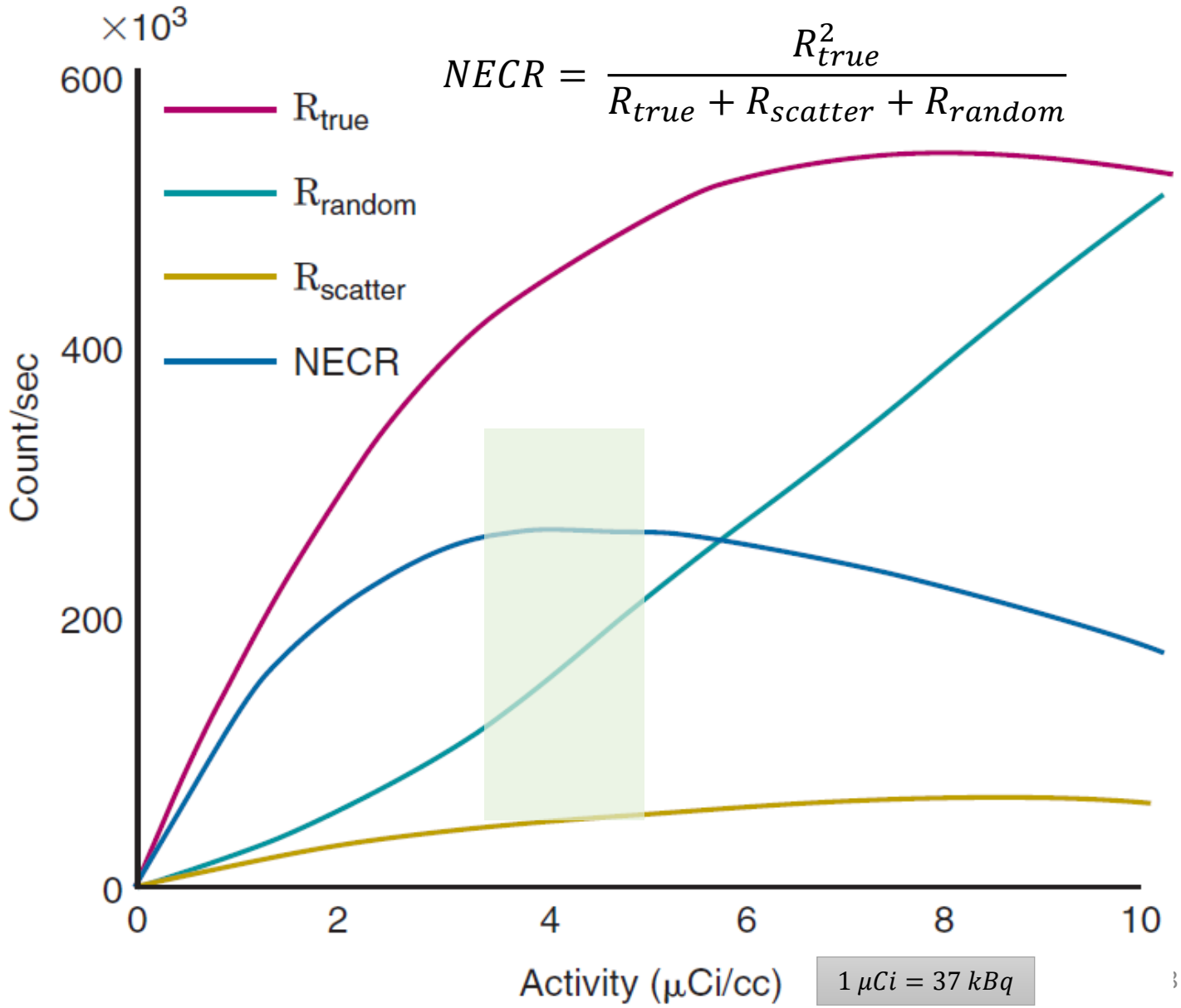
- NECR is related to the SNR ($\propto \sqrt{SNR}$ for a cylinder homogeneously filled with activity)
- It is generally represented as a function of the activity, as both random coincidences and count losses due to dead time are activity-dependent.
- It provides information on the relative proportion of true, random and scattered coincidence events as a function of activity in the field of view.

Useful quantities in PET : NECR

PET only !

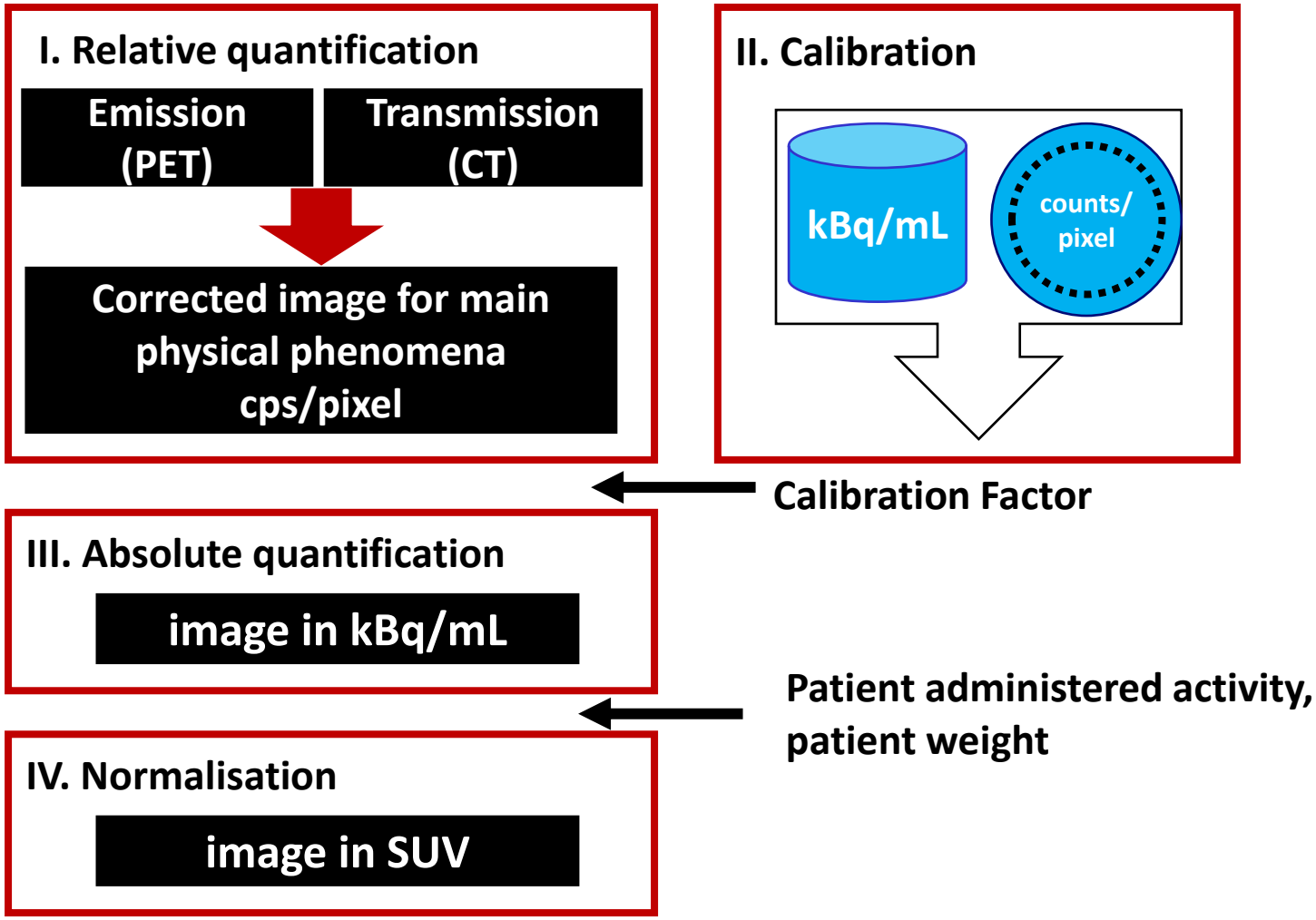
- NECR are different for each scanner and depend on the imaged object and acquisition parameters (energy and timing window, etc).
- At a given activity level, NECR starts to decrease (dead time losses reduce the observed counting rate)
- Peak NECR and corresponding activity are recorded → provide the best SNR.
- For same test object (phantom) → performances of different PET scanners can be compared.

