All I know about

# PET

(and PET/CT,  PET/MR, and SPECT/CT)

Medical Imaging Systems
DTU, November 2024

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## Rigshospitalet, Copenhagen

PET

Entrance 39

Photo: Flying Professor Andreas Kjær



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Thanks to:

GE Medical Systems
CPS Innovation (Bernard Bendriem)
Siemens Medical Solutions
Philips Medico
Impact (www.impactscan.org)
UC Davis, Simon Cherry



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## Overview (0):

- Different kinds of tomography – PET in particular
- Reconstruction from projections, FBP vs. iterative methods
- Positron imaging history
- Raw data structure - sinograms - types of acquisition and presentation
- 2D/3D, advanced data structure – Michelogram
- Resolution and noise

---------------------------------------------------------------------------------

- Scanner physics 1 – PET detectors
- Scanner physics 2 – good, bad, and noise equivalent counts (NEC)
- Attenuation and scatter correction of PET-data
- Hybrid systems – PET/CT- PET/MR - SPECT/CT…    Future ideas



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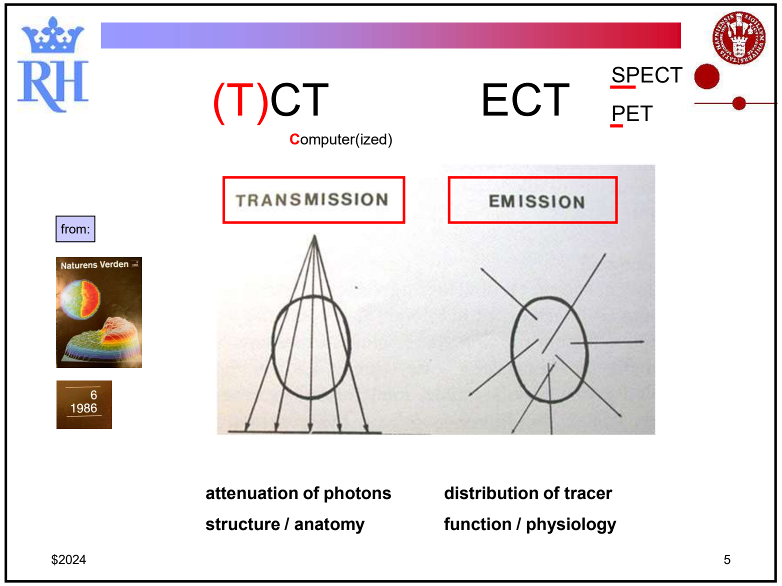
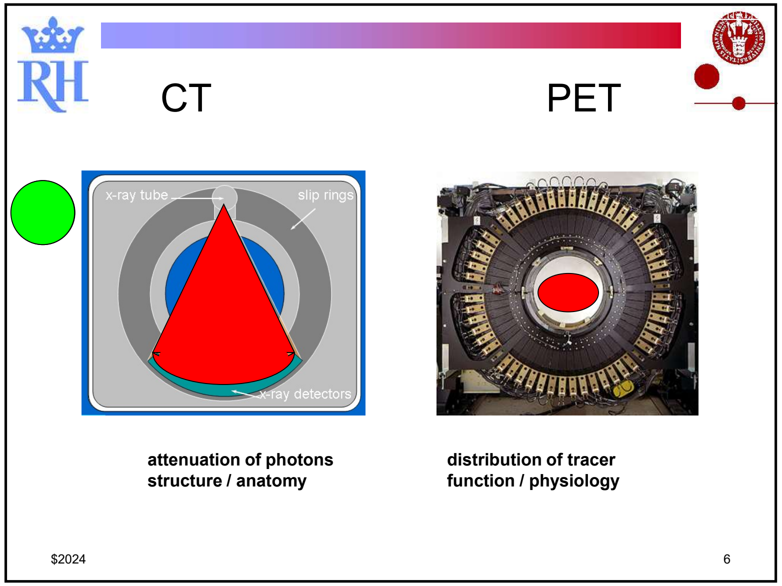

(T)CT
Computer(ized)
ECT
SPECT
PET
from:
Naturens Verden
6
1986
TRANSMISSION
EMISSION
attenuation of photons
structure / anatomy
distribution of tracer
function / physiology
$2024
5

5


CT
PET
x-ray tube
slip rings
x-ray detectors
attenuation of photons
structure / anatomy
distribution of tracer
function / physiology
$2024
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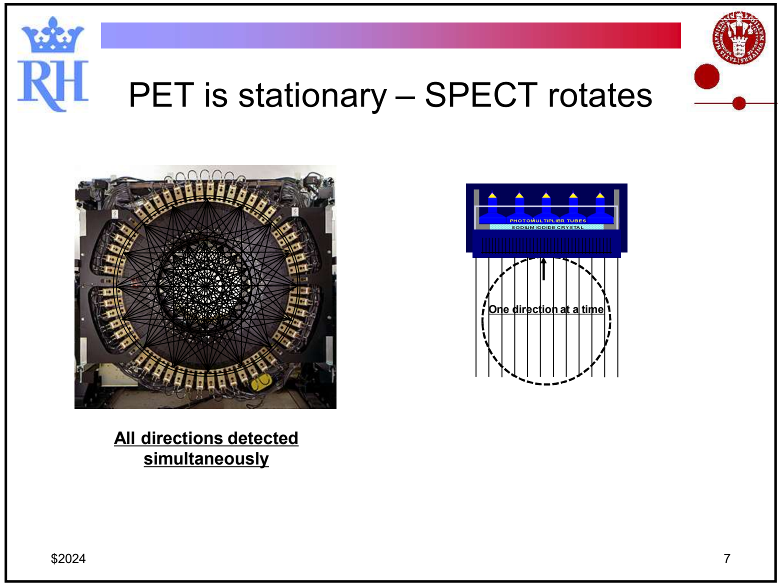
6


PET is stationary – SPECT rotates
All directions detected simultaneously
One direction at a time
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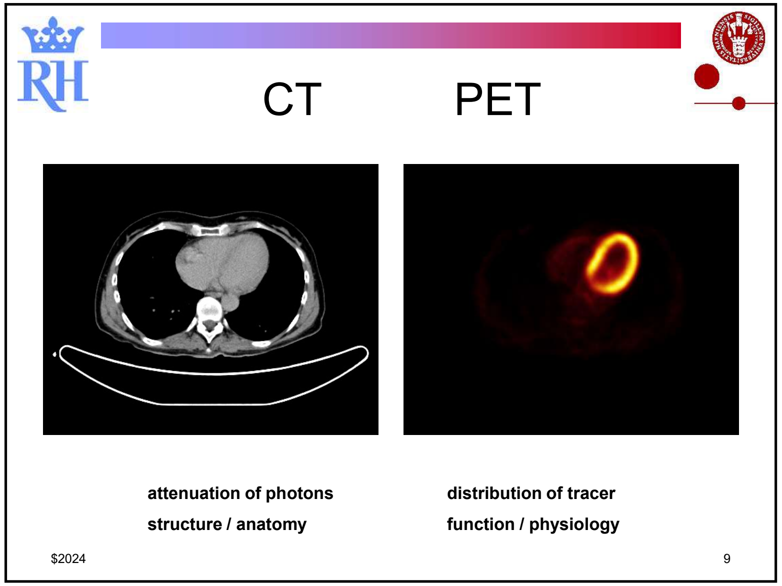
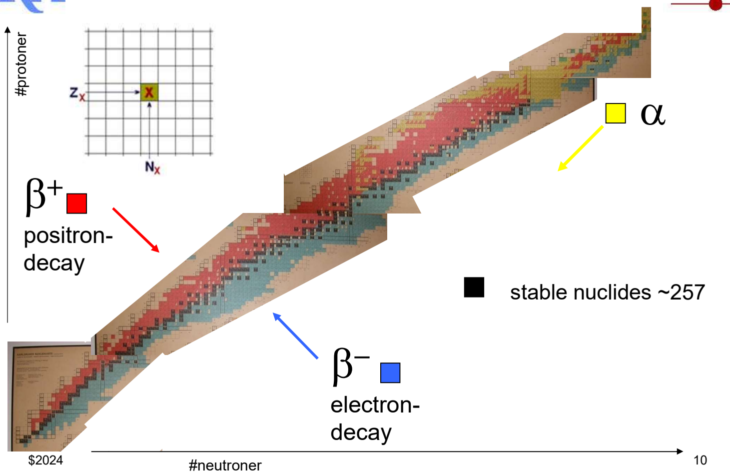

CT
PET
attenuation of photons
structure / anatomy
distribution of tracer
function / physiology
$2024
9

9

## The nuclear chart (N,Z)



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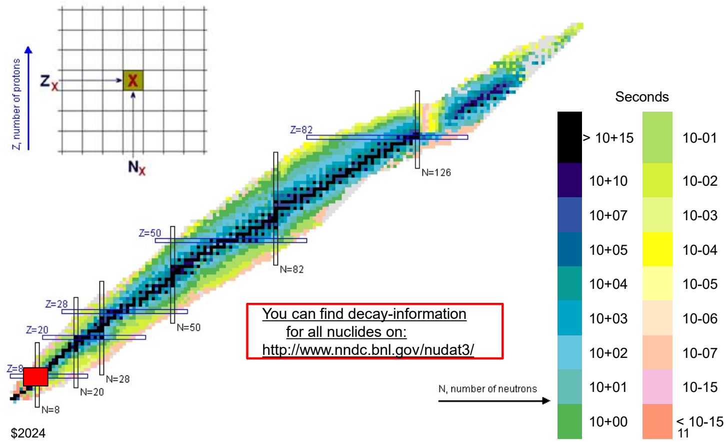
## The nuclear chart (N,Z) - halflives



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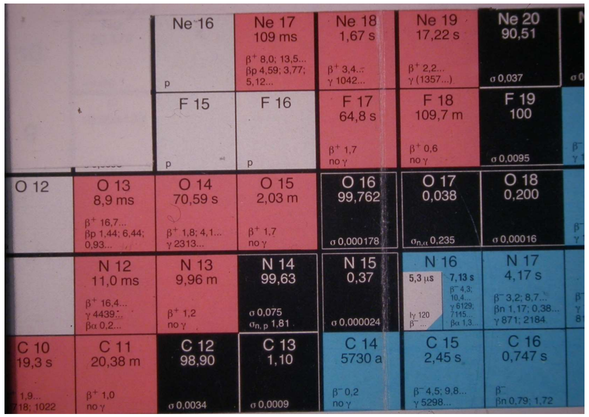
## …magnified



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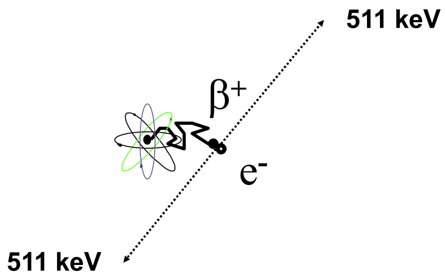
## PET *is really* ART:

**A**nnihilation **R**adiation **T**omography




1955

$E = mc^2$

1905

Result: Two photons on an **almost** straight line that **nearly** contains the point of decay



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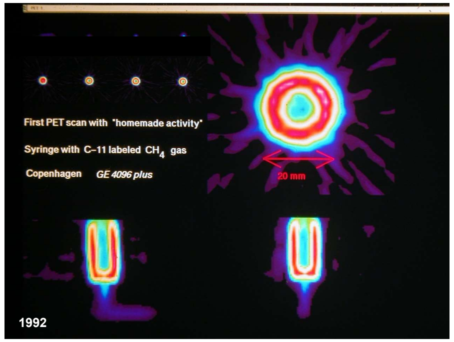
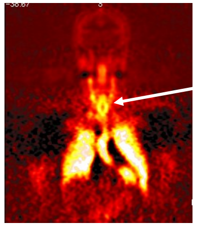
# Positron Emission Tomography (?) or ART

We never detect the positrons directly, only the annihilation photons

Annihilation
Radiation
Tomography



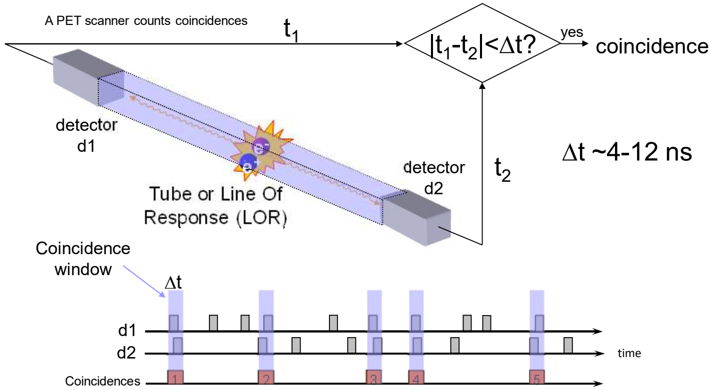



Inhalation of radioactive $\beta^+$ gas





# PET radiation detection

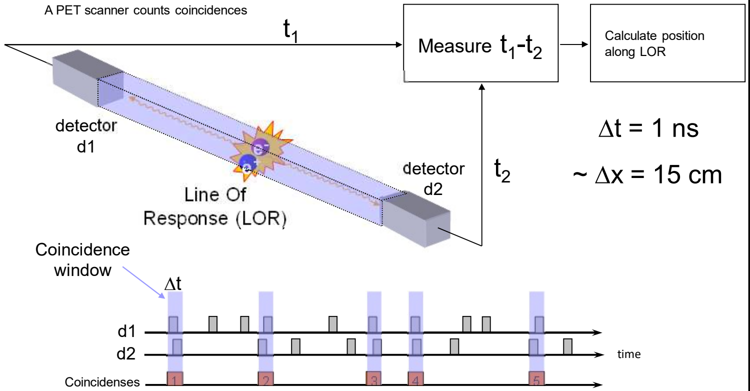



$\Delta t$ ~4-12 ns





# PET detection, Time-of-Flight




$\Delta t$ = 1 ns

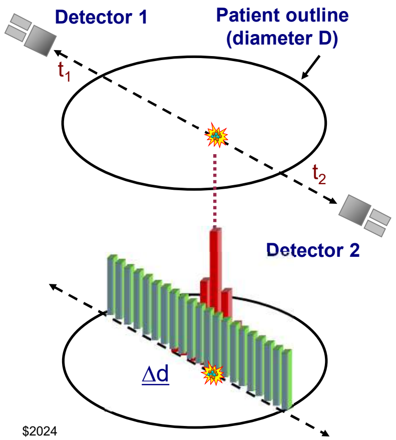
~ $\Delta x$ = 15 cm





# Time of Flight (TOF) PET

– more than just a coincidence...

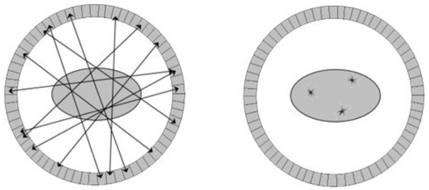



- tried and abandoned in ancient PET times (~1985)
- idea commercially relaunched in 2006 by Philips

| δt (ps) | Δd (cm) | SNR |
|---|---|---|
| 20 | 0.3 | 12 |
| 100 | 1.5 | 5.2 |
| 200 | 3.0 | 3.7 |
| 600 | 9.0 | 2.1 |

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

## Improvement of signal-to-noise ratio: TOF- PET




| δt (ps) | Δd (cm) | SNR |
|---|---|---|
| 20 | 0.3 | 12 |
| 100 | 1.5 | 5.2 |
| 200 | 3.0 | 3.7 |
| 600 | 9.0 | 2.1 |

Best commercial system (2021): $\tau = $ **210 ps** – Siemens Vision (and Quadra)

Potential for $\tau = $ **100 ps** with existing technology in a few years (?)

