IFMP WORKSHOP IN IONIAN UNIVERSITY, CORFU, GREECE

Monday 6/11/2017 12:00

PET BASICS

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The discovery of radioactivity in the late 1890's by Henry Becquerel was the starting point of a wide range of new discoveries and application. One of those was the development of the radioactive tracer principle by George de Hevesy in 1911 which led to the first experiments using a radioactive tracer in humans in 1923. In the following decades the field progressed e.g. with the discovery of the positron or the development of cyclotrons and nuclear reactors. This made it possible to produce artificial radioactive sources in a large amount.

In 1951 Wrenn and colleges published the first application of positrons for brain tumours using coincident detection of the annihilation photons. This was the birth of the technique used in positron emission tomography (PET) and finally led to the development of the first PET scanner in 1975.

A PET relies on the simultaneous detection of two photons travelling in opposing direction originating from positron annihilation. Hence, if these two photons are detected, it is evident that the annihilation has taken place somewhere on a line (also referred to as line of response (LOR)) between the two detectors. In PET coincident photons are detected in a ring geometry or by extended opposing detector arrays from various angles around a positron source. A set of parallel LORs correspond to the projection of the activity distribution from a certain angle. Thereby, it is possible to reconstruct an image of the measured activity distribution using tomographic reconstruction techniques.

In a real setting, photons travelling through an extended object are attenuated according to the properties of its material. One big advantage of coincidence detection is that the probability of attenuation is solely dependent on the attenuation probability across the whole object along the respective LOR. This can be measured using a rotating transmission source e.g. a Ge/Ga 68 source or by computed tomography, used to correct attenuation of the annihilation photons.

Therefore, PET is principally able to quantitatively measure an activity distribution in an extended object.

Positron emission tomography Basics

Ivo Rausch, PhD

Center for Medical Physics and Biomedical Engineering

Overview

1. The Tracer Principle
2. The beta decay
3. Positron emission tomography
4. Reconstruction
5. Detectors
6. System design
7. PET/CT

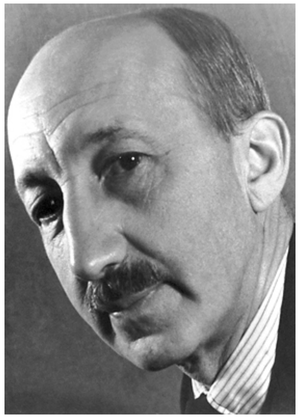
The tracer principle

Use of a radioactive compound to measure in-vivo processes

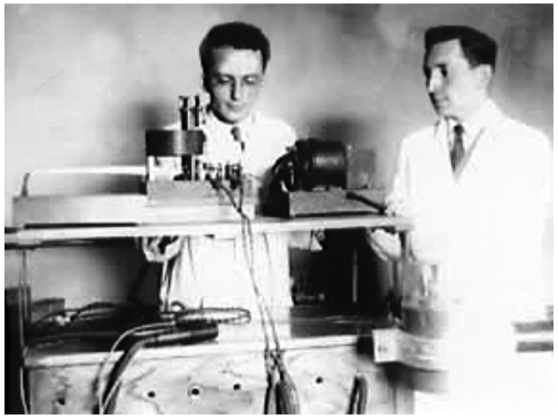
1913 First use of radioactive isotopes by George de Hevesy – works on Pb-salt soluability with a Pb-isotope.

1923 (De Hevesy) Pb-salt uptake in Plants

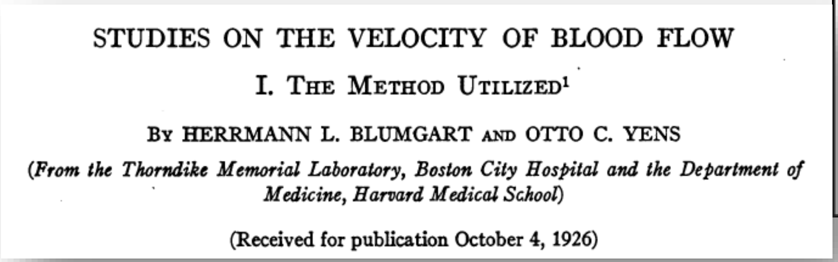
1924 Blumgart and Yens / Weiss – Bi 212 into arm of patient – measured arrival in other



www.nobelprize.org



Patton, JNM 2003



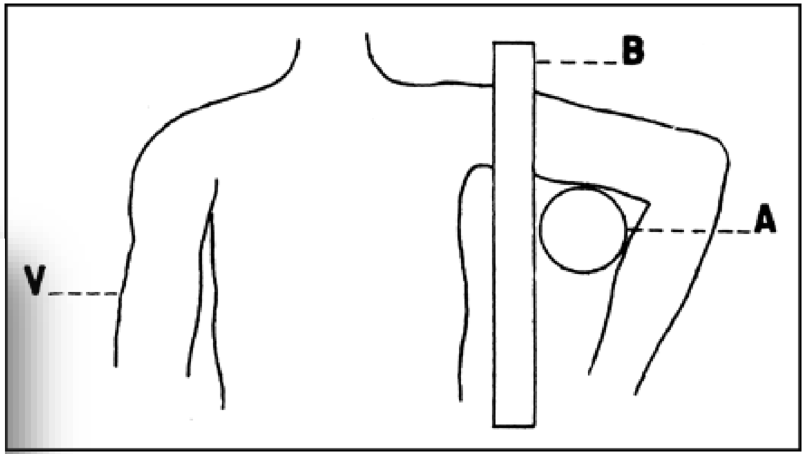
STUDIES ON THE VELOCITY OF BLOOD FLOW

I. THE METHOD UTILIZED[1]

BY HERRMANN L. BLUMGART AND OTTO C. YENS

(From the Thorndike Memorial Laboratory, Boston City Hospital and the Department of Medicine, Harvard Medical School)

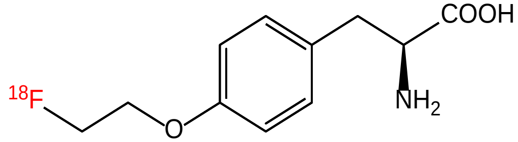
(Received for publication October 4, 1926)



A radioactive tracer can be tracked to study dynamic processes

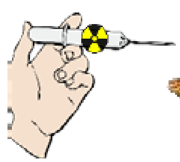
Principle of Nuclear Medicine

Labeled biomolecule = Tracer



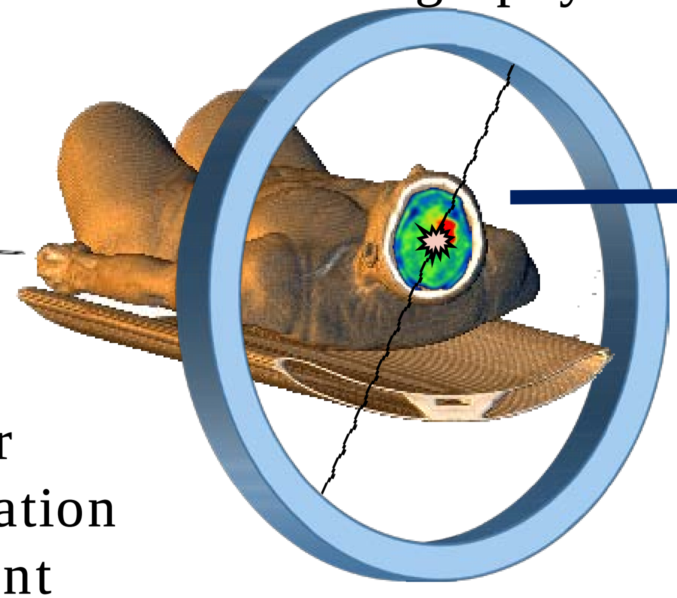
18F

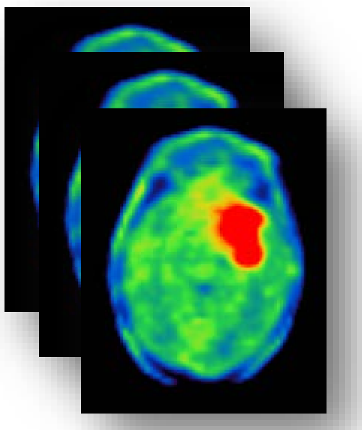
Radioactive isotope



Tracer administration to patient

Emission tomography

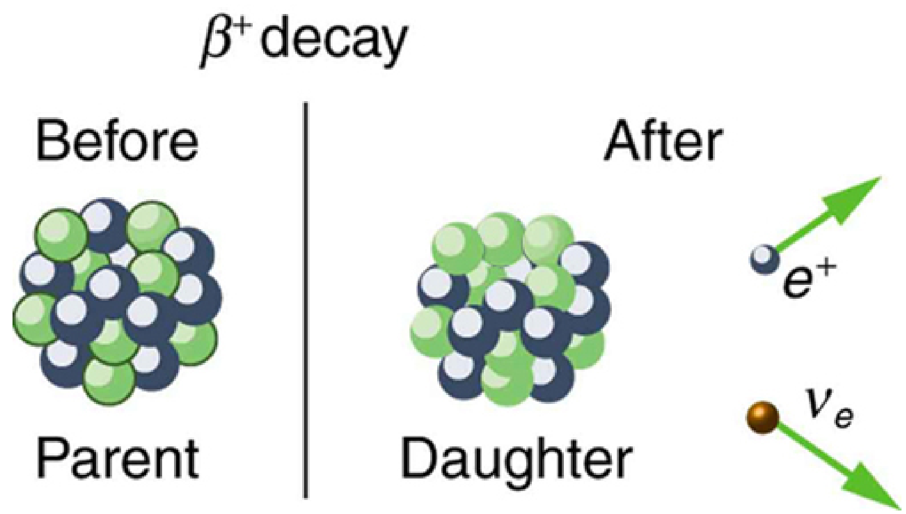




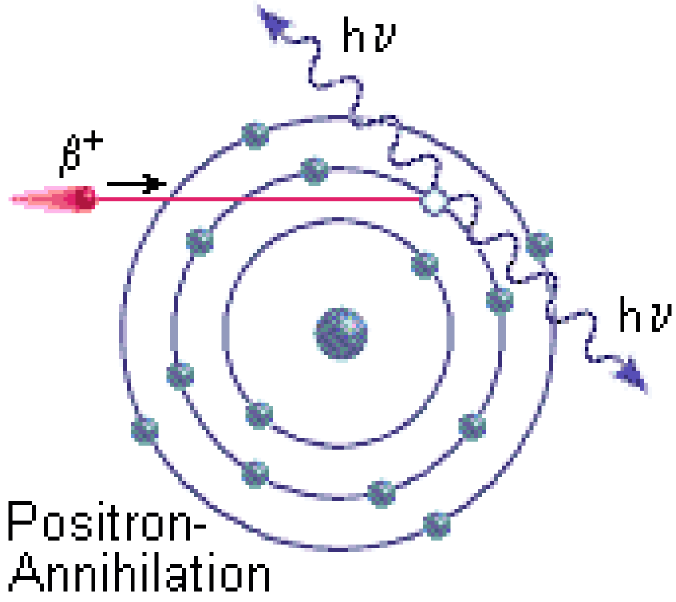
Tracer distribution showing areas of enhanced metabolism

The beta+ decay

For nuclei with a fixed mass number a proton can transform to a neutron = β^+ (and conversely = β^-)



- e^+ antiparticle to e^- -> annihilation
  - $E = mc^2 = 2 \times 511$keV
  - Momentum conservation -> ~ 180°



Beta+ decay: Changing a proton into a neutron

Coincidence counting

First described by Wrenn et al. (Science 1951) for localization of Brain tumors

e^{+} decay leads to 2 perpendicular γ-rays

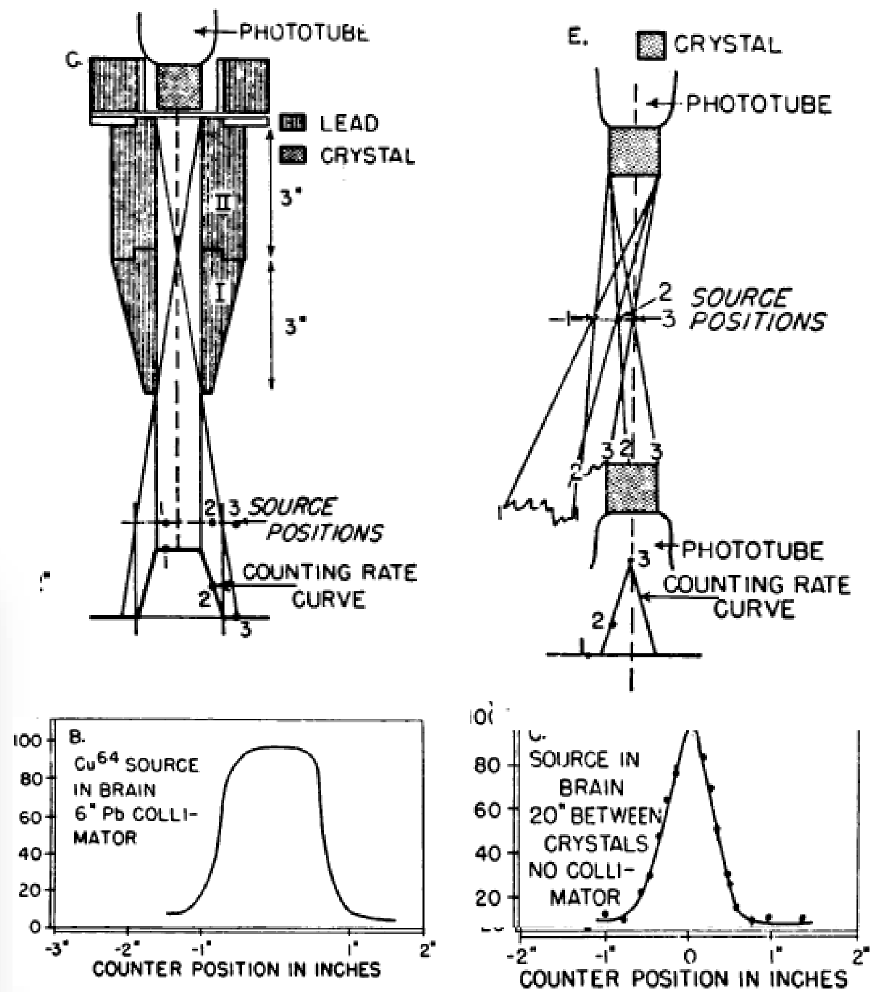
If detected, decay took place on a line between detectors