$$NECR = \frac{R_{true}^2}{R_{true} + R_{scatter} + R_{random}}$$



$1\ \mu Ci = 37\ kBq$

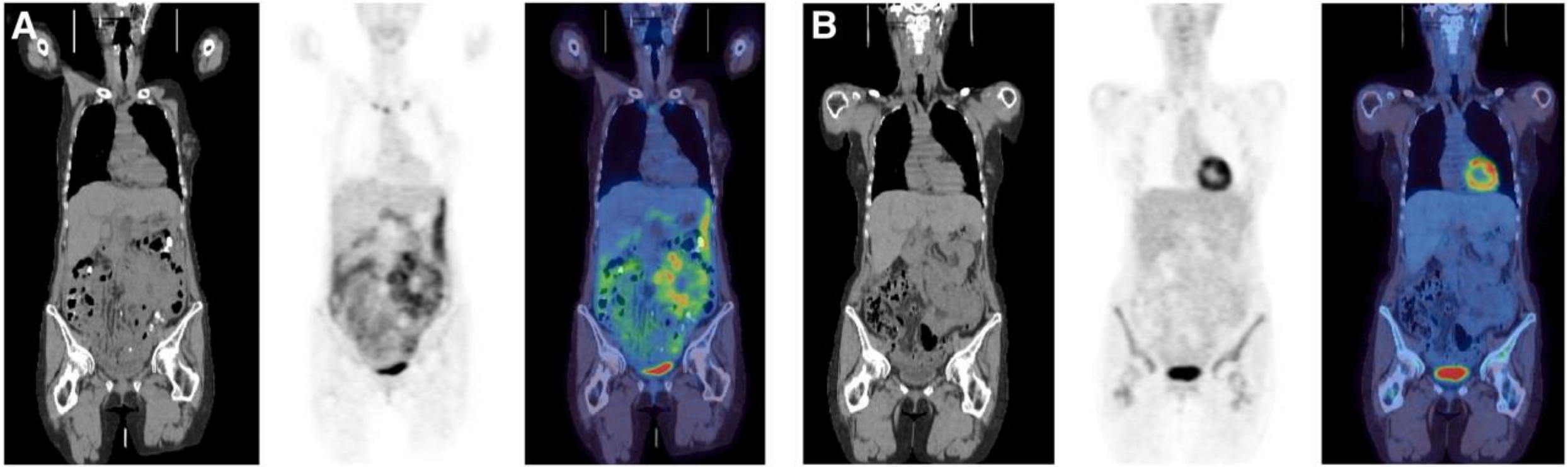
Useful quantities in PET : calibration workflow



Some PET applications

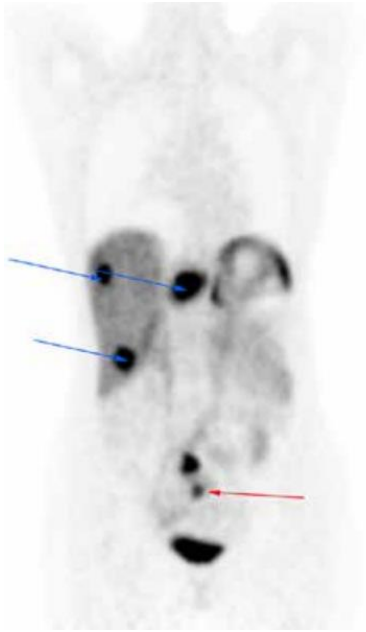
→ oncology, cardiovascular diseases, neurology

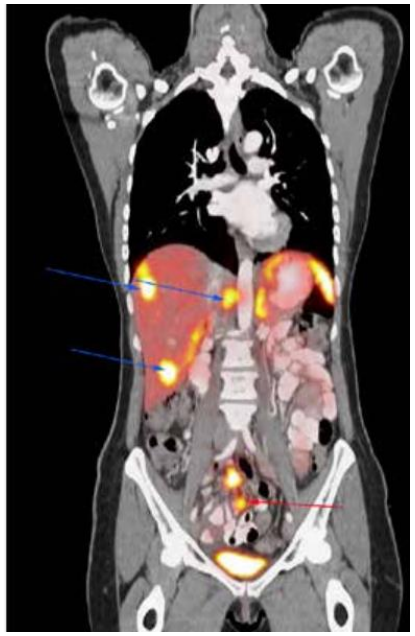
F-18 FDG PET/CT of lymphoma before (A) and after (B) chemotherapy.



https://jnm.snmjournals.org/content/50/Suppl_1/21S

Some PET applications





https://www.uclahealth.org/workfiles/clinical_updates/pharmacology-nuclear/14v1-11_DONTATE.pdf