Figure from Lars Jødal, Ålborg *(included in Klinisk Nuklearmedicin, 2022)*





## Positron Emitting Isotopes

| Isotope | Half-Life | Production |
|---|---|---|
| Carbon-11 | 20.5 min | $^{14}N(p,\alpha)^{11}C$ |
| Nitrogen-13 | 10.0 min | $^{16}O(p,\alpha)^{13}N$ |
| Oxygen-15 | 2.1 min | $^{14}N(d,n)^{15}O$ |
| Fluorine-18 | 110 min | $^{18}O(p,n)^{18}F$ ($F^-$), $^{20}Ne(d,\alpha)^{18}F$ ($F_2$) |
| Gallium-68 | 68 min | Daughter of Ge-68 (271days) |
| Rubidium-82 | 1.3 min | Daughter of Sr-82 (25days) |

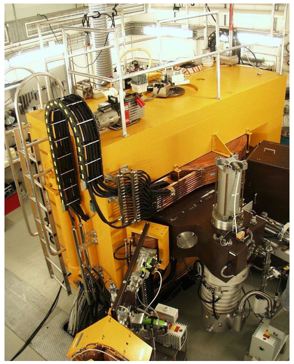
Other: Sc-43/44, Cu-64, Zr-89, I-124…

- Small elements (C,N,O,F) allow "real" biochemistry
- Short half-lives make tracer production an integral part of PET

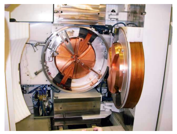




## Cyclotrons



Scanditronix 32 MeV

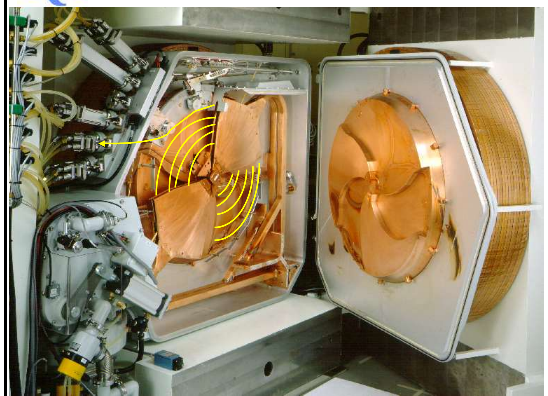


GE Minitrace 11 MeV





## (small) Cyclotron



**Ion Source**

Production of $H^-$

**RF + magnetic field**

Ion acceleration

**Carbon foil**

Electron stripping

$H^- \Rightarrow H^+$ (protons!)

protons do irradiate a

**Target**

# Nuclear Reactions

$^{18}O$ (p,n) $^{18}F$
$^{14}N$ (p,α) $^{11}C$
$^{14}N$ (d,n) $^{15}O$
$^{16}O$ (p,α) $^{13}N$

| | | | | | |
|---|---|---|---|---|---|
| | | | $^{17}F$ 64.49s $β^+$ | $^{18}F$ 109.77m 96.9 % $β^+$ | $^{19}F$ 20.3 ms |
| | | $^{15}O$ 122.24s 99.9 % $β^+$ | $^{16}O$ 99.762 | $^{17}O$ 0.038 | $^{18}O$ 0.200 |
| | $^{13}N$ 9.96 m $β^+$ | $^{14}N$ 99.64 | $^{15}N$ 0.36 | | |
| $^{11}C$ 20.3 m 99.8 % $β^+$ | $^{12}C$ 98.89 | $^{13}C$ 1.11 | $^{14}C$ 5736 a | | |





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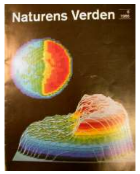
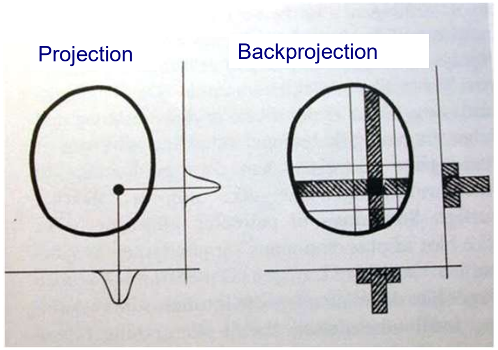
# Principle of image formation!



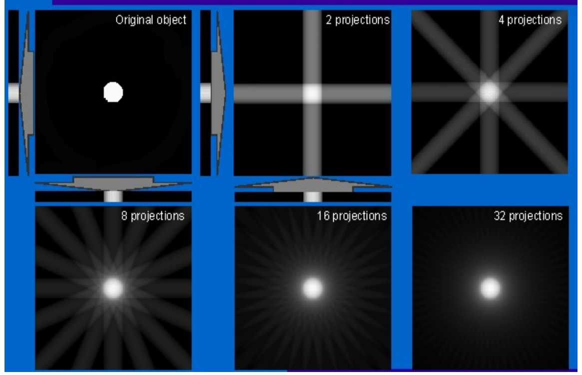

6
1986



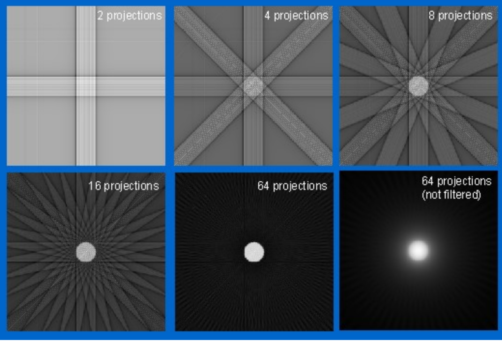





# Back projection



## Filtered back projection



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## Example of FBP

Filtered Back Projection of Xray-data (CT)




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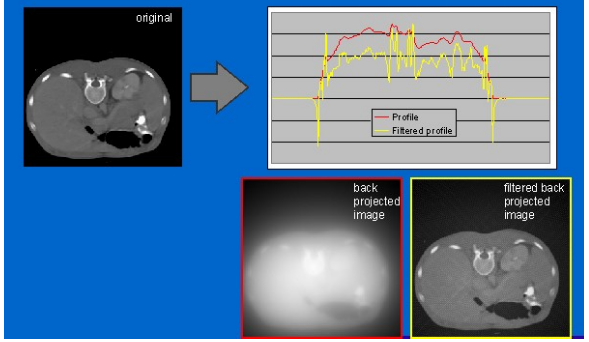
## Filtered back projection



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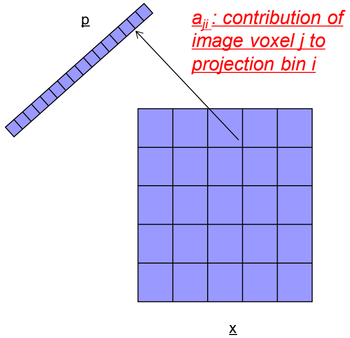
## Iterative Algorithms

- For example, ML-EM, OS-EM,
- Discretize the image into pixels
- Solve matrix equation
  **Ax=p** **( $x=A^{-1}p$ )**
- x = unknowns (pixel values)
- p = projection data
- A = imaging system matrix



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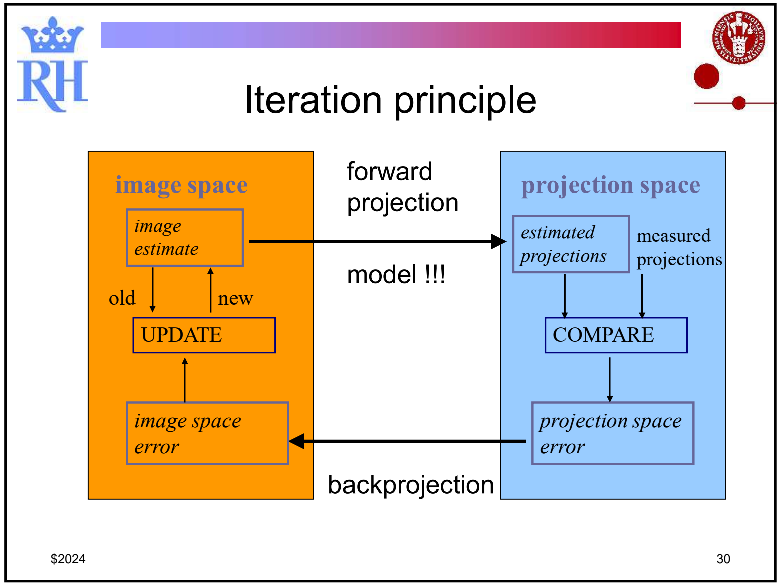
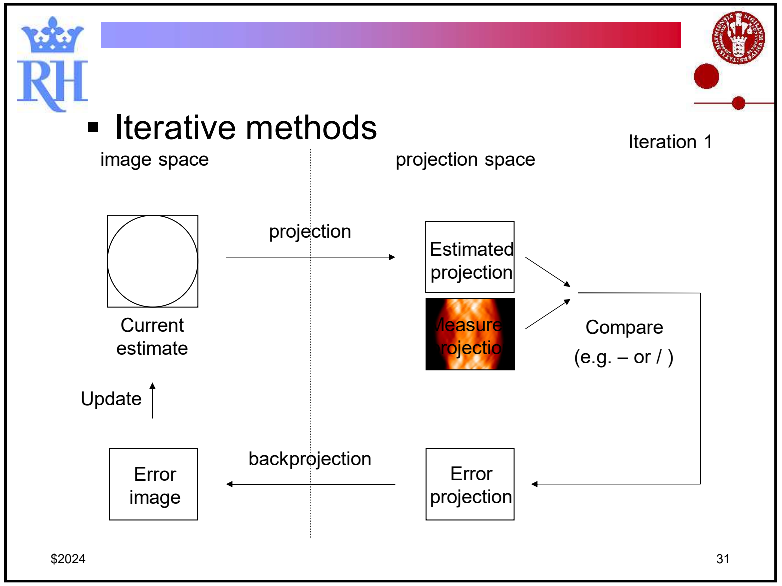

Iteration principle
image space
image estimate
old
new
UPDATE
image space error
forward projection
model !!!
backprojection
projection space
estimated projections
measured projections
COMPARE
projection space error
$2024
30

30


Iterative methods
Iteration 1
image space
projection space
projection
Current estimate
Estimated projection
Compare
(e.g. – or / )
Update
backprojection
Error image
Error projection
$2024
31

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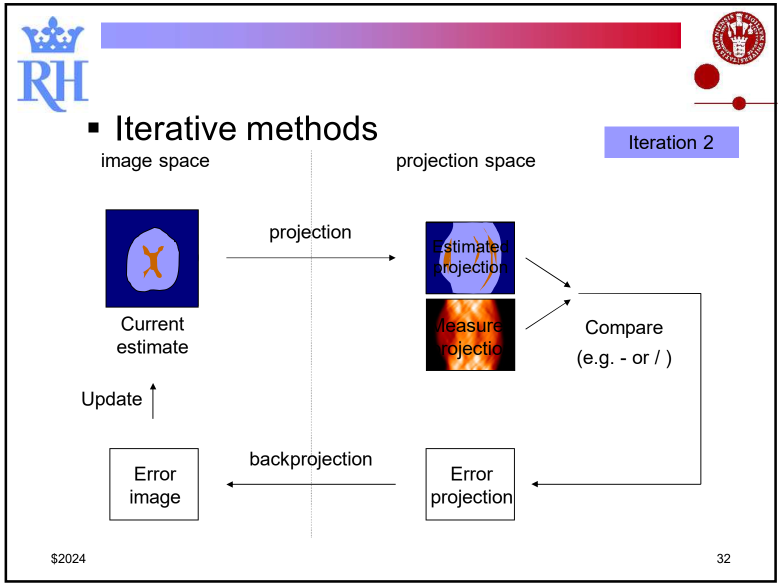
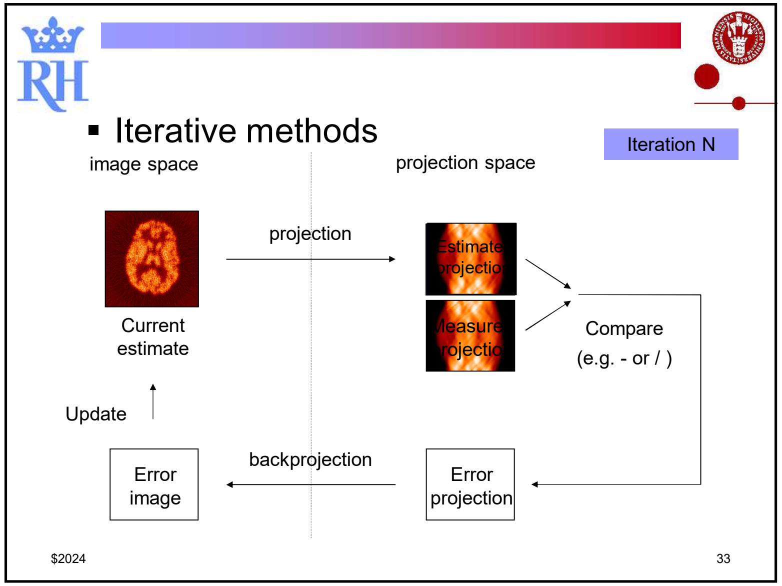

Iterative methods
Iteration 2
image space
projection space
projection
Current estimate
Compare
(e.g. - or / )
Update
backprojection
Error image
Error projection
$2024
32

32


Iterative methods
Iteration N
image space
projection space
projection
Current estimate
Compare
(e.g. - or / )
Update
backprojection
Error image
Error projection
$2024
33

33

# Iterative Recon versus FBP

| | **FBP** Methods | **Iterative** Methods |
|---|---|---|
| **Implementation:** | Simple | Complex |
| **Reconstruction speed:** | Very fast | Slow with ML-EM, fast with OSEM |
| **Imbedded corrections:** | None | anything you can model |
| **Low-count image:** | Noisy | Less noise |
| Reconstruction artifacts: | Streak/spill artifacts | None, regular activity distribution |

FBP reconstructed image

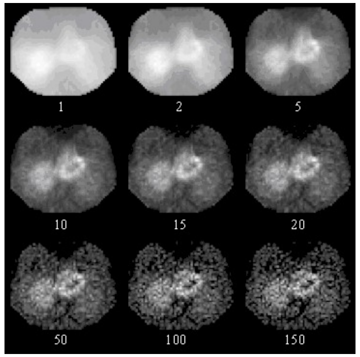
OSEM reconstructed image





# Image at different iteration numbers

**Smooth**
**Low resolution**




**Noisy**
**High resolution**





# Overview (2):

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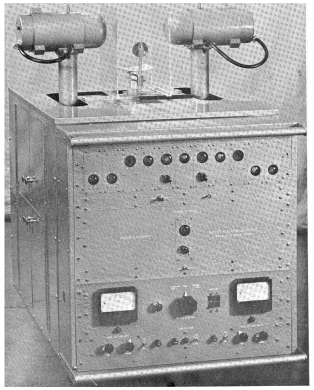
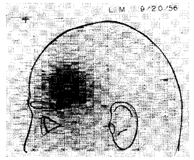
# Positron scanner (*not PET)*

(Brain tumor scanner at MGH 1955- )





Positrocephalogram (PCG) of patient with meningioma

COINCIDENCE SCANNING WITH POSITRON-EMITTING ARSENIC OR COPPER IN THE DIAGNOSIS OF FOCAL INTRACRANIAL DISEASE

By

William H. SWEET, John MEALEY, Jr.,
Gordon L. BROWNELL and Saul ARONOW
Departments of Surgery and Medicine, Harvard Medical School, and the Neurosurgical Service and Physics Research Laboratory of Massachusetts General Hospital, Boston, Massachusetts, U. S. A.

*Abstract*

This is a report on coincidence counting in man of the paired annihilation gamma rays from positron-emitting copper or arsenic. We discuss the relevant biological behavior of inorganic arsenate and arsenite, of copper versenate, and the results of using these substances during automatic scanning to localize intracranial masses.