Equivalent to a projection

The Use of Positron-emitting Radioisotopes for the Localization of Brain Tumors[1]

Frank R. Wrenn, Jr.,[2] Myron L. Good, and Philip Handler

Division of Neurosurgery, Departments of Physics and Biochemistry and Nutrition, Duke University, Durham, North Carolina



Coincidence counting requires no collimation

PET principle

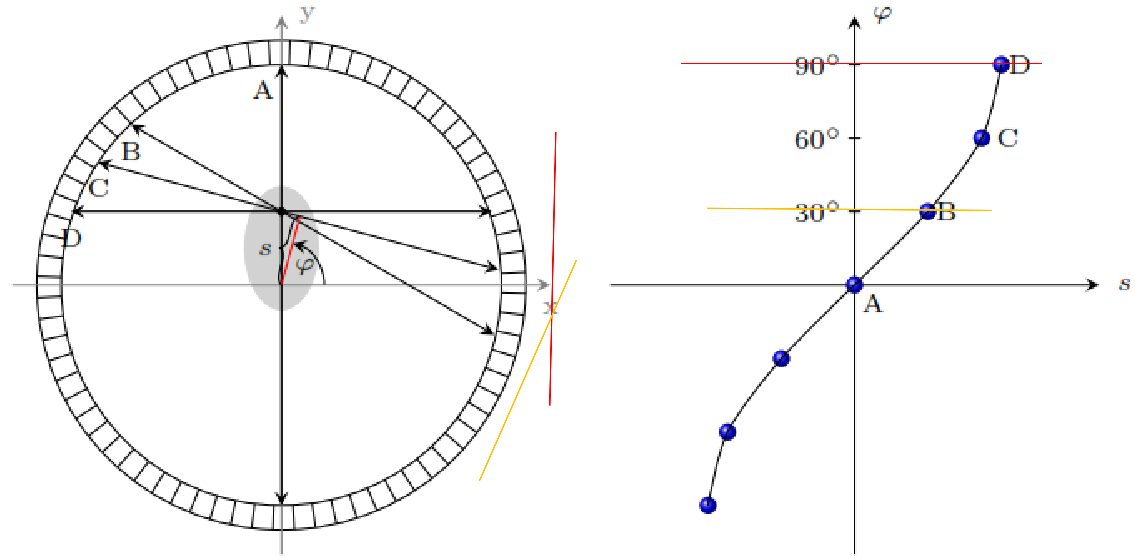
PET relies on detection of two photons from positron annihilations

Most common: ring geometry

Annihilation on a line (LOR) between the detectors

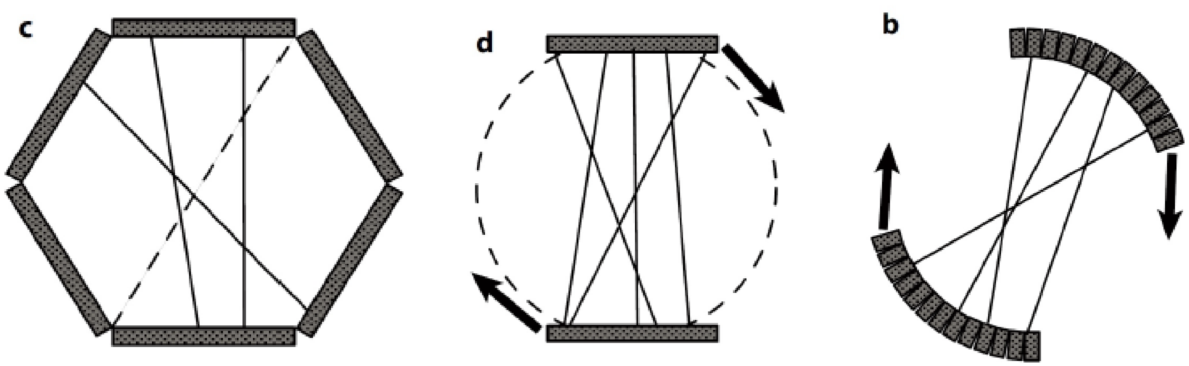
Parallel lines belong to same projection

Data most common represented as “Sinograms”



(a) LORs in the scanner (b) Sinogram

Courtasy Albert Hirtl



Multiple projections are acquired using a detector ring

The fist PE(T)T

First described by Phelps et al. JNM 1975

Prototype of a positron emission transaxial tomograph (PETT)

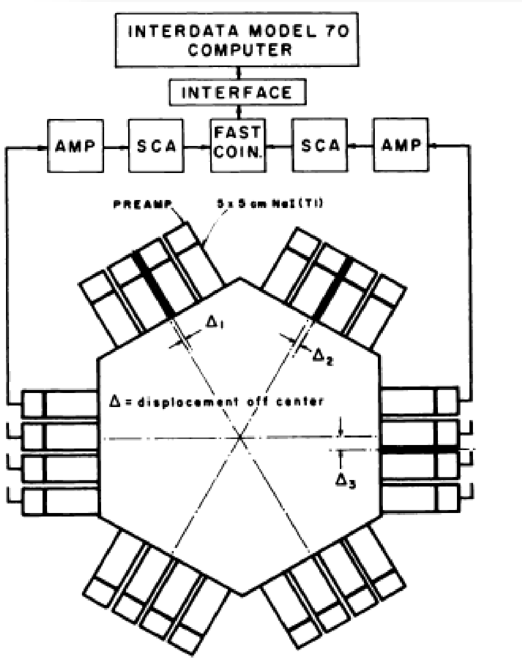
Tested on phantoms and dogs

Reconstructed using Fourier transformation and attenuation corrected using ^{64}Cu source

APPLICATION OF ANNIHILATION COINCIDENCE DETECTION TO TRANSAXIAL RECONSTRUCTION TOMOGRAPHY

Michael E. Phelps, Edward J. Hoffman, Nizar A. Mullani, and Michel M. Ter-Pogossian

Washington University School of Medicine, St. Louis, Missouri



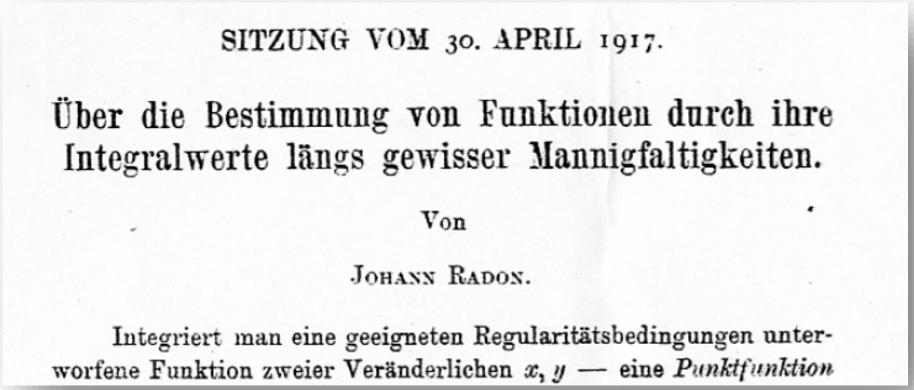
The first positron emission tomograph was described in 1975

Image reconstruction

General Problem:

Get a 2D image out of 1D projections

- In principle solved mathematically by Radon 1917
- Radon transformation



SITZUNG VOM 30. APRIL 1917.

Über die Bestimmung von Funktionen durch ihre Integralwerte längs gewisser Mannigfaltigkeiten.

Von

JOHANN RADON.

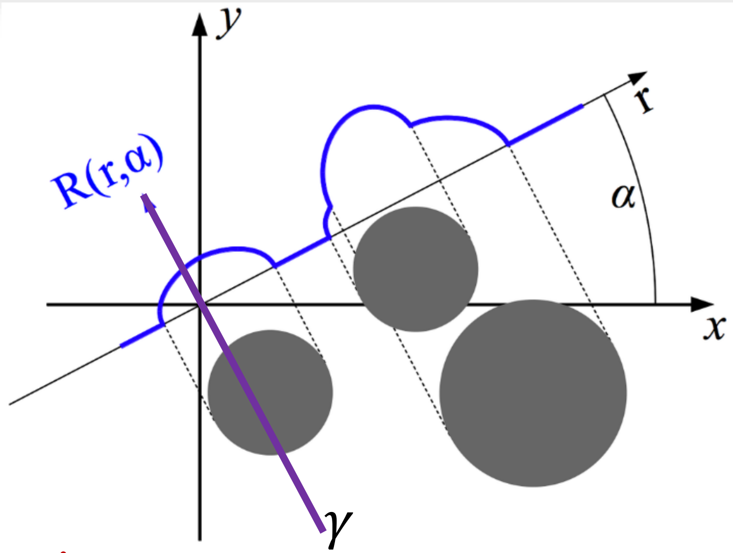
Integriert man eine geeigneten Regularitätsbedingungen unterworfene Funktion zweier Veränderlichen x, y — eine *Punktfunktion*

Activity distribution

$$R(\alpha, r) = \int_{\gamma} f(x, y) d\gamma$$

Projections

Line integral through activity concentration = Projection



Invers Radon transformation = FBP

Image reconstruction: FBP

Back projection -> Blurred images

Solution: FBP

Inverted radon transformation

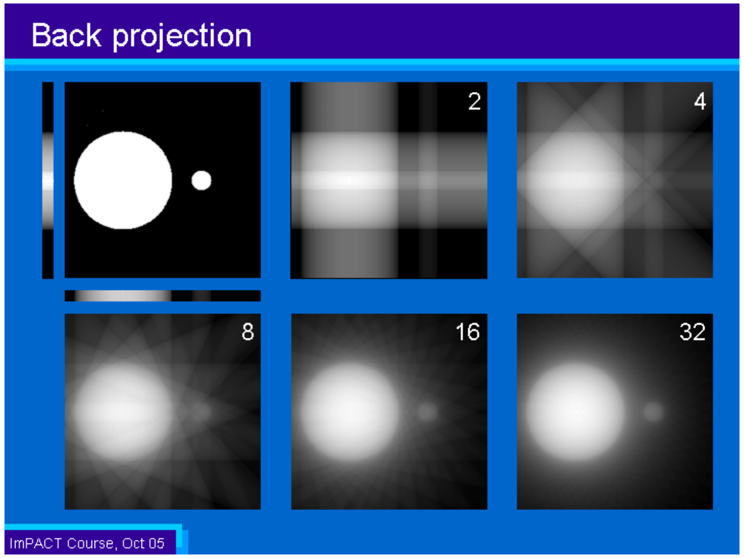
$$f(x,y) = \frac{1}{4\pi^2} \iint G(\alpha,\omega)\, e^{i\omega(x \sin\alpha - y \cos\alpha)} |\omega| d\omega d\alpha$$

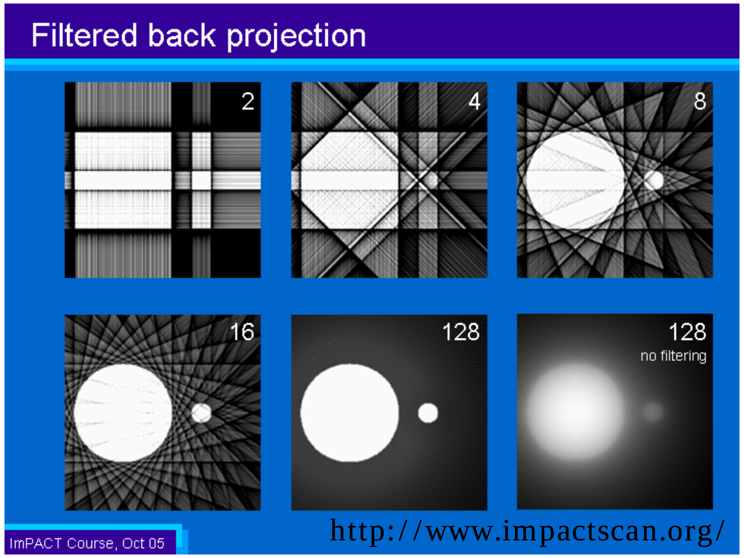
Filter!!!