Ga-68 DOTATATE PET/CT of neuroendocrine tumour

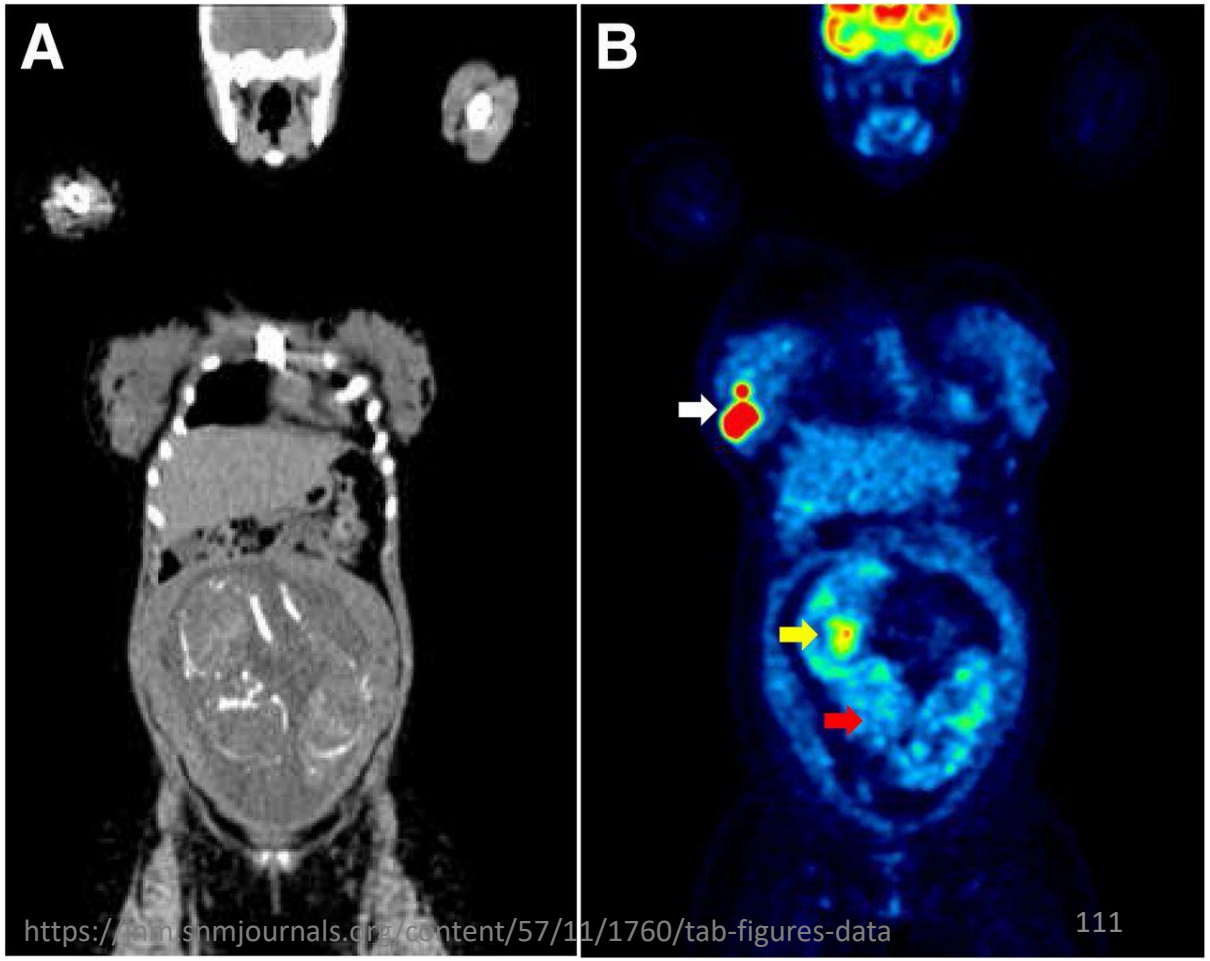
^{18}F-FDG of a pregnant woman with large B-cell non-Hodgkin lymphoma.

CT (A) and PET (B) image of 29-y-old woman with diffuse while expecting twins (about 25 wk pregnant). White arrow points to lymphoma mass.

Red arrow: fetal ^{18}F-FDG uptake in brain.

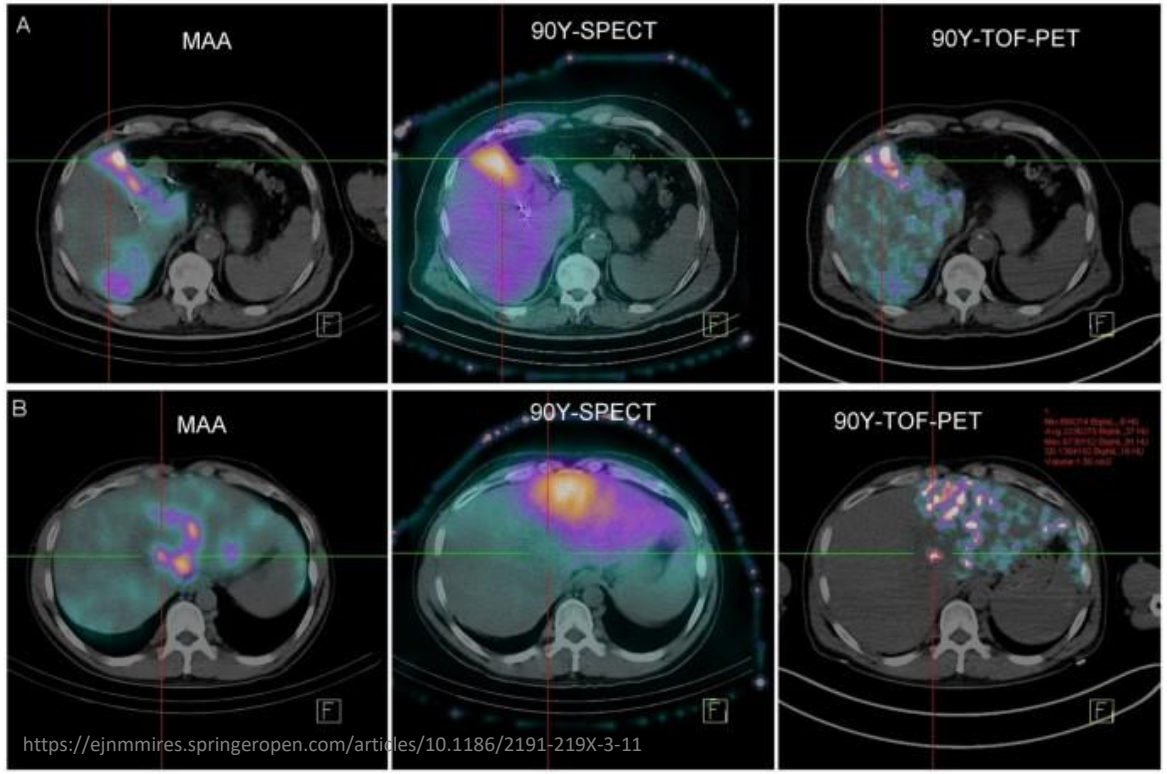
Yellow arrow: fetal ^{18}F-FDG uptake in myocardium of same fetus.

Skeletons of the twins are visible on CT scan.



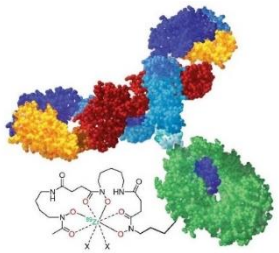
https://jnm.snmjournals.org/content/57/11/1760/tab-figures-data