Radioassay of biopsies of the principal normal cephalic tissues, of various types of neoplasms, of hematomas, abscesses and zones of demyelination were carried out. With arsenic the ratios of concentrations of tumor to normal brain were up to 30 for meningiomas. The remaining main tumor types, in order of decreasing concentrations of isotope, were acoustic neuroma, glioblastoma, metastatic malignancy and astrocytoma. The high tumor uptake with arsenic persists long enough so that repeat scans one day after injection are valuable. The muscle : brain ratio of concentrations of circa 3 is high enough to interfere with the accuracy of diagnosis in lesions beneath the lower temporal and especially the upper nuchal masses of muscle. Hematomas, abscesses and zones of demyelination also have high enough ratios to permit localization in the majority of patients. The results on biopsies containing copper versenate showed similar ratios insofar as ascertainable from fewer samples. The meningiomas are a probable exception, yielding lower ratios with the copper.

On the basis of radioassay both of urinary excretion and of the full range of tissues obtainable at autopsy we compute the local whole-body radiation with $As^{74}$ to be about 3.2 rads after the usual scanning dose of 2.3 mC/70 kg. The kidney receives about 12.7 and the liver 9.7 rads. The corresponding figures for $Cu^{64}$ are 0.325 rads to the whole body, but with a dose to the liver of 3.2 rads because this organ takes up about half of the administered versenate.

The automatic scan includes in 2 simultaneously evolving side views a coincidence count or positrocephalogram (PCG) and a plot of the asymmetry of the total gamma radiation, an asymmetrogammagram (AGG). A sagittal PCG is also taken. The lateral scan requires 40 minutes, the sagittal 20 minutes.

Of the more than 3000 scans carried out we report here only the 285 performed in the last 3½ years on a special group of 334 patients, who nearly all proved to have

(IAEA meeting 1959)

MEDICAL
RADIOISOTOPE SCANNING

Proceedings
of a seminar jointly organized by
The International Atomic Energy Agency and the World Health Organization
Vienna, 25 — 27 February, 1959

PCG:

A "routine" examination!

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## Anger camera (Rev.Sci.Instr. 1957)

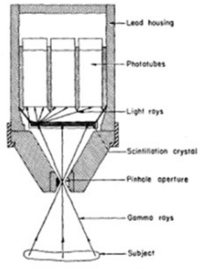


Fig. 1. Sectional drawing of scintillation camera.

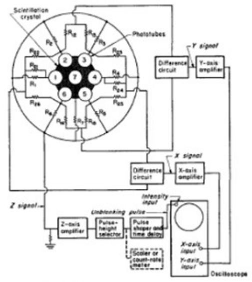


Fig. 2. Block diagram of electronic circuit.

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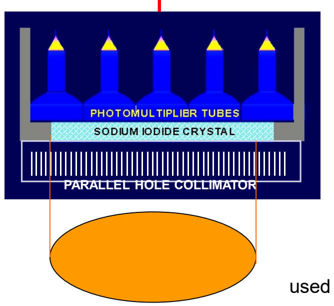
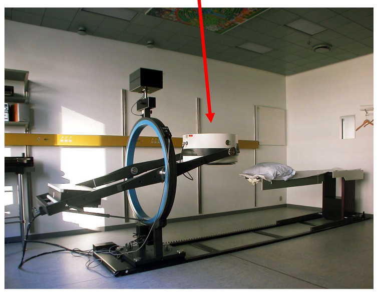
## Gamma camera principle

position sensitive photon-detector



used for planar imaging or tomography (SPECT)

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NEW POSITRON TECHNIQUE

The Anger positron camera has proven to be of considerable value in high-sensitivity scanning.[3] This camera, shown in Figure 12, consists of a conventional Anger camera coupled


Figure 12. Anger positron camera. The crystal matrix is used to select and position pulses from the Anger scintillation camera. (3)

with a second matrix of sodium-iodide detectors. Only pulses in the scintillation camera which are coincident with pulses in the detector matrix are recorded. The position of the pulses are adjusted according to the location of the detector in the second matrix. By a simple control, it is possible to focus on various planes within the object. Because of the very-wide-

Gamma camera for positron imaging:

NOT a recent invention

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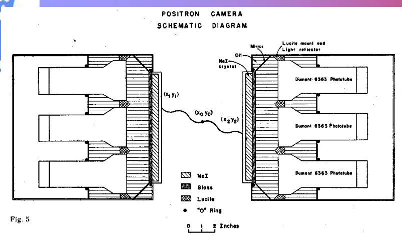


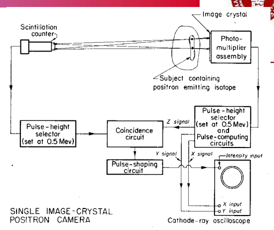


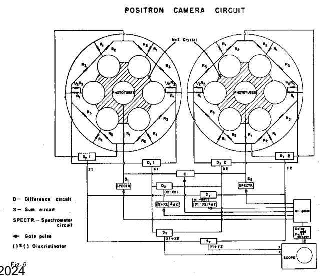


Principles proposed by Hal Anger 1959



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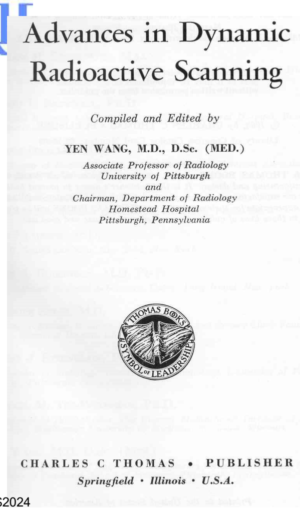
# 1968 PET


Advances in Dynamic Radioactive Scanning

*Compiled and Edited by*

YEN WANG, M.D., D.Sc. (MED.)

*Associate Professor of Radiology*
*University of Pittsburgh*
*and*
*Chairman, Department of Radiology*
*Homestead Hospital*
*Pittsburgh, Pennsylvania*

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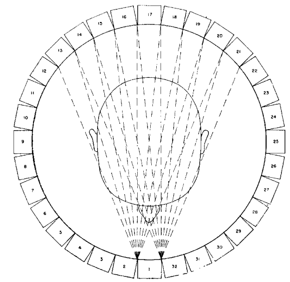

FIGURE 13. (a and b) Multicrystal positron detector of Brookhaven design. Each NaI detector and phototube feeds pulses into a coincidence matrix. Coincidences are stored in a magnetic drum memory and subsequent calculation permits the original isotope distribution to be reconstructed. (4)



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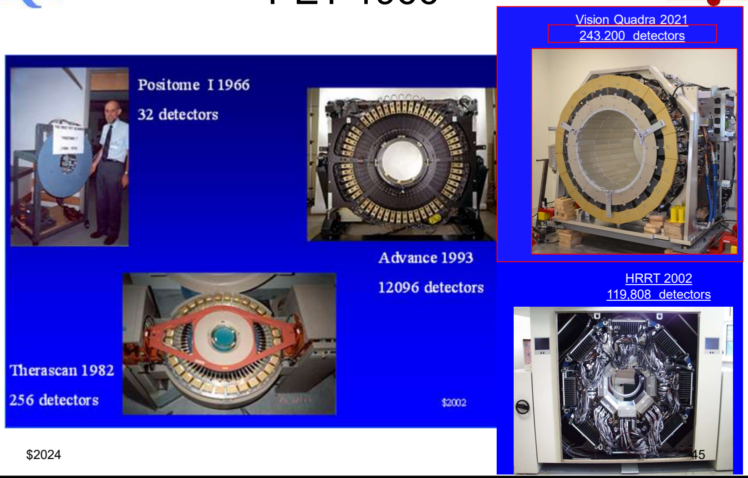
# PET 1966 -



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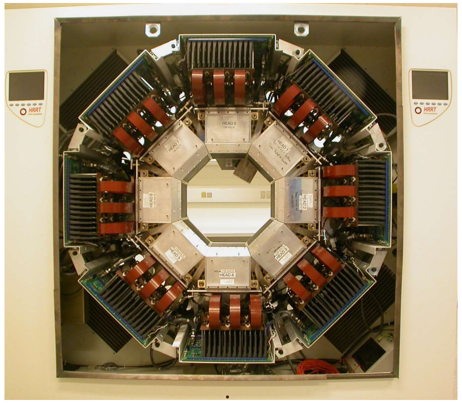
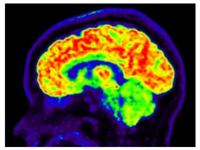
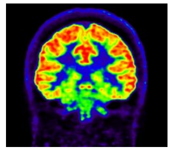
# Special Brain scanner (HRRT)







119.808

Detector elements



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Time to breathe…

[Reykjavik, 25. August 2011$]



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## Overview (3):

- Different kinds of tomography – PET in particular
- Reconstruction from projections, FBP vs. iterative methods
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- 2D/3D, advanced data structure – Michelogram
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- Scanner physics 1 – PET detectors
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- Attenuation and scatter correction of PET-data
- Hybrid systems – PET/CT- PET/MR - SPECT/CT… Future ideas



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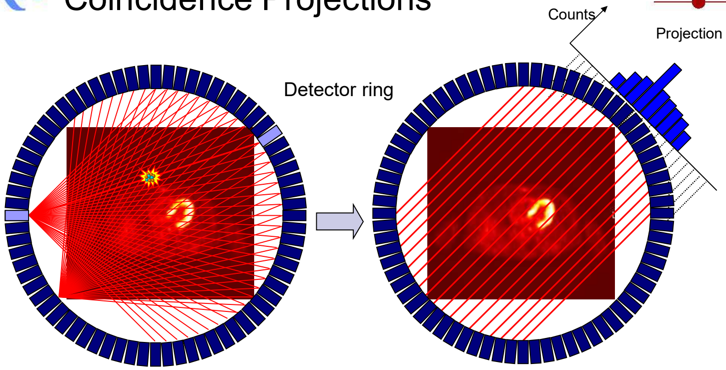
## Coincidence Projections




Coincidence events determine sampling paths (**Lines Of Response**)

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



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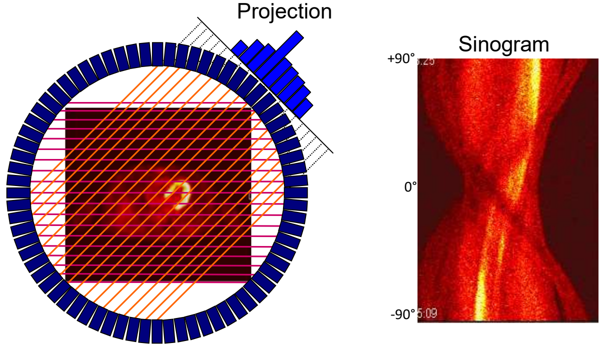
## Data-Sorting Sinogram




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



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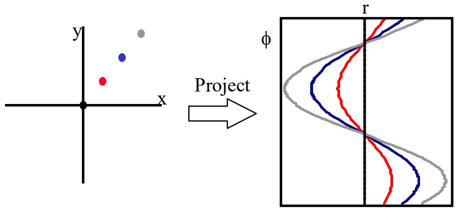
## Sinogram

Real

Space




Radon

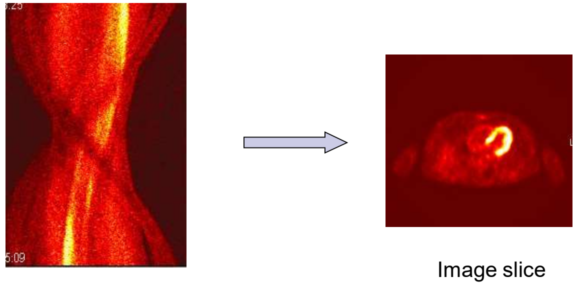
transform

Point in center: straight line

Off-center: sine curve, amplitude proportional to radius



## Image Reconstruction



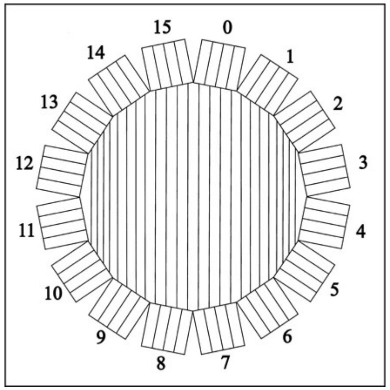
Sinogram

Image slice



## Geometric correction

Interpolation needed before reconstruction

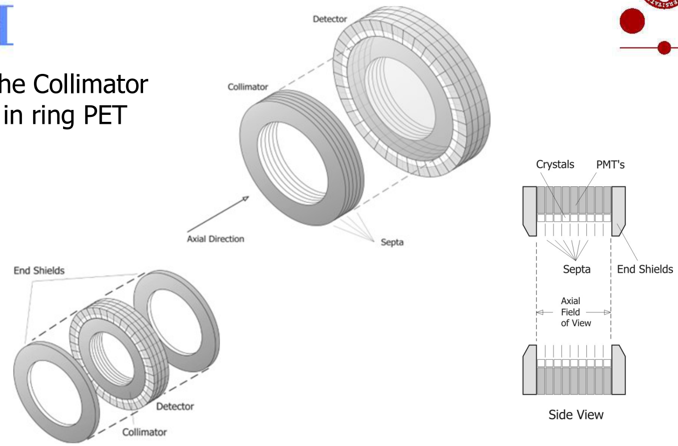



The sampled LORs are not equidistant, but become closer towards the edges.

The projections must be resampled prior to or during reconstruction

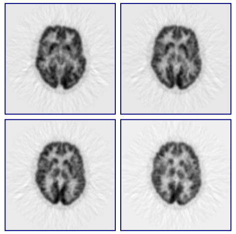


## The Collimator in ring PET



## *Static Frame Acquisition*

- Set of slices in a single FOV
- No patient table motion
- ➢ Brain scan
- ➢ Heart examinations (myocardial perfusion, metabolism and viability)



Adjacent brain PET static slices

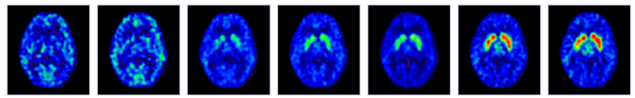




## *Dynamic Frame Acquisition*

- Set of slices over time in a single FOV (like a movie)
- No patient table motion
- Start data acquisition as the tracer is administered
- ➢ Quantitative flow study (blood or other fluid): brain or heart

Cerebral dynamic PET scan
Tracer is $^{18}$F-labeled D2 dopaminergic receptor ligand
Finding: caudate and putamen normal tracer uptake



time





## *Gated Acquisition*

- Set of slices over time in a single FOV (like a movie)
- No patient table motion
- ➢ Heart imaging without cardiac motion blurring
- ➢ Myocardial perfusion, metabolism and viability

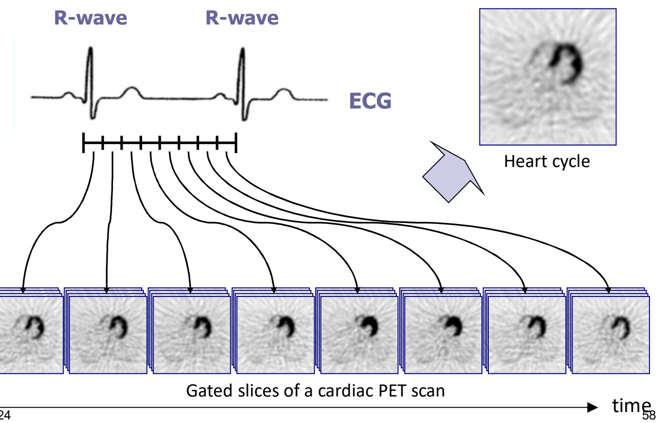
+

Electrocardiogram





## *Gated Acquisition*




Gated slices of a cardiac PET scan

# List Mode data (LM)

- List mode is an alternative way to store data during acquisition
- In the sinogram, events are counted in each matrix element. In List Mode, the two addresses (the detector numbers) of the two detectors involved are written to a continuous datastream.
- Every millisecond a timestamp is added to the stream
- Signals from cardiac or respiratory monitoring may be added

