Biomedical Imaging

Nuclear Imaging (I)

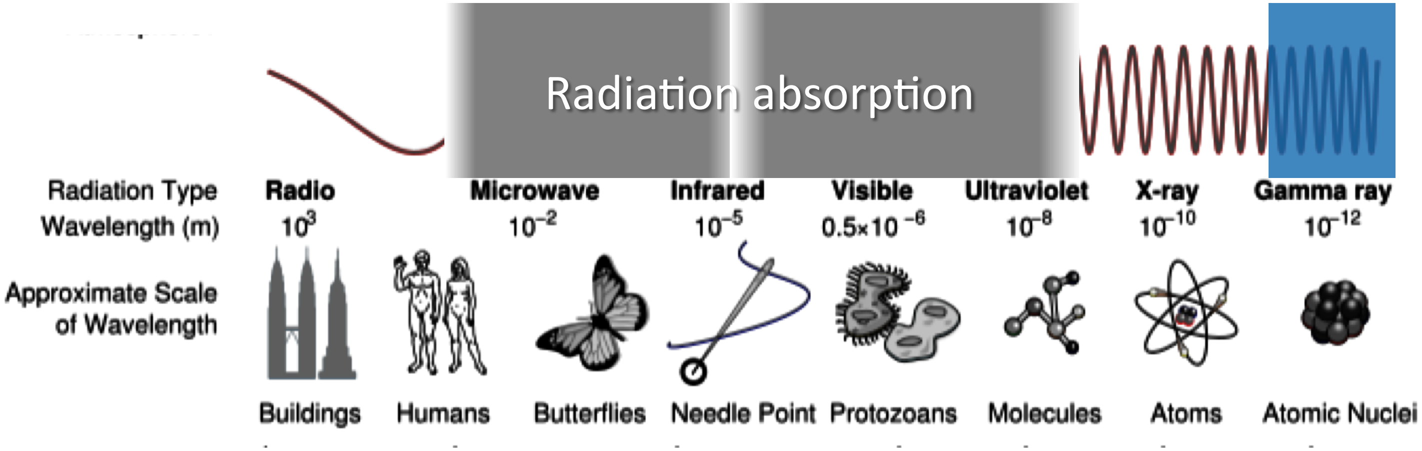
Sebastian Kozerke / Markus Rudin

Institute for Biomedical Engineering, University and ETH Zurich, Switzerland

Today's Learning Objectives

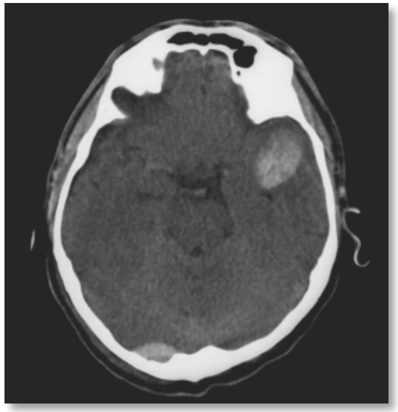
- **Review radioactivity, physical and biological half-life, radioisotopes**
- **Relate geometrical collimation, spatial resolution and PSF**
- **Describe scintillation detection and energy filtering**
- **Derive image reconstruction in SPECT, PET** (compare with CT)
- **Implement CT-based attenuation correction for PET** (Exercise)

Biomedical Imaging

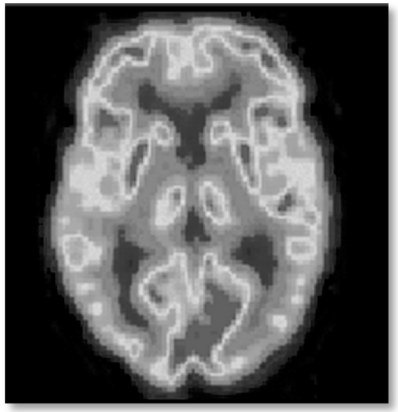


Magnetic Resonance

XR/CT



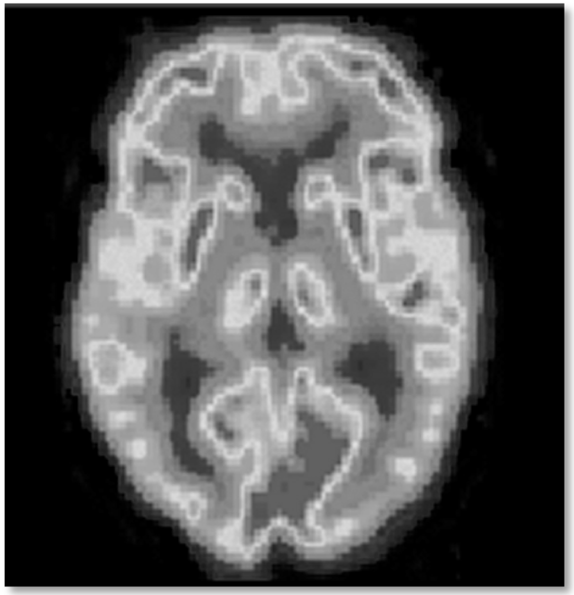
Nuclear Imaging



Nuclear imaging

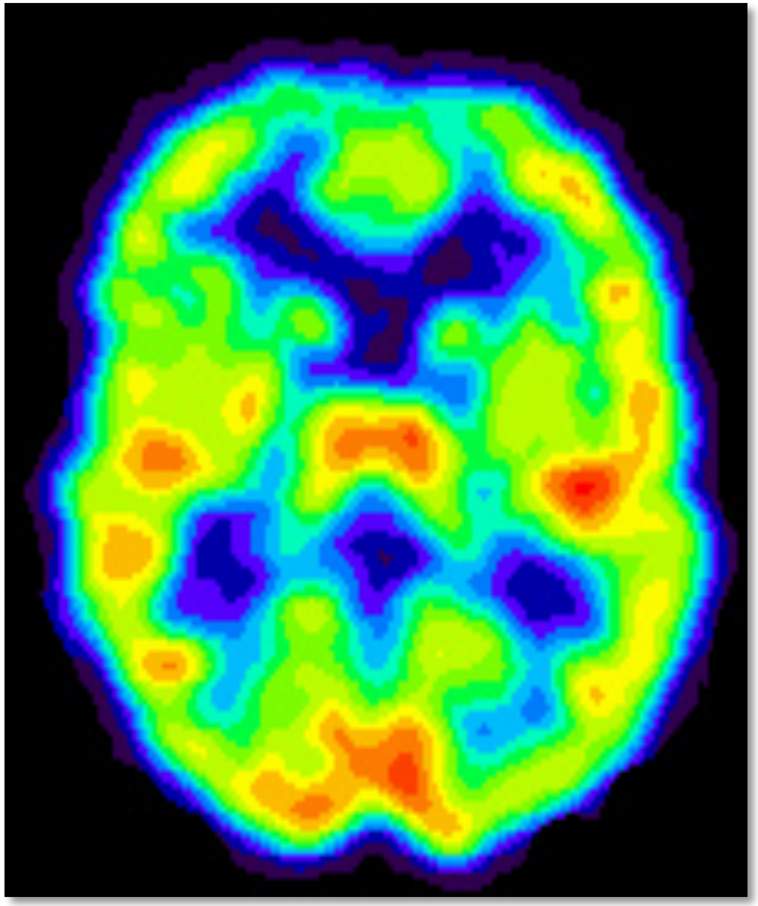
- Exogenous tracer as only source of imaging signal
  - distribution of radiotracer in tissue upon intravenous injection
  - radiotracer are compounds that contain metastable/instable nucleus
  - γ-emitter or positron emitter
  - tracer concentration: **pmol - nmol**

▶ **Molecular and perfusion imaging**

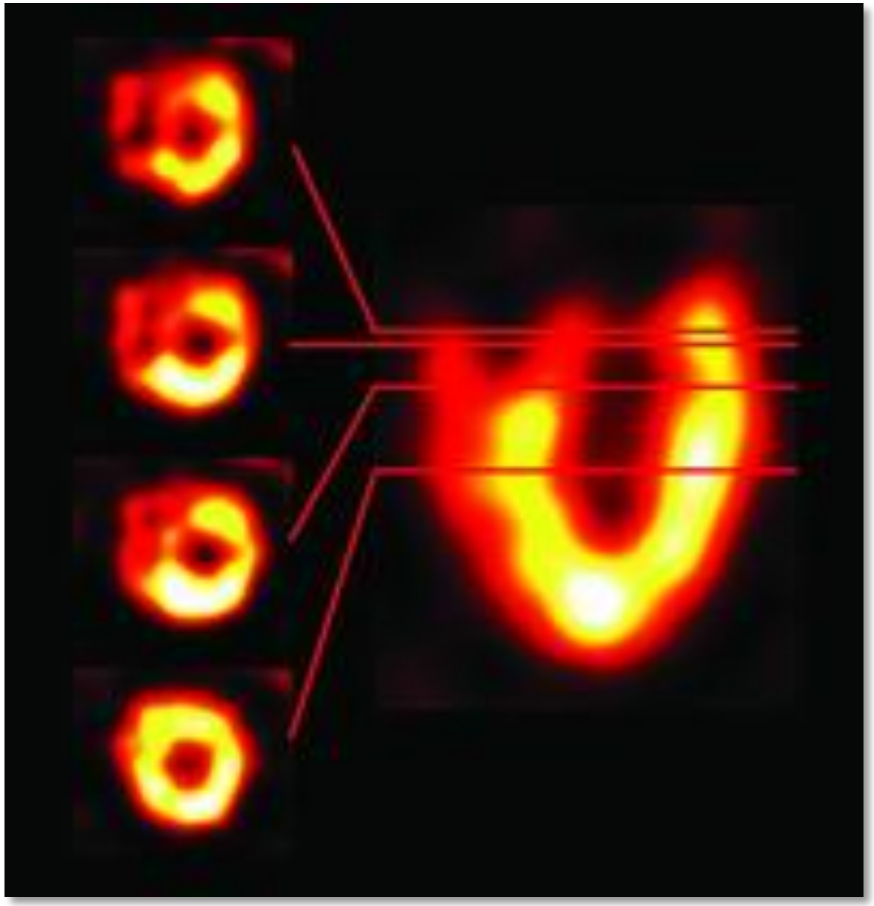


Nuclear imaging

Brain

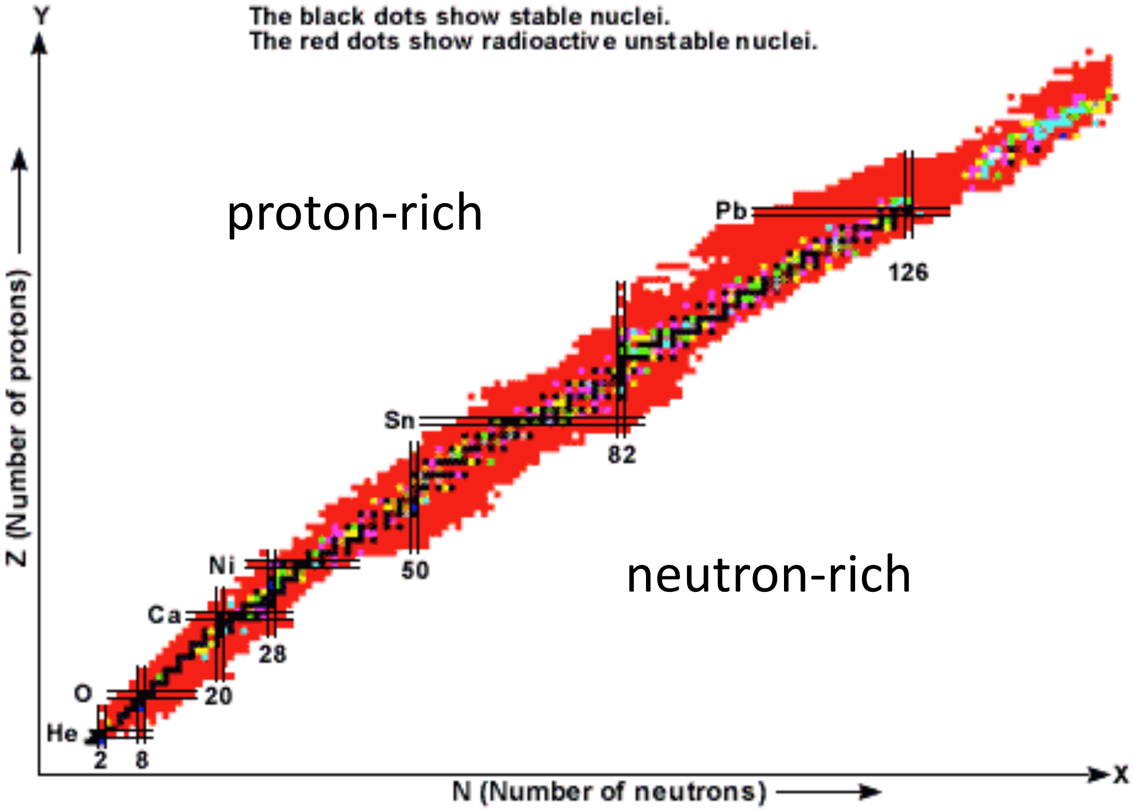


Heart



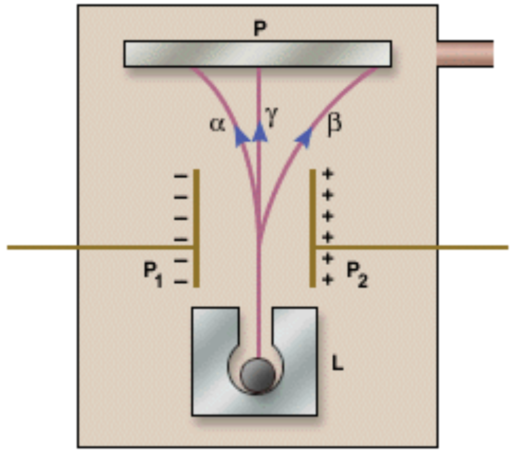
Radioactivity

Radioactive nuclei



Decay modes

α: helium 4-nuclei
β: electrons e^-
γ: photons



α, β and γ radiations

Radioactivity

- First-order kinetics of radioactive decay:

$$\frac{dN}{dt} = -\lambda \cdot N \quad \rightarrow \quad N(t) = N_0 e^{-\lambda t}$$

- Radioactivity = number of disintegrations per unit time:

$$Q = -\frac{dN}{dt} = \lambda \cdot N$$

Units:	Curie (Ci)	1 Ci = $3.7 \cdot 10^{10}$ disintegrations/s (=activity of 1g ^{226}Ra)
	Becquerels (Bq)	1 Bq = 1 disintegration/s

- **Physical half-life time**:

$$\mathbf{N(t_{1/2}) = \frac{N_0}{2} = N_0\, e^{-\lambda \cdot t_{1/2}} \quad \rightarrow \quad t_{1/2} = \frac{\ln(2)}{\lambda}}$$

Biological half-life time

- Physical half-life time:

$$t_{1/2} = \frac{\ln(2)}{\lambda}$$

- Biological half-life time:

$$t_{1/2,\text{bio}} = \frac{\ln(2)}{\lambda_{\text{bio}}}$$

- Combined tracer exposer:

$$N(t) = N_0 e^{-\lambda t} \cdot e^{-\lambda_{\text{bio}} t}$$

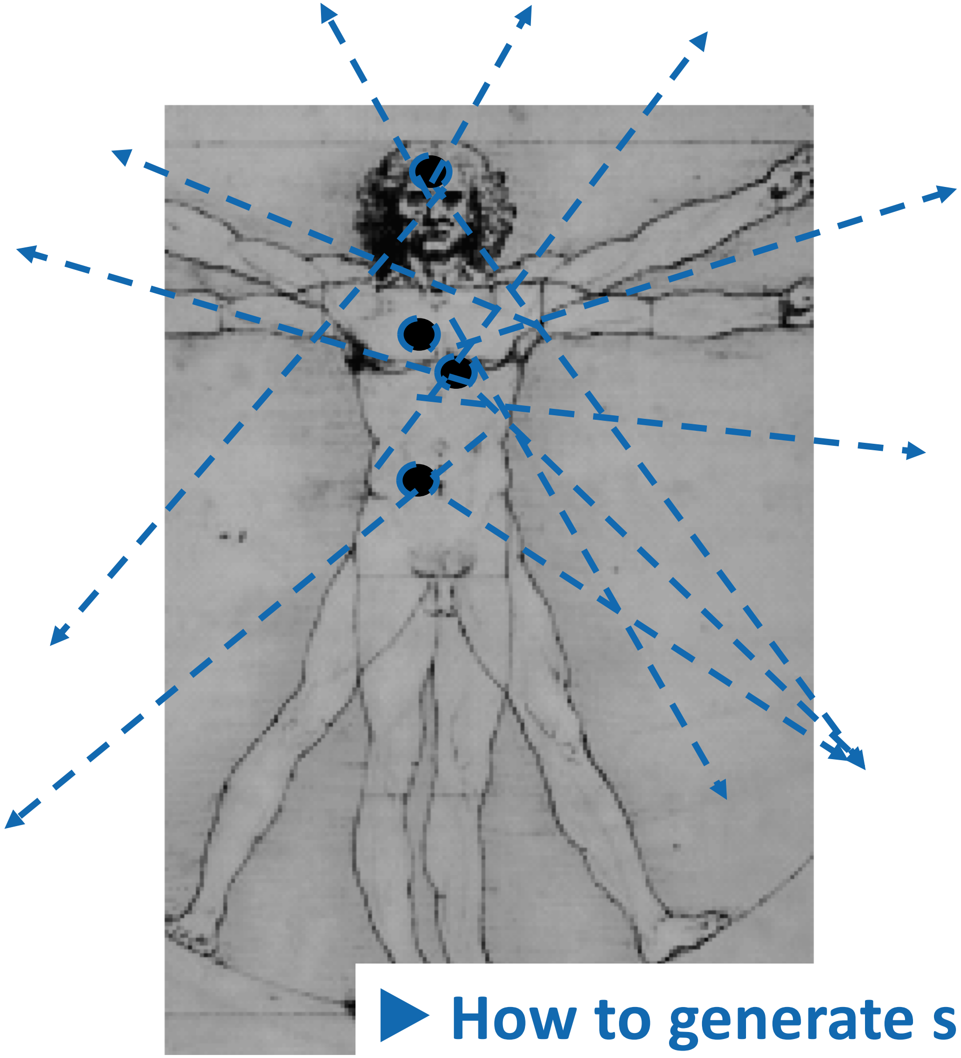
- **Effective tracer half-life time:**

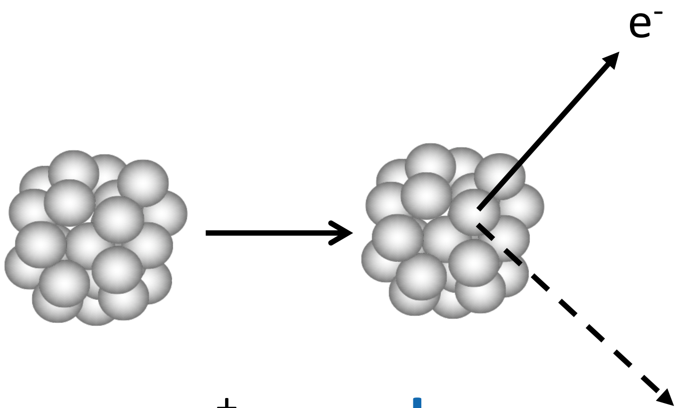
$$\mathbf{t_{1/2,eff} = \frac{t_{1/2} \cdot t_{1/2,bio}}{t_{1/2} + t_{1/2,bio}}}$$