Projections in Frequency space

Filter:

- ➢ reduces low frequencies = blurring
- ➢ enhances high frequencies = sharp edges
- ! Enhances noise
- ! Limited # projections -> Cut of frequency





FBP is fast and easy but sensitive to noisy data

Iterative Reconstruction

Getting a projection from an image can be written as a matrix multiplication

System-matrix: representing the PET

$$g_i = \sum_{j=1}^{K} c_{ij} \lambda_j$$

Projection

Image (activity distribution)

Problem:

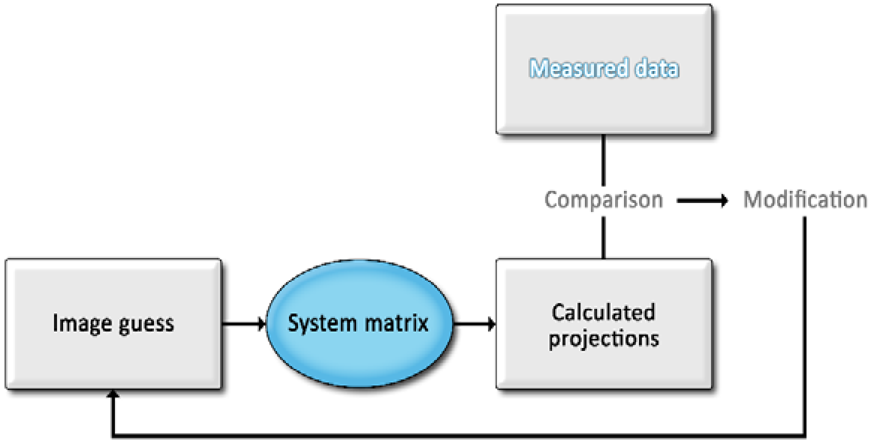
inversion of matrix not possible!!!

Solution:

Iteratively finding the image which fits the measured projections

Advantages:

- less affected by noice
- physical properties (scattering, absorbtion, resolution…) can be directly implemented into sytem-matrix



Changing a activity distribution until it fits the measured data

The OS-EM algorithm

Maximum likelihood expectation maximisation
Algorithm for iterative reconstruction described by Sepp and Vardi 1982

Maximum Likelihood Reconstruction for Emission Tomography

L. A. SHEPP AND Y. VARDI

'revious models for emission tomography (ET) do not dis- porate timing information and correct for positron r

Image update:

comparing and correcting with all projections

- slow convergence

Ordered Subset:
A compromise described by Hudson and Larkin 1994: a subset of projections is taken for correction

Accelerated Image Reconstruction Using Ordered Subsets of Projection Data

H. Malcolm Hudson and Richard S. Larkin

-We define ordered subset processing for standard fast Fourier transforms. Related approaches to the s

- Good noise properties + fast convergence

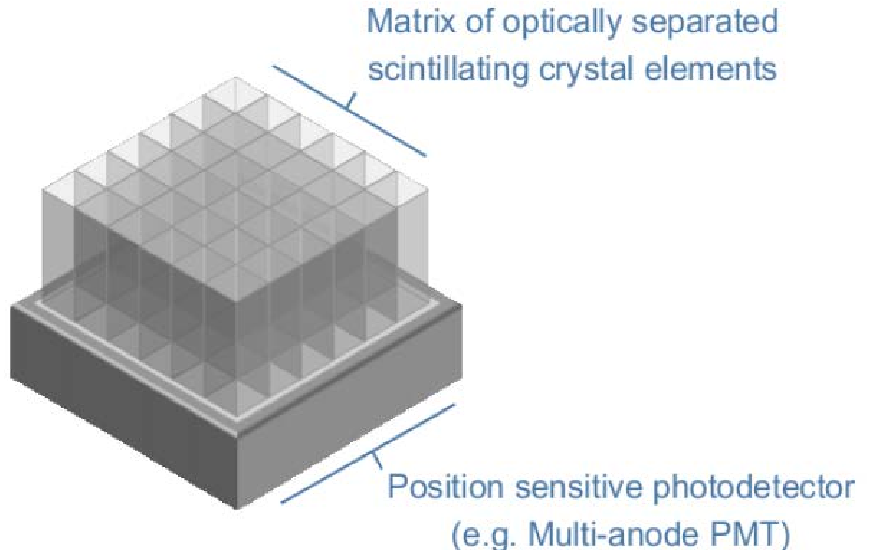
EM is the how to update the image, OS is for acceleration

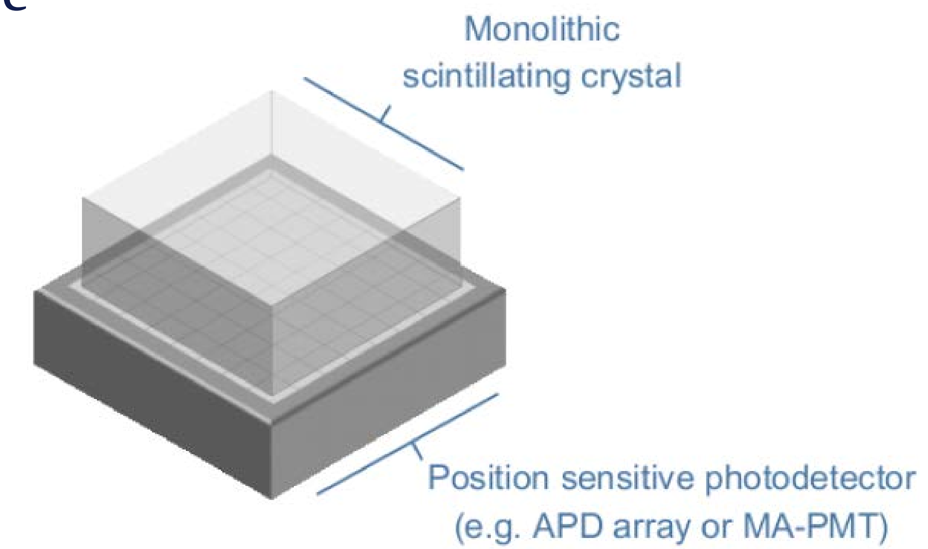
PET detectors

Transfer 511keV photons into electric signal

Most common devices consist of:

- Scintillator:
  converts high energy photons into visible light
- Photo detector:
  converts visible light into electric signal





A detector converts a 511 keV photon into an electrical signal

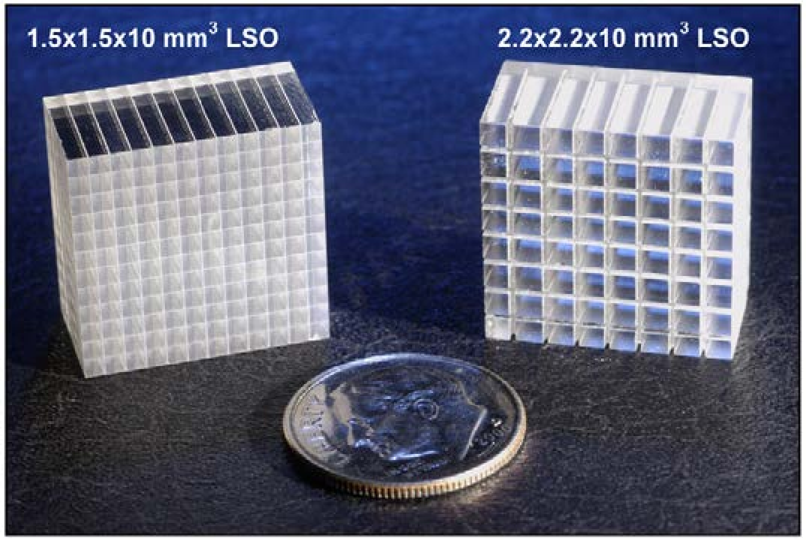
Scintillator materials

Scintillator material needs certain properties

High interaction property with 511keV
- Density -> stopping power

High light output
- Energy resolution
- Spatial resolution

Fast scintillation
- Dead time
- Timing resolution



Scintillator	Decay time (ns)	Attenuation coefficient (cm^{-1})	Light output (photons/MeV)
NaI(Tl)	230	0.35	41000
BGO	300	0.95	7000
GSO	60	0.70	10000
BaF_2	2	0.45	2000
LYSO, LSO	40	0.86	26000
$LaBr_3$	20	0.47	60000

Fast scintilators with high light output

Photo multiplier tubes (PMTs)

Most commonly used

1. Photocathode: converts visible light quants into free electrons
2. Electric field: accelerates electrons towards the dynode (an anode)
3. Dynode: electron impact causes secondary electron production (amplification)
4. Anode: collects the electrons -> electric signal

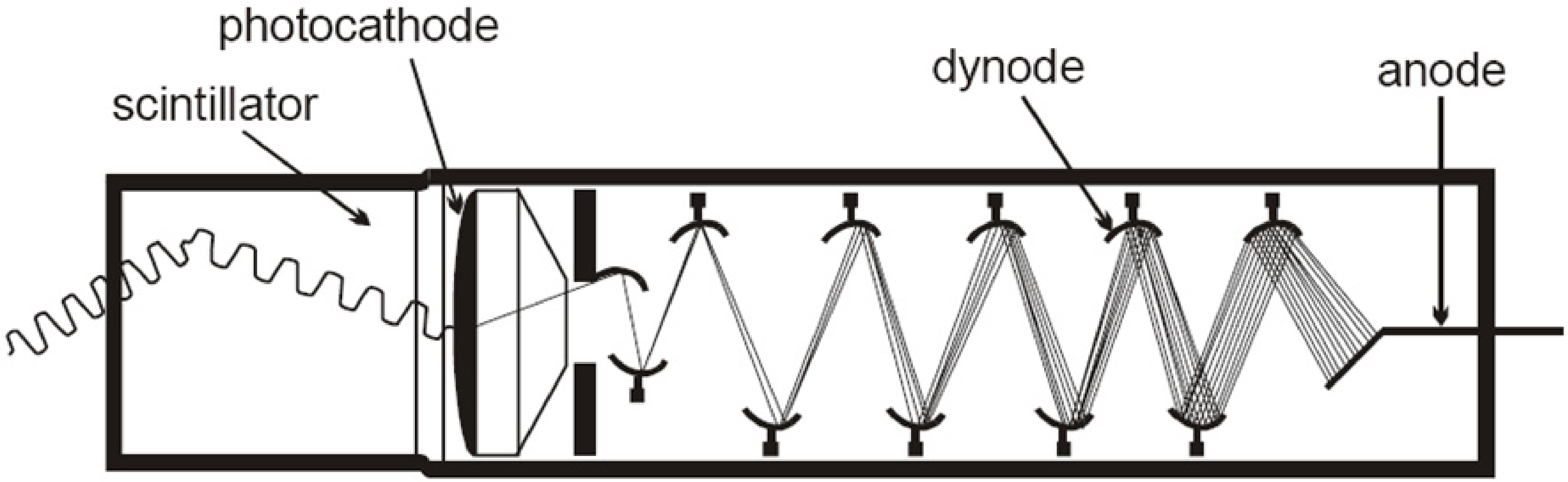


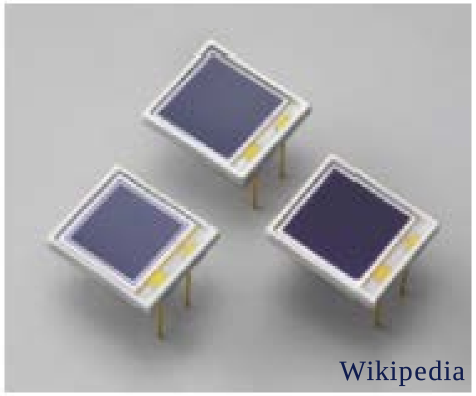
Image: http://nsspi.tamu.edu/nsep/

Electron acceleration and amplification

Alternatives to PMTs

APD: Averlange photo detectors

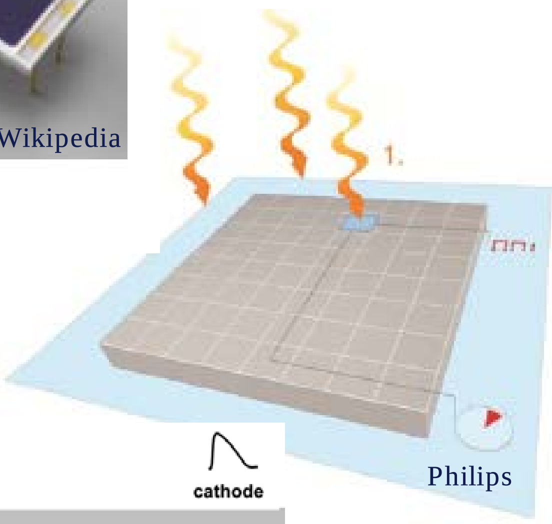
- ➢ Based on semiconducturs
- \+ better spatial resolution
- − low gain
- − slow compared to PMTs



APD

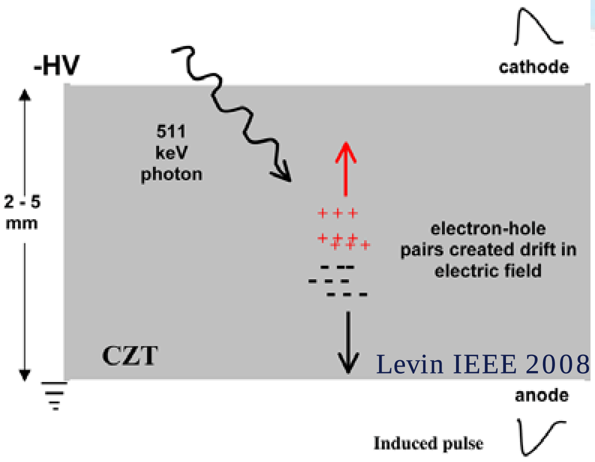
SiPM: Silicon Photomultiplier

- ➢ Grid of APDs operated in “Geiger-mode”
- \+ analog or digital readout
- \+ fast