- After the acquisition, the LM-file can be replayed and sorted into sinograms
- This allows dynamic and gated studies to be acquired without assumptions about time frames and number of gating bins
- In some cases it may even save raw data storage capacity



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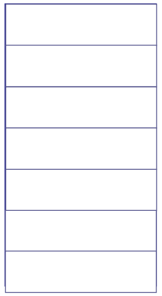
# *Whole-Body Acquisition*

- Metastatic spread of cancer
- Set of slices in multiple FOVs
- Step-by-step (or continuous) tabletop motion during acquisition



Whole-body scan



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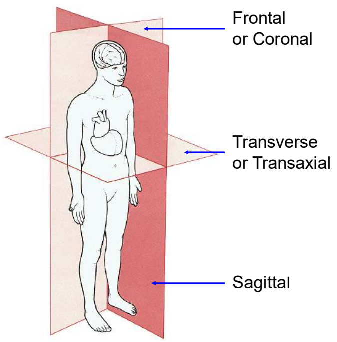
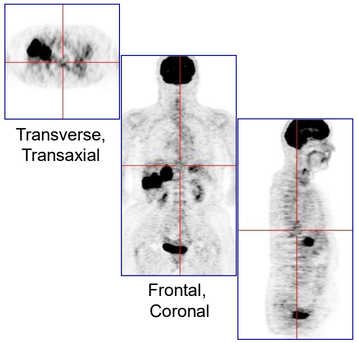
# Body Tomographic Planes



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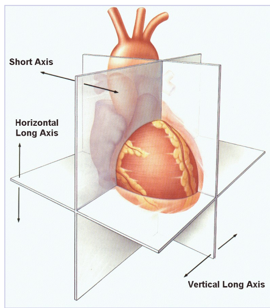
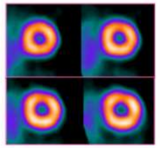
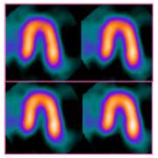
# Tomographic Planes for the Heart

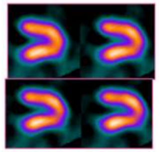


Short Axis (SA)



Horizontal Long Axis (HLA)



Vertical Long Axis (VLA)



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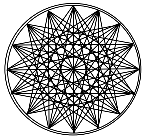
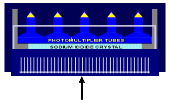
## Comparison of PET and SPECT:



all directions simultaneously



én retning ad gangen

**+ PET**

1: Higher sensitivity, with "electronic collimation"

2: Fast dynamic scans

3: "Biological" tracers with C-11, N-13, O-15, F-18

4: Quantitative technique, with attenuation correction

**+ SPECT**

1: Dual isotopes possible

2: Tc-99m generator + kits !

3: Less expensive to run

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## Overview (4):

- Different kinds of tomography – PET in particular
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- Scanner physics 1 – PET detectors
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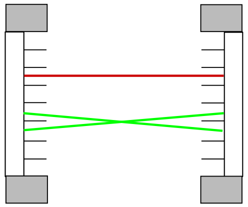
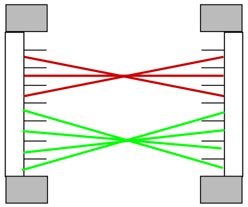
## 2D Imaging



**High Resolution Mode**
- **Direct ΔZ = 0**
- **Cross ΔZ = ±1**
- **Limited Sensitivity**



**High Sensitivity Mode**
- **Direct ΔZ = 0, ±2**
- **Cross ΔZ = ±1, ±3**
- **Increased Sensitivity**

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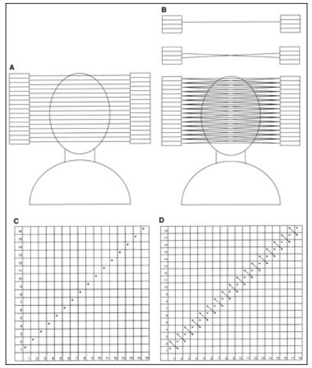
## Michelogram – direct and cross slices



Direct only Direct and Cross

The diagram shows all possible combinations of two detector rings.

The ones "allowed" are marked with a "*".

Combinations that add to one sinogram are connected with a line between the points

Shown examples are the simple **direct slices** (diagonal in diagram) and

simple **cross slices**

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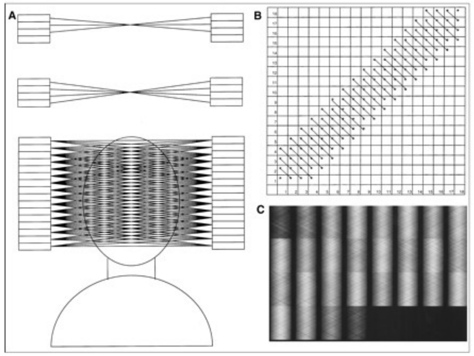
## Michelogram – 2D ”span 7”



The number of combinations involved in direct and cross slices is known as the ”**SPAN**”

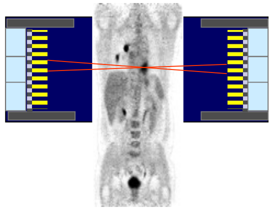
-in this case **7**

Note how the sensitivity decreases towards the edge of the axial Field-of-View



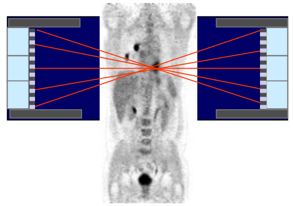


## 2D / 3D



**2D ACQUISITION MODE**
septa employed
low acceptance solid angle

*[NOT used anymore]*

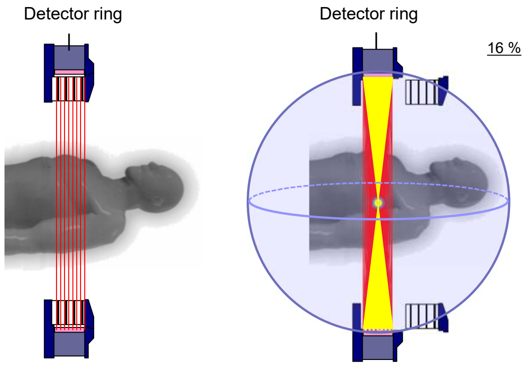


**3D ACQUISITION MODE**
no septa
High(er) acceptance solid angle





## 2D/3D Volume Acquisition (GE Advance, 1993)




2D acquisition
(Septa installed)

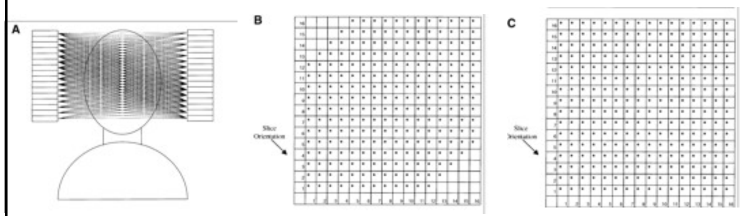
3D acquisition
(Septa removed)





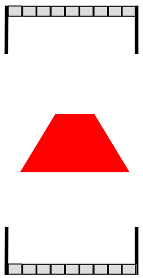
## Michelogram – 3D, RD11 and RD15

RD = Ring Difference



In 3D, where larger angles (ring differences) are allowed, the michelogram becomes populated further away from the diagonal – eventually completely filled.

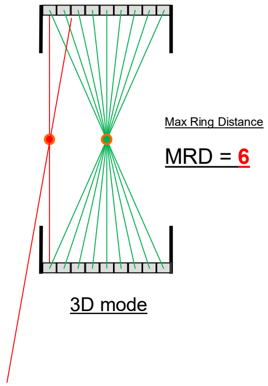
## Sensitivity in ”3D” is position dependent



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

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

(we are not allowing all angles)




3D mode

3D mode

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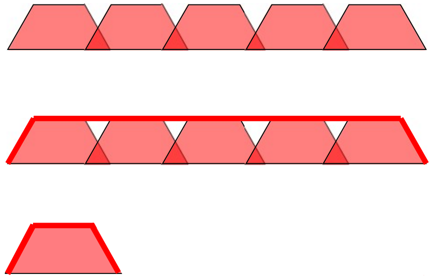
## - and therefore we need ”overlap” in whole-body scanning



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

”Flow motion”

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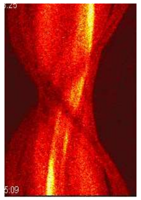
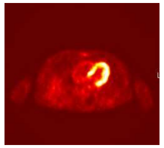
## Image Reconstruction





- Filtered Back-Projection methods:
  - 2D Filtered Back-Projection (2D FBP)
  - 3D Filtered Back-Projection (3D FBP)
- Iterative Reconstruction methods:
  - Maximum Likelihood Expectation Maximization (ML-EM)
  - Ordered Subsets Expectation Maximization (OSEM)
  - Full 3D iteration

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## Overview (5):

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- Scanner physics 1 – PET detectors
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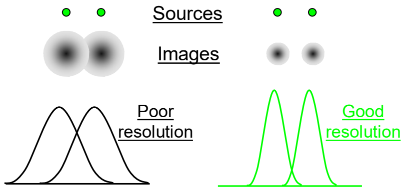
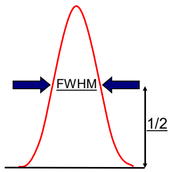
## Spatial Resolution

- ~~How small an object can you see in PET?~~
- Ability to separate two objects close together: ***Resolution***




Line profile of a point source (PSF)

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



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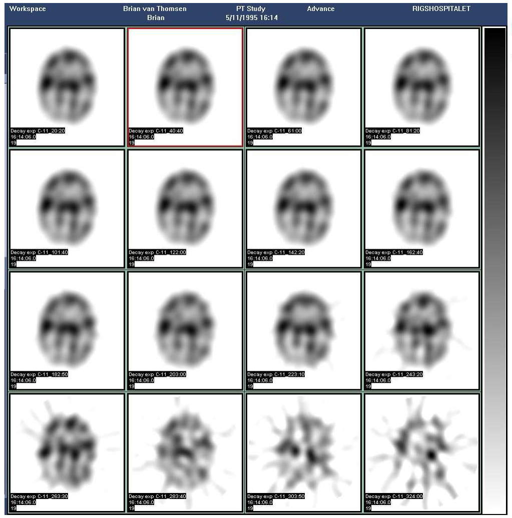
Filtering is a balance between noise and resolution (FWHM)



20 mm



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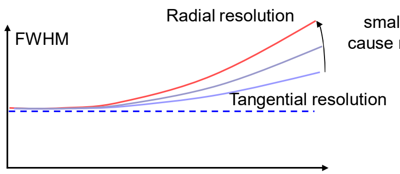
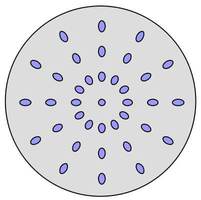
## Radial Vs Tangential Resolution




Plot of resolution versus radial position



Smearing of point sources within the FOV

- Radial resolution degrades toward the edge of the field-of-view.
- Tangential resolution is almost constant within the field-of-view.



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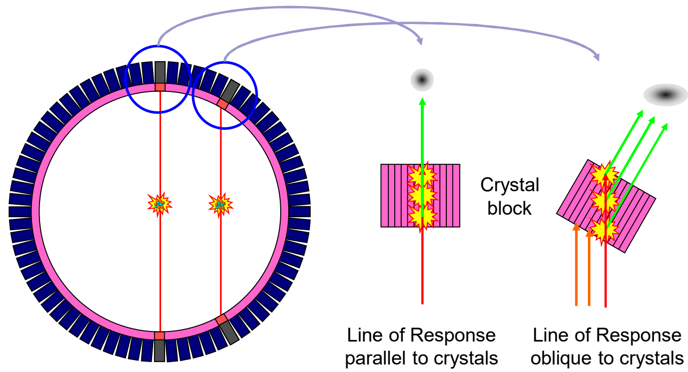
## Radial Vs Tangential Resolution




Line of Response parallel to crystals axis

Line of Response oblique to crystals axis

Detector ring



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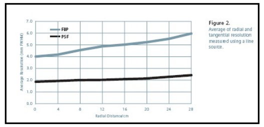
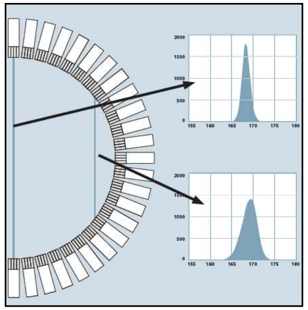
## Results of modeling PSF in reconstruction

(example: Siemens “High definition” recon)

Measured PSF





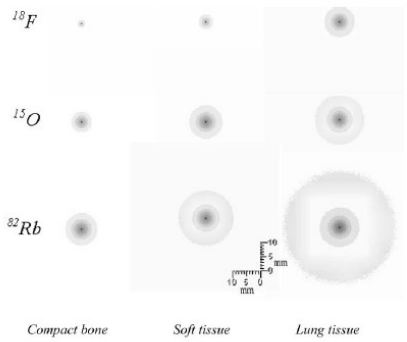




## Positron flight in human tissues

Sanchez-Crespo A et al. Eur J Nucl Med Mol Imaging (2004)

**Fig. 1.** Monte Carlo-calculated distribution of annihilation events around a positron point source embedded in different human tissues as seen in the image plane of a PET camera








## Effect of positron energy

Iida-phantom

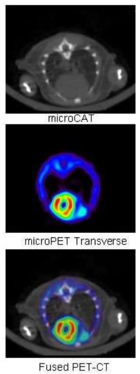
| $^{18}F$ | $^{68}Ga$ | $^{120}I$ |
|---|---|---|
| $E_{max}$= 0.63 Mev | 1.90 Mev | 4.59 Mev |



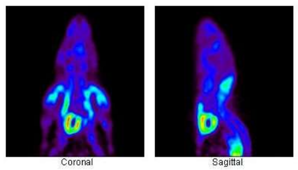


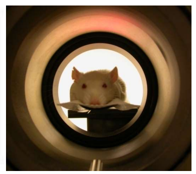
## Mouse Heart PET/CT: 28g Mouse

Image courtesy of David Stout
Crump Institute for Molecular Imaging, Los Angeles CA




microPET® Focus™220 Mouse FDG Images
Living mouse, non-gated



Similar devices have been installed at the Panum Institute

# Overview (6):

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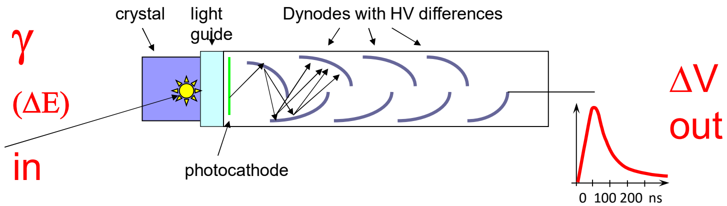
# Detection of 511 keV photons

- First, we need to stop the photons
  - That requires some high Z, high density material
  - which converts the energy to low energy photons

- Then this signal must be amplified and digitized
  - Two options:
    - photo multiplier tube (PMT) or
    - solid state detectors (APD, SiPM)



# Scintillation detector




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



# Evolution of PET-detectors

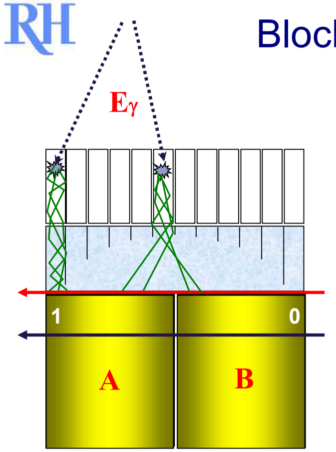
**Therascan**
1981 (89)
single detector
20*35 mm
total # 256

**4096+**
1991
4*4 block
6*12 mm
total # 4096

**Biograph Hirez**
2005
13*13 block
4*4 mm
total # 24336

**Biograph Vision**
2018
(4*2) 5*5 miniblock
3.2*3.2 mm
total # 60800

## Block Concept




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

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

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



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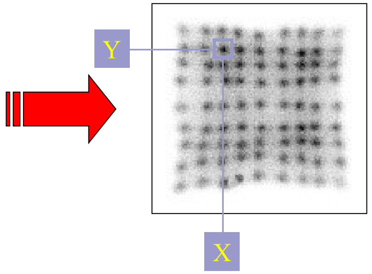
## Flood Histogram / Position Map

Anger Logic

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

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



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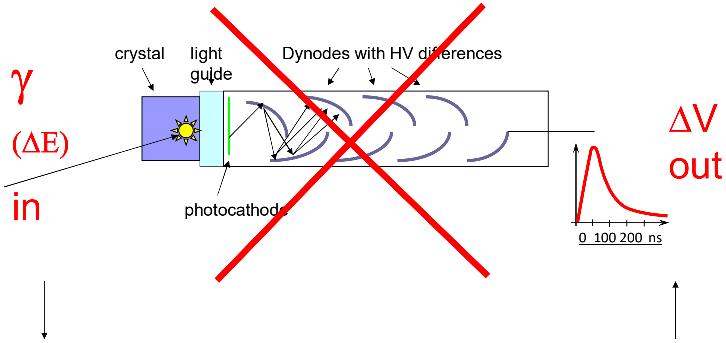
## Scintillation detector




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

Not effective in a MAGNETIC FIELD !