Radioisotopes

Radioisotope	Energy (keV)	Half-life	Production
^{67}Ga	93, 185, 300	3.3d	cyclotron
^{99m}Tc	140	6h	generator
^{111}In	173, 247	67h	cyclotron
^{123}I	160	13h	cyclotron
^{133}Xe	81	5.2d	reactor
^{201}Tl	60, 83	73h	cyclotron

Challenge

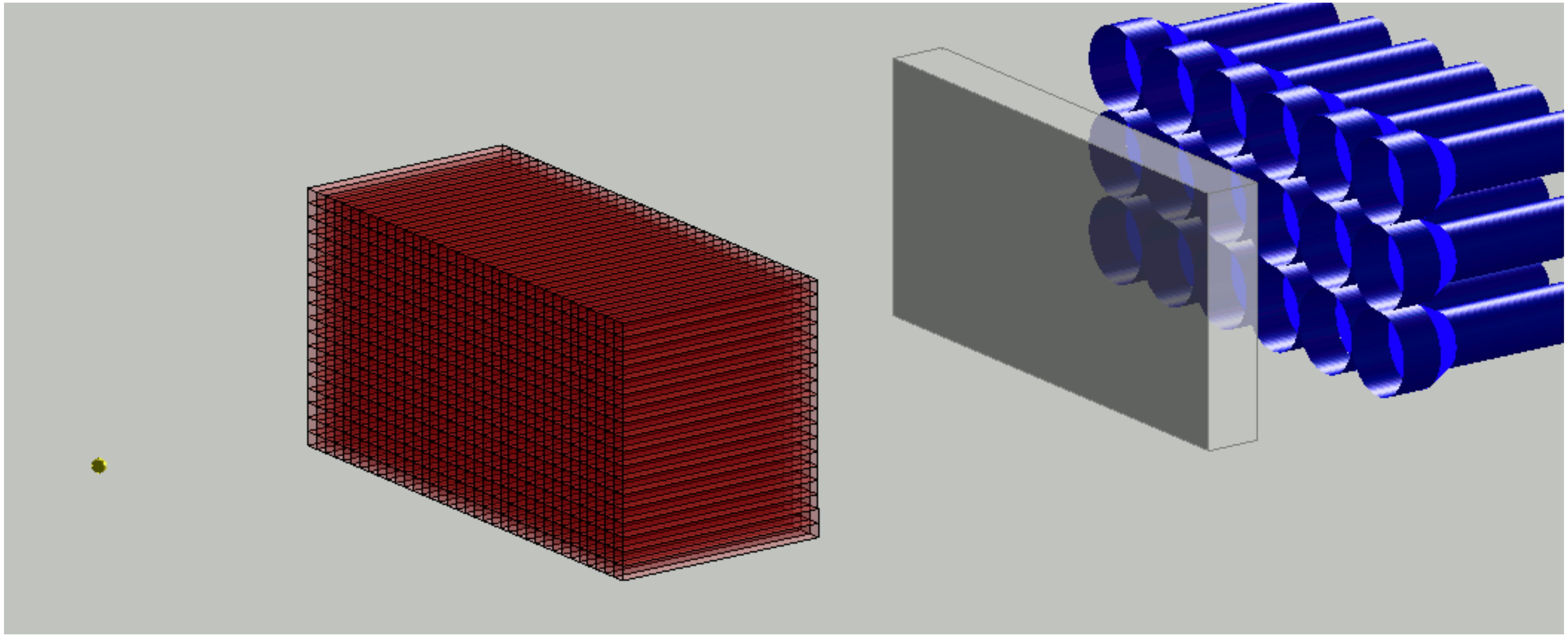




$$n \rightarrow p^{+} + e^{-} + h \cdot \nu$$

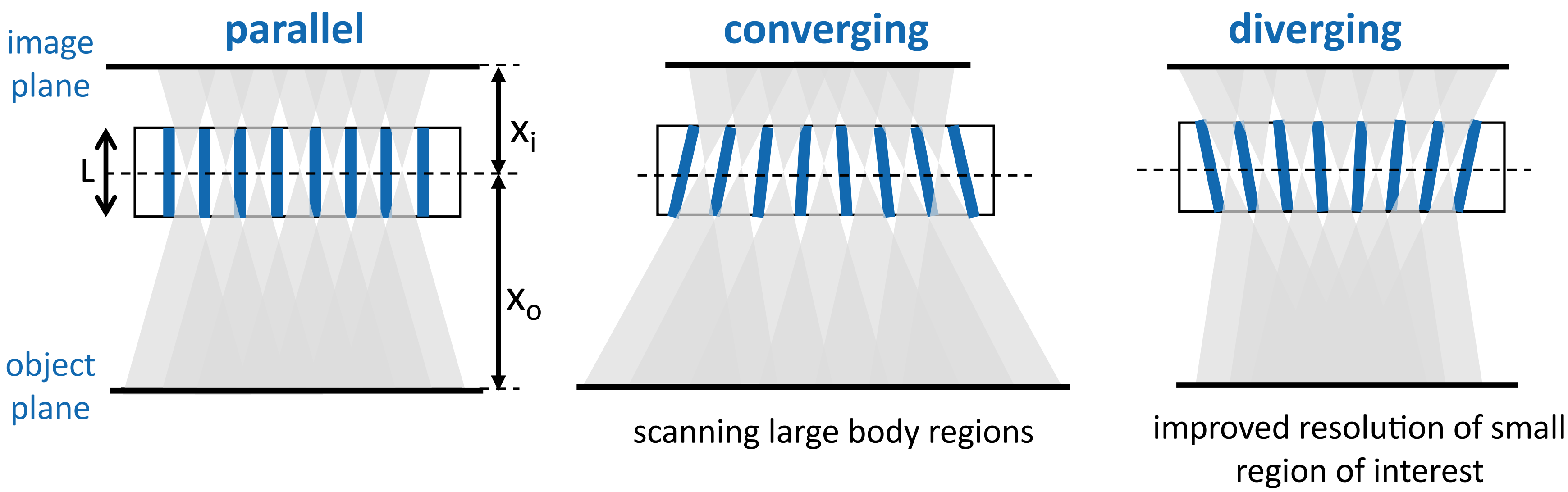
▶ **How to generate spatial resolution?**

Collimation



- **Geometrical collimation provides spatial information at the expense of reduced sensitivity** (only a small fraction of decays will be detected)

Collimator geometries

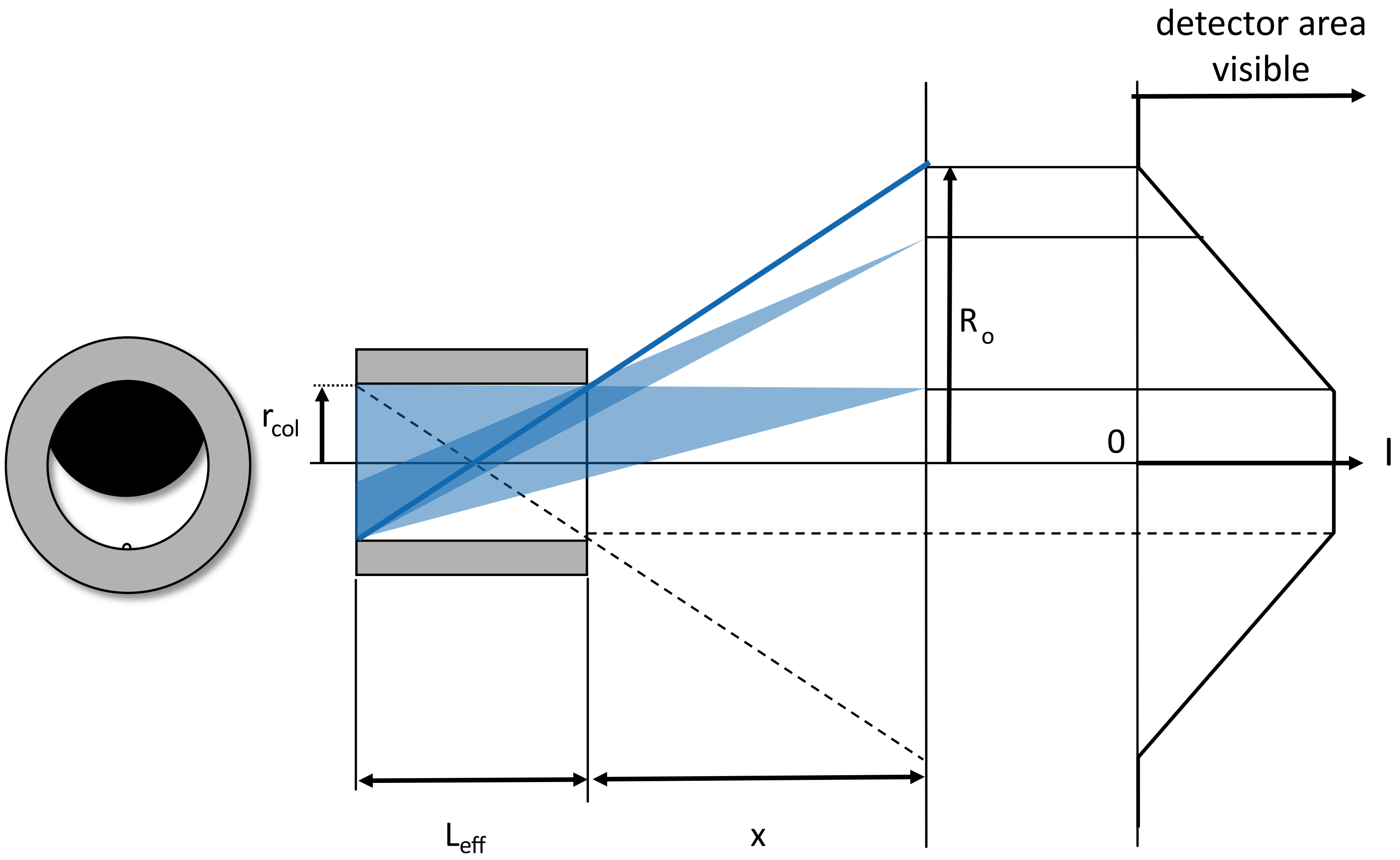


- Ratio of object size to image size depends on **collimator geometry** and **distance of object plane-collimator plane x_o** and **image plane-collimator plane x_i**

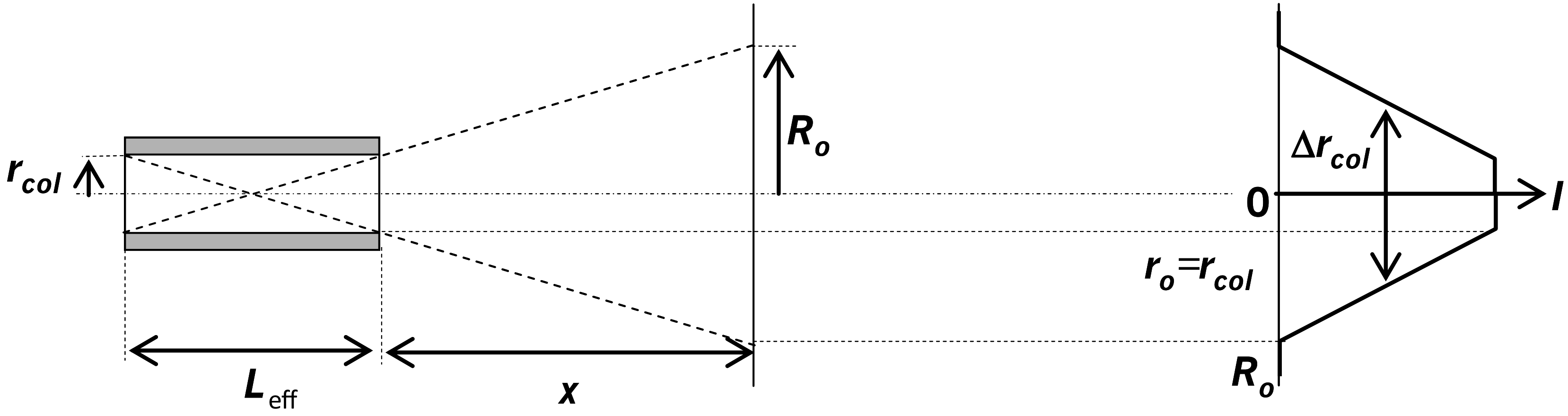
- Effective septal length (L_{eff}) is slightly shorter than the actual physical length (L) of the septa due to residual γ-ray transmission:

$$L_{eff} = L - \frac{2}{\mu_{septa}}$$

Geometrical collimation



Point-spread function



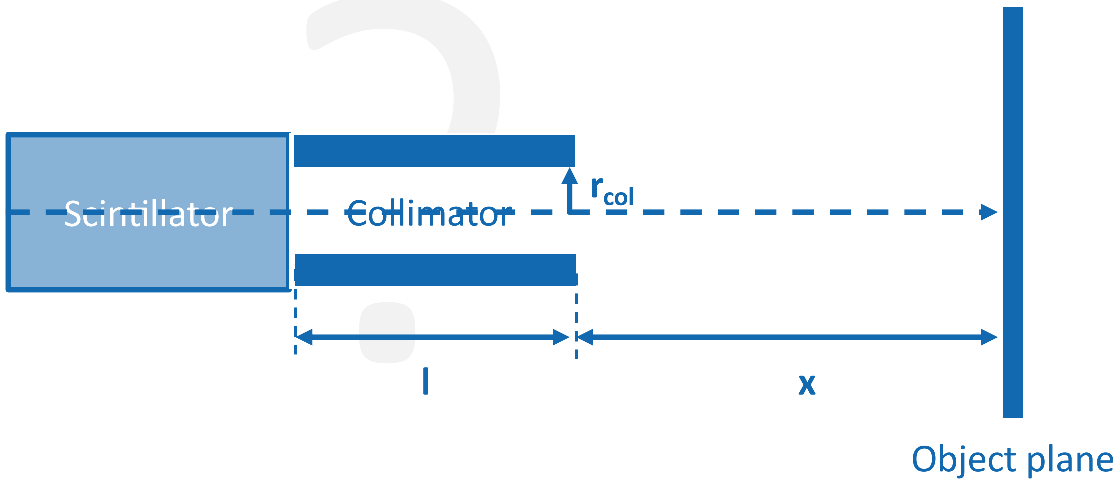
- **Point-spread function (PSF)** with full-width-at-half-maximum of Δr_{col}

$$R_0(x) = \frac{2 \cdot r_{col}}{L_{eff}}\left(x + \frac{L_{eff}}{2}\right) \qquad \Delta r_{coll}(x) = \frac{2 \cdot r_{col}}{L_{eff}}(x + L_{eff})$$

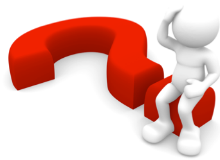
Clicker Activity (5 min)

Assume a cylindrical collimator of a radius of r_{col}=2mm and length of l=40mm. The object plane shall be at a distance of x=60mm from the collimator. What is the maximal distance from the collimator axis, at which the scintillation crystal still detects incoming γ-photons?