Direct semiconductor detectors

- \+ high spatial resolution
- − low efficiency

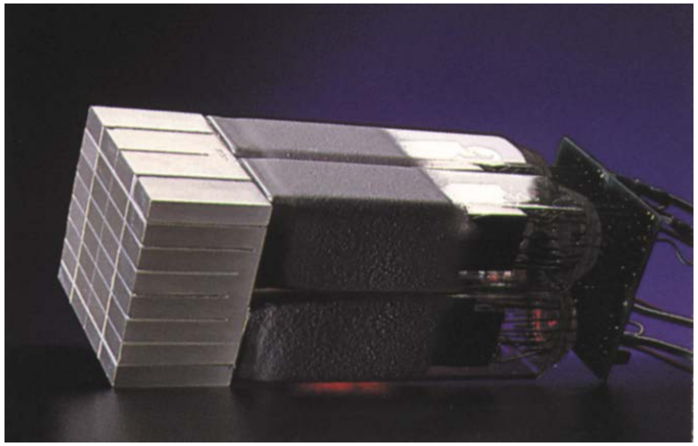


There are alternatives to PMTs based on semiconductors

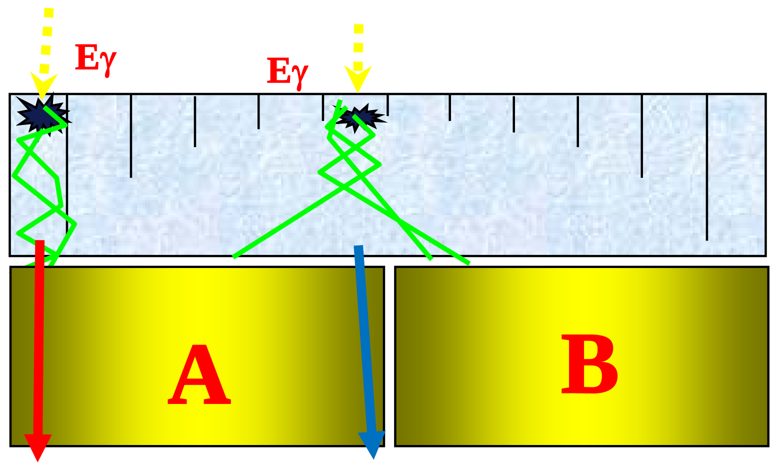
PET system design

One scintillator crystal mounted on four PMT

- Detector block

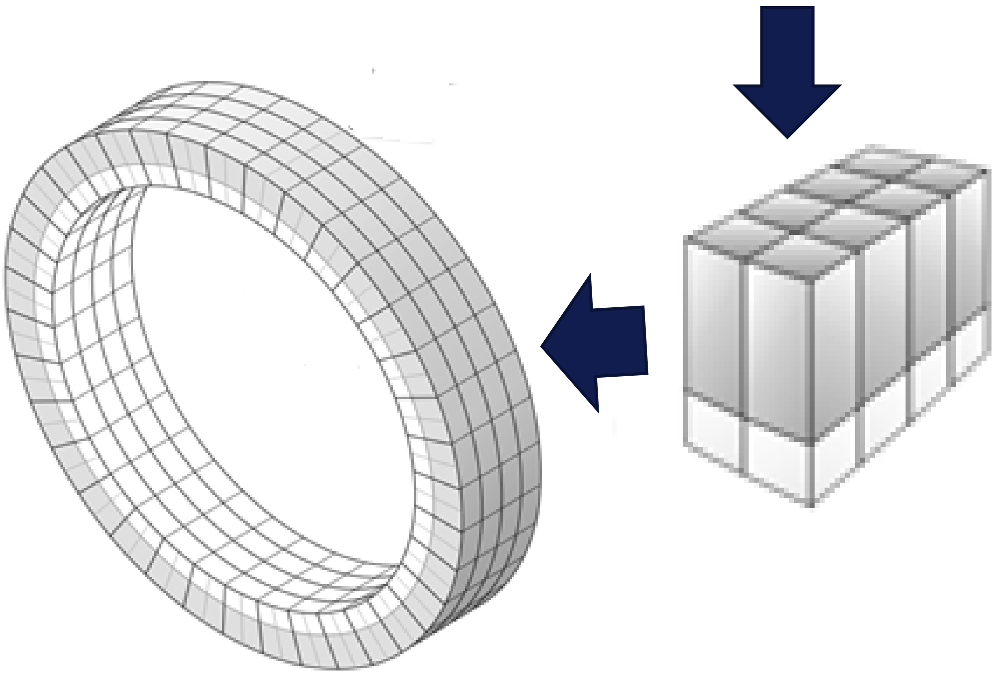


Position of photon interaction – Anger logic



X1 = 100 / (100 + 0) = 1   X2 = 55 / (55 + 45) = 0.55

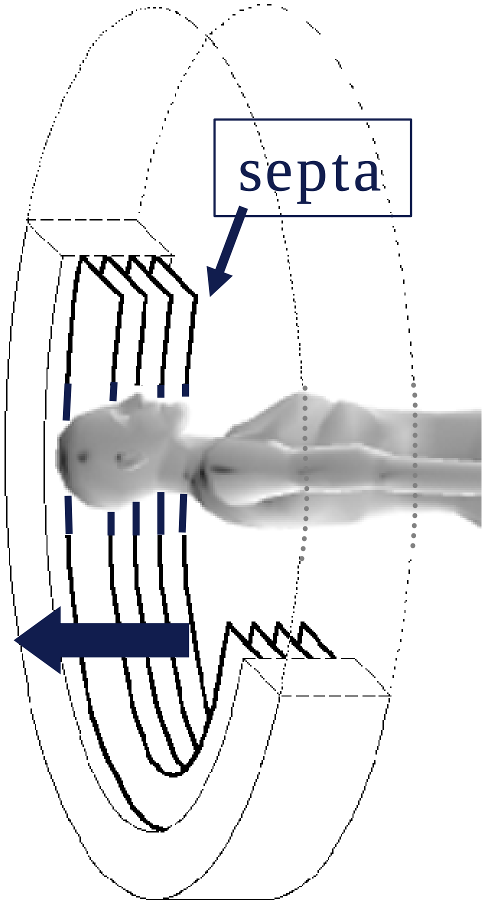
Courtasy: Mauritio Conty



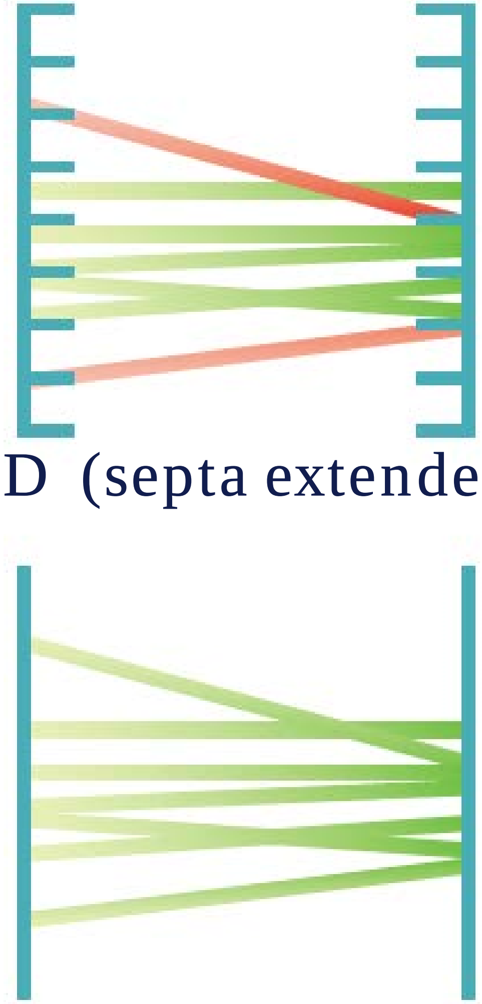
All clinical PET/CT today are whole-body ring systems

2D- vs 3D PET

Courtesy T.Beyer (Vienna)



Multi-ring tomograph
+ retractable septa

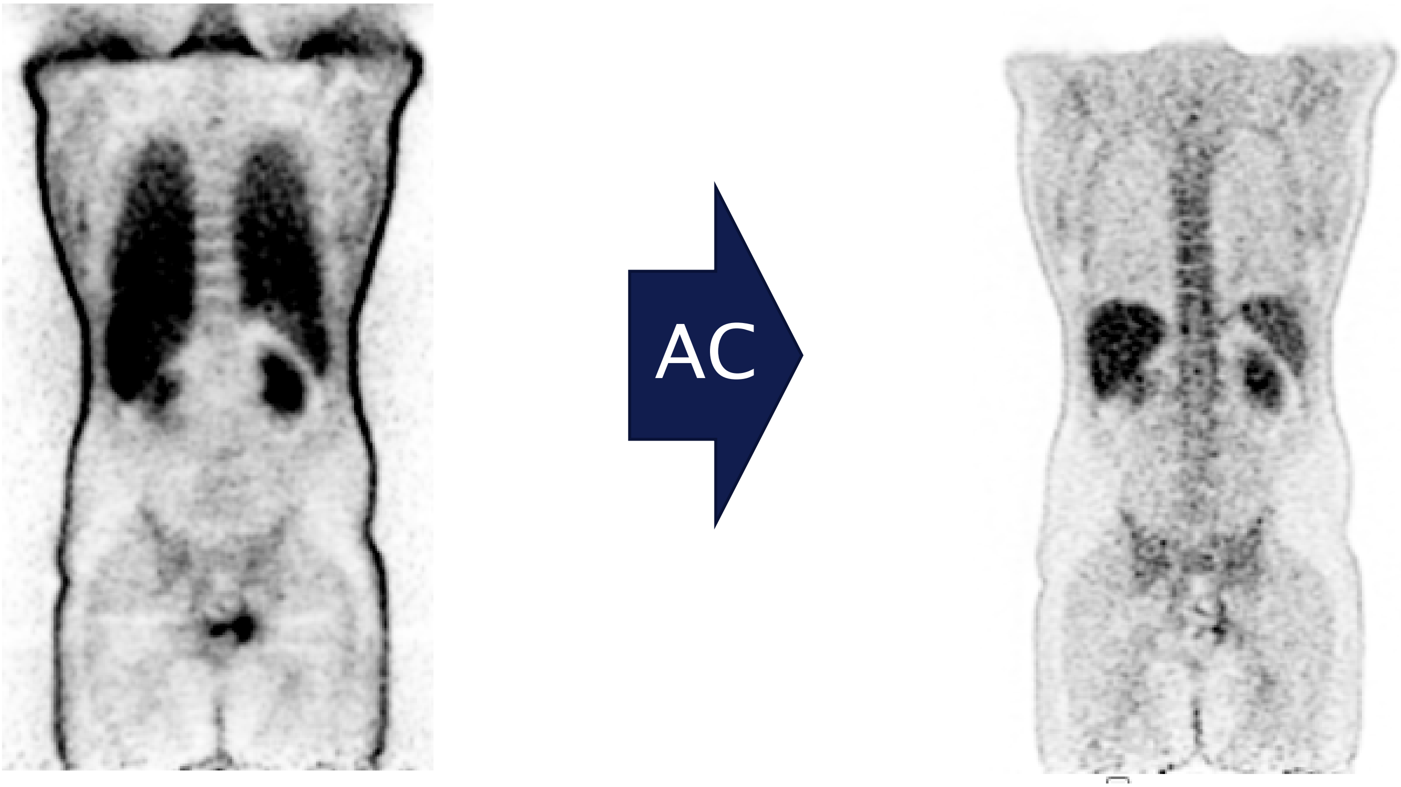


- increased sensitivity
- increased background
- increased deadtime
- out-of-field activity
- 3D reconstruction
- non-uniform response
- BGO works for brain
- LSO/GSO for whole-body

State-of-the-art PET: 3D (no septa) for increased sensitivity

Attenuation correction (AC)

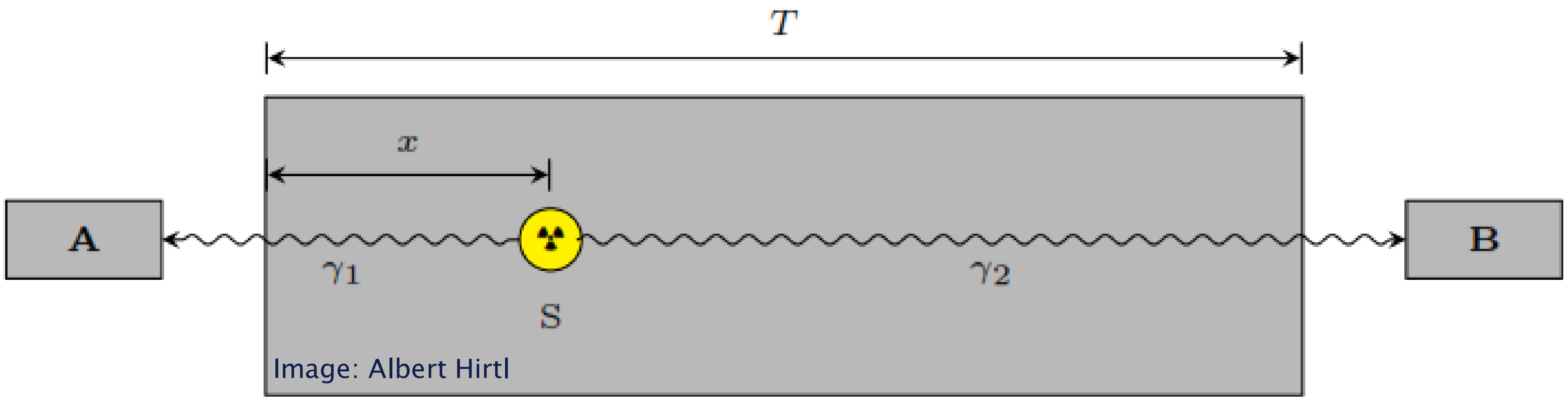
Attenuation correction is essential for quantitative PET data