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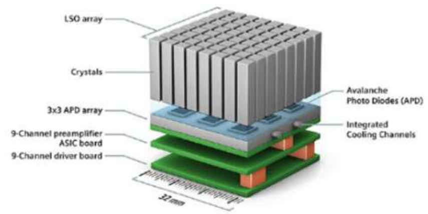
## "MR-friendly PET detector"



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# Basic PET Detector technologies

Solid-state photo-multipliers (SSPMs) can be fabricated from small silicon sub-pixels to replace PMTs making them attractive for **PET+MR and TOF-PET**:

- fast, low-jitter time response
- magnetic field immunity
- small form-factor

**Technical challenges:**

- Readout circuits/ASIC development
- Multiplexing options
- Handling multi-crystal events
- MR compatible architecture

| | PMT | SSPM SiPM | APD |
|---|---|---|---|
| Detection efficiency | 25% | 50% | 50% |
| Coincidence timing res. | 550ps | 250ps | 1000ps |
| Gain | $10^6$ | $10^5$-$10^6$ | $10^2$ |
| Height | 100 mm | 2 mm | 2 mm |
| Magnetic Sensitivity | High | Low | Low |
| Noise | Low | Low | High |
| Cost | Low | High | High |

GE imagination at work

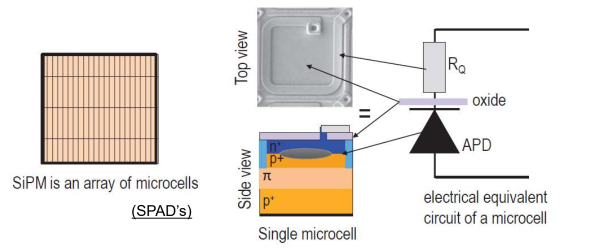




# SiPM = Silicon PhotoMultiplier

HAMAMATSU

## SiPM structure




Copyright © Hamamatsu Photonics K.K. All Rights Reserved. 6





First characterization of a digital SiPM based time-of-flight PET detector with 1 mm spatial resolution 3063

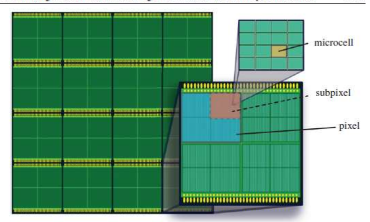
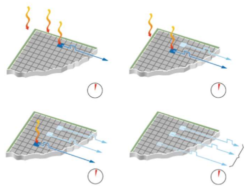



**Figure 1.** Schematic representation of the digital silicon photomultiplier (dSiPM) array. The larger inset depicts a zoom on a single die consisting of four pixels. Each pixel contains 6396 microcells (a number of which are shown in the smaller inset) that are arranged into 4 subpixels.

1 Tile
16 dies
4 pixels
4 subpixels
~1600 microcells

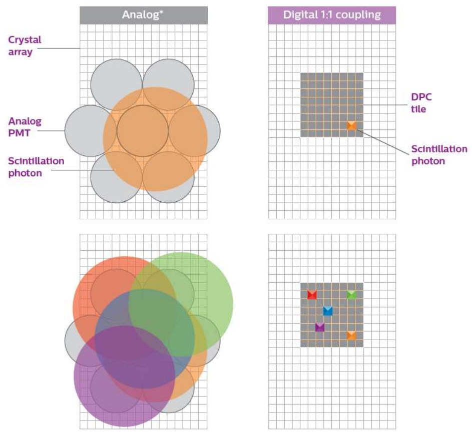
## Philips Vereos Digital PET dSiPM







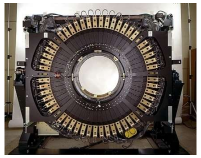
# Shared PMTs versus 1 to 1 coupling



# PET Detector Components

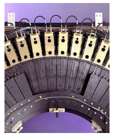
Crystal elements

and photomultiplier tubes



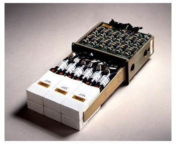
Detector ring

Detector block



Module array

Detector blocks and front-end electronics

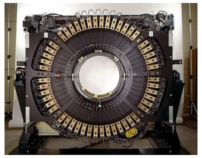


Detector module





# PET (example: GE Advance)



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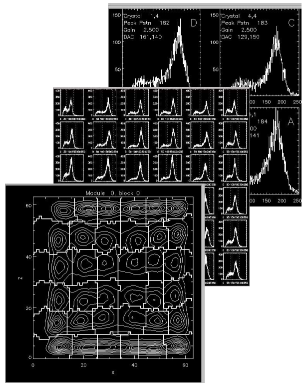
336 *

PMT-gain

Energy-windows

Uniformity

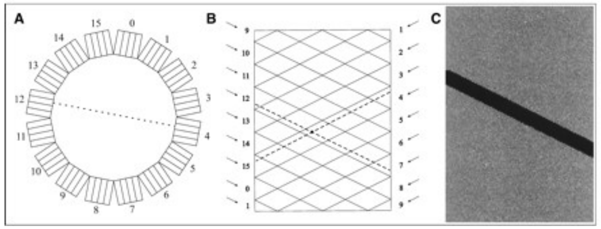


Every pair of blocks is tuned for coincidence timing



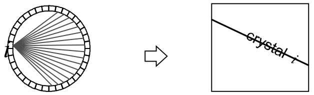


# Block contribution to sinogram




All the contributions from a single detector will be on a line, angled as shown. Due to sensitivity differences a certain "rhombic" structure will be visible in the sinogram.

One defective block will show up as a black, empty area in the sinogram

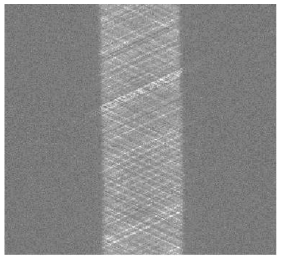




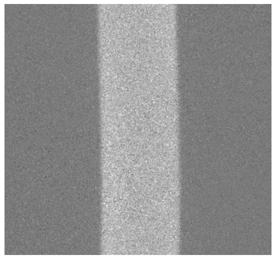



# Normalisation correction

– Compensates systematic efficiency variations (system geometry, crystal efficiency)



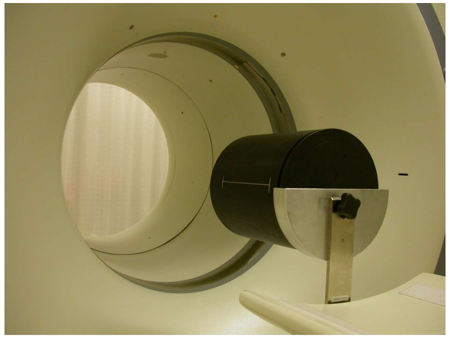
Sinogram **before** normalisation correction



Sinogram **after** normalisation correction

## Siemens Biograph uses $^{68}$Ge cylinder

- but recently intrinsic radiation from Lu-176 (crystals!) is utilized over night

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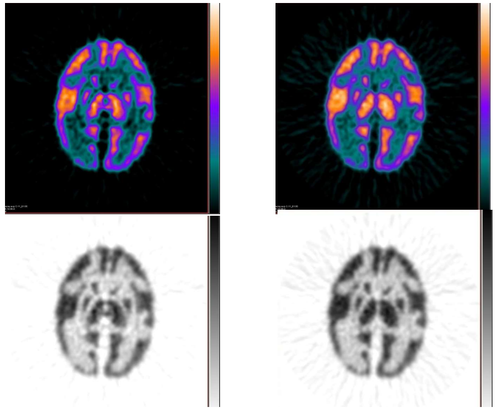
## Effect of Normalisation



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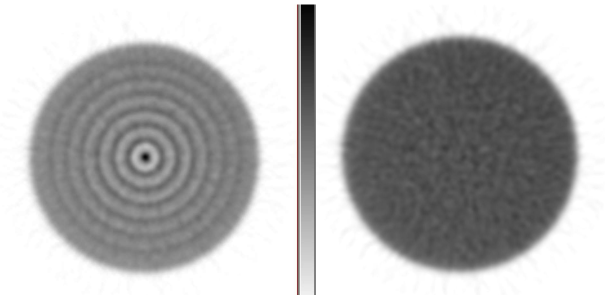
## Uniform phantom – very sensitive to NORM



**without** **with**

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## Overview (7):

- Different kinds of tomography – PET in particular
- Reconstruction from projections, FBP vs. iterative methods
- Positron imaging history
- Raw data structure - sinograms - types of acquisition and presentation
- 2D/3D, advanced data structure – Michelogram
- Resolution and noise

---

- Scanner physics 1 – PET detectors
- Scanner physics 2 – good, bad, and noise equivalent counts (NEC)
- Attenuation and scatter correction of PET-data
- Hybrid systems – PET/CT- PET/MR - SPECT/CT… Future ideas

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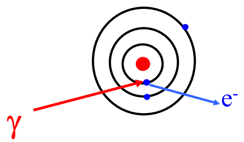
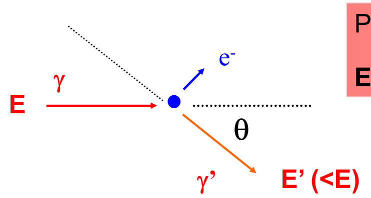
## Two processes stop photons in tissue:

**Absorption:**




Simple,
no parameters

**Compton scattering:**




Parameters

**E' and θ**

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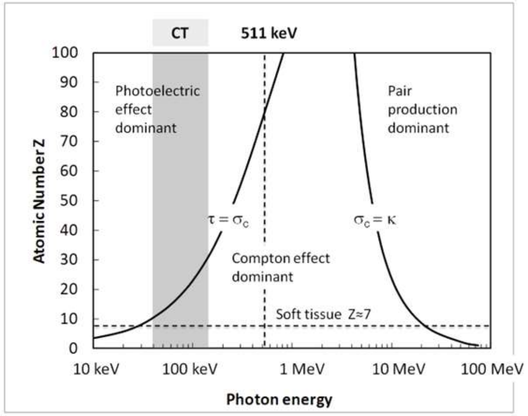
## Photon interactions - (E,Z) dependency

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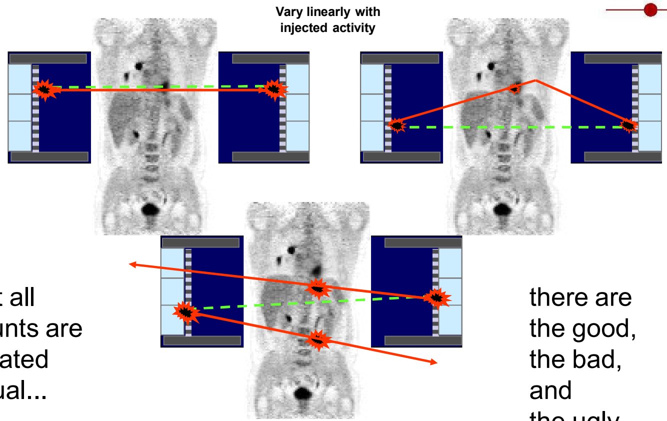
Trues Coincidence

Scatter Coincidence

Vary linearly with injected activity



Not all counts are created equal...

there are the good, the bad, and the ugly counts

Random Coincidence

Vary quadratically with injected activity and linearly with coincidence window

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## The ideal scintillation detector has

- High element no (Z)
- High density (ρ)

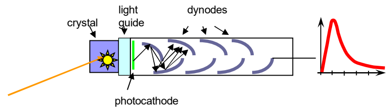
Good absorption
⇒ High sensitivity

- Short decay of light
- High ligth output
- Low price

⇒ Less Deadtime, fast counting

⇒ Narrow coincidence window
⇒ less Randoms

⇒ Good energy resolution
⇒ Scatter rejection

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## PET Detector Scintillator Materials

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

"New" promising crystal materials: $LaBr_3$, $CeBr_3$ and TlBr

BGO may have a come-back

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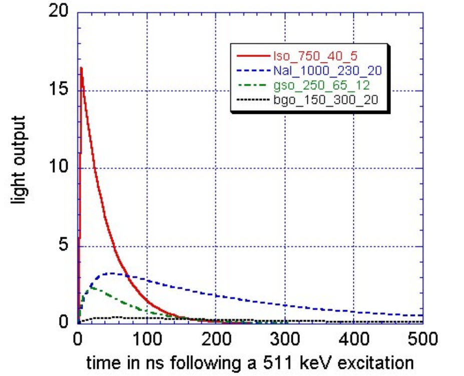
## Scintillator Light Output

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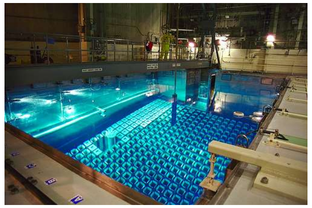
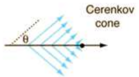
## Cerenkov photons






$$\cos\theta = \frac{c}{vn}$$

v = particle velocity
n = index of refraction of the medium

For water with n=1.33, the limiting angle for high speed particles is given by:

$$\theta = \cos^{-1}\frac{1}{1.33} = 41.2°$$

The threshold particle speed for Cerenkov radiation is v = c/n, which for an electron in water gives a threshold particle kinetic energy of 0.26 MeV.

$$\beta = 0.752,\ E_{electron} = \gamma m_e c^2 = \frac{1}{\sqrt{1-\beta^2}} m_e c^2 = (1.52)(0.511\ \text{MeV}) = .775\ \text{MeV}$$

Kinetic energy = 0.775 MeV - 0.511 MeV = 0.26 MeV

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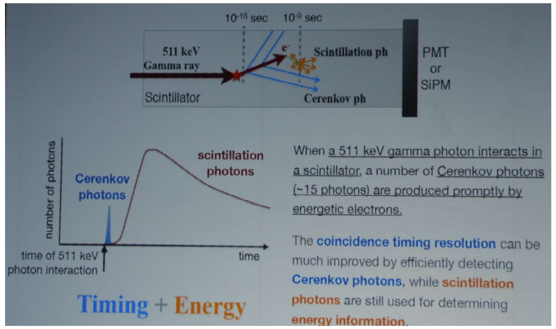
## Timing with Cerenkov




Kwon et al, MIC 2016

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## TOF scan with Cerenkov photons

14 October 2021 https://doi.org/10.1038/s41566-021-00871-2

ARTICLES NATURE PHOTONICS

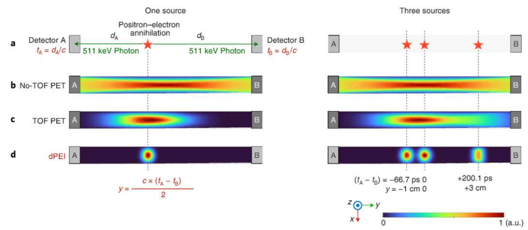


**Fig. 1 | Basis for direct imaging of positron-emitting radiotracers using ultrafast timing. a**, Detection of back-to-back annihilation photons by a pair of radiation detectors and the source location-dependent arrival times of the two photons. **b**, Simulations showing the probability distribution of source locations for a detected event (9.6×9.6 $mm^2$ detector area, detector separation = 96 mm) in conventional PET imaging where no timing information is available. When multiple sources are present (right hand side), it is not possible to discriminate them without further measurements from different detector orientations. **c**, Partial localization when TOF information is added (the example shown has a timing resolution of 210 ps, corresponding to 3.15 cm spatially). **d**, The new modality, dPEI, in which the timing resolution of 32 ps allows the event to be localized within 4.8 mm, providing the basis for direct image generation without image reconstruction. The three sources can now be clearly resolved from a single measurement. The two-dimensional sensitivity maps presented are computed by simulation using the stated geometry and are calculated by integrating the three-dimensional distributions across the detector width perpendicular to the figure. The lower intensity and vertical elongation of the source located at +3 cm reflects the geometric response of coincidence detection for a pair of rectangular detectors. c, speed of light.