- 16 mm
- 8 mm
- 4 mm
- 2 mm

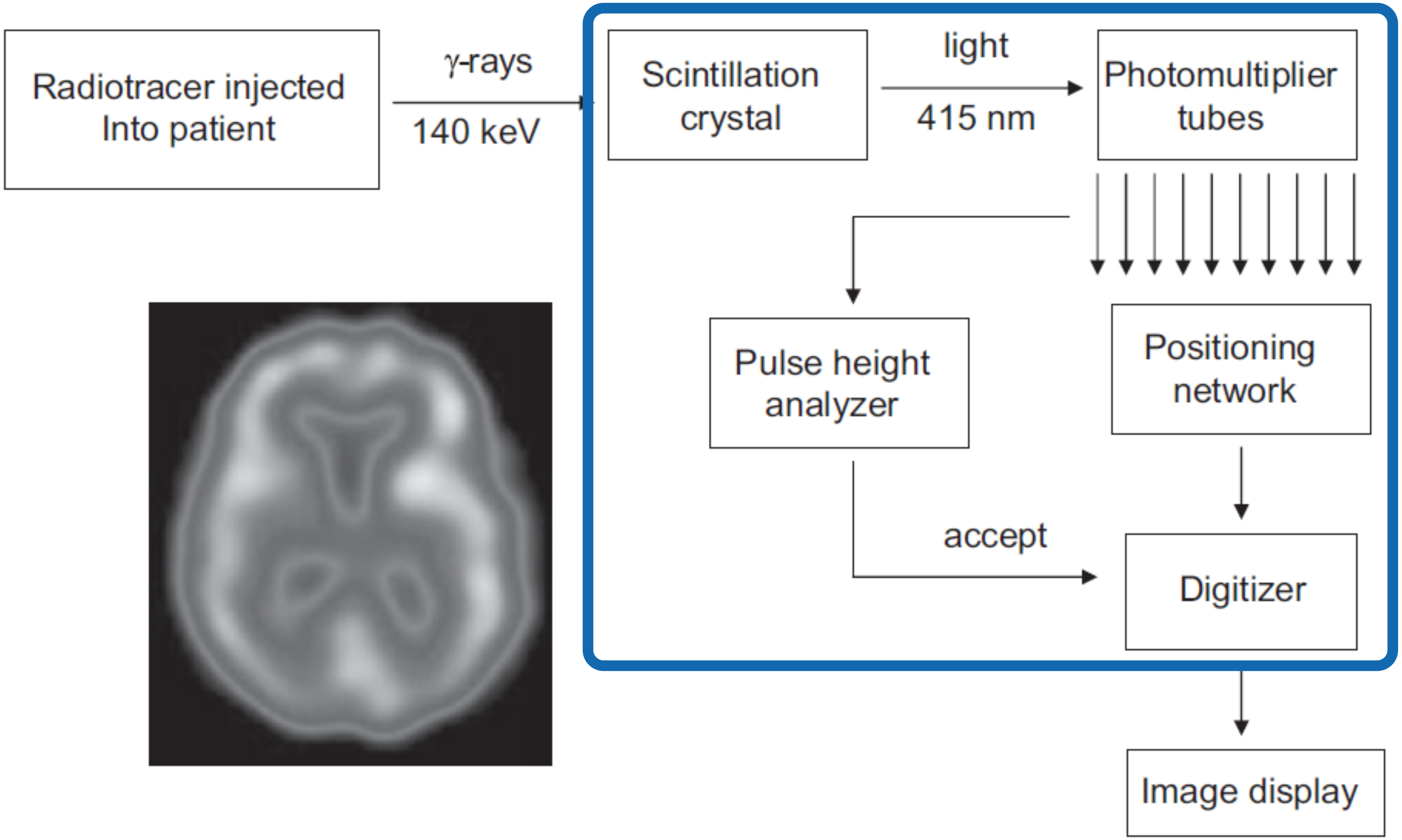


ETH Edu

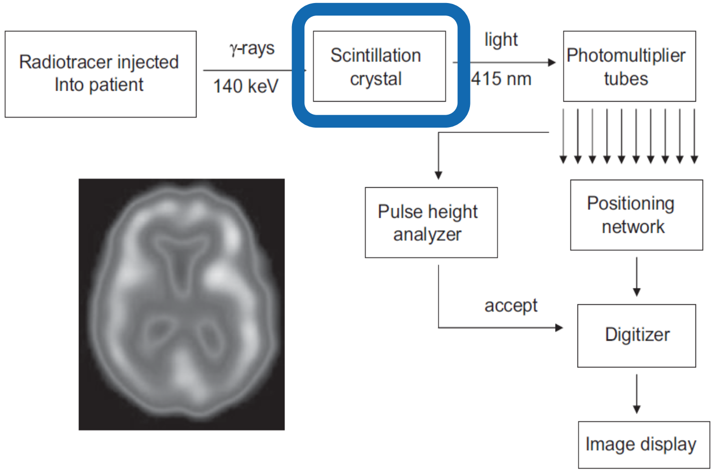


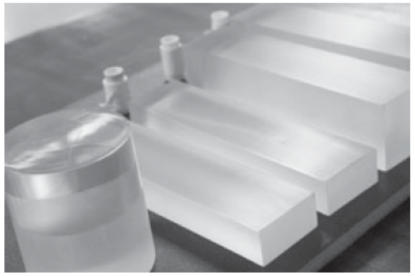
Gamma camera

Gamma camera

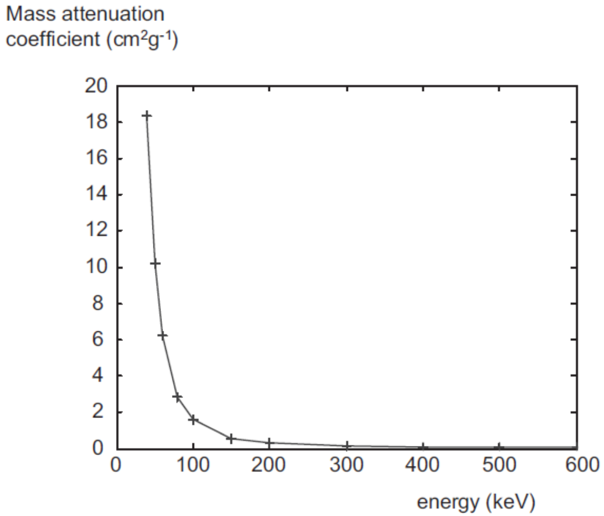


Scintillation detection





NaI(Tl)

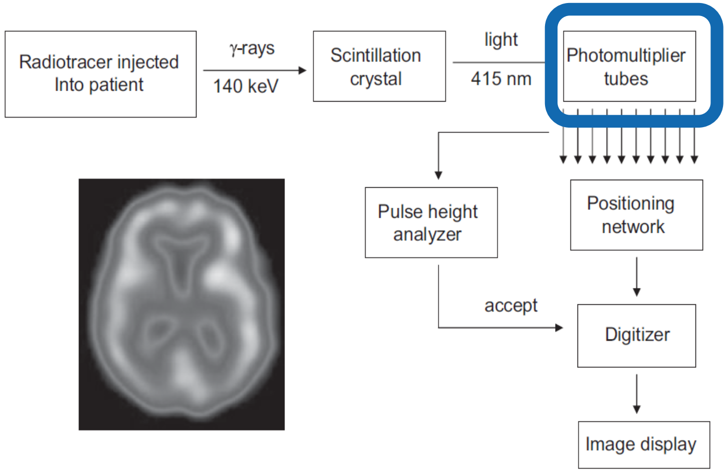


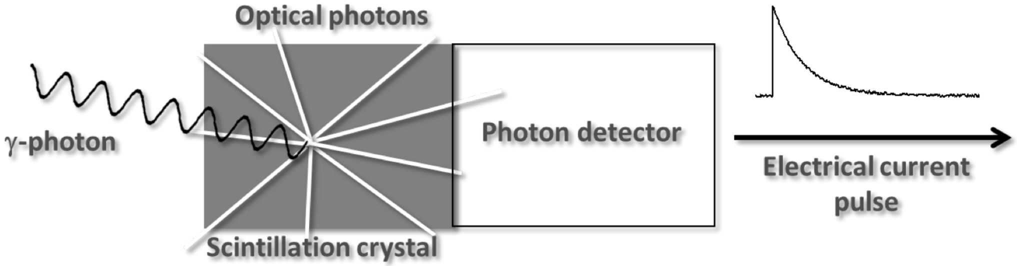
- **Photo effect** and **Compton scattering** cause excited electronic states in scintillation crystal ▶ **photon emission** (e.g. 415 nm for NaI(Tl))
- **Detection efficiency ε:**

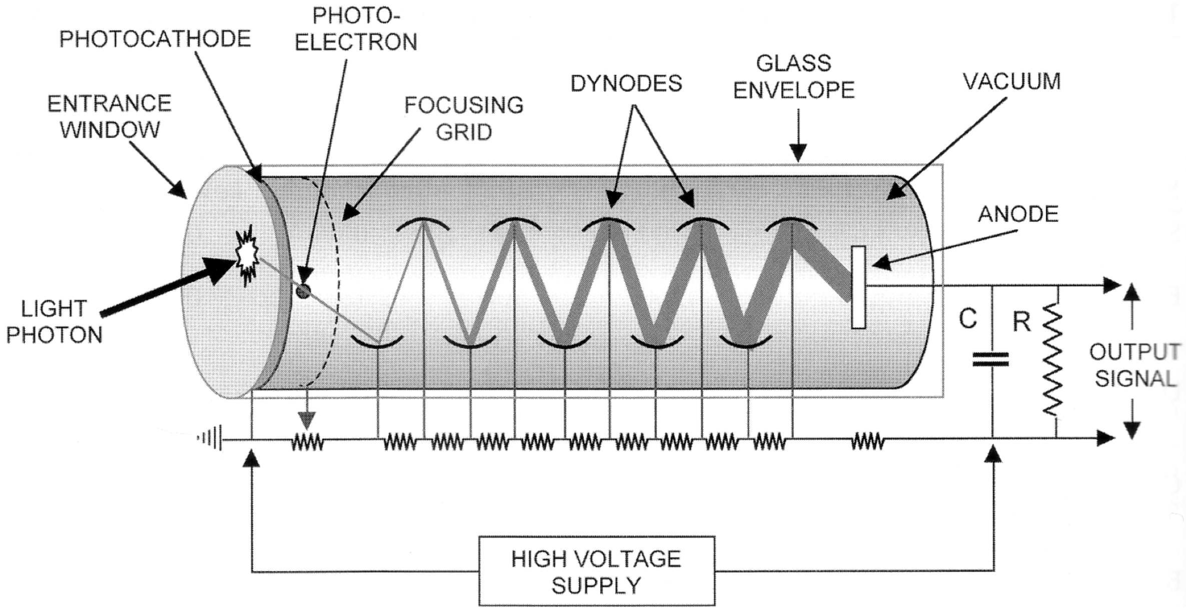
$$\varepsilon = 1 - e^{-\mu_{crystal} \cdot d_{crystal}}$$

$\mu_{crystal}$: attenuation coefficient
$d_{crystal}$: crystal thickness

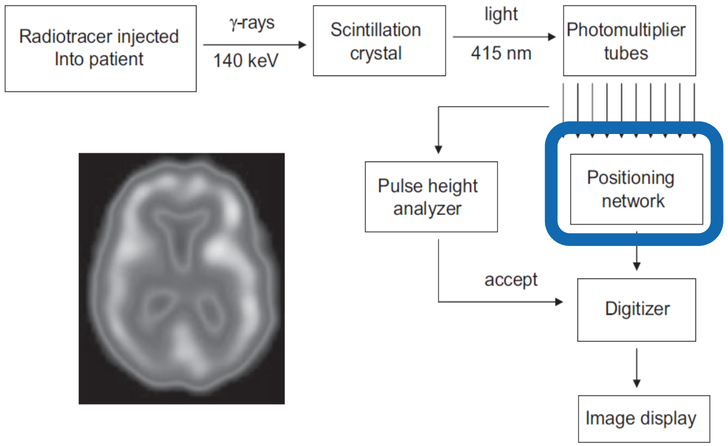
Photomultiplier tube (PMT)

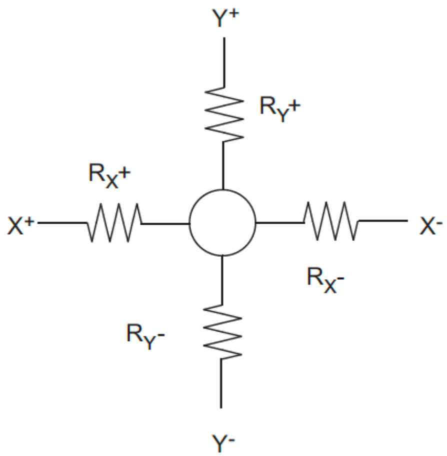


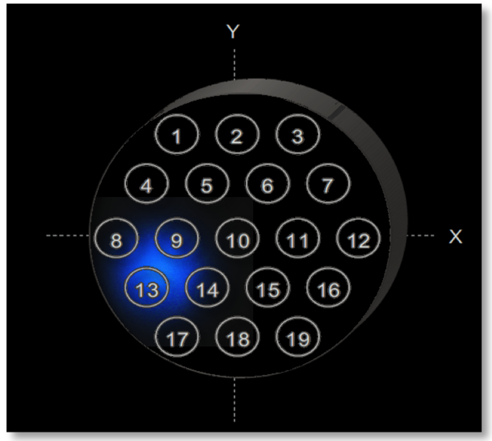




Positioning network



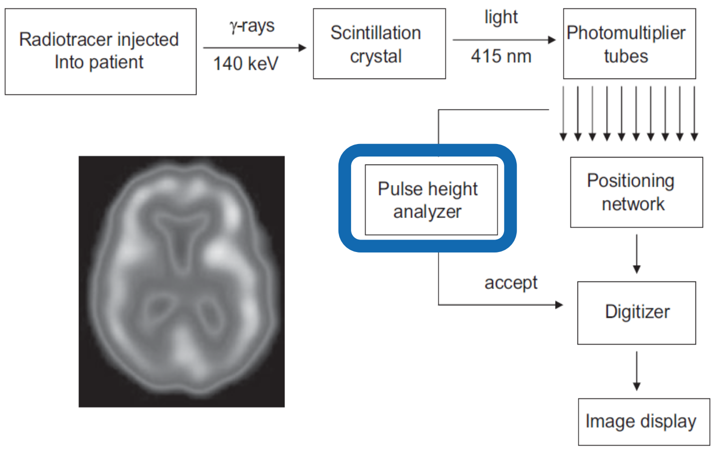


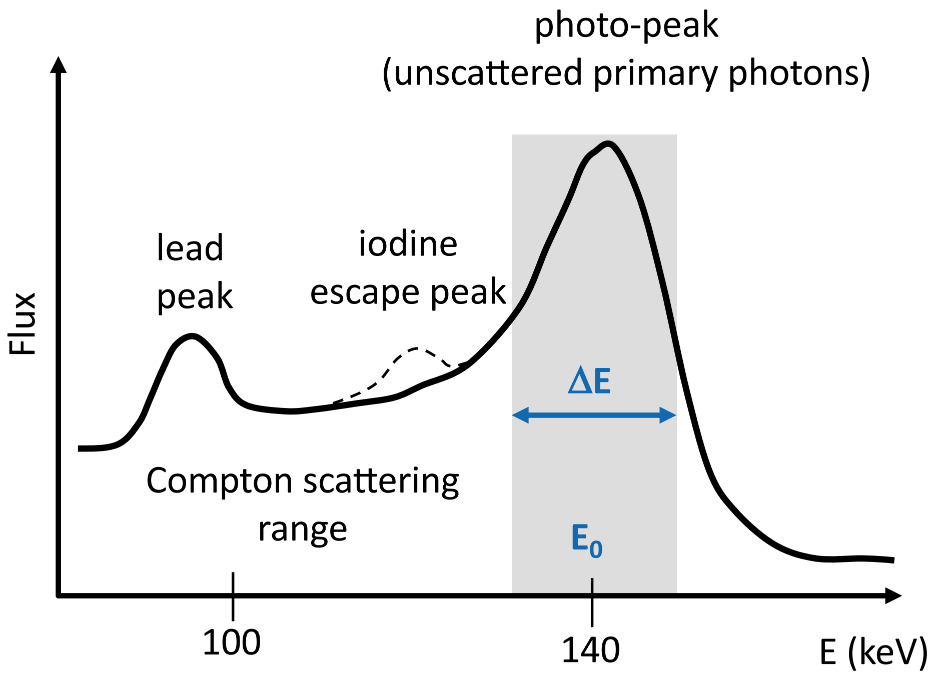


- Spatial response is inferred by **combined analysis of output** of all photomultiplier tubes
- **Location along X and Y** is determined according to:

$$\mathbf{X} = \frac{\mathbf{X}^{+} - \mathbf{X}^{-}}{\mathbf{X}^{+} + \mathbf{X}^{-}} \quad \mathbf{Y} = \frac{\mathbf{Y}^{+} - \mathbf{Y}^{-}}{\mathbf{Y}^{+} + \mathbf{Y}^{-}}$$

Pulse height analyzer





- **Pulse height (Z-signal)** is sum of output of all PMTs:

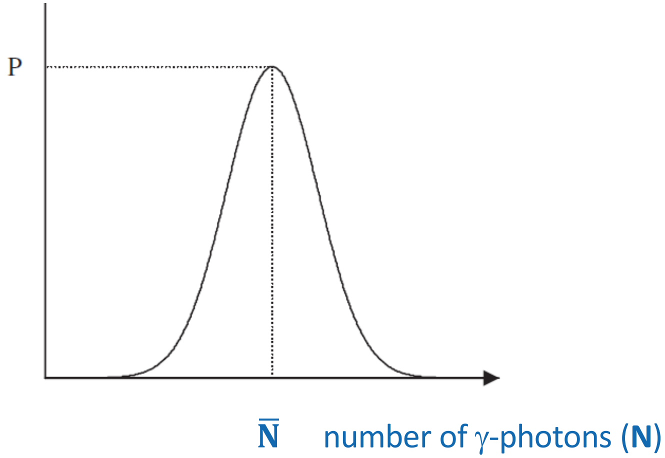
$$Z = \sum X^{+} + X^{-} + Y^{+} + Y^{-}$$

- **Energy resolution** of PMT: $\dfrac{\Delta E}{E_o} = \dfrac{1}{\sqrt{p \cdot N_{light}}}$