Non-attenuation corrected | Attenuation corrected

Attenuation correction (AC)

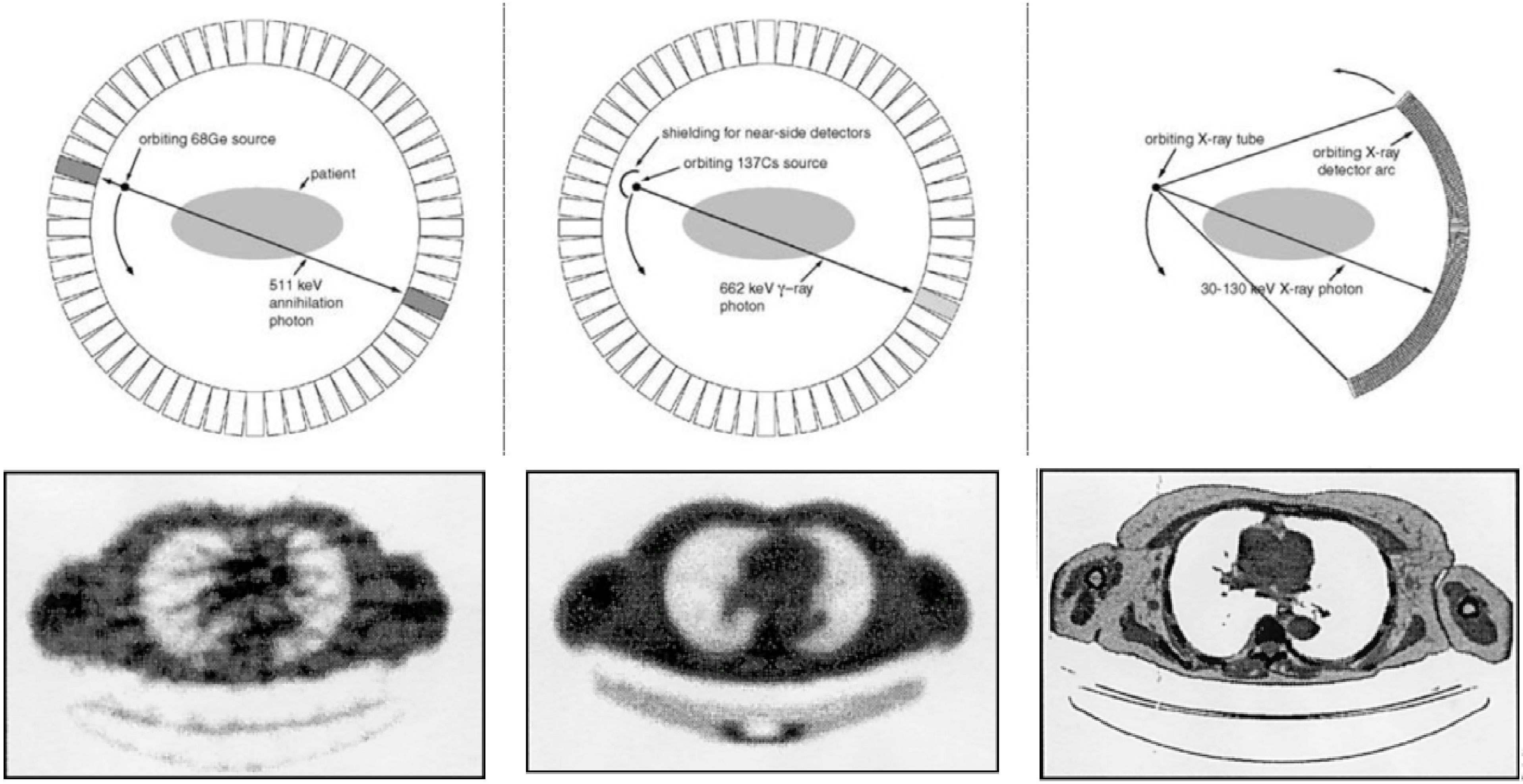
Both annihilation photons need to be detected for a valid event



$$P_{detect} = P_{detect\gamma_1} \cdot P_{detect\gamma_2} = e^{-\mu x} \times e^{-\mu(T-x)} = e^{-\mu T}$$

Probability dependent on total attenuation through the object

Attenuation correction



(a) ^{68}Ge/^{68}Ga positron source (b) ^{137}Cs gamma-ray source (c) 120 kVp x-ray source

AC is done using a transmission scan

Type of events in a PET system

True coincidences are usable

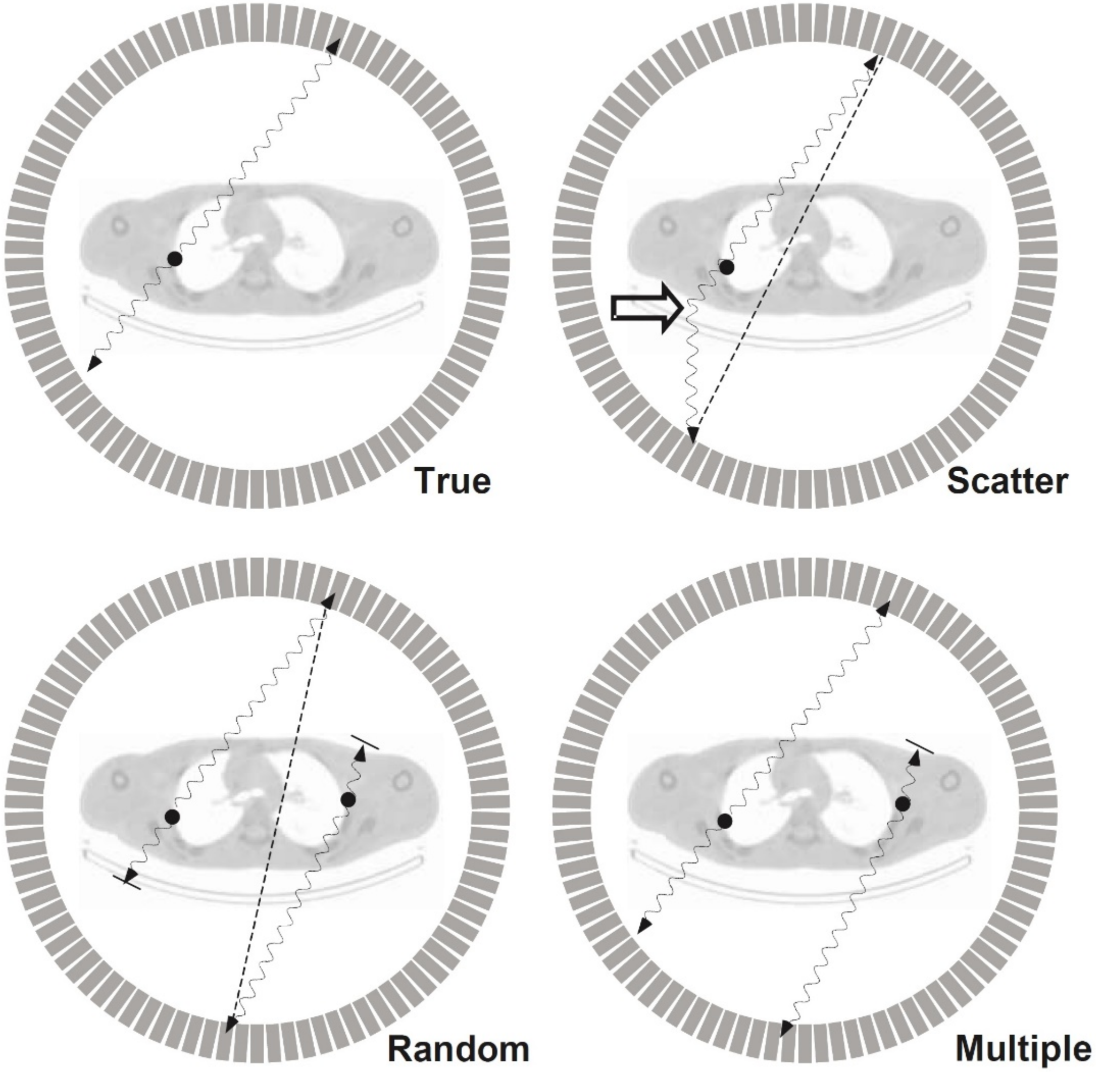
- Time window ~4ns
- Energy window ~450keV-630keV

Scatter

- minimized by energy window
- Correction by simulation

Random

- Minimized by timing window
- Correction by estimation from delayed timing window



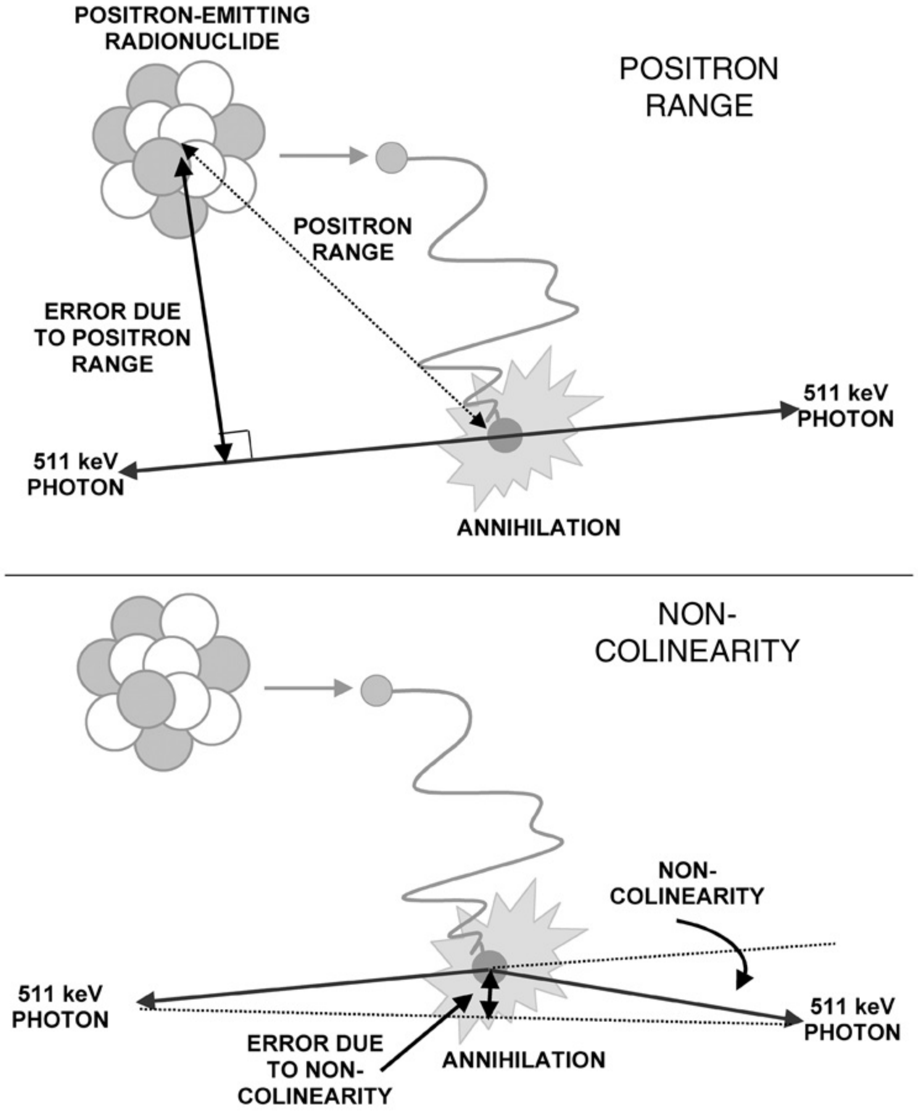
Not every count is a usable count

Limiting Factors

Positron Range:

Depending on E_{kin} of positron

Nuclide	Mean range
18-F	0.6 mm
68-Ga	2.9 mm
11-C	1.1 mm



Non collinearity:

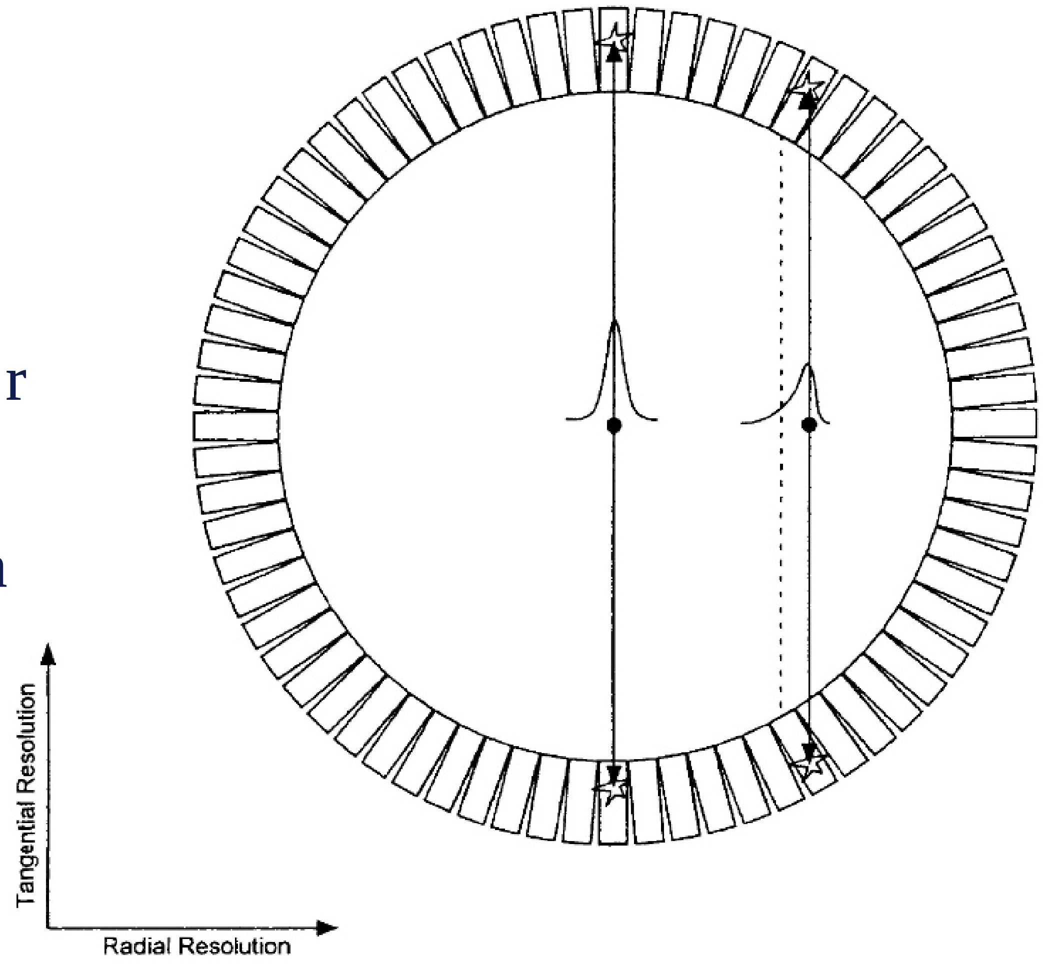
- Residual momentum of positron causes deviation from 180°-preservation of momentum
- Nearly Gaussian (FWHM~0.5°)
- Depending on ring diameter

Positron emission ≠ positron annihilation

Limiting factors

Detector parallax:

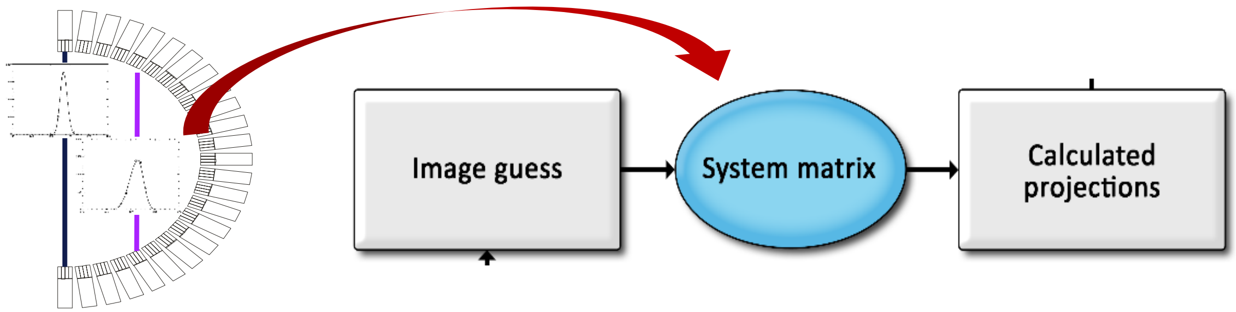
- Detectors shifted in angle
- Photon passing first scintillator -> wrong LOR
- asymmetric response function



Resolution depends on system design and geometry

Point spread function (PSF)

Incorporation of the PSF into system matrix

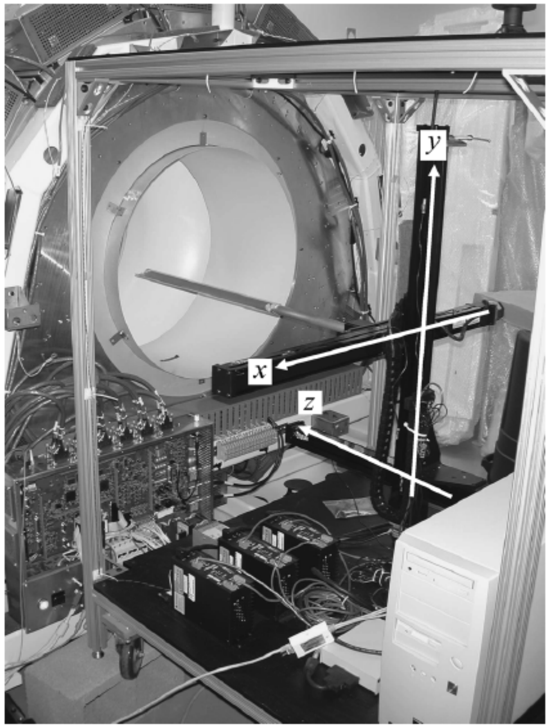


PSF: measured, MC simulations, modelled

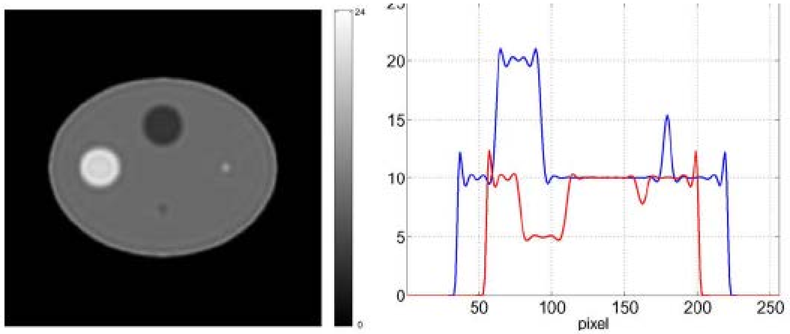
- ➢ accounting for varying spatial resolution

E.g. Siemens TrueX Algorithm (now "HD PET")

- + better resolution -> detectability of small volumes
- – Gibbs artifacts at sharp edges



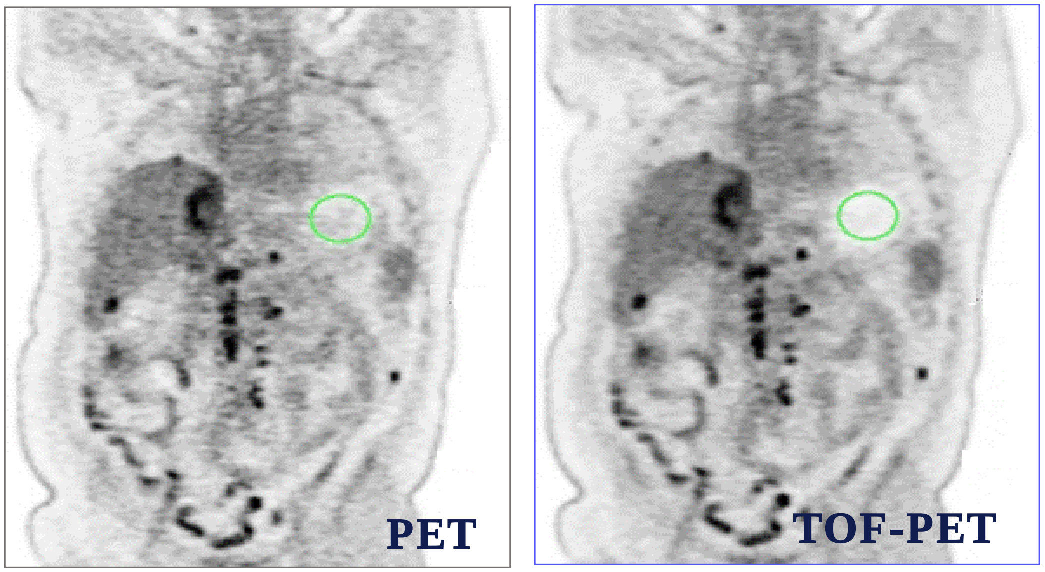
Panin et al. IEEE 2006



Tong et al. IEEE 2011

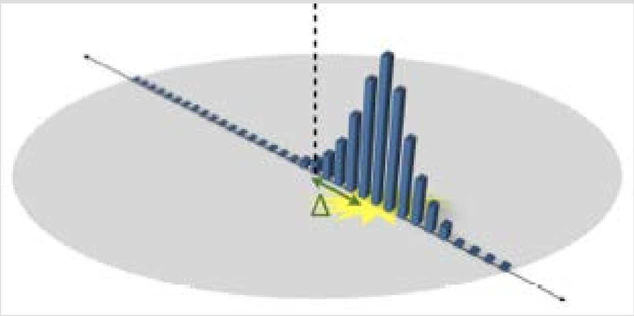
Time-of-flight

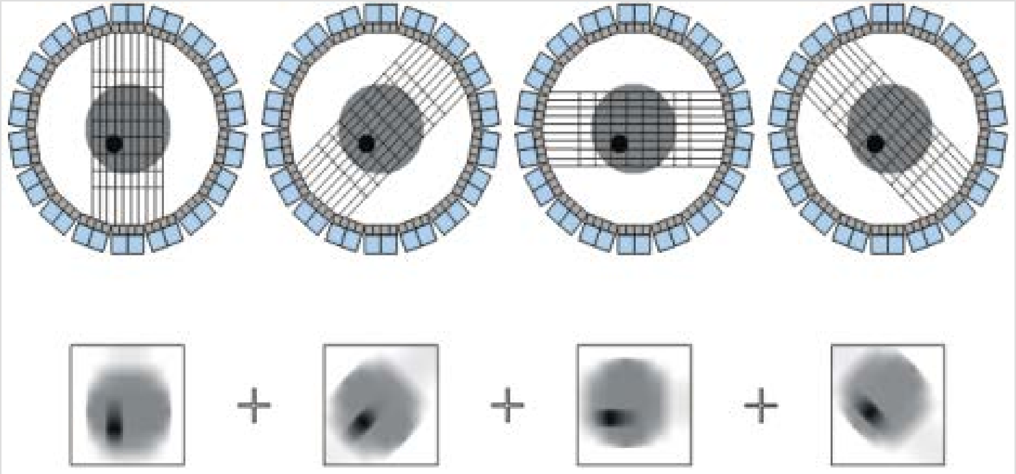
$$SNR_{TOF} \cong \sqrt{\frac{D}{\Delta x}} \cdot SNR_{conv}$$

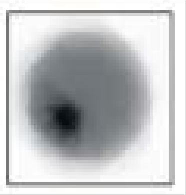


BMI 30

Time-of-flight PET





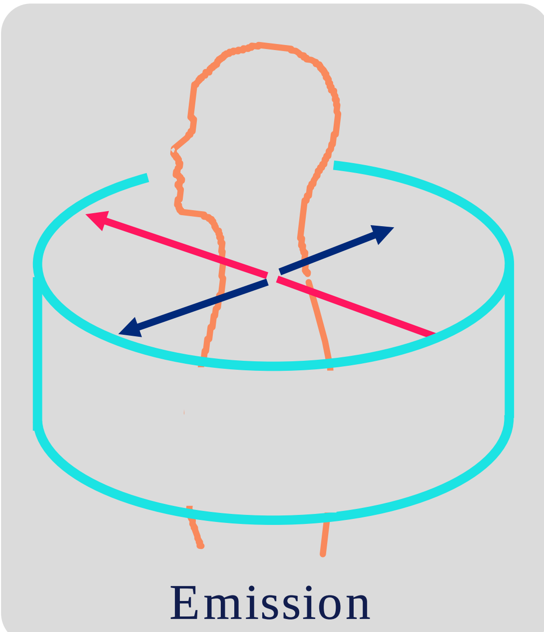


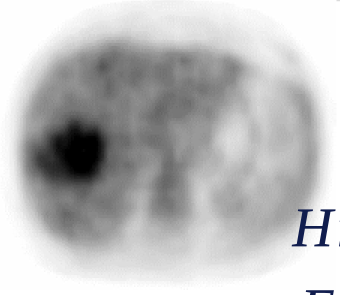
TOF-PET improves SNR (not spatial resolution)

Why PET/CT?