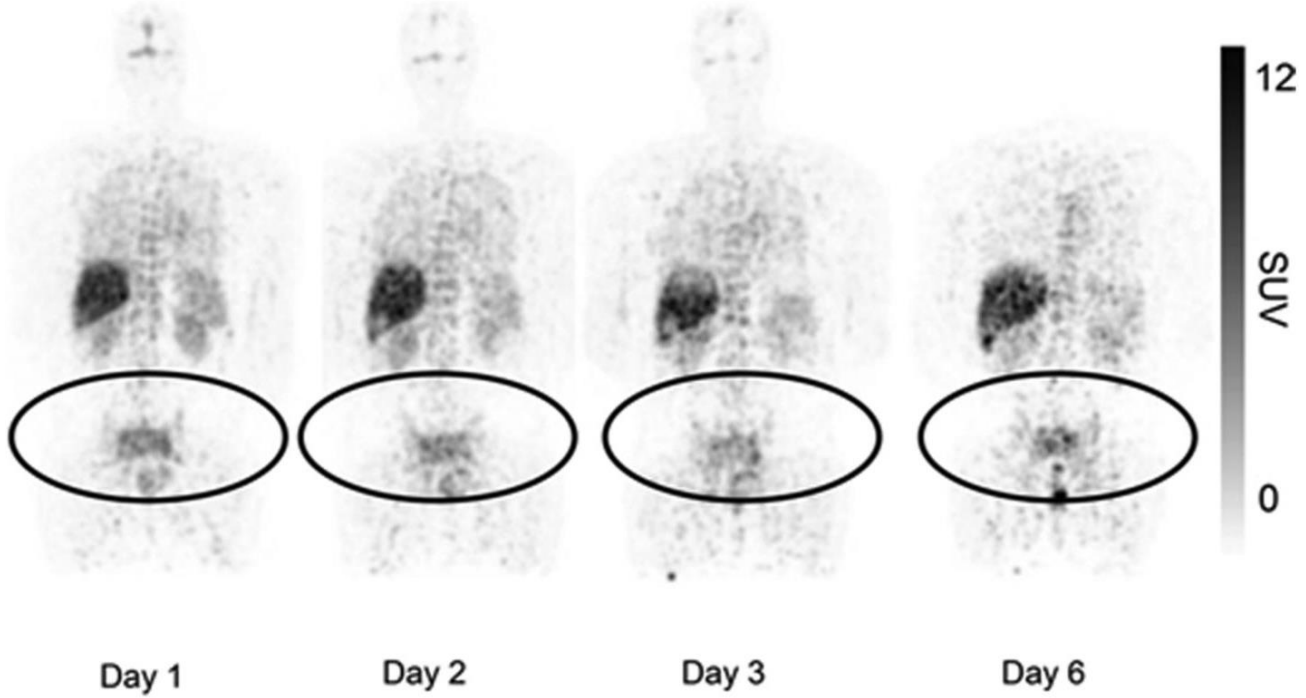
Some PET applications



Y-90 PET of post-treatment of hepatocellular carcinoma (radioembolisation) + post-treatment SPECT + pre-treatment SPECT

Use PET radionuclides to mark antibodies (e.g. with Zr-89).
Study the possible outcomes of immunotherapy / immunoradiotherapy.





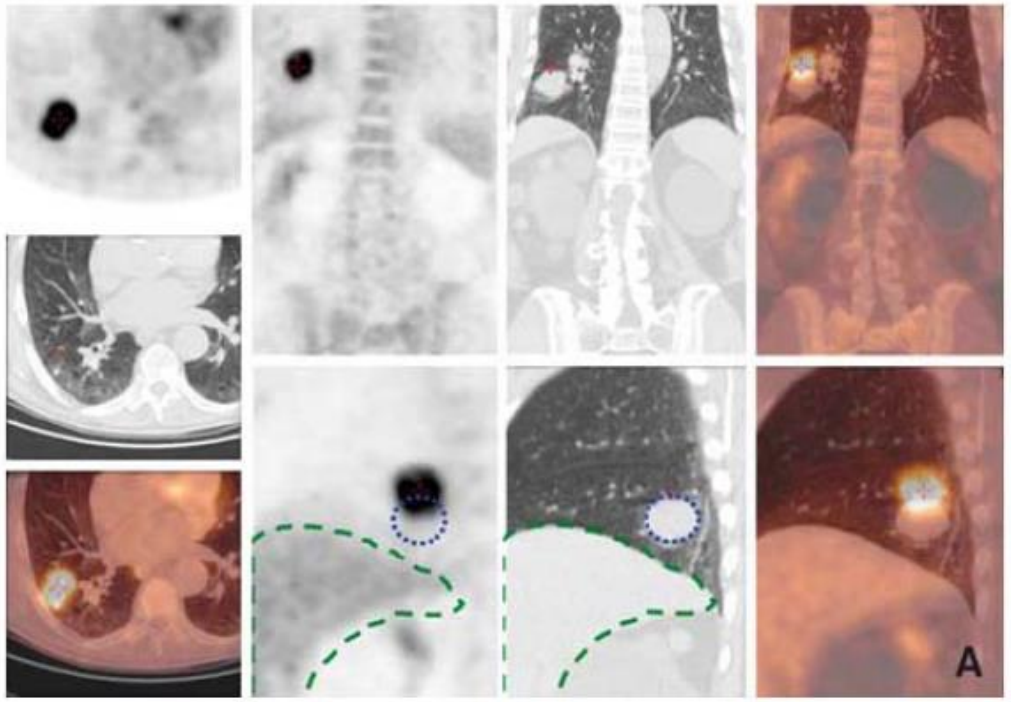
https://jnm.snmjournals.org/content/62/4/438

Some PET applications

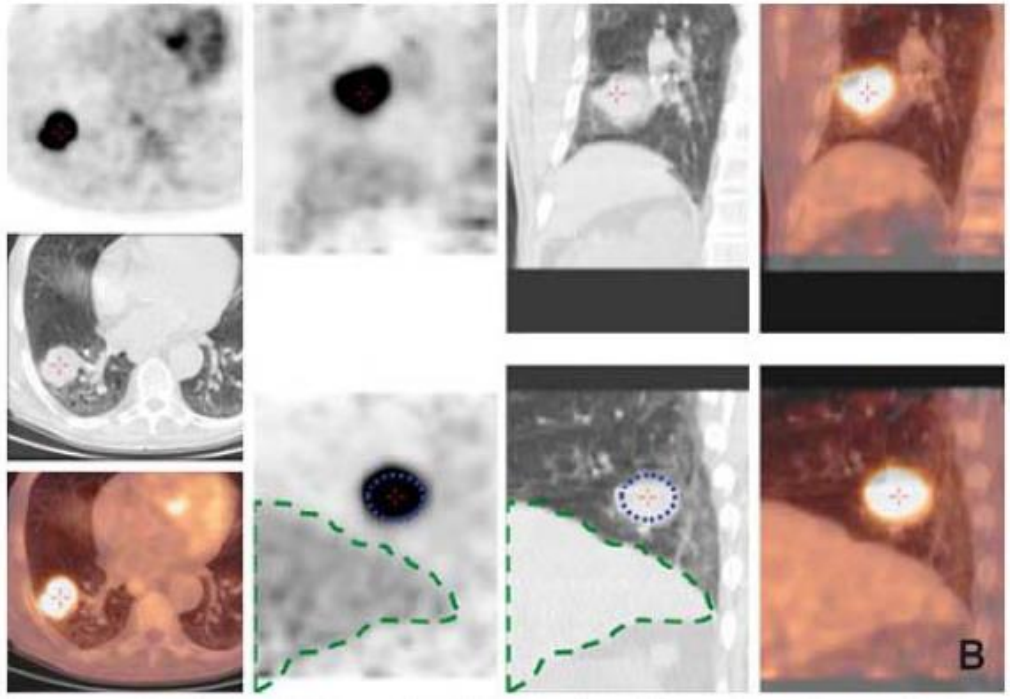
Patient motion and respiratory motion can have big impact on PET/CT images:

- PET : normal breath (~minutes)
- CT : breath hold can be used (~sec)