ΔE	FWHM of energy peak of primary γ-quanta
E_0	Average energy of primary (unscattered) γ-photons
N_{light}	Number of light photons produced by γ-quantum
p	Probability that light photon induces electron in PMT

Signal-to-noise ratio and spatial resolution

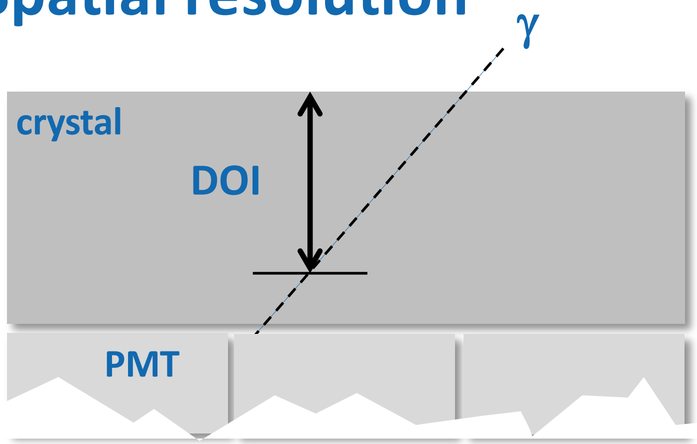
- **Poisson distribution**



- **Signal-to-noise ratio (SNR)**

$$\mathrm{SNR} = \frac{\bar{N}}{\sqrt{\bar{N}}} = \sqrt{\bar{N}}$$

- **Spatial resolution**

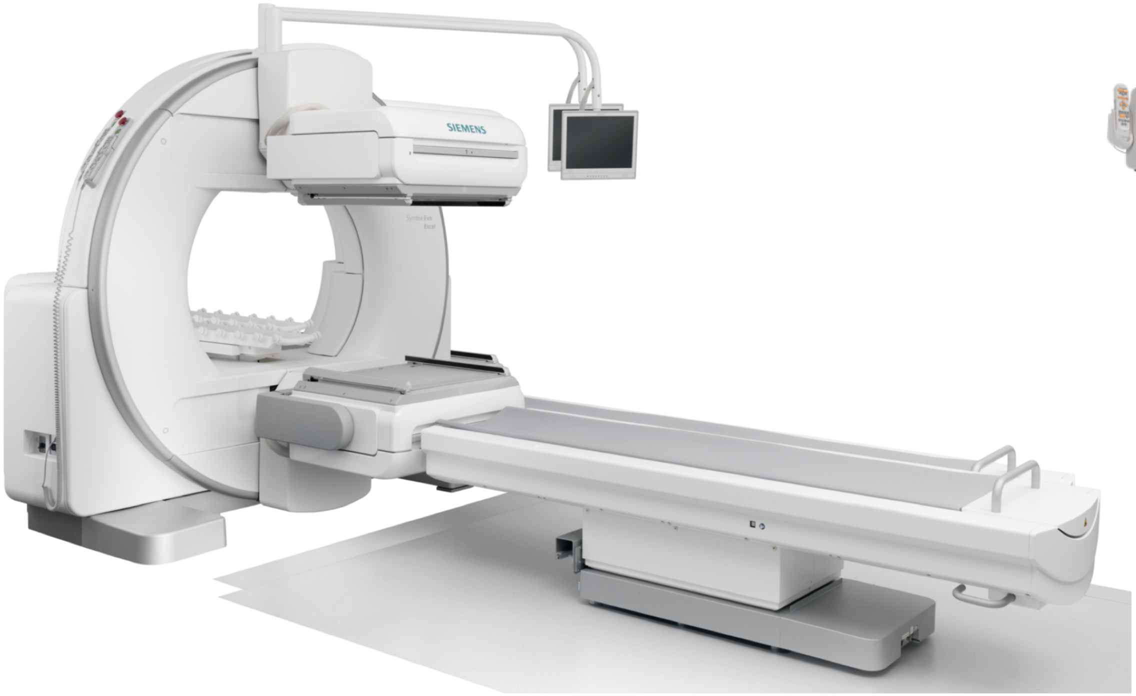


$$R = \sqrt{R_{detect}^2 + R_{coll}^2}$$

R_{coll} (see above), $R_{cdetect}$ reflect uncertainty in measurement location of scintillation event (depth of interaction DOI error; error in PMT estimation)

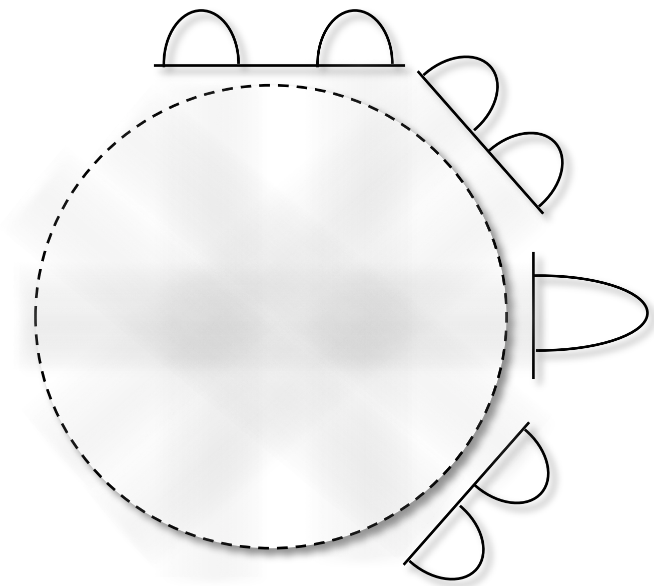
Single photon emission computer tomography (SPECT)

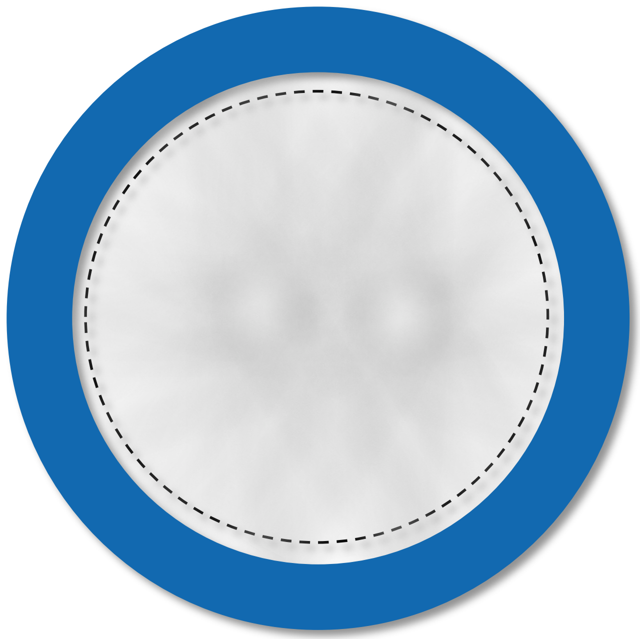
SPECT



▶ **Systems with rotating gamma camera**

SPECT image reconstruction

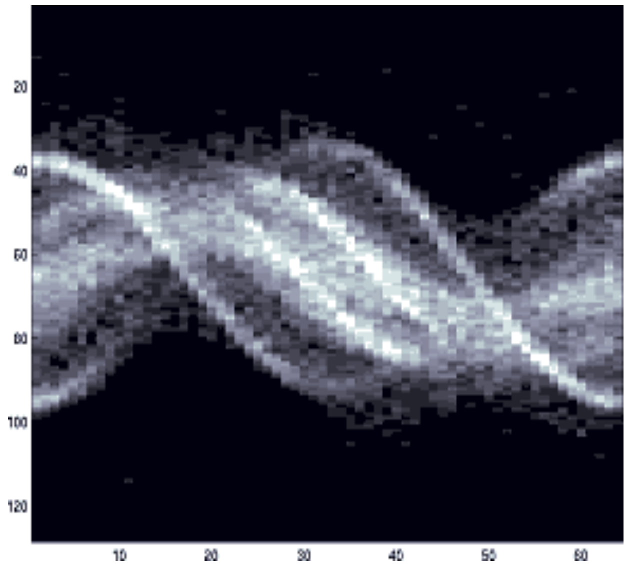




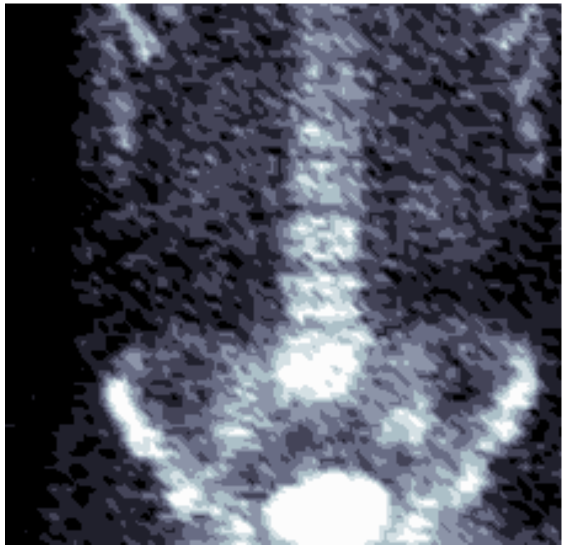
▶ Image reconstruction using Filtered Backprojection

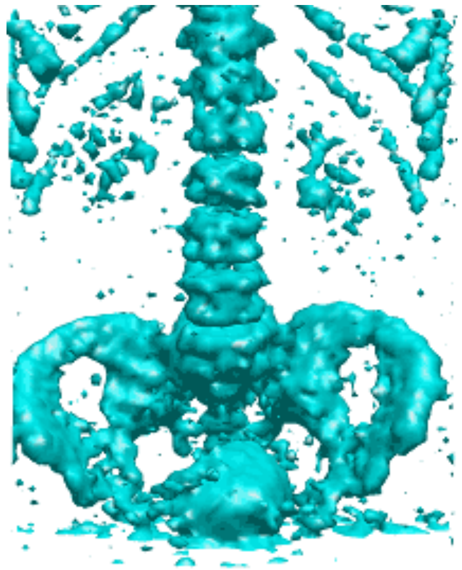
SPECT 3D reconstruction

Sinogram



Reconstruction

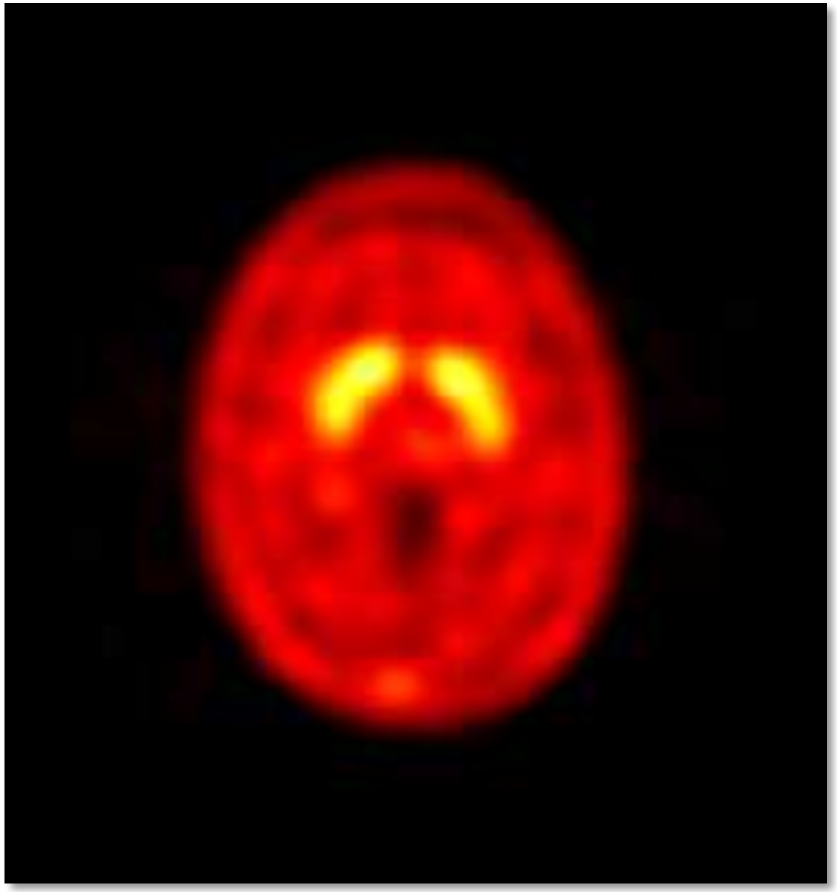




human skeleton using ^{99m}Tc based bone tracer

http://www.physics.ubc.ca

SPECT applications



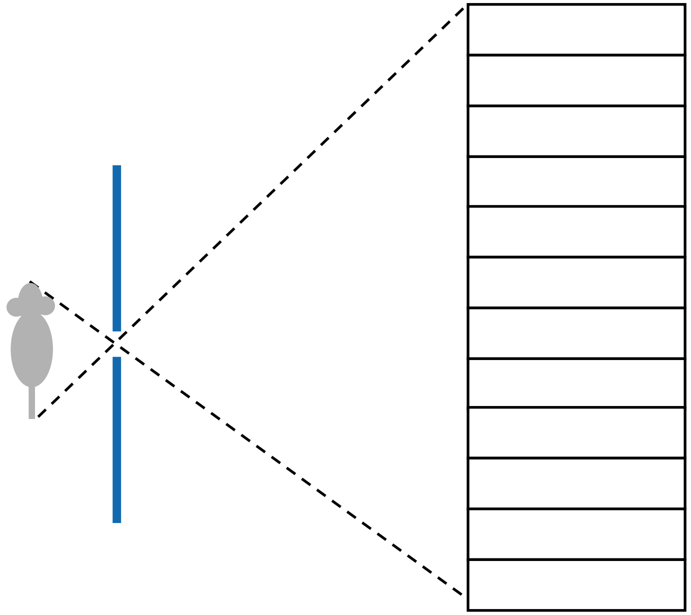
Dopamine transporter imaging

SPECT radioligand is derivative of tropane ligand family and labeled with ^{99m}Tc reflects location of dopamine transporter in caudate putamen.

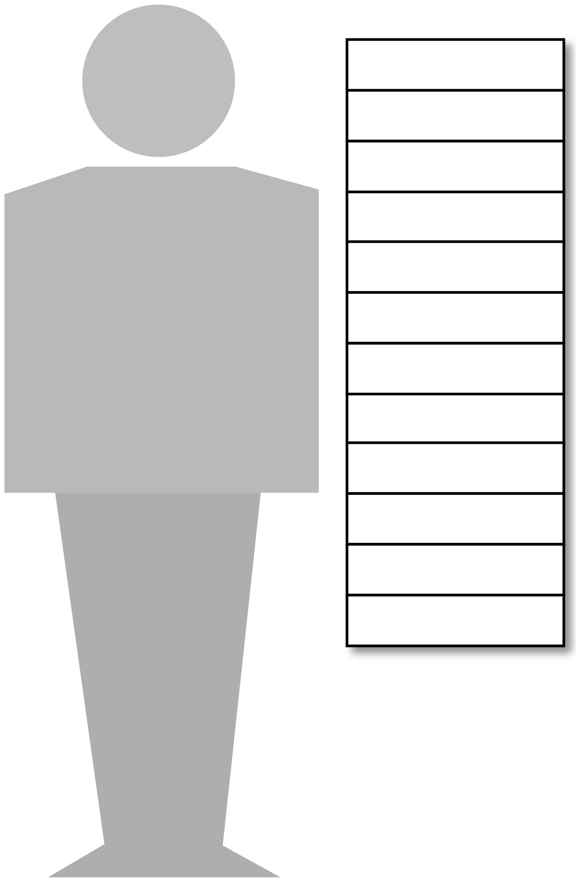
▶ in Parkinson patients receptor density is significantly reduced.