Courtesy T.Beyer (Vienna)

Positron Emission Tomography





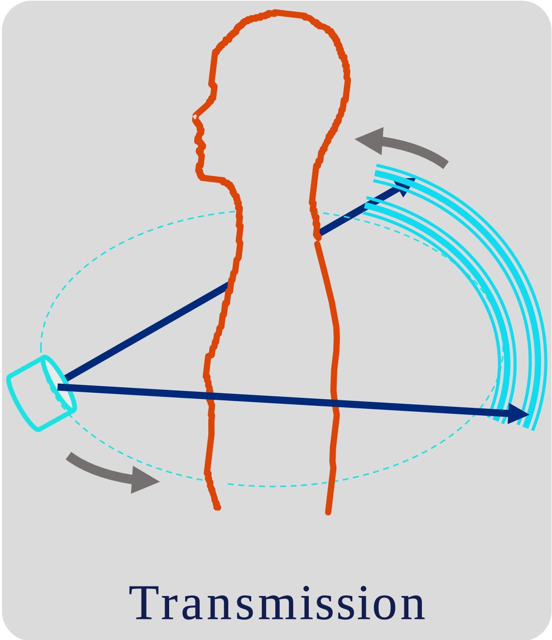
Functional anatomy

Changes in metabolism

High functional resolution

Early detection is possible

Computed Tomography



Spatial anatomy

Changes in anatomy

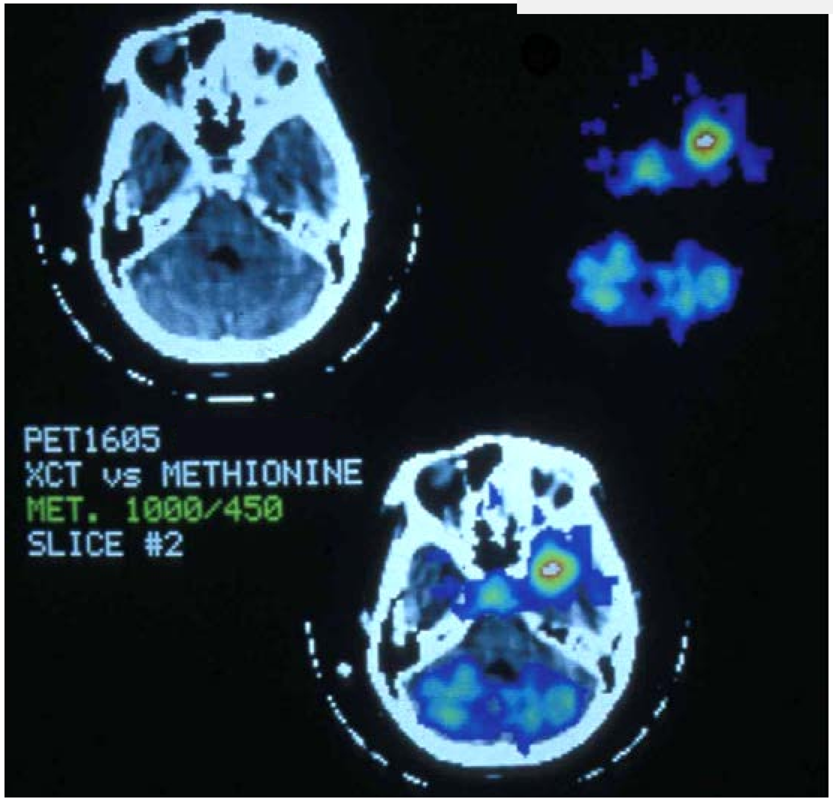
High spatial resolution

Late(r) anatomical changes

PET/CT is *function* plus *anatomy*

Early PET/CT development

Courtesy T.Beyer (Vienna)



A combined CT and PET system developed by Prof. Teruo Negai (Dept of Radiology, Gunma University, Japan) in 1984.

The device incorporated CT and PET scanners from Hitachi Inc and the patient bed moved on floor-mounted rails between the PET and CT.

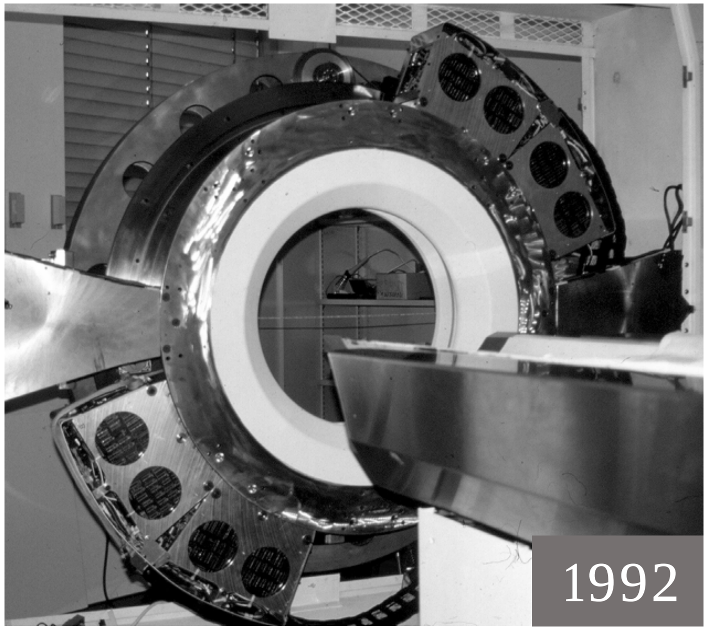
Fusion images of a patient with a brain tumor.

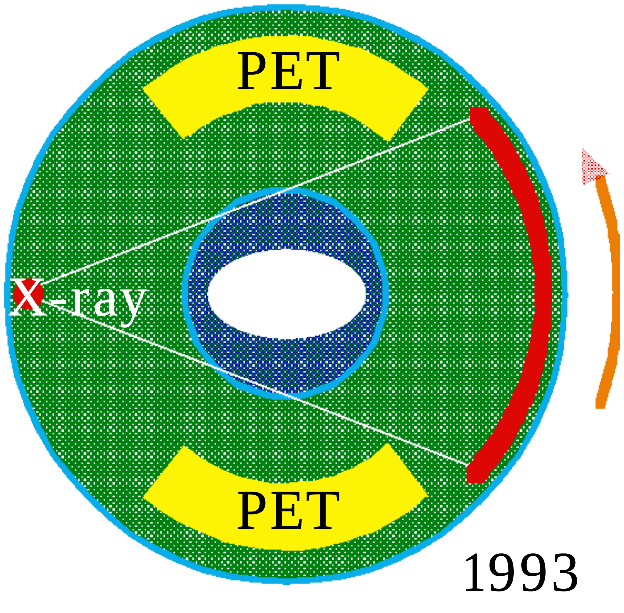
^{11}C-methionine PET and CT acquired in the same examination.

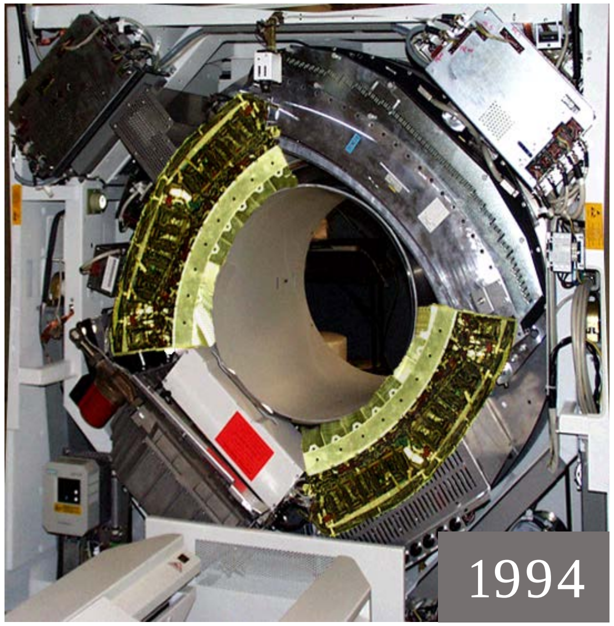
Courtesy Prof. Y Sasaki

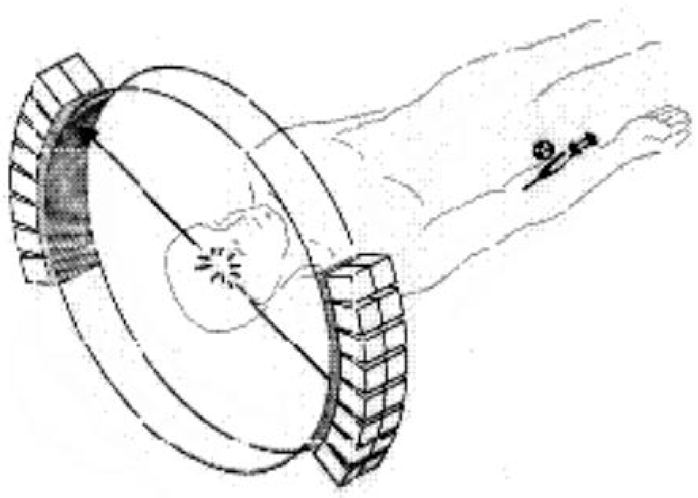
Prototyping PET/CT

Courtesy T.Beyer (Vienna)









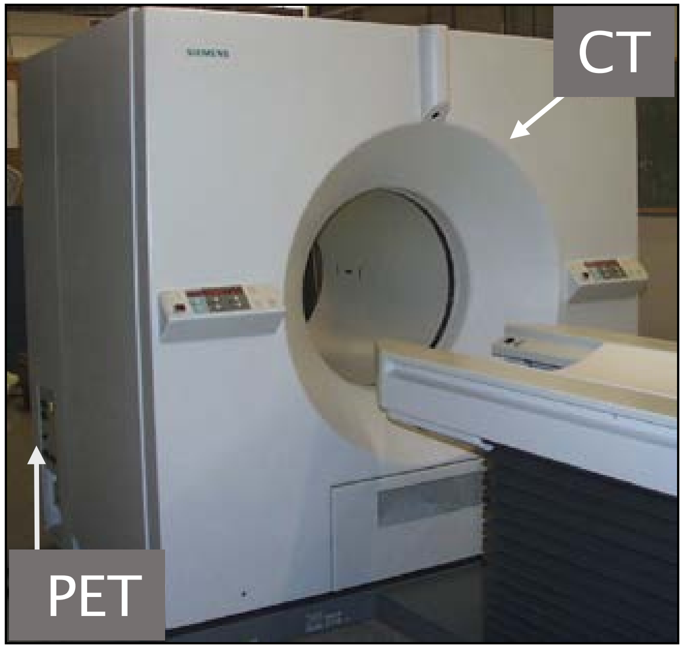
A rotating PET scanner using BGO detectors,
Townsend DW et al, JNM 30, 1993

The evolution of a PET/CT concept:1992-4

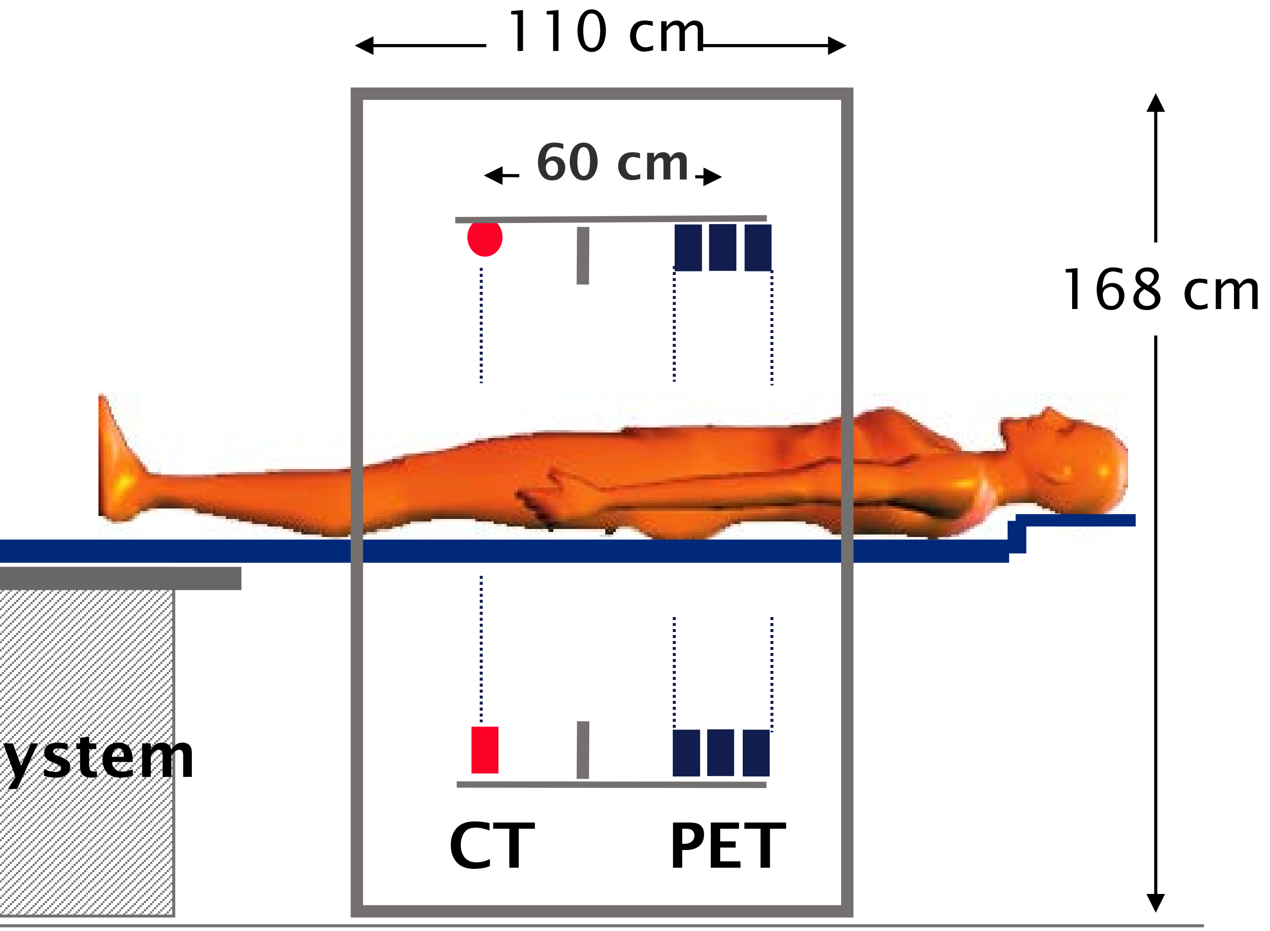
- Routine oncology imaging (whole-body)
- Complementary PET/CT
- Accurate, fast CT-based quantitation