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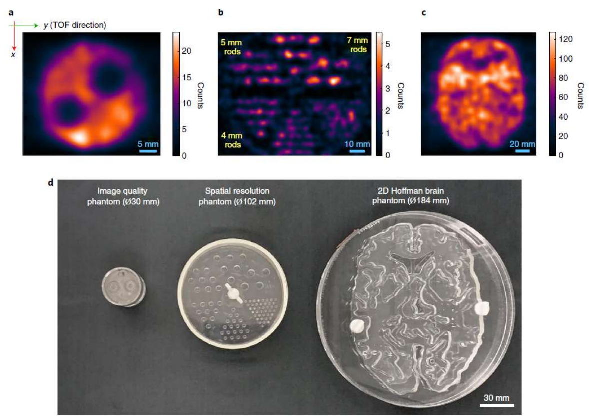
## TOF scan with Cerenkov photons

14 October 2021 https://doi.org/10.1038/s41566-021-00871-2

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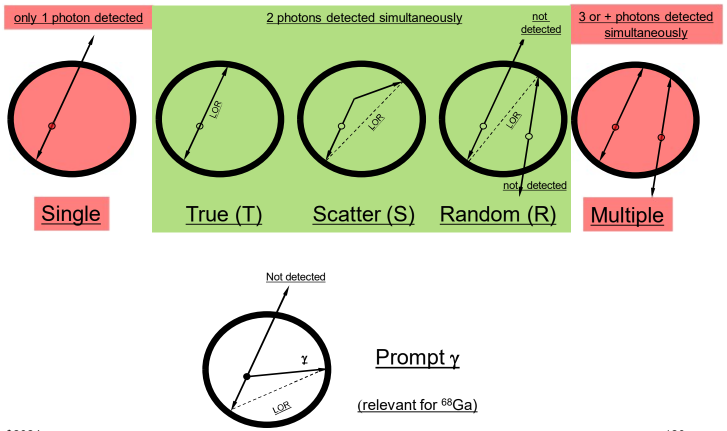
## Types of "events"




Prompt γ

(relevant for $^{68}$Ga)

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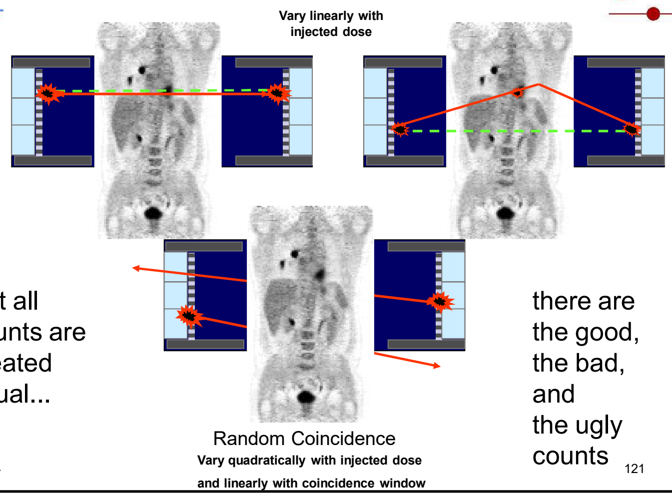


Not all counts are created equal...

there are the good, the bad, and the ugly counts

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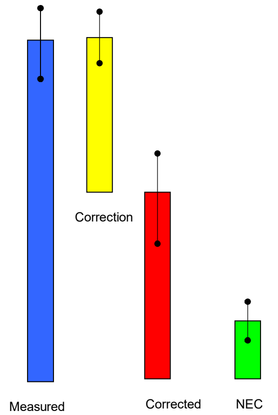
## Noise Equivalent Counts (NEC)

When correcting for randoms and scatter, counts are subtracted

But the noise (uncertaincy) is added!

The result is of less value than if the same #counts were measured directly

NEC is the number of GOOD counts to which the result is equivalent (i.e. same COV)



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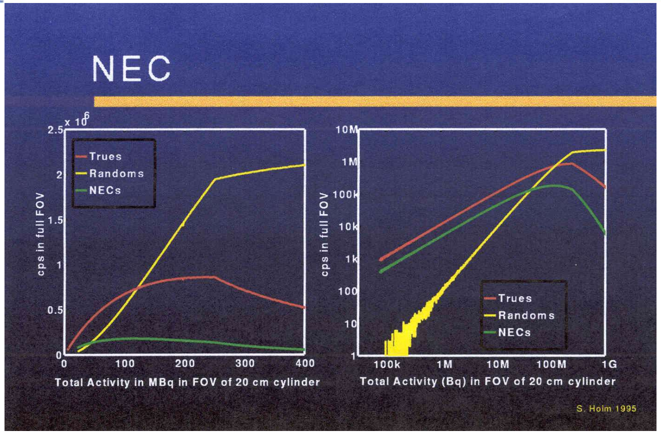




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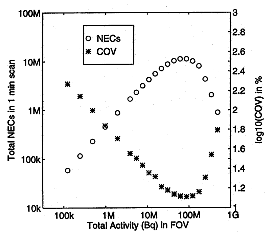
## Noise Equivalent Counts (or count rate)

$$SNR^2 = NECR \cdot \Delta t = \left[\frac{T^2}{(P + kR)}\right]\Delta t = \left[\frac{T^2}{(T + S + (k+1)R)}\right]\Delta t$$

- k = 0 (R is estimated from singles)
- K = 1 (R measured in delayed window)

- NEC actually "reflects" the noise!



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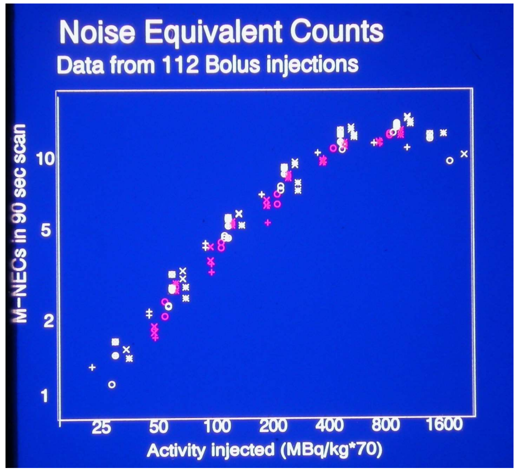




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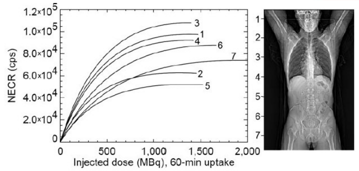
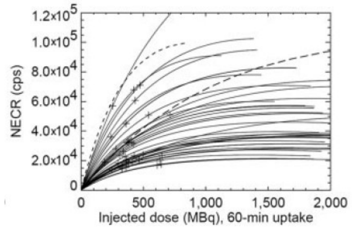
Optimizing Injected Dose in Clinical PET by Accurately Modeling the Counting-Rate Response Functions Specific to Individual Patient Scans

Charles C. Watson, PhD[1]; Michael E. Casey, PhD[1]; Bernard Bendriem, PhD[1]; Jonathan P. Carney, PhD[2]; David W. Townsend, PhD[3]; Stefan Eberl, PhD[4]; Steve Meikle, PhD[4]; and Frank P. DiFilippo, PhD[5]

J Nucl Med 2005; 46:1825–1834



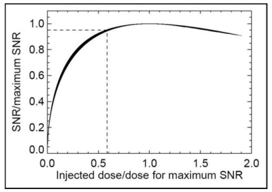




**FIGURE 3.** Relative response curves for 163 scans on conventional LSO PET/CT scanner, obtained by scaling SNR (1*R* case) and $D_{inj}$ by their values at peak response.

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Time to breath…

[Reykjavik, 25. August 2011$]

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## Overview (8):

- Different kinds of tomography – PET in particular
- Reconstruction from projections, FBP vs. iterative methods
- Positron imaging history
- Raw data structure - sinograms - types of acquisition and presentation
- 2D/3D, advanced data structure – Michelogram
- Resolution and noise

-----------------------------------------------------------------------------------

- Scanner physics 1 – PET detectors
- Scanner physics 2 – good, bad, and noise equivalent counts (NEC)
- Attenuation and scatter correction of PET-data
- Hybrid systems – PET/CT- PET/MR - SPECT/CT… Future ideas

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## PET is a quantitative technique

(although most people don't care these days...)

IF all the necessary corrections are applied:

- Deadtime
- Geometry, Normalization
- Randoms subtraction
- Attenuation and scatter
- Decay
- …

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# Attenuation and Scatter

- It is a paradox in our terminology that from a *physics* point of view, attenuation (in NM) is caused mainly by scattering processes (and only partly by absorption)
- but in our *correction* procedures:
  - Attenuation is "lack of counts" that we must restore while
  - Scatter is a surplus of counts (in wrong places) to be removed
- Correcting one without the other will give wrong results



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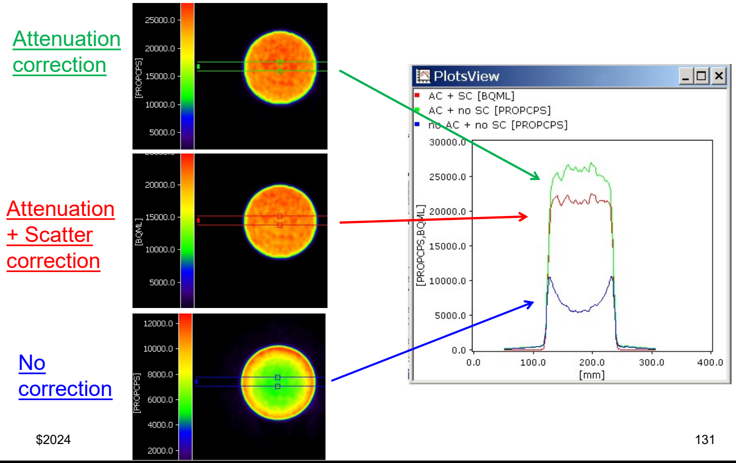
# Attenuation and Scatter



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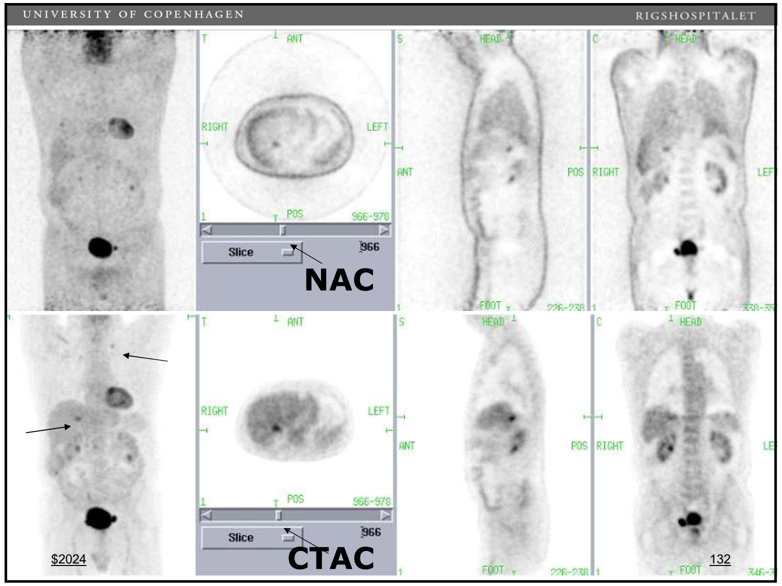




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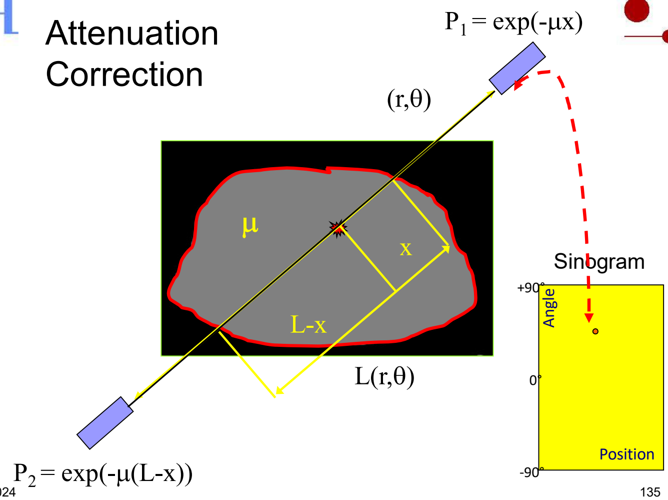
# Attenuation Correction



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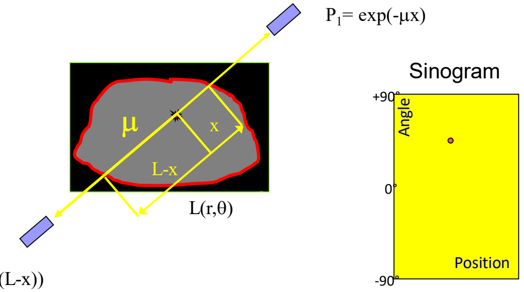
## Probability of a coincidence:

$P(r,\theta) = P_1 * P_2 = \exp(-\mu x) * \exp(-\mu(L-x)) = \exp(-\mu L)$ [independent of x !]



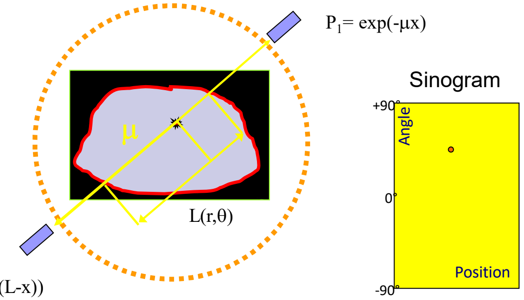





## Probability of a coincidence:

$P(r,\theta) = P_1 * P_2 = \exp(-\mu x) * \exp(-\mu(L-x)) = \exp(-\mu L)$ [independent of x !]