PET with synchronized respiratory gating

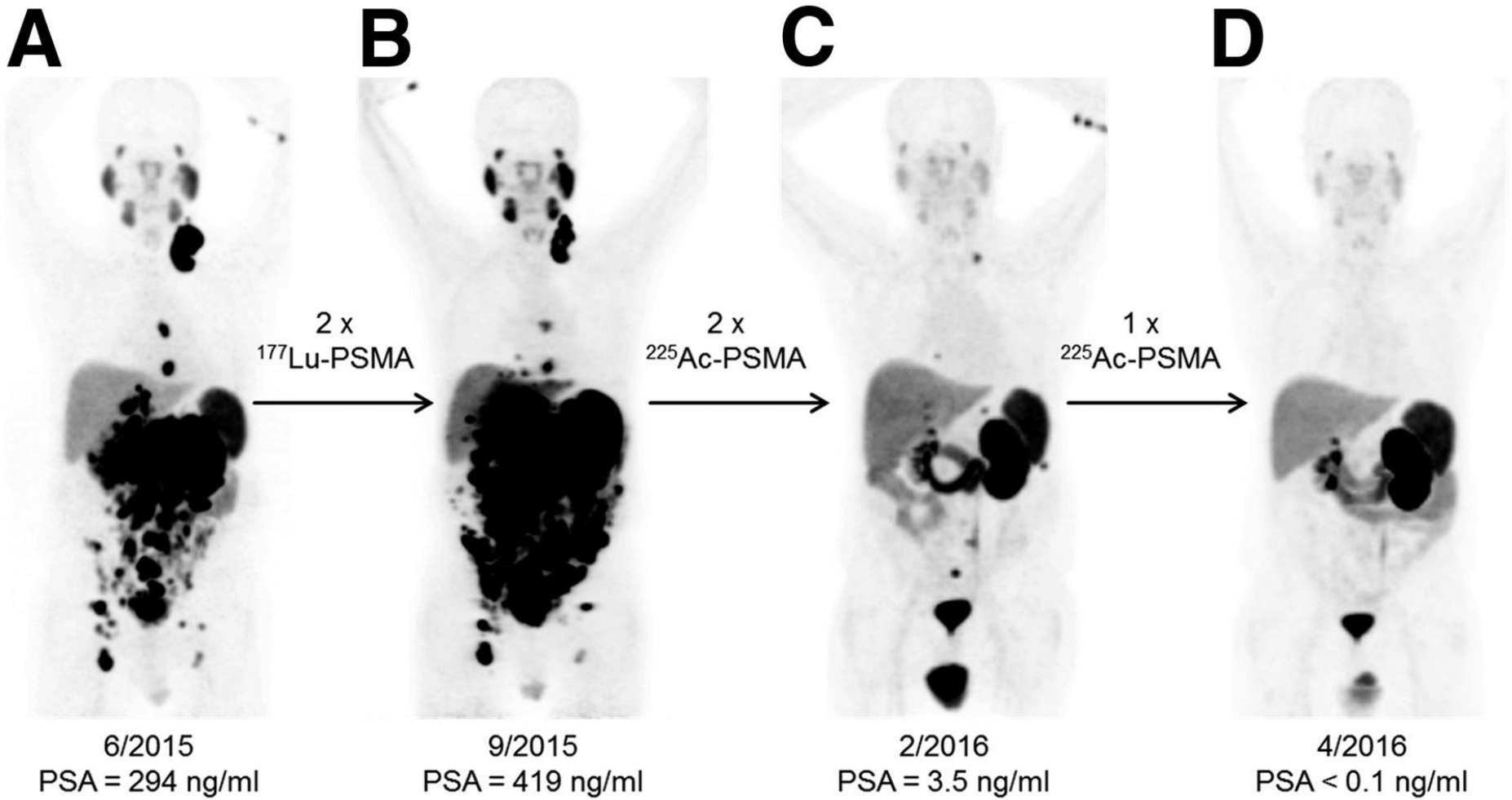


Without respiratory synchronization



With respiratory synchronization

BONUS: radionuclide therapy, the future of NM?