MicroSPECT

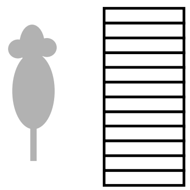
Pinhole



Standard detector

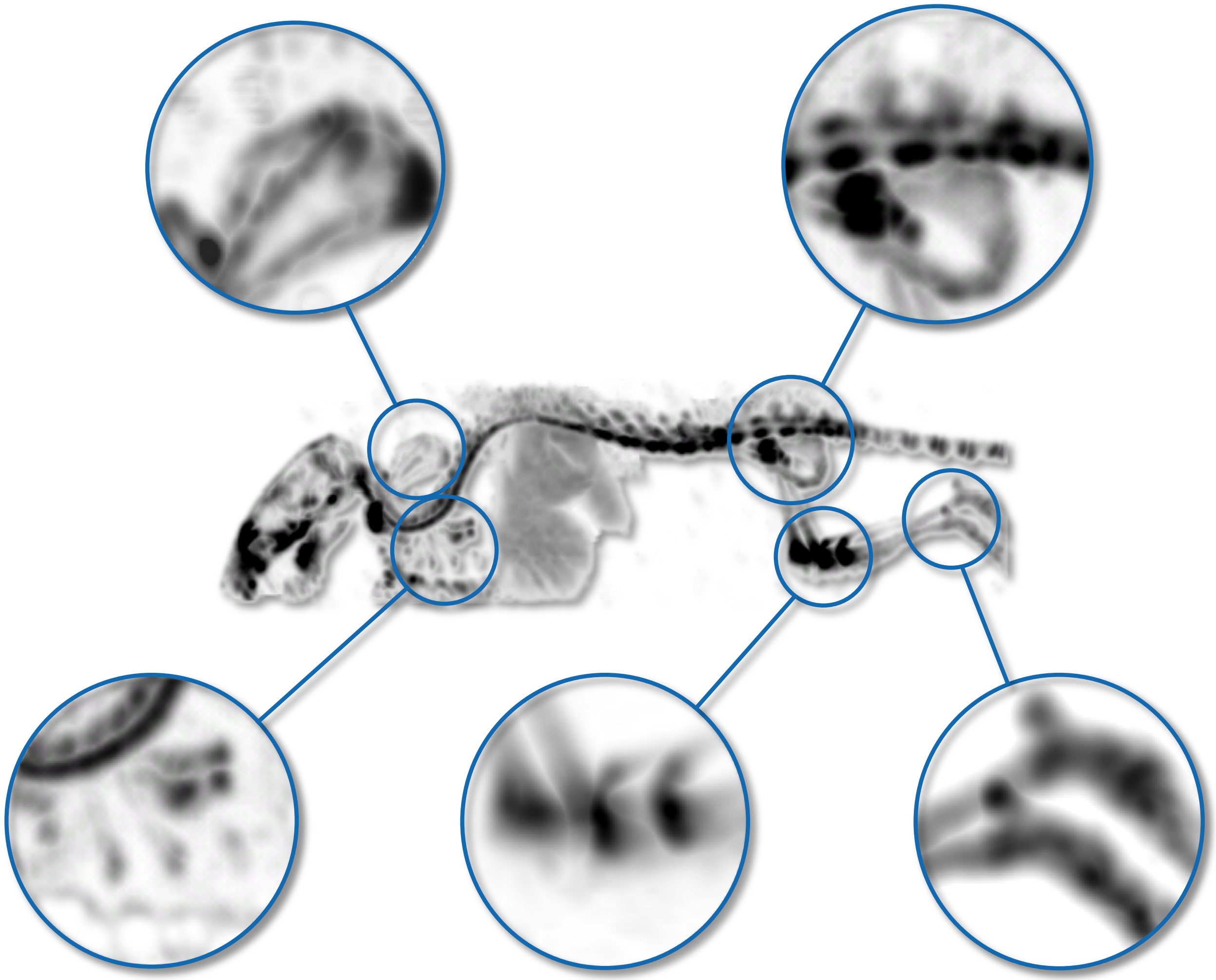


Miniaturized detector



MicroSPECT

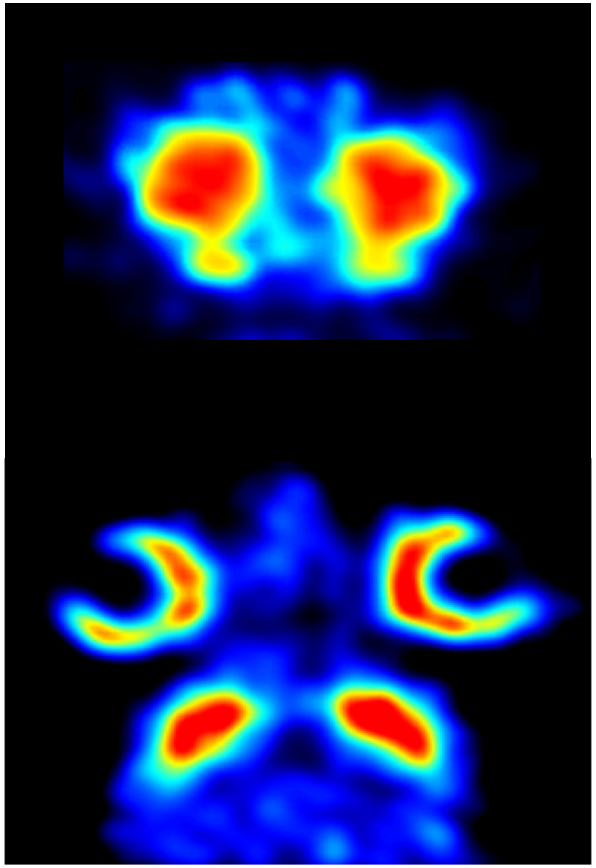
High-resolution mouse imaging



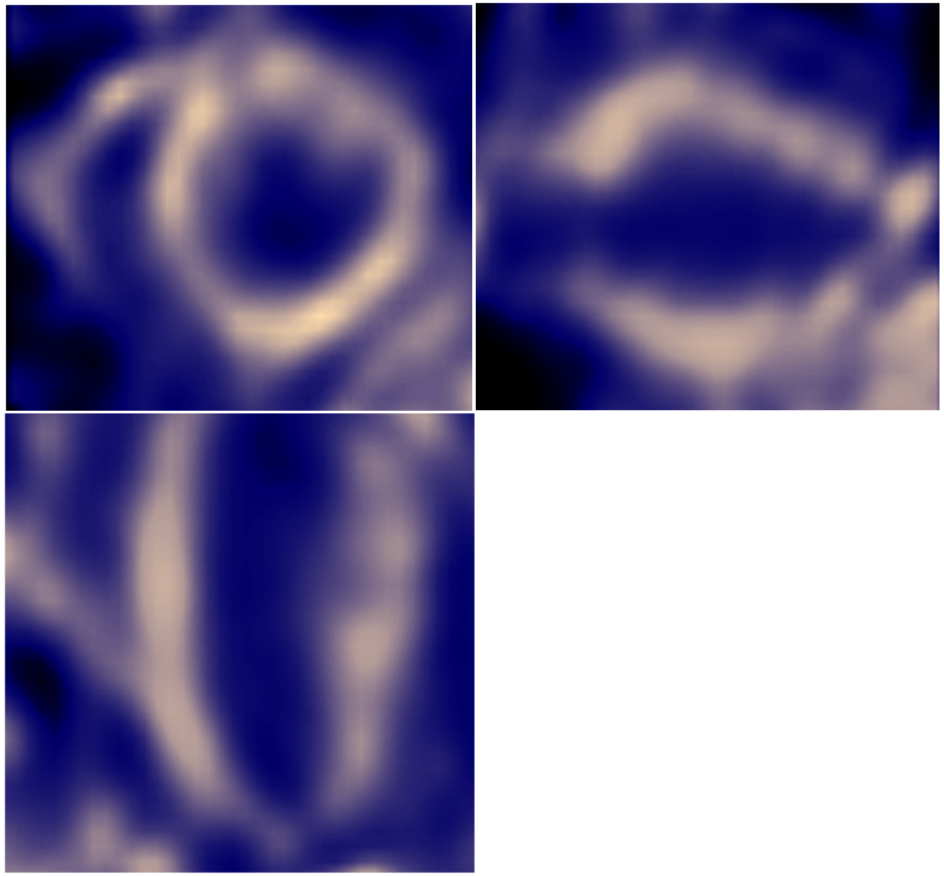
courtesy F Beekman

MicroSPECT

Mouse brain
dopamine transporter



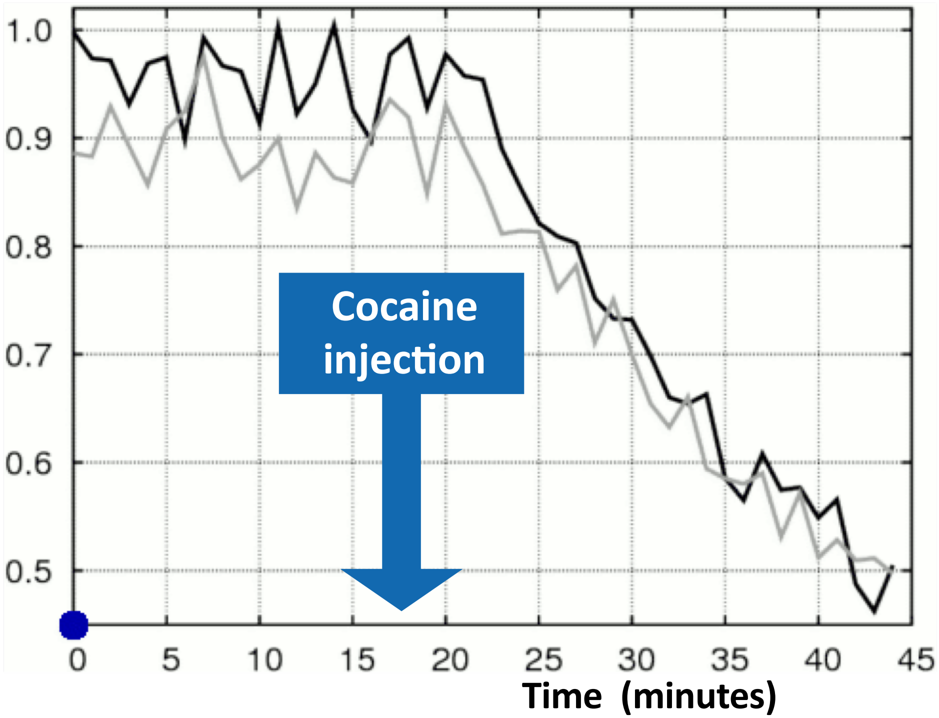
Mouse heart
perfusion

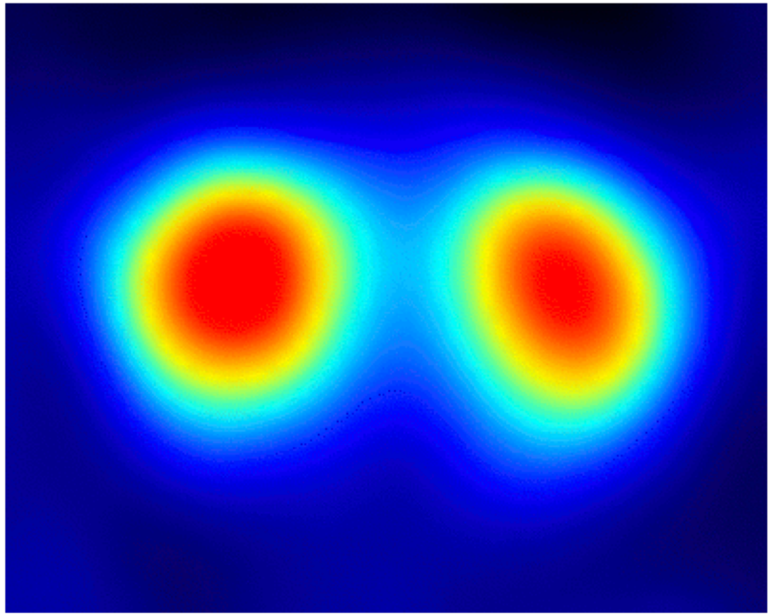


Molecular Imaging Laboratories courtesy F Beekman

MicroSPECT

Dynamic SPECT of dopamine transporters in mouse brain





Left Caudate Putamen
Right Caudate Putamen

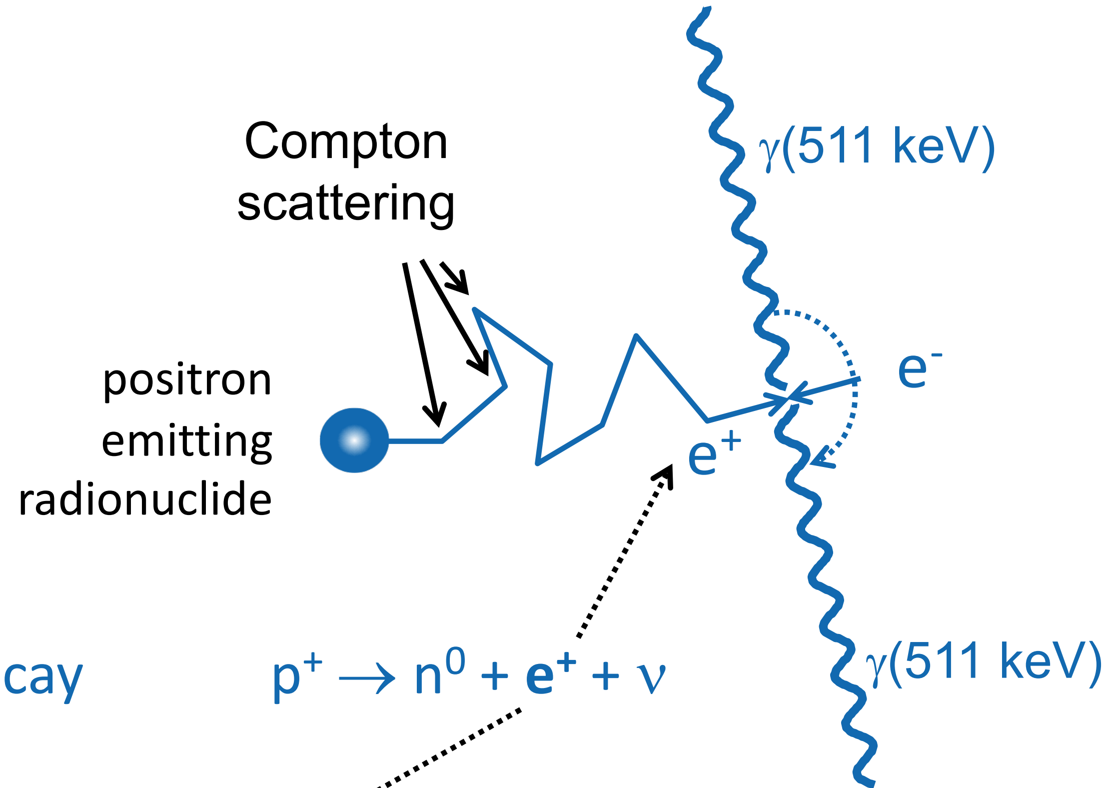
MILabs Molecular Imaging Laboratories courtesy F Beekman

Positron emission tomography (PET)

Positron emitters

Radionuclide	Half-life	E_{max} (MeV)	e^+ decay (%)
^{11}C	20.4 min	0.96	100
^{13}N	10 min	1.20	100
^{15}O	2 min	1.73	100
^{18}F	110 min	0.63	97
^{22}Na	2.6 y	0.55	90
^{62}Cu	9.7 min	2.93	97
^{64}Cu	12.7 h	0.65	29
^{68}Ga	67.6 min	1.89	89
^{76}Br	16.2 h	Various	56
^{82}Rb	1.3 min	2.60, 3.38	96
^{124}I	4.2 d	1.53, 2.14	23

Positron annihilation



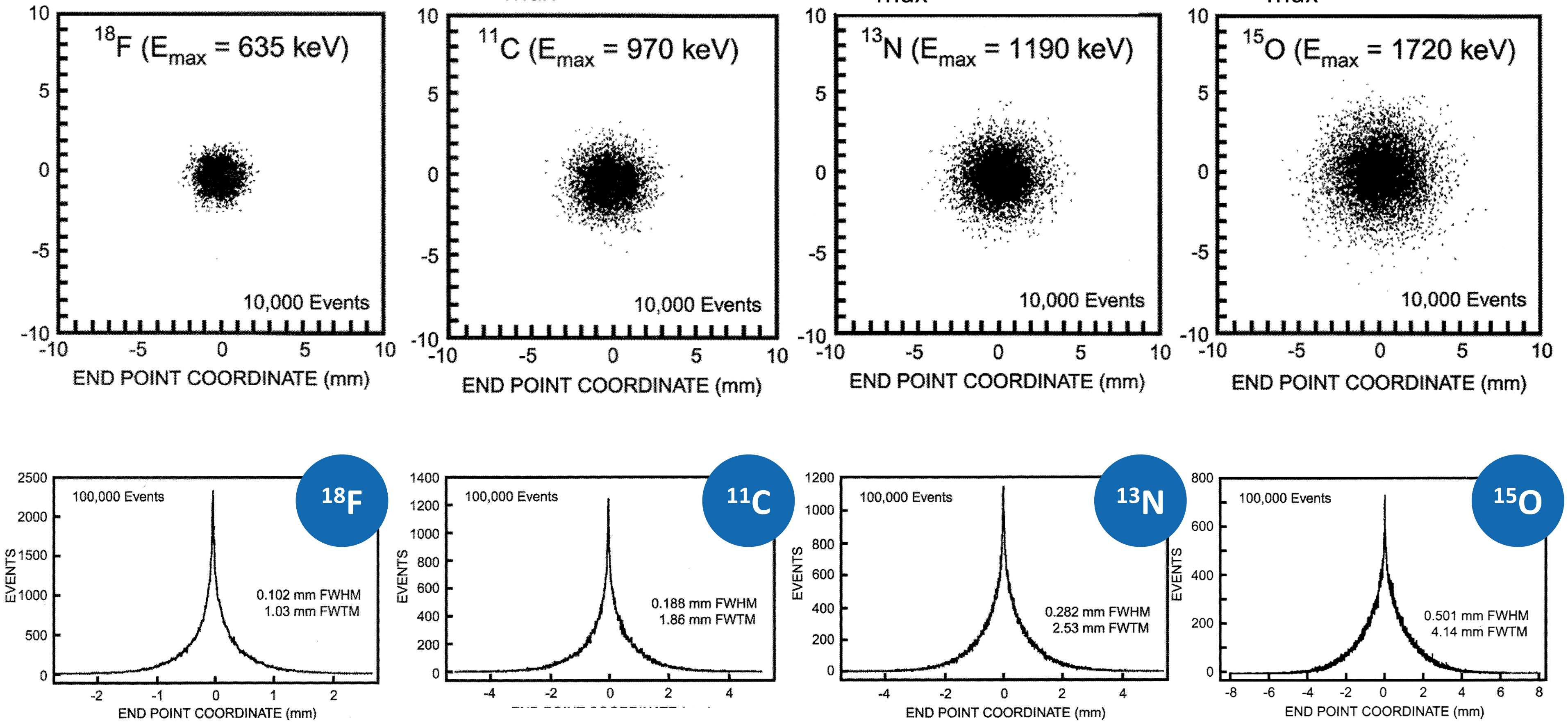
- nuclear decay $p^+ \rightarrow n^0 + \mathbf{e^+} + \nu$

- annihilation $\mathbf{e^+ + e^- \rightarrow \gamma + \gamma}$

- Coincidence detection of **two g-photons** gives information on location of positron-electron annihilation (<u>not</u> on location of radionuclide)