- and therefore easily measured with external (rotating) pin/point source
- and corrected: each line of response multiplied by its own $\exp(\mu L)$





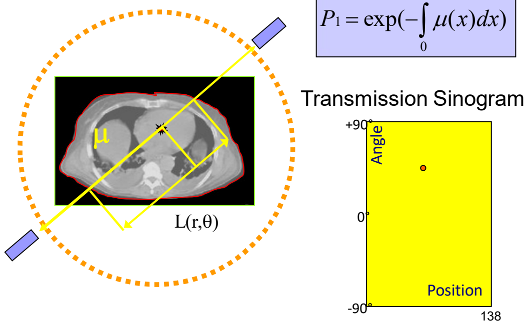



## If μ is not a constant (and it IS NOT):

$$P_1 * P_2 = \exp(-\int_0^x \mu(x)dx) * \exp(-\int_x^L \mu(x)dx) = \exp(-\int_0^L \mu(x)dx)$$

still independent of the source position

$$P_1 = \exp(-\int_0^x \mu(x)dx)$$



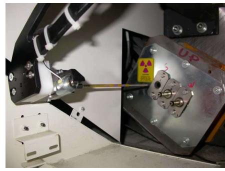

$$P_2 = \exp(-\int_x^L \mu(x)dx)$$





## GE used $^{68}$Ge Pin sources

GE 4096 (by hand)



GE Advance and GE Discovery LS

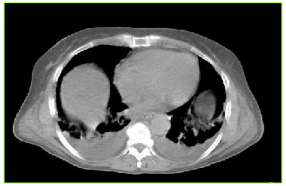
(3 pins, automated complex robotic arm)

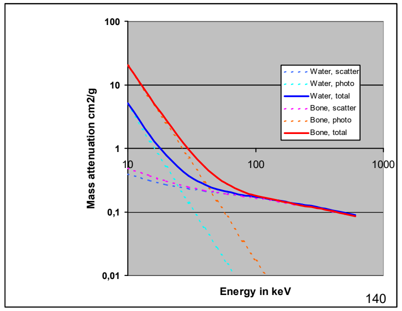
GE Discovery ST etc.

(1 pin in trunk)

# CT scans are μ-maps (in HU)

They can be used for attenuation correction – essentially noise free
But: $\mu(511\ keV) \neq \mu(80\ keV)$, therefore a scaling is required
Soft tissue and bone (and contrast) scale differently
Not one simple scaling factor, but a lookup table for $\mu(HU; kV_p)$









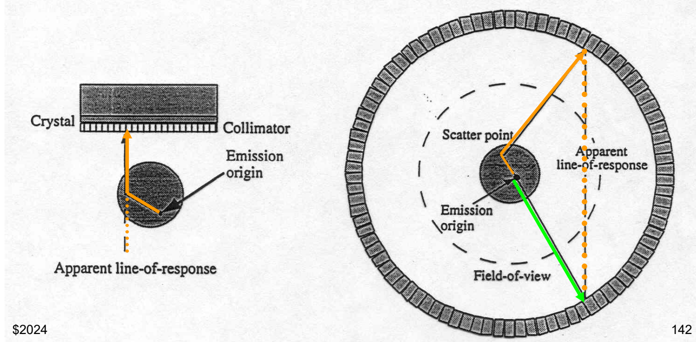

# Scatter in

## SPECT

## PET

appears "inside" the object

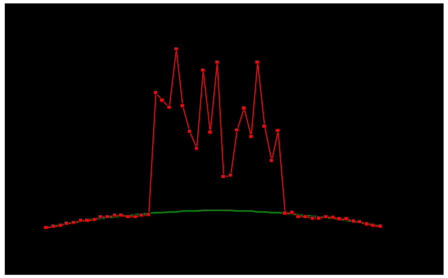
may appear outside object








# Scatter Correction by Function Fitting

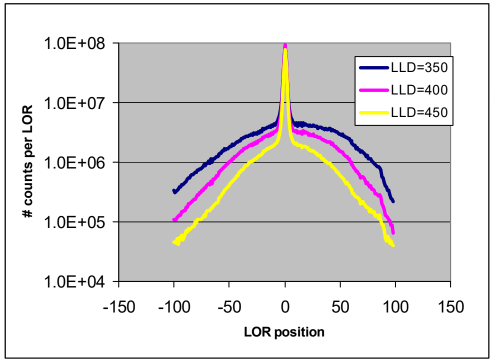


- Fit data to projection tails
- This requires tails!
- More elaborate methods model the scatter from detailed knowledge of the object



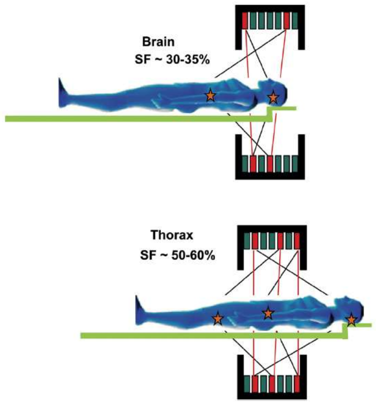


# Scatter removal by energy discrimination




(keV)

## Scatter fractions in 3D PET

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## Scatter correction techniques

- Metz / Wiener filtering
- Asymmetrical energy window
- Dual energy window
- Dual photopeak window
- Weighing of detected events (WAM)
- Channel ratio method
- Photopeak energy distribution analysis
- Position dependent scatter correction
- Stationary / Non-stationary deconvolution
- Iterative reconstruction techniques
- Neural network
- Pixel by pixel spectral analysis
- Regularized deconvolution-fitting method
- Scatter-free imaging (CFI)
- Holospectral imaging
- Factor analysis of medical image sequences
- **Single scatter simulation techniques**

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## Overview (9):

- Different kinds of tomography – PET in particular
- Reconstruction from projections, FBP vs. iterative methods
- Positron imaging history
- Raw data structure - sinograms - types of acquisition and presentation
- 2D/3D, advanced data structure – Michelogram
- Resolution and noise

---

- Scanner physics 1 – PET detectors
- Scanner physics 2 – good, bad, and noise equivalent counts (NEC)
- Attenuation and scatter correction of PET-data
- Hybrid systems – PET/CT- PET/MR - SPECT/CT… Future ideas

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## PET/CT scanner:

First "physicist's" PET-CT was constructed by Townsend, Beyer, Kinahan et al in Pittsburgh 1994-

We (Rigshospitalet) got a prototype from GE in 2001

Today commercial devices exist from:

- GE
- Siemens
- (Philips)
- United Imaging
  and a few others
- \- with more than 10000 installations worldwide
- Since 2005, almost NO stand-alone PETs have been installed

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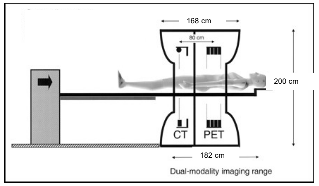
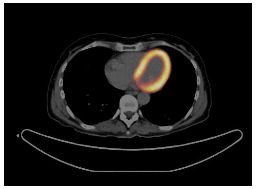
# PET/CT (or SPECT/CT) scanner:



(Townsend et al 2004)

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

Anatomical localisation of tracer – Attenuation correction

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# PET/CT: GE Discovery LS

Advance NXI + Lightspeed plus

Detector material BGO

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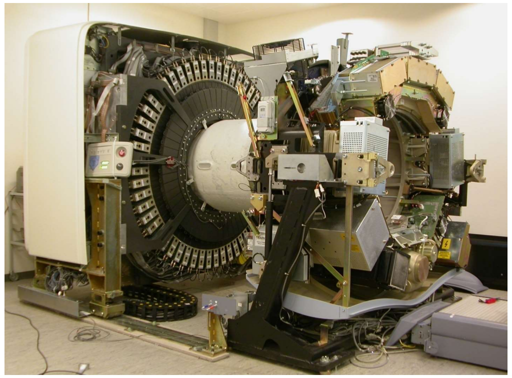
# Inside Discovery LS



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# PET/CT (images from around 2005)

Herlev
Hillerød
Vejle (2)
Århus RT

Philips Gemini (KAS Herlev)

Siemens Biograph (RH)

RH (6)
Næstved (2)
Århus PET (4)
Herning
Herlev (3)
Glostrup

Unknown company:
Viborg
Esbjerg
Åbenrå
...

GE Discovery (Milano San Raffaele)

Odense (5)
Ålborg (2)
Køge (2)
Hvidovre
Gentofte
Bispebjerg (3)
Herlev RT

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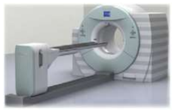
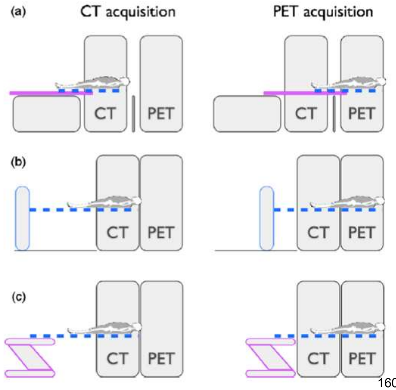
## PET/CT instrumentation: adding CT

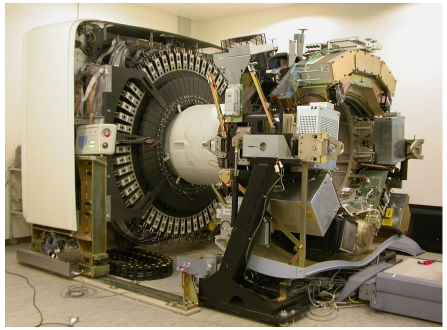
- Important design criterion: keeping the patient position (height) stable






## PET/CT alignment /registration



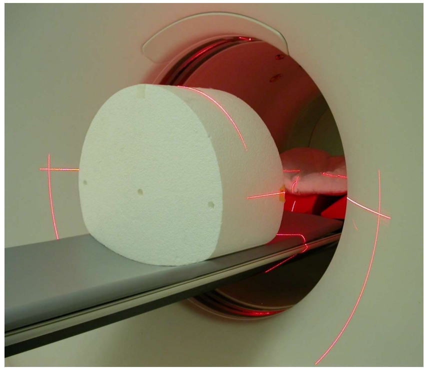
Not likely to change spontaneously.

For **GE** and **Siemens**: Only opened by service. Must be measured after "invasive procedures"

**Philips** Gemini designed to scan in the separated position also.



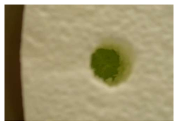
## GE PET – CT alignment



GE Discovery aligns CT with PET transmission using the built-in Ge-68 line sources.

No (other) activity is required
The phantom contains 5 glass spheres

Newest GE-scanners use similar phantom with Ge-68 spheres





## Siemens PET – CT alignment

Siemens Biographs have no transmission sources.

Instead 2 Ge-68 line sources mounted in a black box are used.

They are visible on both PET and CT, and an automated algorithm provides the correction

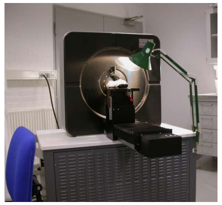
# Philips PET – CT alignment

- Special service tool holding 6 Na-22 point sources
- Registration performed at 1 year interval

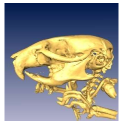


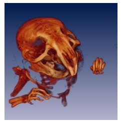


# Small Animal PET-CT

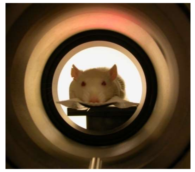


CT resolution down to 15 μ





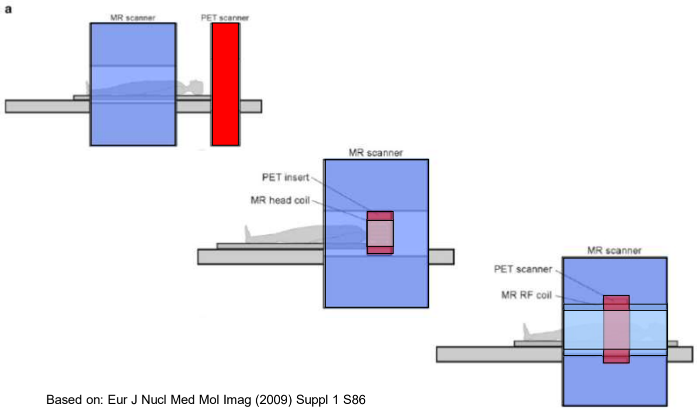
PET resolution < 2 mm







# Potential PET-MR configurations

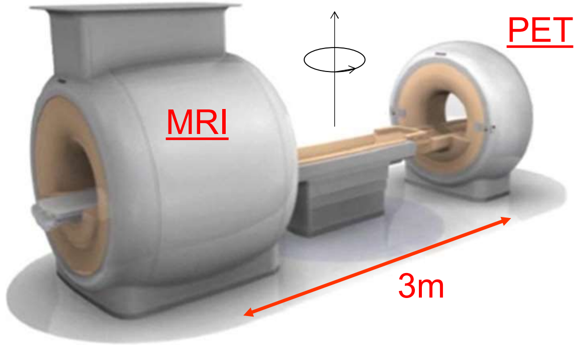



Based on: Eur J Nucl Med Mol Imag (2009) Suppl 1 S86





# PET-MR: the "easy" solution



## PET-MR: the ”easy” solution

Philips Medical, exhibition RSNA 2012

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## (real) PET-MR

- Siemens made a prototype combination in 2007:
- 3 T MR scanner with brain coil
- PET ”insert” between coil and magnet
- Requires detector insensitive to magnetic field
- In 2011, Siemens made an integrated system (APD)
- In 2014, GE followed (SiPM – TOF possible)

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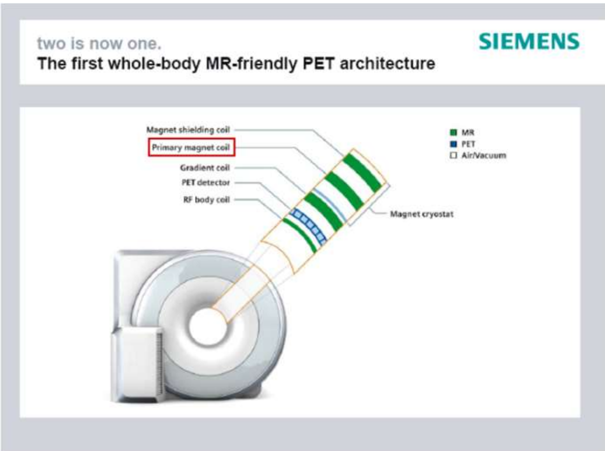


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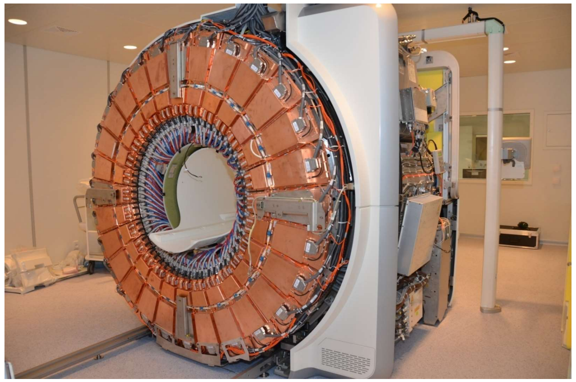
## PET/MR



All PET electronics is encapsulated in a Faraday cage to avoid RF-interference

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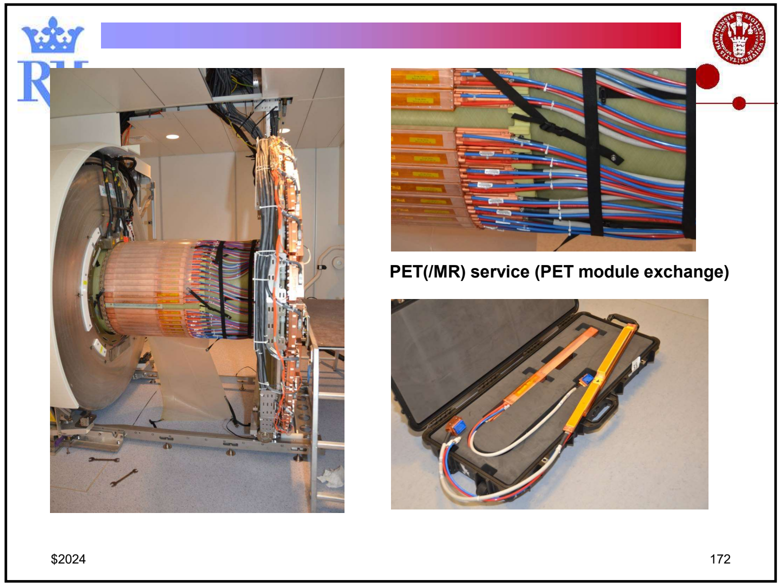