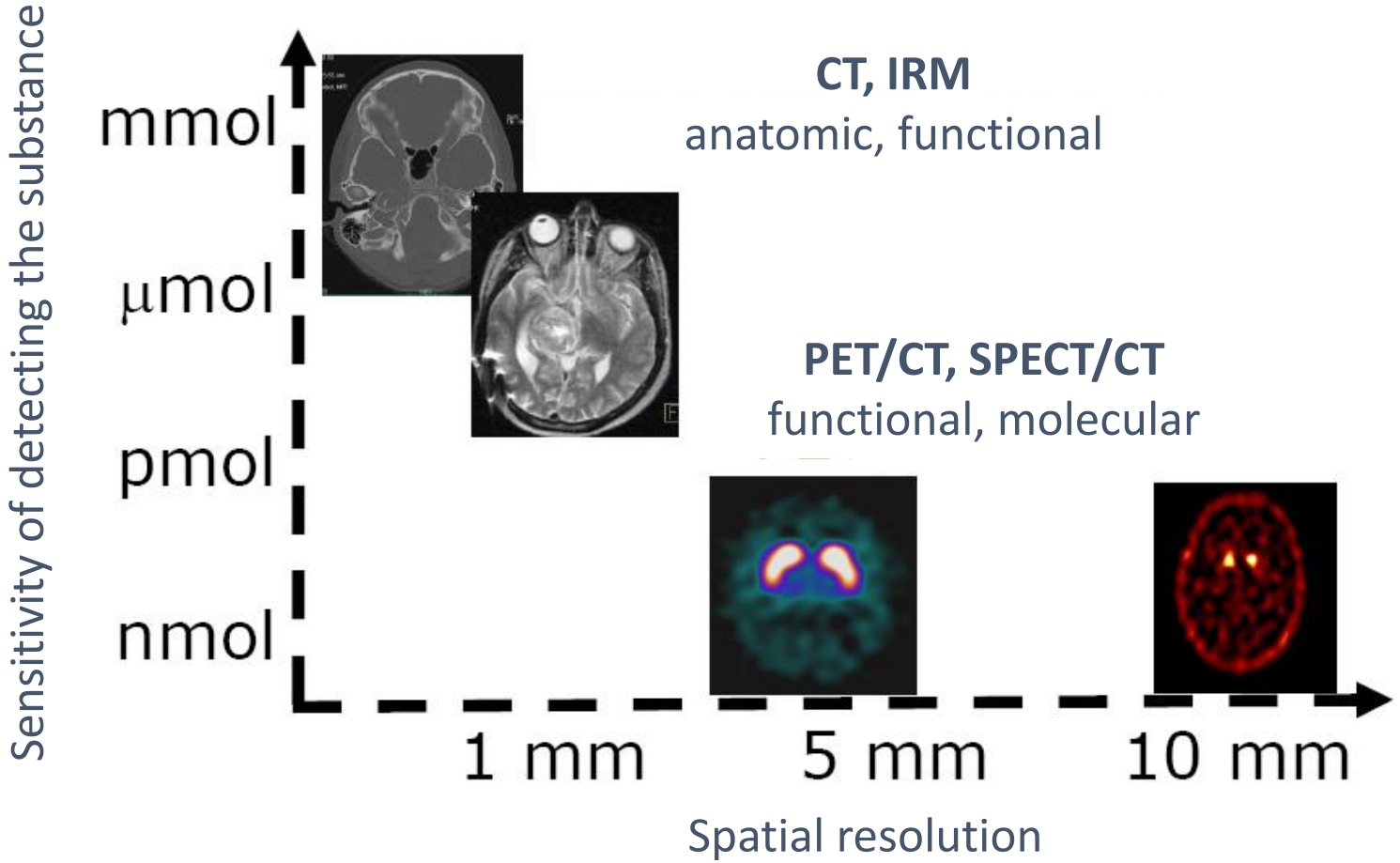


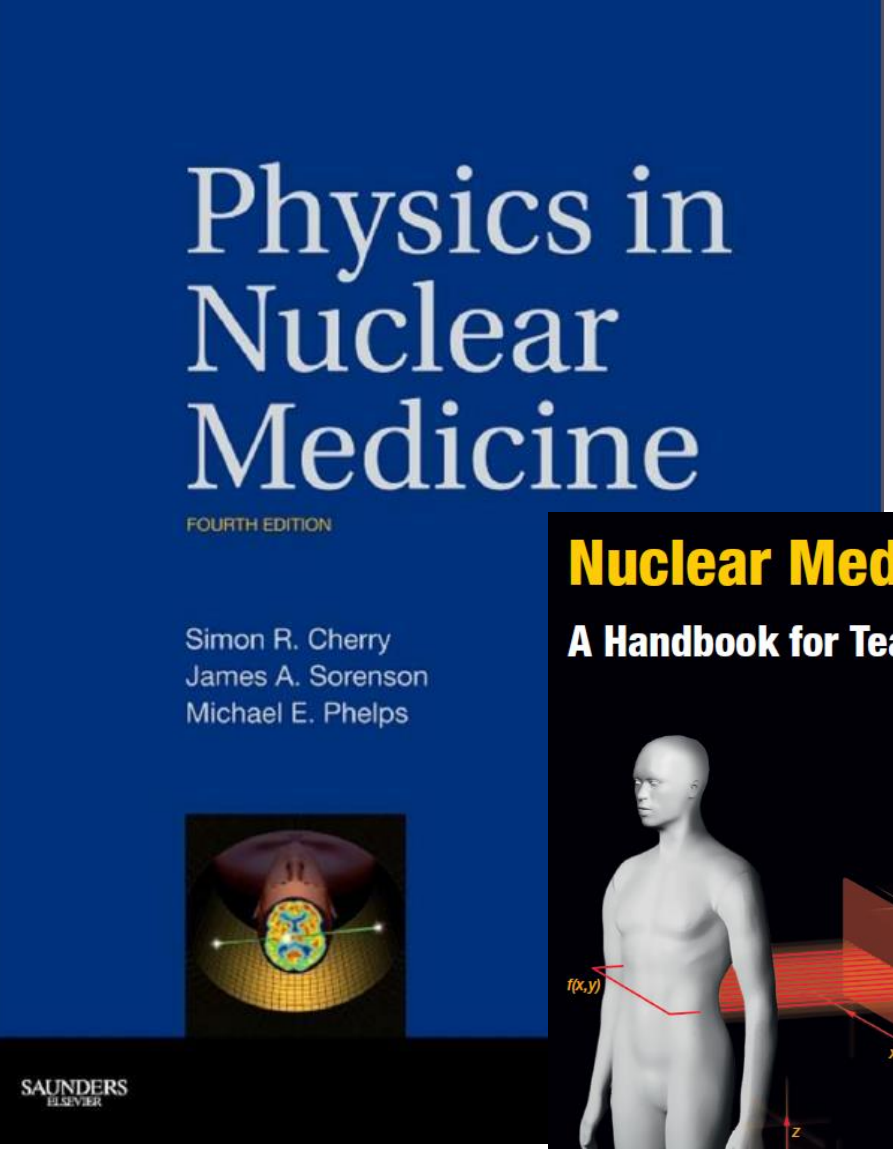
68Ga-PSMA-11 PET/CT scans of patient B. In comparison to initial tumor spread (A), restaging after 2 cycles of β-emitting 177Lu-PSMA-617 presented progression (B). In contrast, restaging after second (C) and third (D) cycles of α-emitting 225Ac-PSMA-617 presented impressive response.

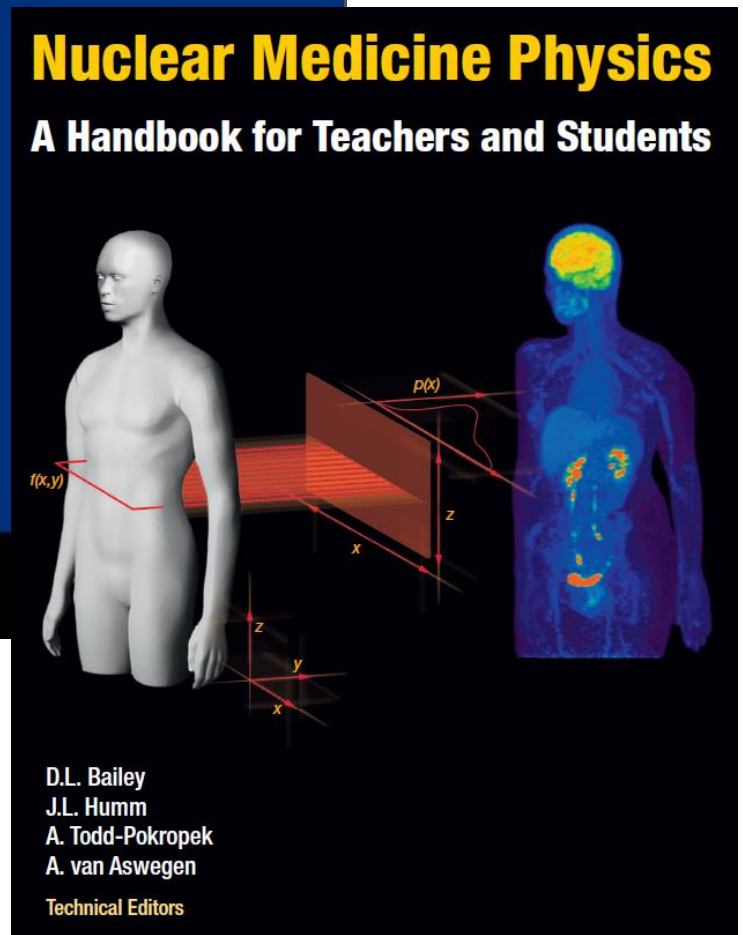
https://jnm.snmjournals.org/content/57/12/1941

Some PET applications

Short comparison of imaging modalities







Material and slides adapted from
Dr. Silvano Gnesin (CHUV/IRA).