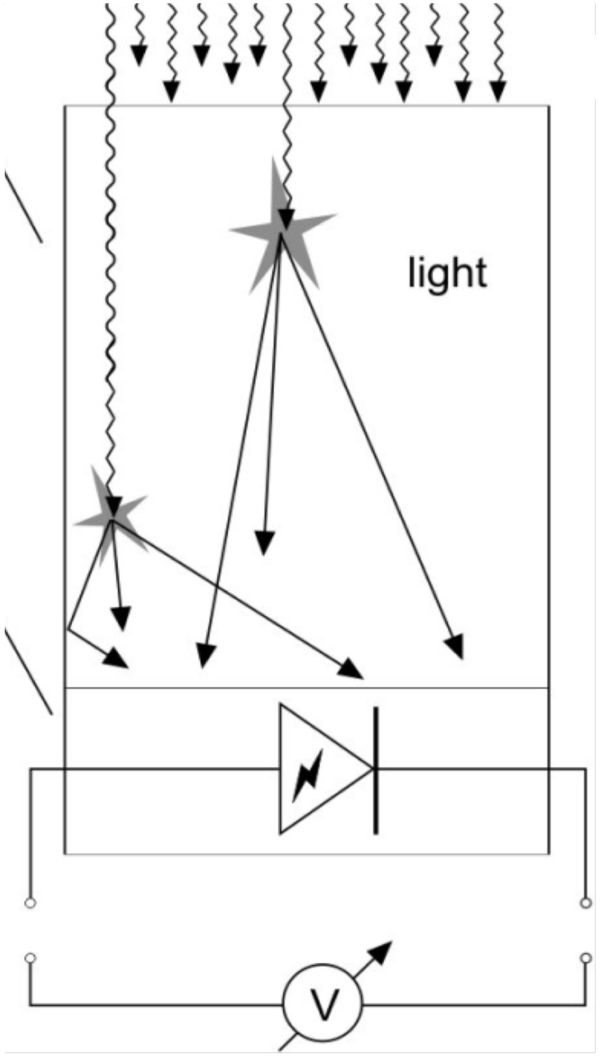
Positron annihilation range

E_{max}=635keV | E_{max}=970keV | E_{max}=1190keV | E_{max}=1720keV



Levin, Hoffmann, Phy Med Biol 44: 781-799 (1999)

Coincidence detection



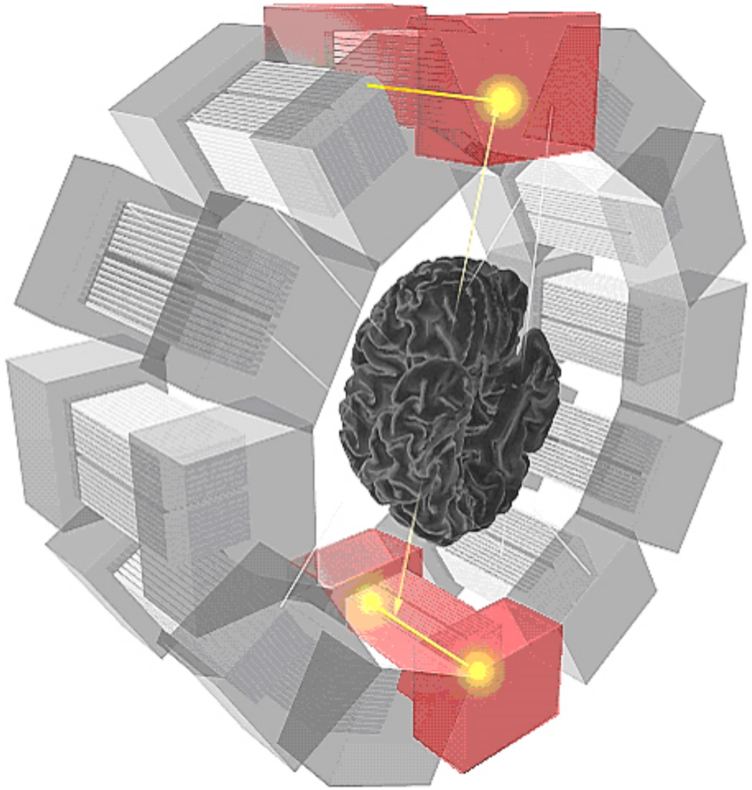
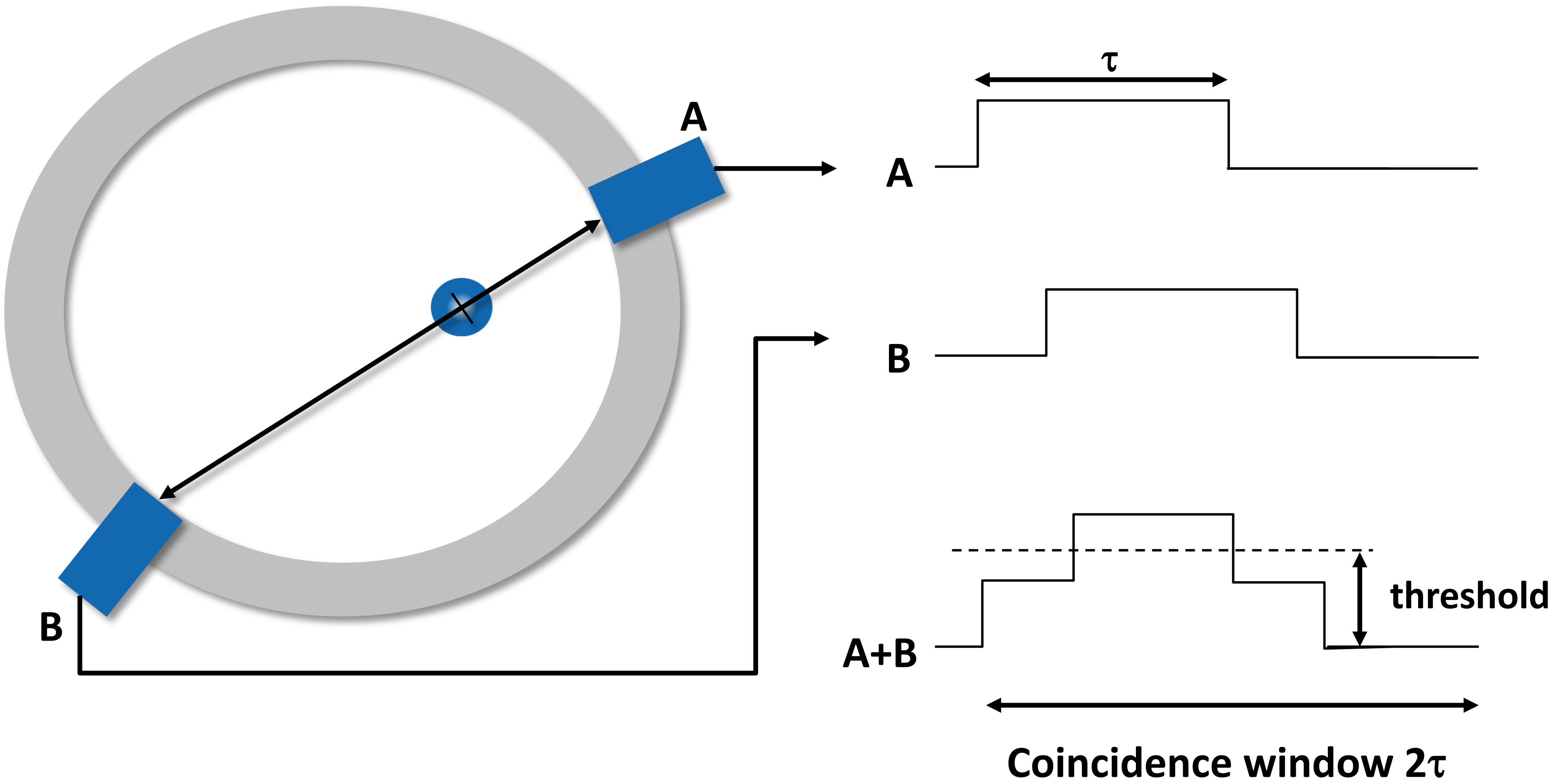


Image courtesy of HUG

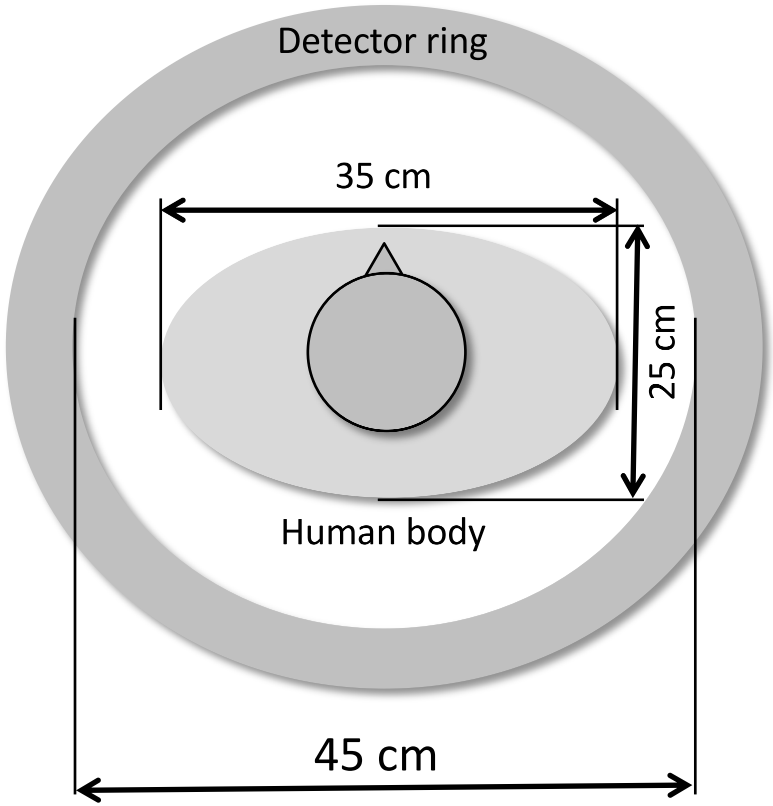
Coincidence detection



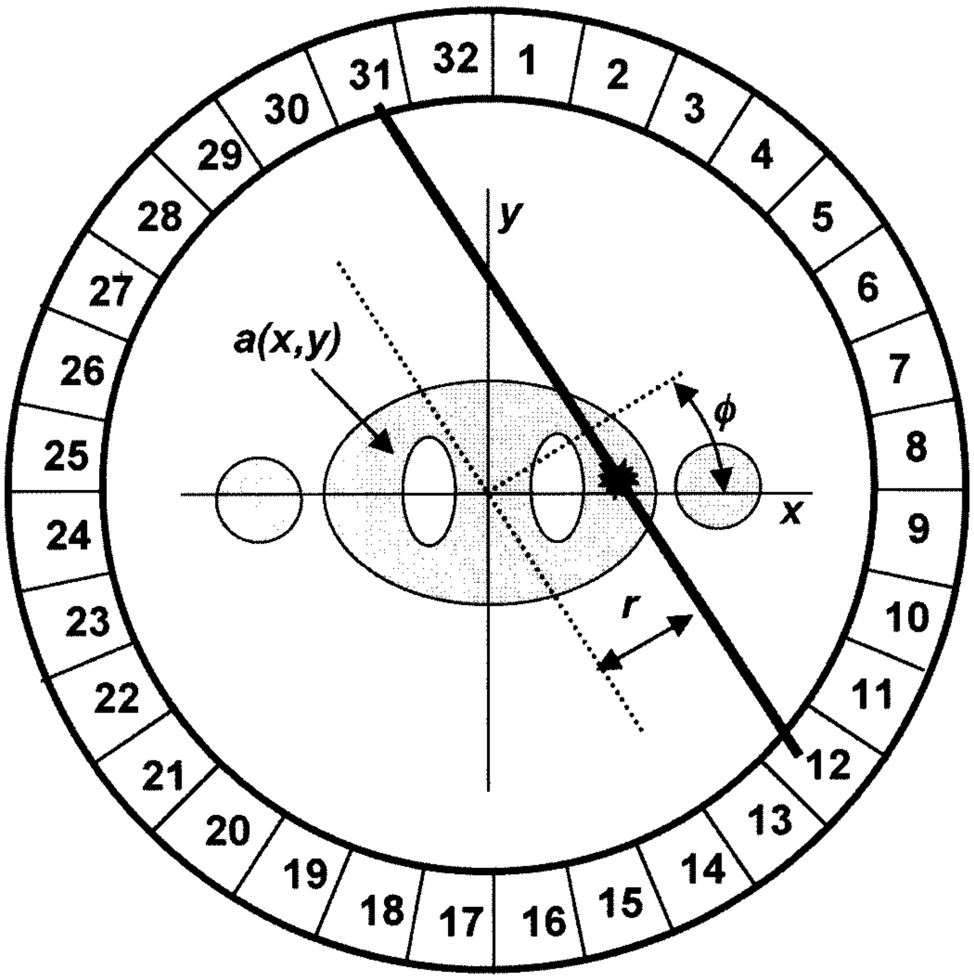
Clicker Activity (5 min)

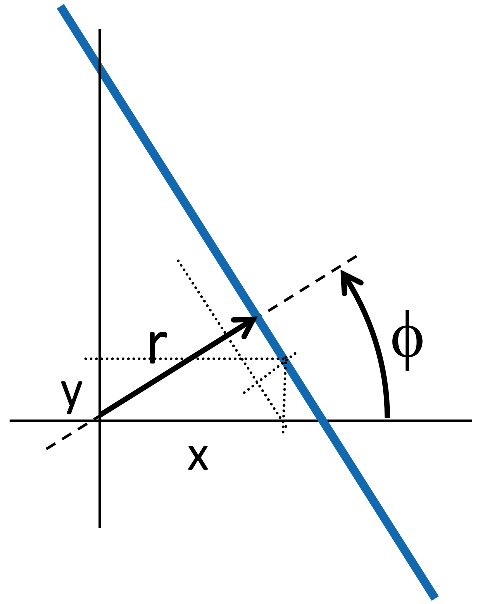
What is the maximum possible time difference of scintillation events in this example?

- 12 ns
- 24 ns
- 1.2 ns
- 2.4 ns



Line of Response (LoR)