The SMART PET/CT

Courtesy T.Beyer (Vienna)

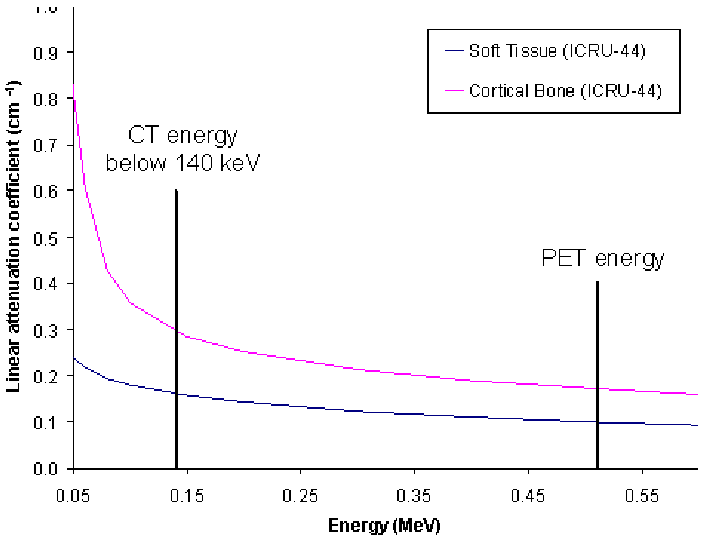


SMART
→ Somatom CT
→ Advanced Rotating Tomograph (PET)

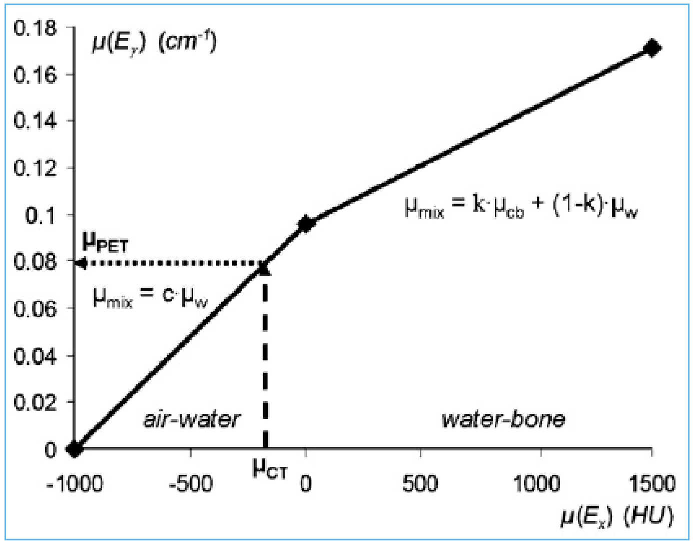


CT based AC

Courtesy T.Beyer (Vienna)

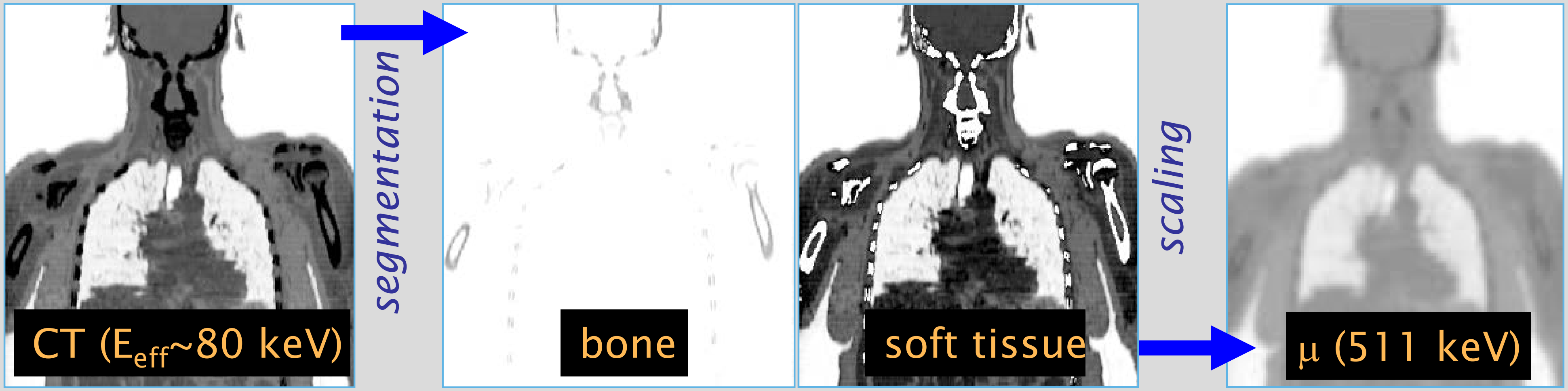


Kinahan P et al, Sem Nuc Med XXXIII, 2003



Townsend DW, PMB 53: R1-39, 2007

bi-linear segmentation-scaling approach to CT-AC



Early PET/CT concepts

Courtesy T.Beyer (Vienna)

1998-2000

300 oncology patients

~50% with CT contrast

Torso exam in 60 min

CT: 80 cm = 4 min,

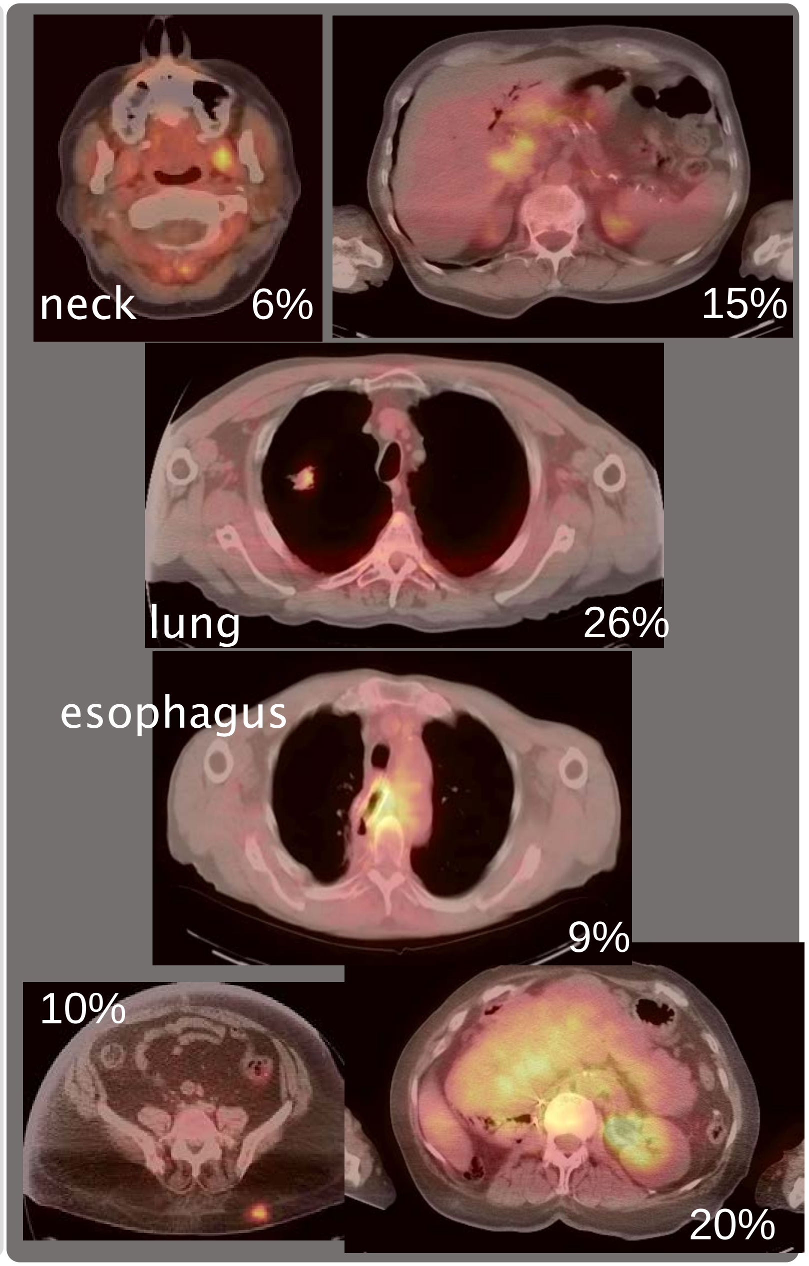
PET: 7 beds = 50 min

BGO: 7x7x20 mm^3

1-slice CT, 15 kW

Power of fused images

CT-based artifacts



RSNA 2000

PET/CT systems

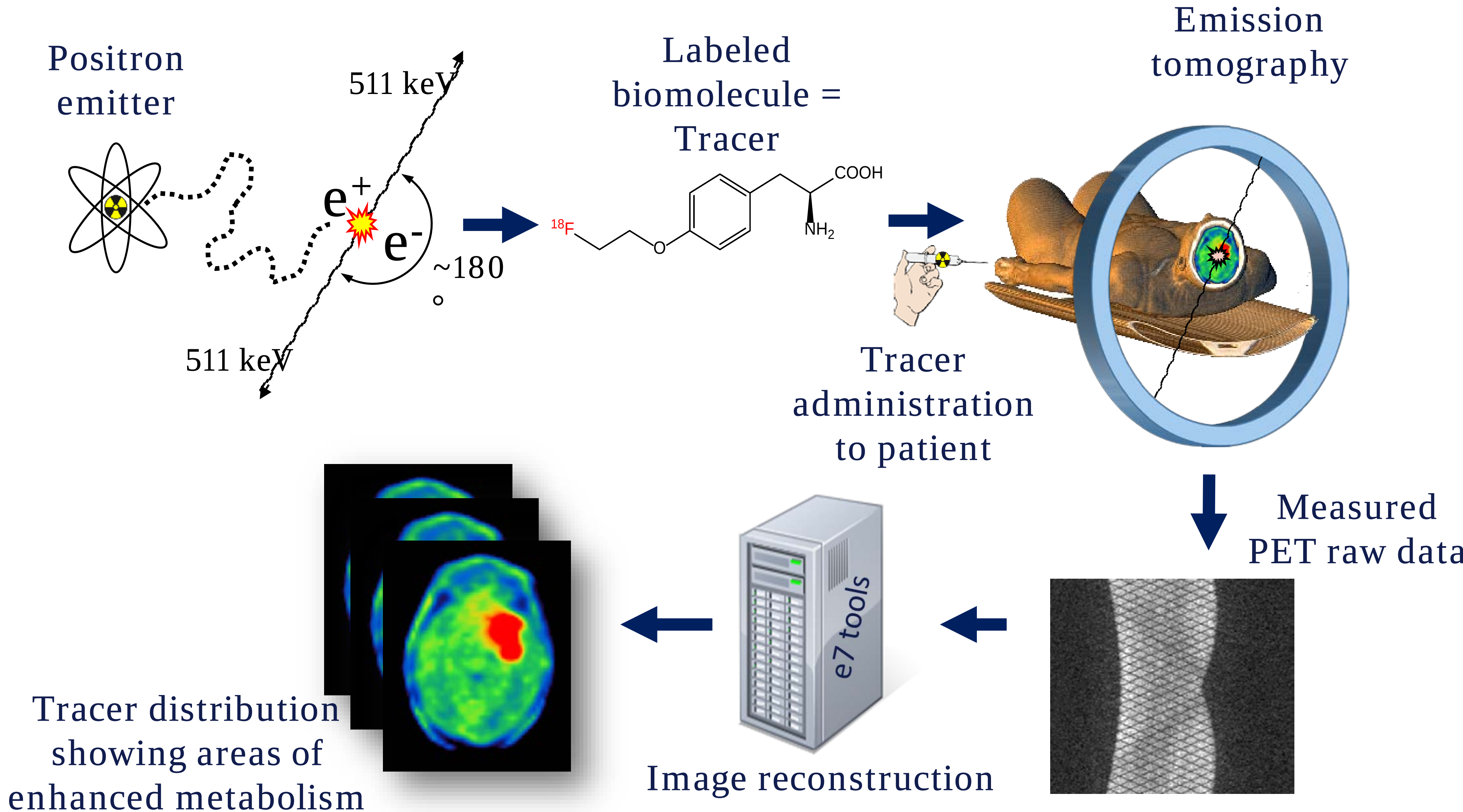
Courtesy T.Beyer (Vienna)




Discovery VCT	Ingenuity TF	AnyScan	Biograph mCT
CT: 16-128 slices	CT: 16-128 slices	16-slice CT	CT: 20-128
70 cm patient port	70 cm (85 cm) patient port	70 cm diameter patient port	78 cm patient port
250 kg table weight limit	215 kg table weight limit	250 kg table weight limit	250 kg table weight limit
170 cm co-scan range	190 cm co-scan range	360 cm co-scan range	170 cm co-scan range
24 rings of LYSO(Ce)	44 rings of LYSO(Ce)	24 rings of LYSO(Ce)	52 rings of LSO (Ce) crystals
4.2 x 6.3 x 25 mm^3	4.0 x 4.0 x 22 mm^3	3.9 x 3.9 x 20 mm^3	4.0 x 4.0 x 20 mm^3
Time-of-flight	Time-of-flight		Time-of-flight
15.1 cm axial FOV	18 cm axial coverage	23 cm axial coverage	21.6 cm axial coverage
70 cm transaxial FOV	67 cm transaxial FOV	55 cm transaxial FOV	70 cm transaxial FOV
PET resolution model	PET resolution model		PET resolution model

High-end PET combined with high-end, multi-slice CT

Summary



Tracer distribution showing areas of

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