Reference textbooks:
Physics in Nuclear Medicine (4th edition)
by S.R. Cherry, J.A. Sorenson, and M.E. Phelps
ISBN: 978-1-4160-5198-5

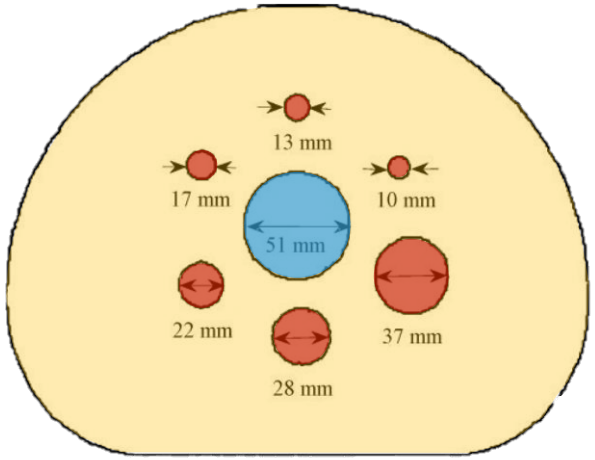
Nuclear Medicine Physics:
A Handbook for Teachers and Students
By D.L. Bailey, J.L. Humm, A. Todd-Pokropek, A. van Aswegen, IAEA (2014).

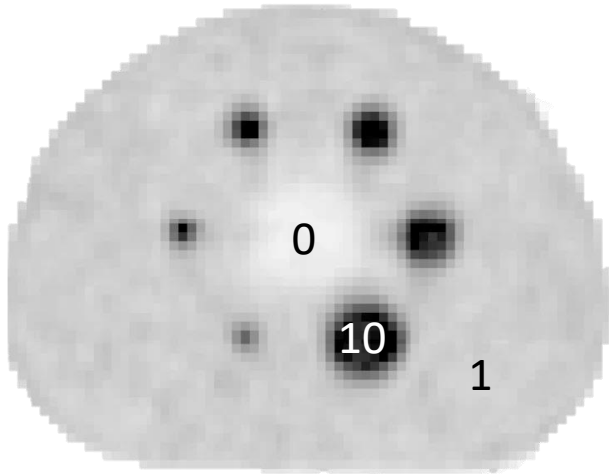
Other sources:
«Cours de Radiophysique Medicale - Médecine nucléaire & Radiochimie»,
IRA / HESAV TRM.

Example of medical physicist task : optimisation

NEMA phantom:

- Activity concentration spheres/BG = 10:1



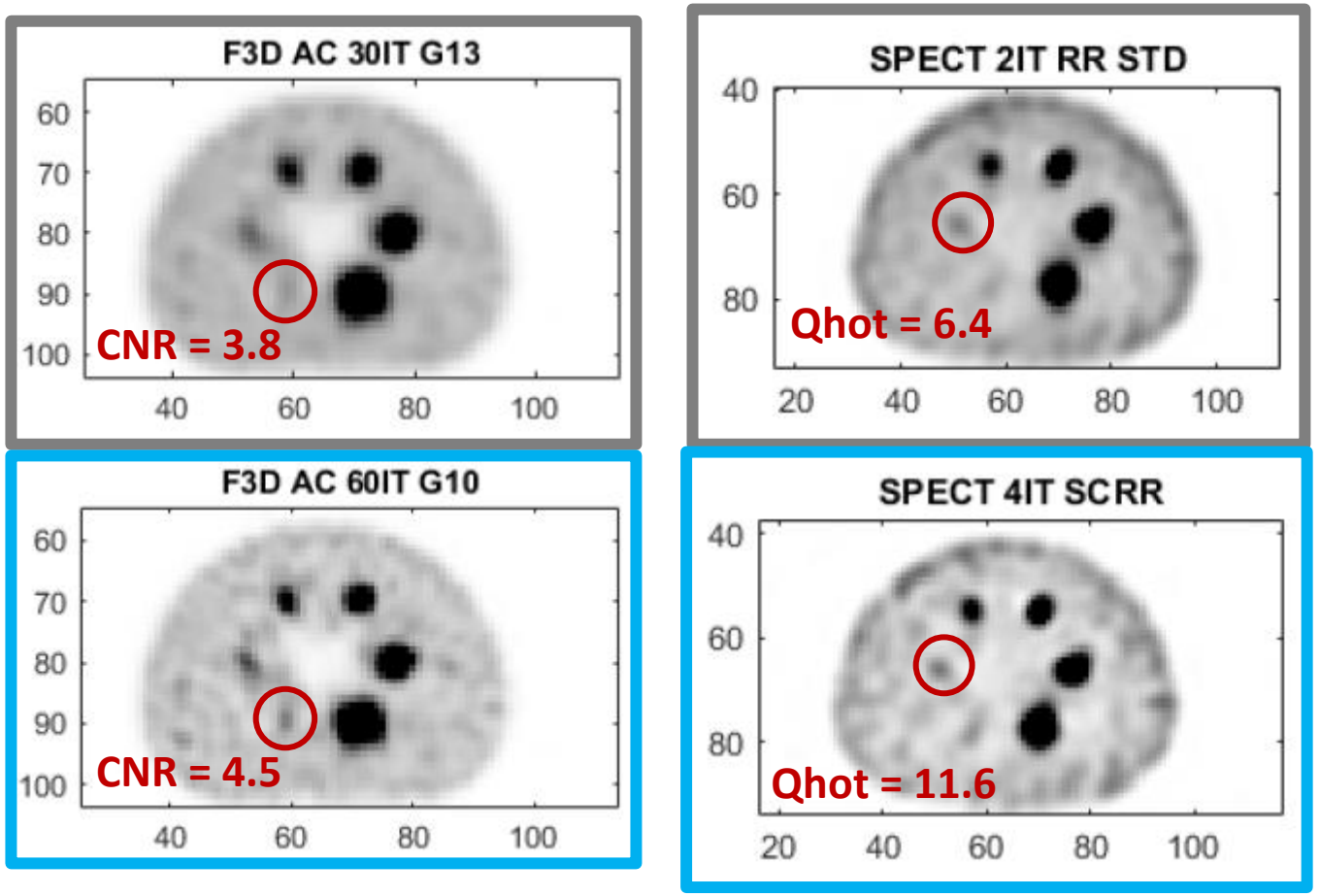


S. Medici, S. Gnesin. Impact of clinical protocol optimization in SPECT and PET: a multi-centre and multi-device study. Swiss Congress of Radiology 2023

Protocol optimisation

$$CNR_{\text{sphere}} = \frac{\bar{S}_{\text{sphere}} - \bar{S}_{\text{BG}}}{SD_{\text{BG}}}$$

$$Q_H(\%) = \left(\frac{\frac{S_{\text{sphere,meas}}}{S_{\text{BG,meas}}} - 1}{\frac{S_{\text{sphere,true}}}{S_{\text{BG,true}}} - 1} \right) \cdot 100$$