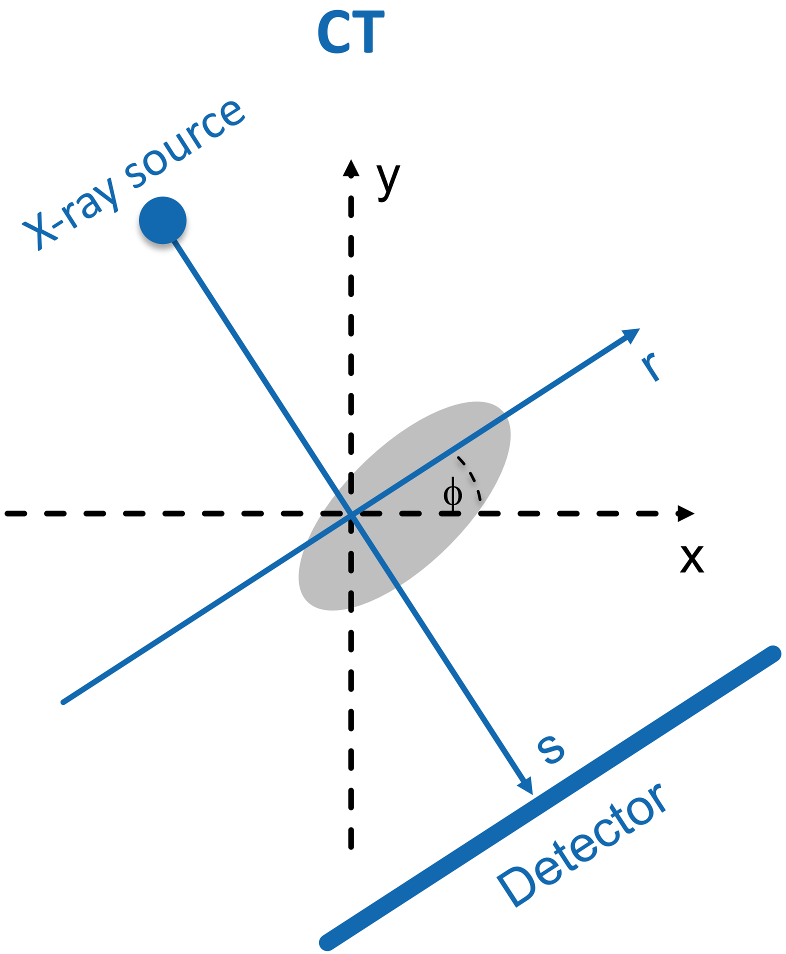


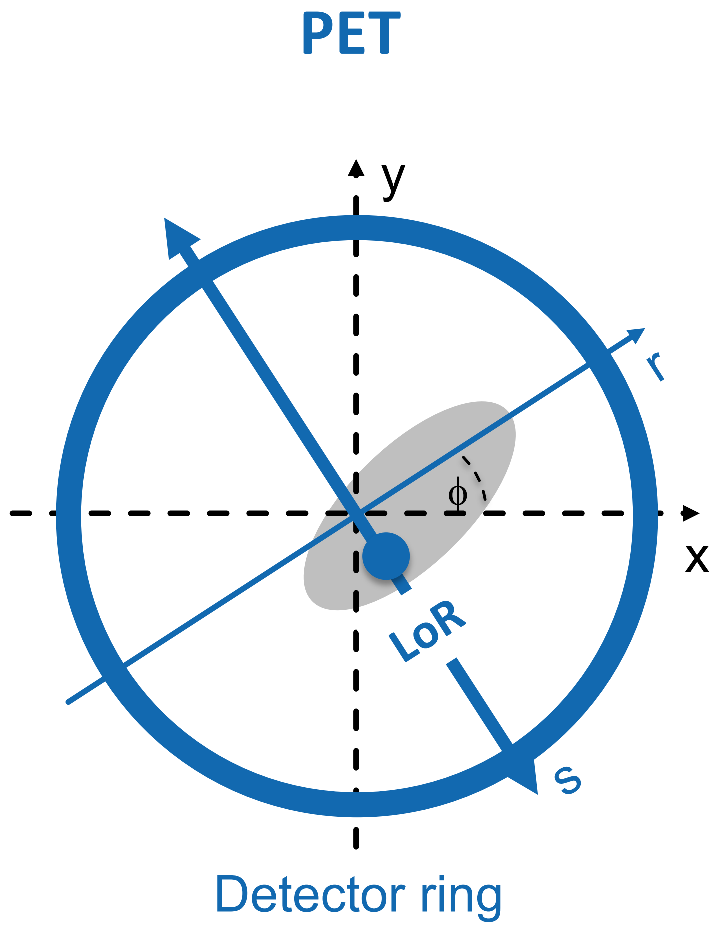


$$\mathbf{r = x \cdot cos\varphi + y \cdot sin\varphi}$$

ETH zürich | University of Zurich UZH

Image reconstruction



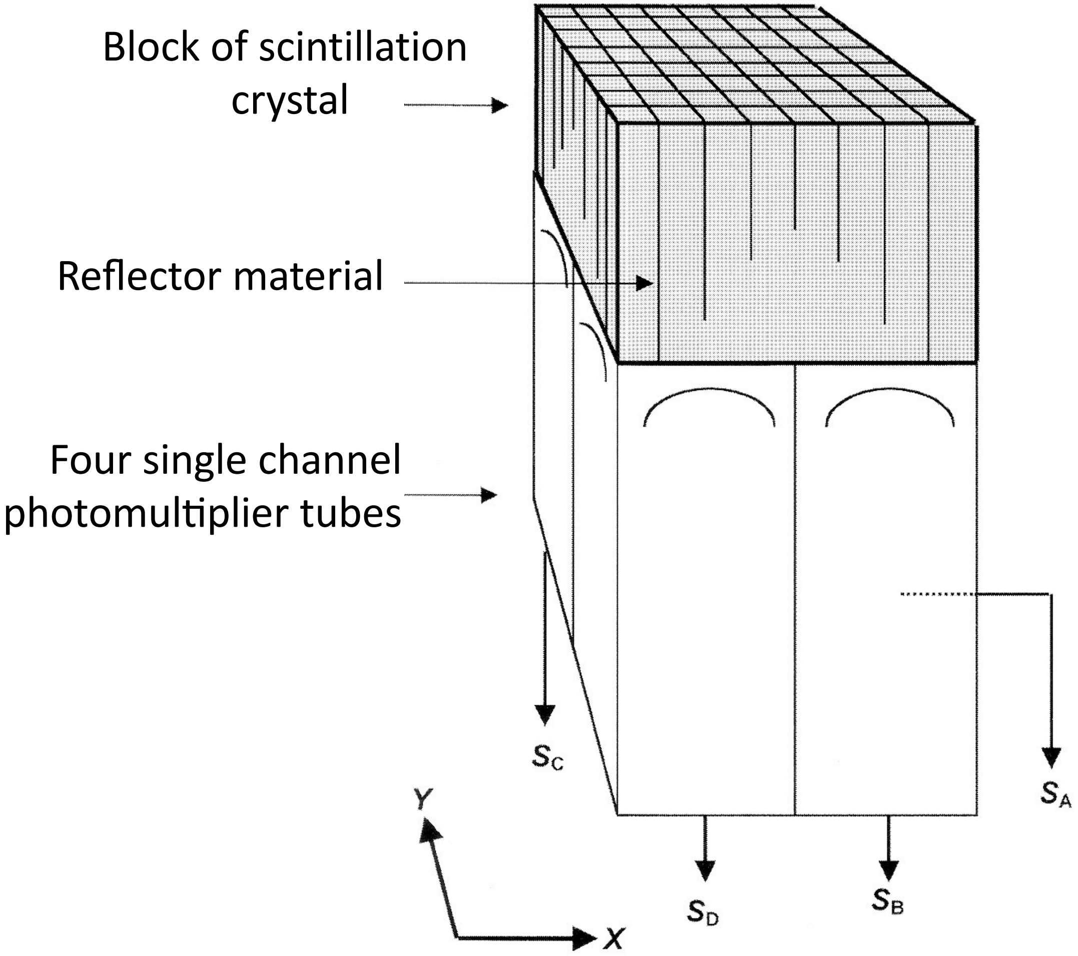


▶ **Image reconstruction using FBP**

Scintillation crystals

Scintillation crystal	Density g/cm^3	Light ϕ per 511 keV	Decay time (ns)	Linear attenuation (cm^{-1})
Sodium Iodide NaI(Tl)	3.67	19400	230	0.34
Bismuth Germanate BGO	7.13	4200	300	0.96
Lutetium Orthosilicate LSO	7.40	13000	47	0.88
Gadolinium Orthosilicate GSO	6.71	4600	56	0.70

Detector



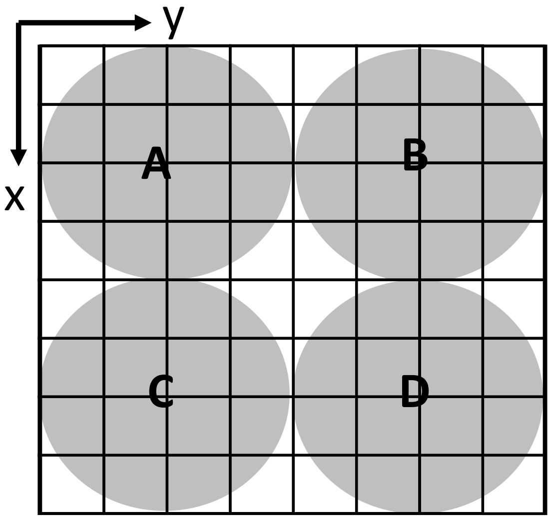
S_C	S_A
S_D	S_B

Geometrical information

$$x = \frac{S_A + S_B - S_C - S_D}{S_A + S_B + S_C + S_D}$$

$$y = \frac{S_A - S_B + S_C - S_D}{S_A + S_B + S_C + S_D}$$

Geometric correction

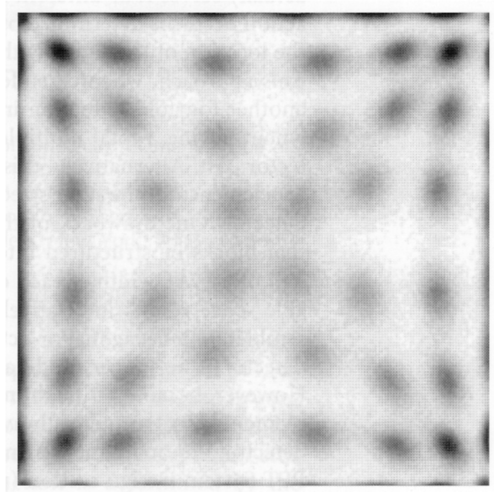


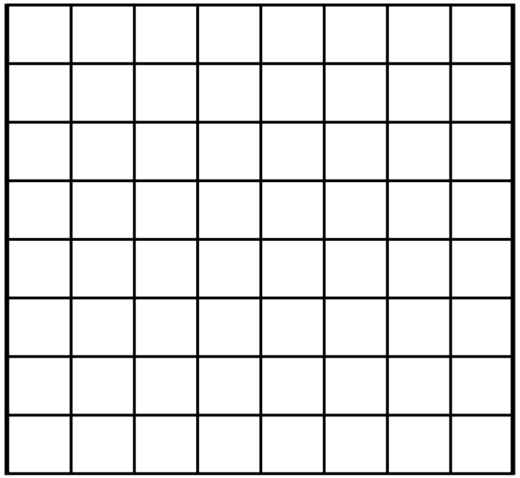
Derivation of geometrical information

$$x = \frac{S_A + S_B - S_C - S_D}{S_A + S_B + S_C + S_D}$$

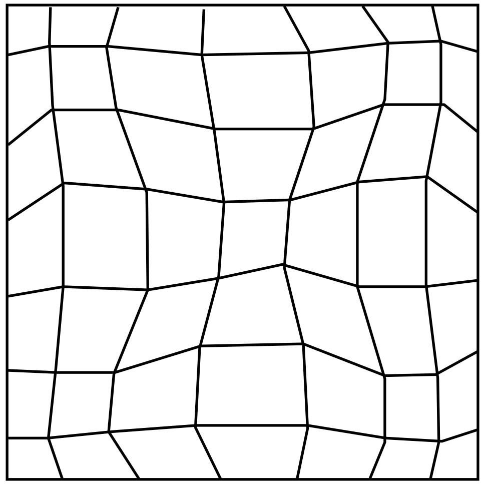
$$y = \frac{S_A - S_B + S_C - S_D}{S_A + S_B + S_C + S_D}$$