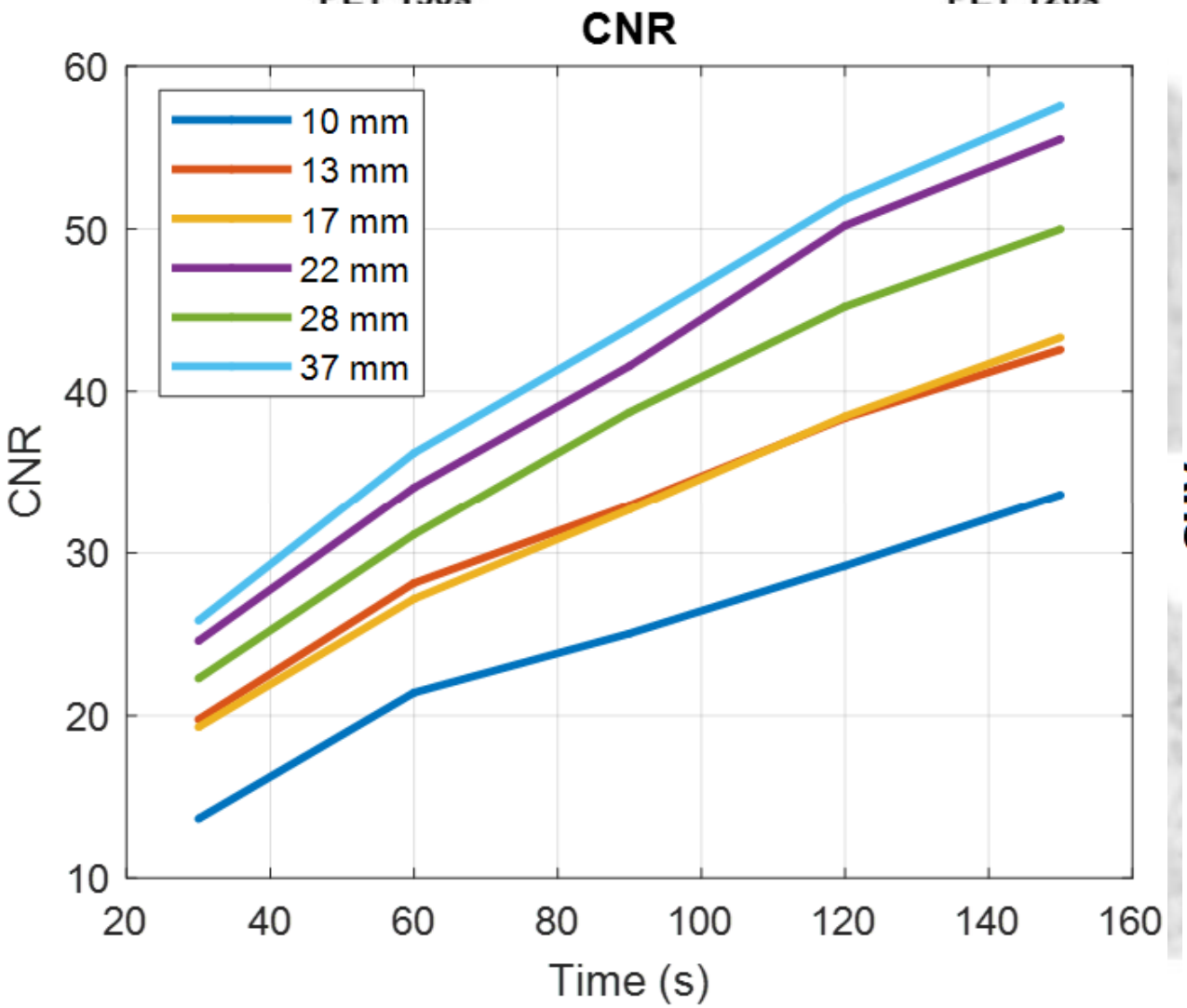


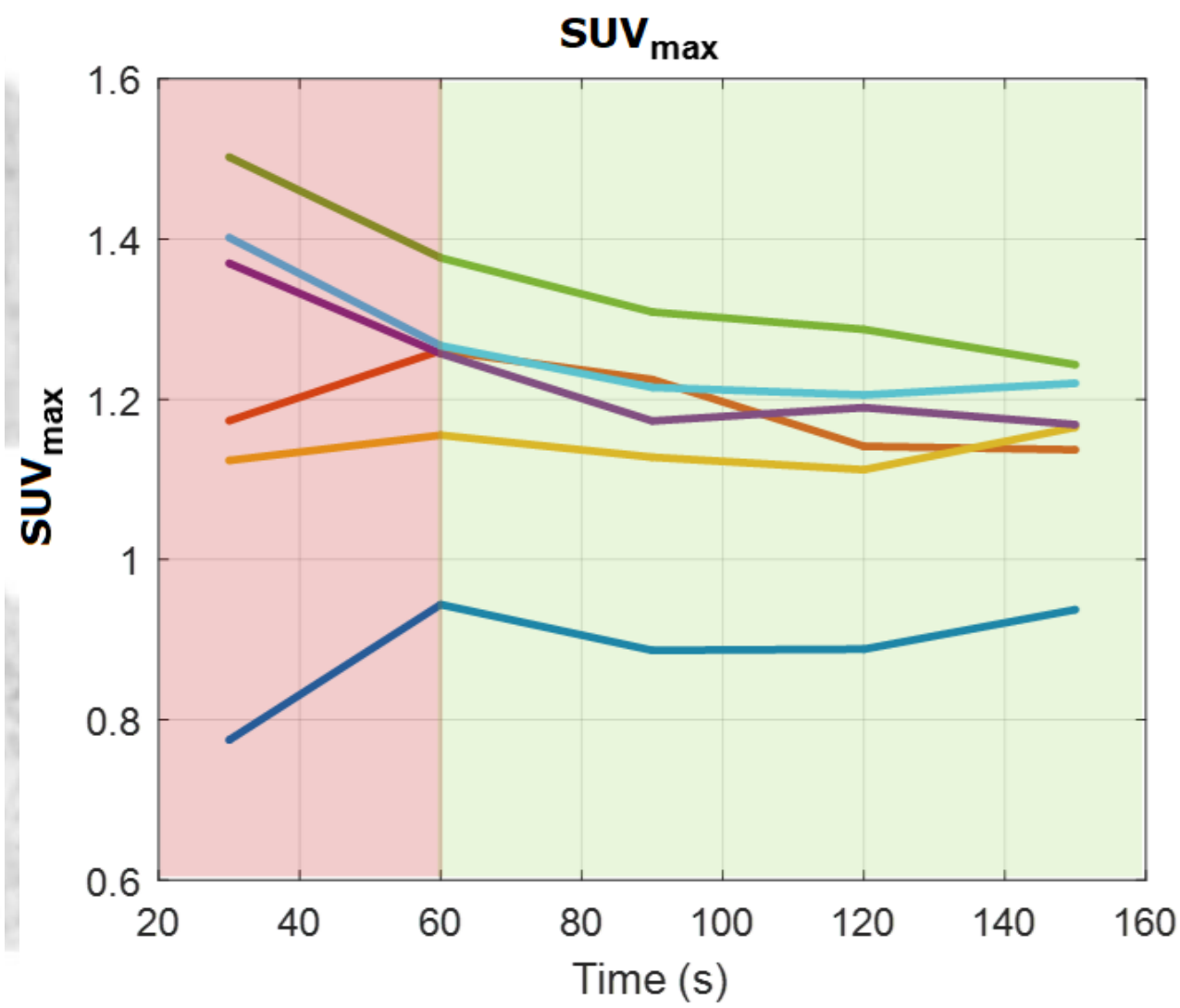
Examples of image quality improvement (CNR and Q_{hot}) by optimising reconstruction parameters

S. Medici, S. Gnesin. Impact of clinical protocol optimization in SPECT and PET: a multi-centre and multi-device study. Swiss Congress of Radiology 2023

PET: statistics vs. IQ

IQ preserved → margin for **dose reduction**





S. Medici, S. Gnesin. Impact of clinical protocol optimization in SPECT and PET: a multi-centre and multi-device study. Swiss Congress of Radiology 2023