Flood histogram

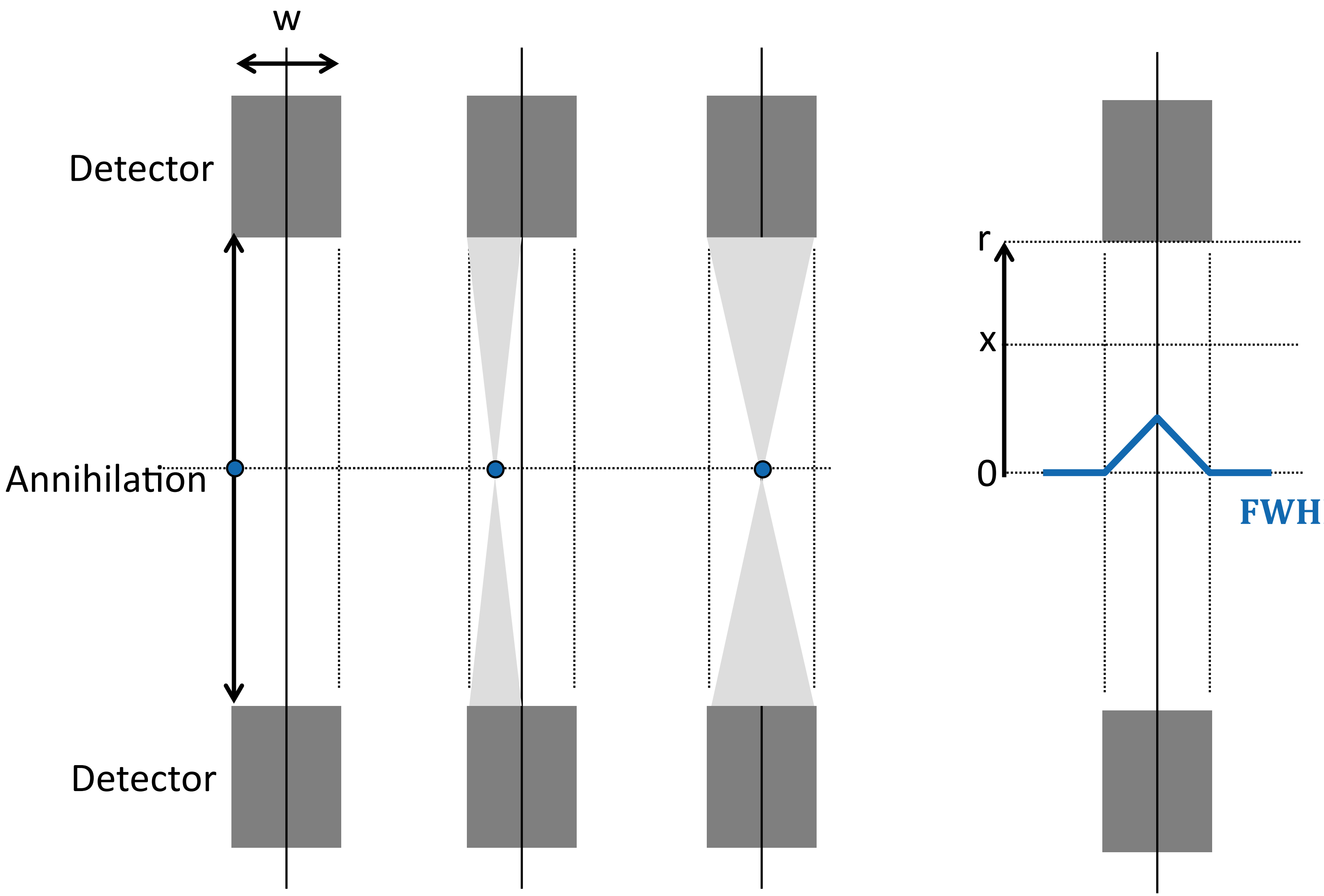




Correction

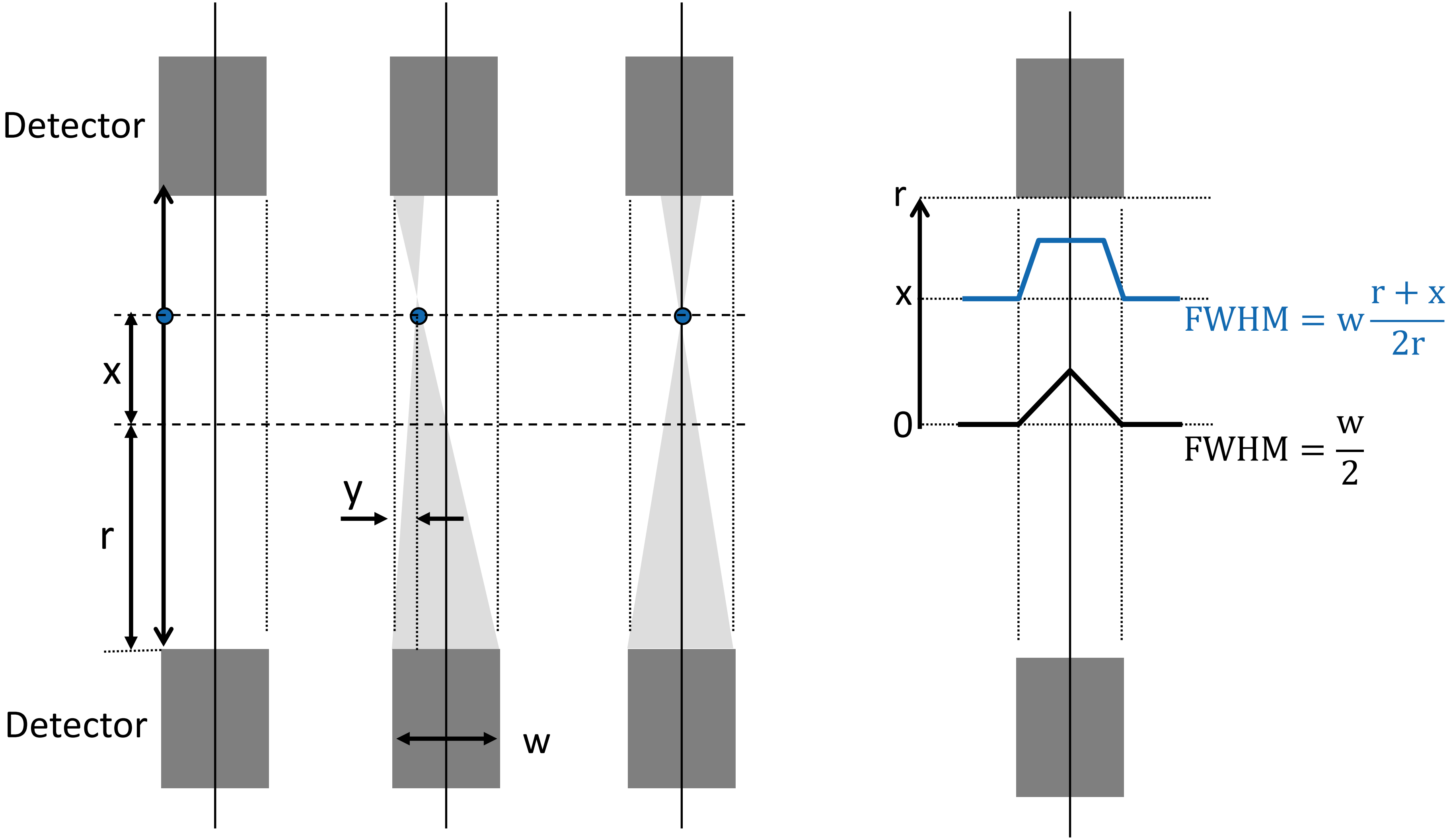


Point-spread function



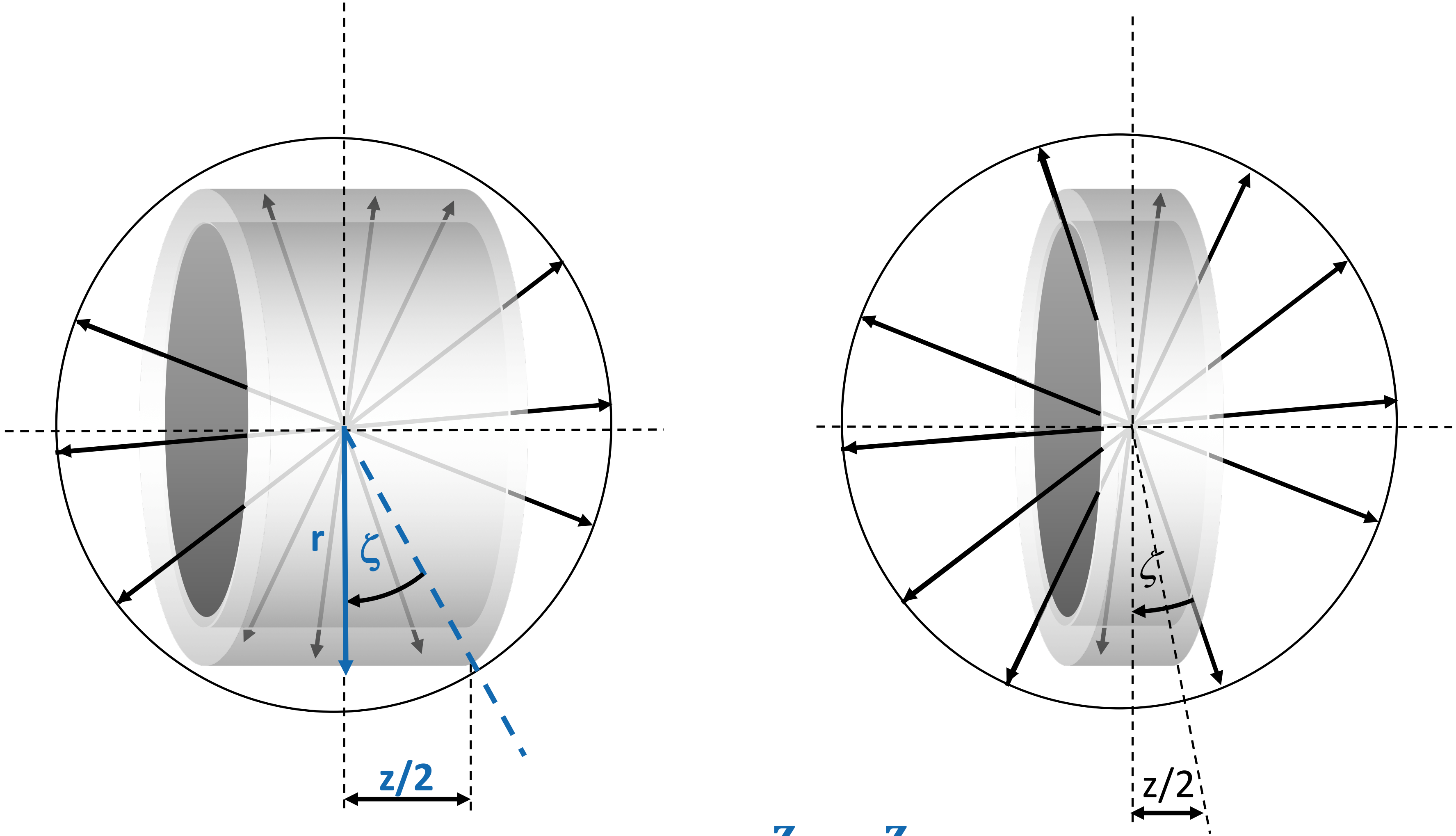
$$\mathbf{FWHM} = \frac{\mathbf{w}}{\mathbf{2}}$$

Point-spread function



$$\frac{y}{w} = \frac{r-x}{2r} \qquad \mathrm{FWHM} = w - y = w - \frac{r-x}{2r}w = w\frac{r+x}{2r}$$

Axial coverage



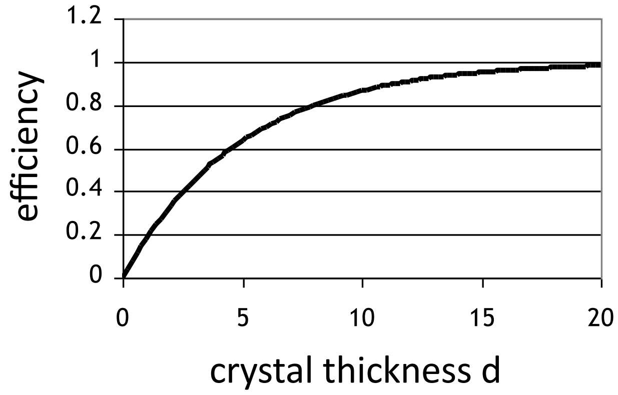
$$\tan\zeta = \frac{z}{2r} = \frac{z}{D}$$

Detection and geometric efficiency

- ## Detection efficiency

$$\varepsilon = \left(1 - e^{-\mu \cdot d}\right) \cdot \phi$$ single detector

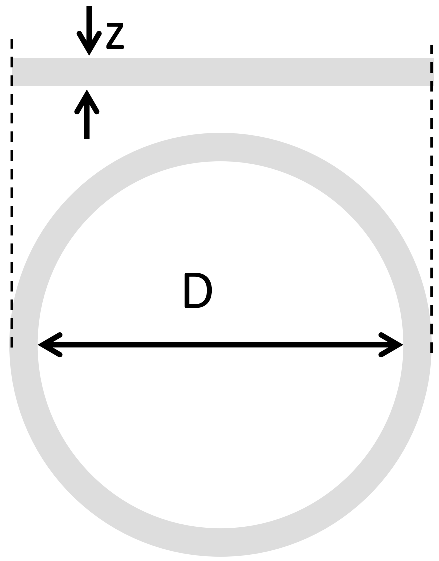
$$\varepsilon^2 = \left(1 - e^{-\mu \cdot d}\right)^2 \phi^2$$ coincidence detector



Fraction of events within energy window: Φ
Attenuation by scintillation crystal: μ

- ## Geometric efficiency

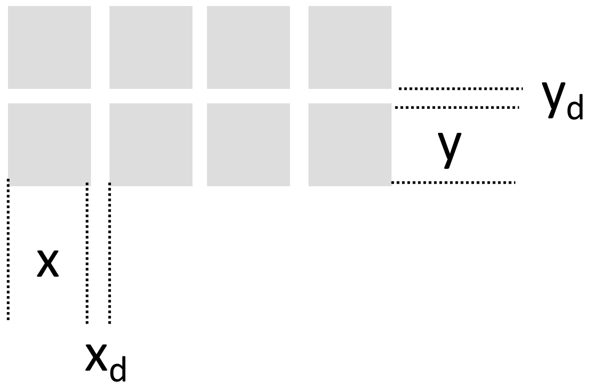
$$\Omega = \sin\left(\tan^{-1}\left(\frac{z}{D}\right)\right)$$



Total sensitivity

- **Radial coverage**

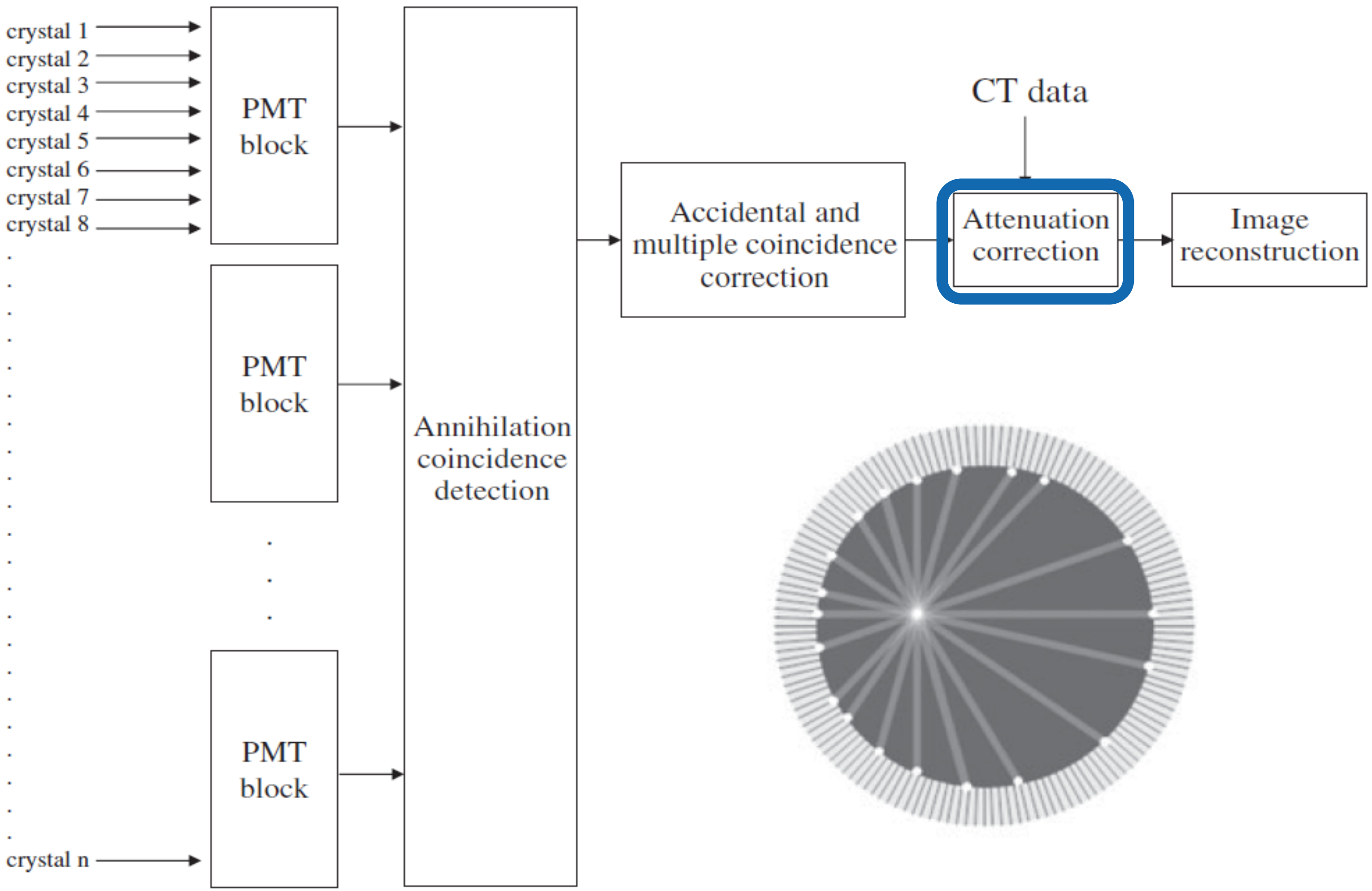
$$\vartheta = \frac{x \cdot y}{(x + x_d) \cdot (y + y_d)}$$



- **Total sensitivity**

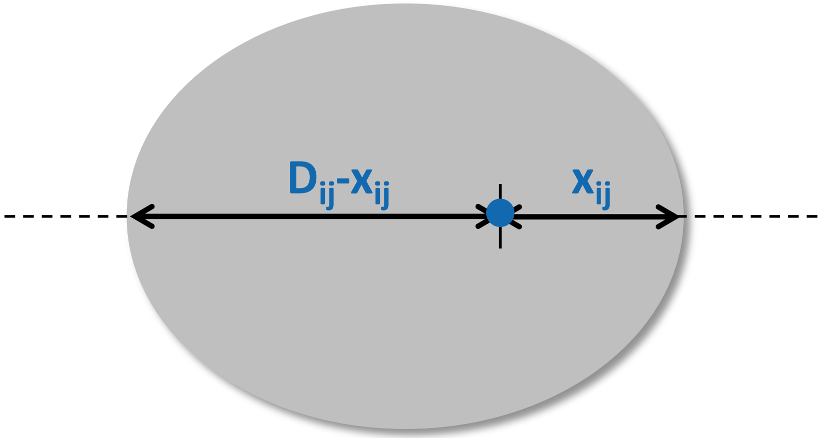
$$\boxed{\eta = \varepsilon^2 \cdot \vartheta \cdot \Omega}$$

Attenuation correction



Attenuation correction

- **Loss of γ-photons due to Compton scattering**



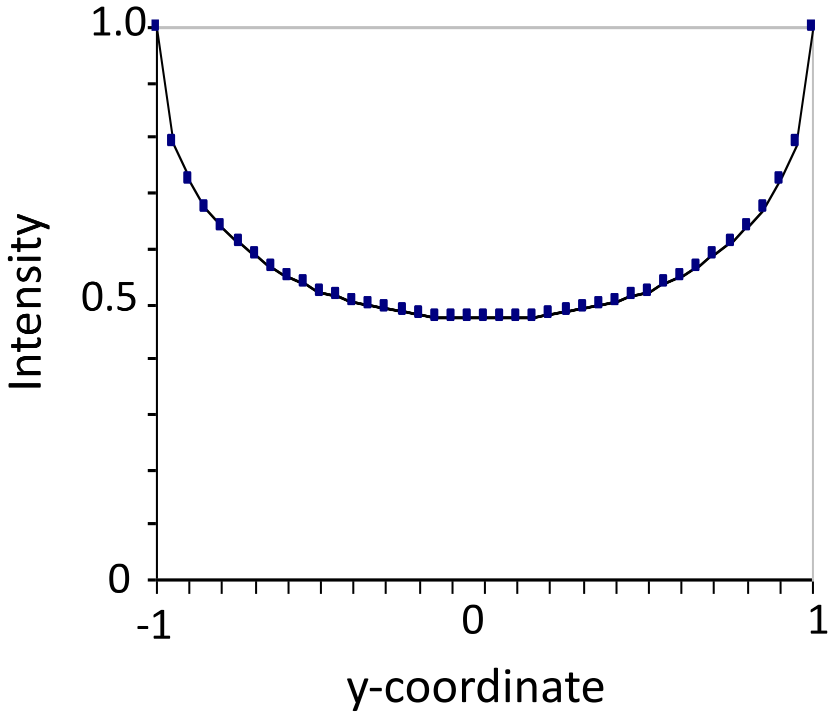
$$\mathbf{p_{1ij} = e^{-\mu \cdot x_{ij}}}$$

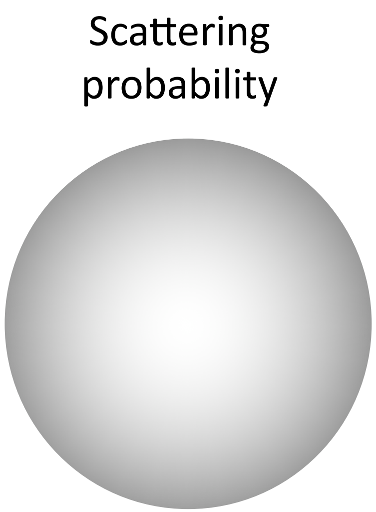
$$\mathbf{p_{2ij} = e^{-\mu \cdot (D_{ij} - x_{ij})}}$$

- **Total scattering probability**

$$\boxed{\mathbf{p_{ij} = p_{1ij} \cdot p_{2ij} = e^{-\mu \cdot D_{ij}}}}$$

Attenuation correction



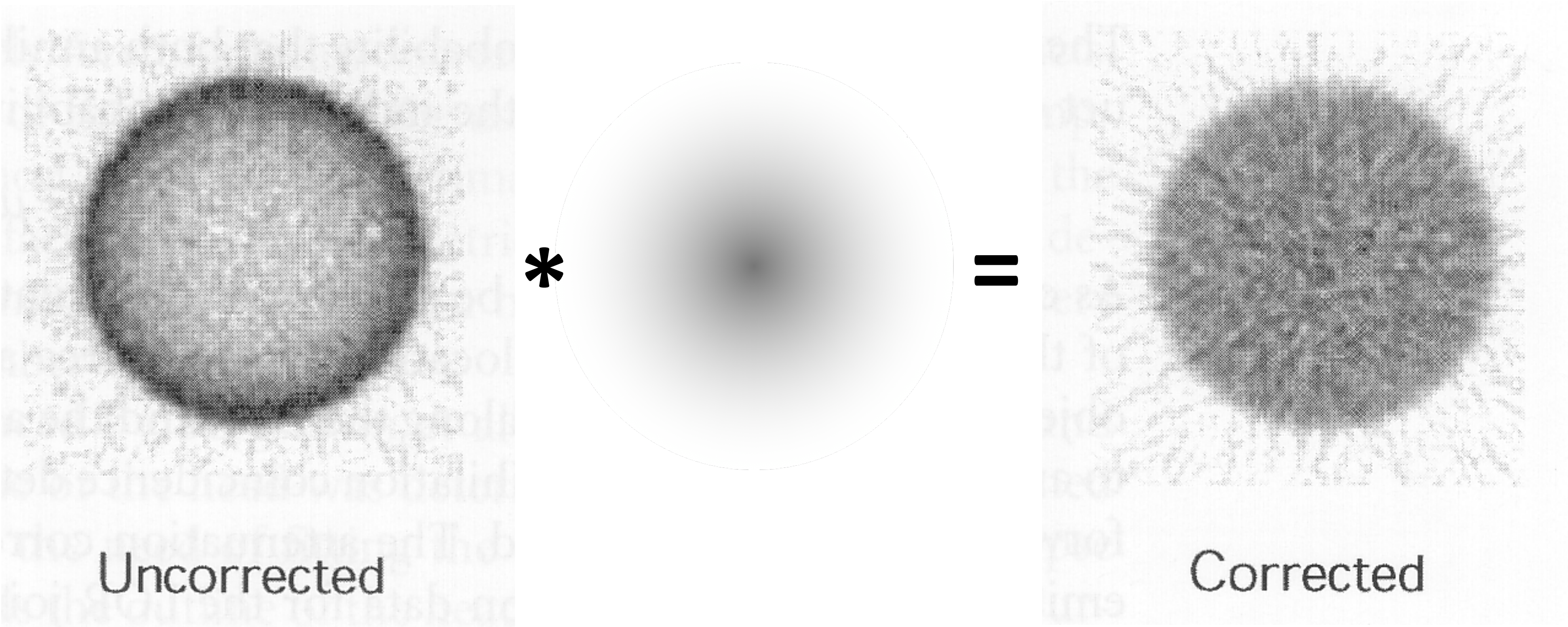


- **Attenuation correction**

$$\boxed{a_{ij} = \frac{1}{p_{ij}} = e^{\mu \cdot D_{ij}}}$$

Attenuation correction

Attenuation correction



“The most important slides”