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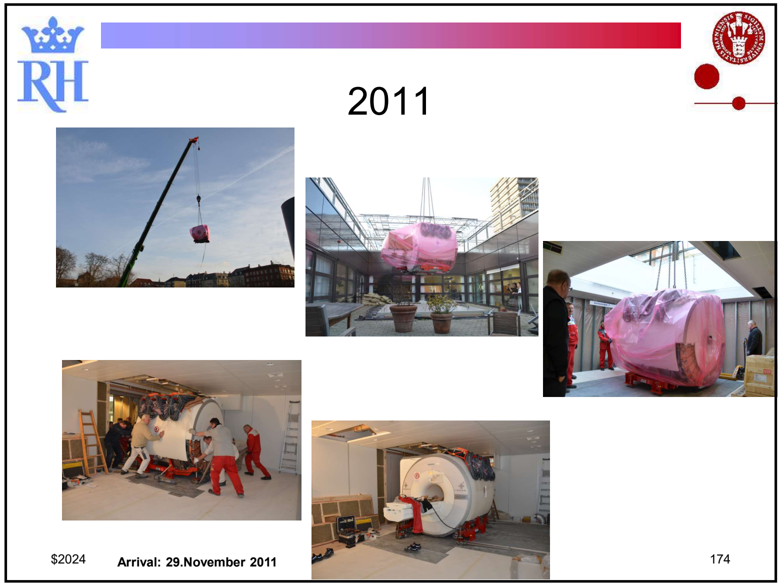


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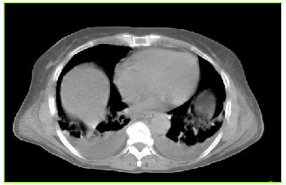
# With PET/CT:

A CT scan is a μ-map (expressed in HU)
A scaling for energy difference between CT and PET is required
Soft tissue and bone (and contrast) scale differently
⇒ (only) minor errors in quantitation of PET images

GE Discovery LS (2001)





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# In PET/MR:

Attenuation correction is a challenge (and still a research topic)

MR images (in general) are NOT μ-maps

Bone, Air, and Metal implants show almost same MR-signal: ~0
- but they have very different influence on PET attenuation



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# SPECT/CT

- serves the same dual purpose of
  Anatomical localisation of tracer and
  Attenuation correction

- AC is not as simple or ”exact” as in PET
  because we have only one photon
- With CT and iterative recon, quantitation is feasible



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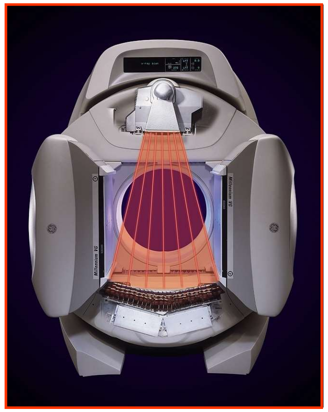
# SPECT/CT (GE Hawkeye)



X-Ray Tube is mounted on the same gantry as the gamma cameras

A ‘CT scan’ takes 15 s / cm

With 1 inch crystals, “PET” is possible



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# SPECT/CT

Siemens

Philips

Symbia

Precedence =

Skylight SPECT + Brillance CT

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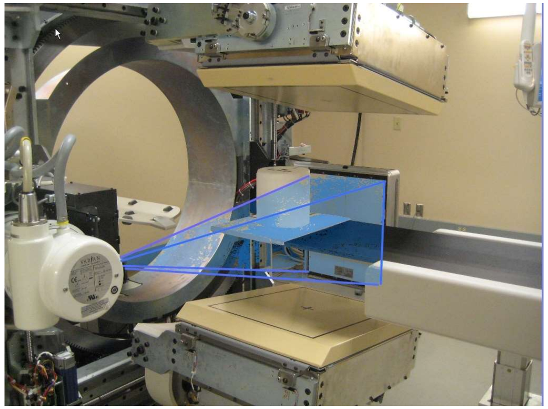
# BrightView XCT SPECT/CT



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# Combinations...

PET-CT / SPECT–CT / PET–MRI / SPECT-MRI


$2024 Exhibition EANM October 2012 187

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# PET / SPECT / CT

for small animals


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## VECTor: A Preclinical Imaging System for Simultaneous Submillimeter SPECT and PET

Marlies C. Goorden*[1], Frans van der Have*[1,2], Rob Kreuger[1], Ruud M. Ramakers[1,2], Brendan Vastenhouw[1,2], J. Peter H. Burbach[3], Jan Booij[4], Carla F.M. Molthoff[5], and Freek J. Beekman[1,2]

J Nucl Med 2013; 54:306–312
DOI: 10.2967/jnumed.112.109538

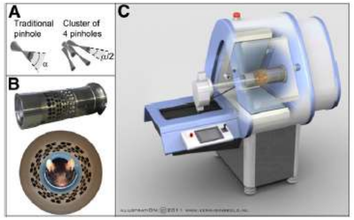


**FIGURE 1.** Integration of clustered-pinhole collimator into existing SPECT/CT platform. (A) Traditional pinhole with opening angle α and cluster of 4 pinholes with approximately same field of view and opening angle α/2. (B) Clustered-pinhole collimator optimized for imaging SPECT and PET tracers, into which mouse is placed. (C) Collimator mounted in SPECT/CT system.

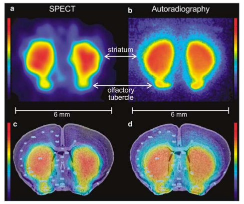


**Figure 2** High resolution *in vivo* imaging of striatal DAT (left) compared with DAT autoradiography (right).



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## MILabs G-SPECT

- Game-Changing SPECT

?




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## Spectrum Dynamics D-SPECT


CZT

= CdZnTe

Solid state detector
at room temperature



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## Spectrum Dynamics Veriton-CT

CZT = CdZnTe





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# PET / SPECT / CT

AnyScan

Mediso
Budapest

Exhibition at
EANM 2008

Still marketed


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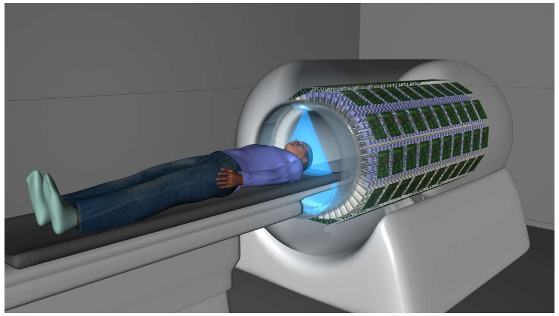
# Total-Body PET

EXPLORER



UCDAVIS
UNIVERSITY OF CALIFORNIA

BERKELEY LAB

Penn
University of Pennsylvania

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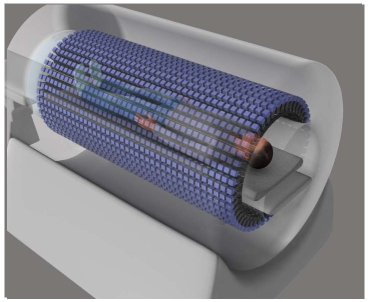
# Maximizing Sensitivity by Total-Body PET



**~40-fold increase**
**for adult total-body imaging**

**~20-fold increase**
**for pediatric total-body imaging**

**~4-fold increase**
**for single organ imaging**

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# Completed EXPLORER Scanner

**System:**
Ring diameter: 78.6 cm
Transaxial FOV: 68.6 cm
Axial FOV: 194.8 cm

# of crystals: 564,480
# crystal blocks: 13,440
# of SiPMs: 53,760

80 detector row CT

UNITED IMAGING

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## Sligthly less ambitious: 1 m FOV

**Arrived at RH on August 17, 2021**


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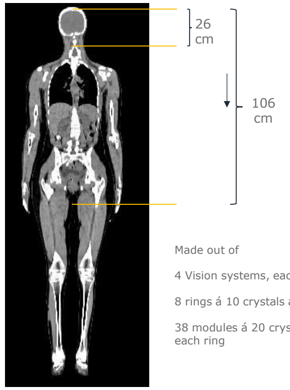
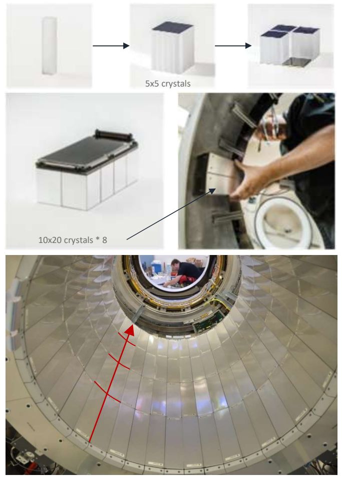
3.2-mm crystal Vision technology




Made out of

4 Vision systems, each with:

8 rings á 10 crystals axial

38 modules á 20 crystals in each ring

# crystals: 243.200 (ca. 368 kg)

[(5x5) * (2x4) * 8 * 38] * 4 stk * 0.15 cm³ * 7.4 g/ cm³

Bonus-info: ca. 15 MBq Lu-176

Dosis rate in center < 1 μSv/h

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## Specs?

Practically identical with Siemens Vision for

Spatial resolution
Energy resolution
Timing (for TOF)

Major difference (obviously):

# Sensitivity

What is sensitivity?
something about… counts per Bq in known geometry
preferably just one number

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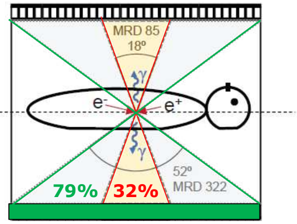
## Sensitivity for point source in center

Ø82 cm




L = 106 cm

Expanding

MDR = Max Ring Difference

from 85 to full value of 322

Increases the sensitivity at the **center** by a factor of 2.5, but it still drops to 0 at the edge.

*In a Vision, MDR = 79.*

*Now: Quadra = 1.08 Vision*

*Future: Quadra ~ 3 * Vision*

Figure based on Prenosil et al. JNM 2021

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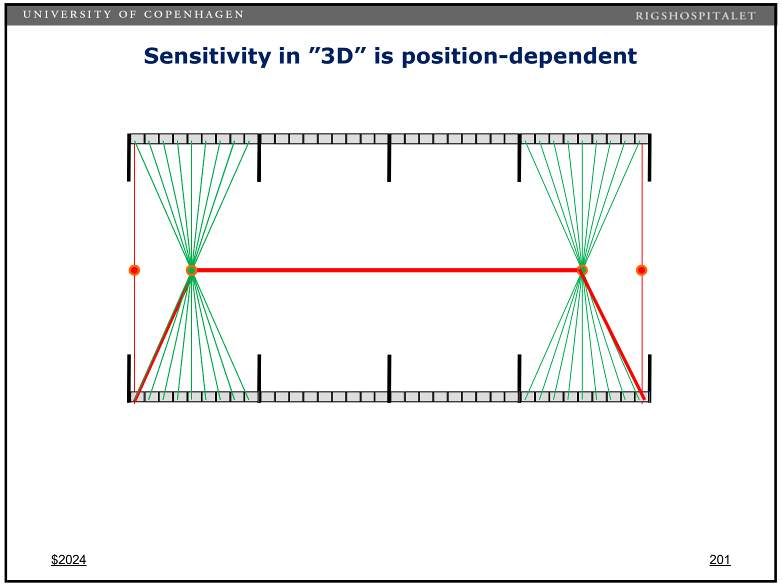
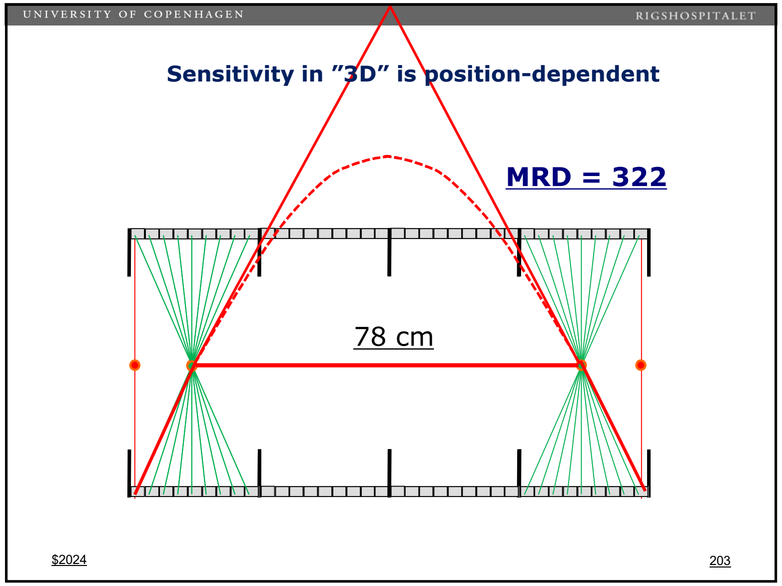
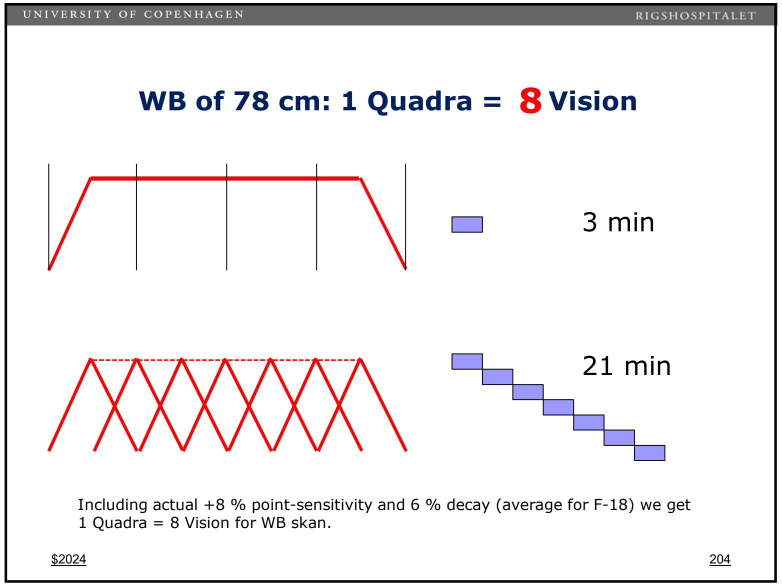


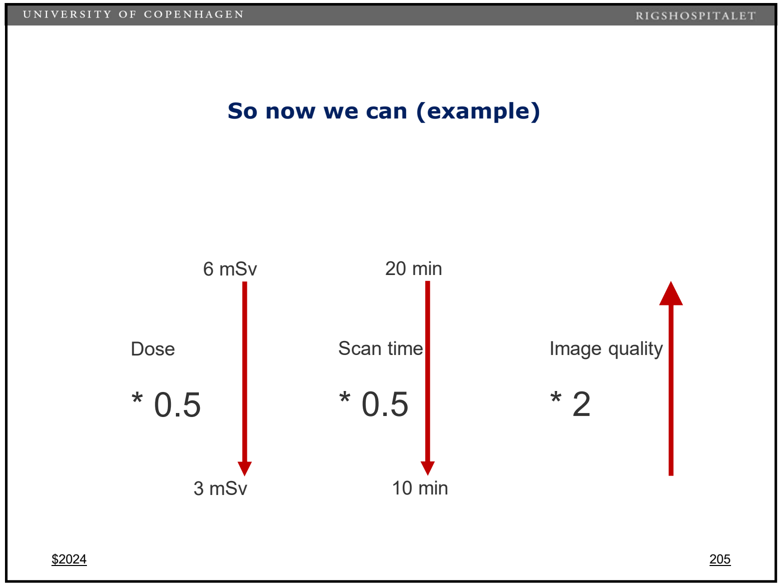

201




203




204

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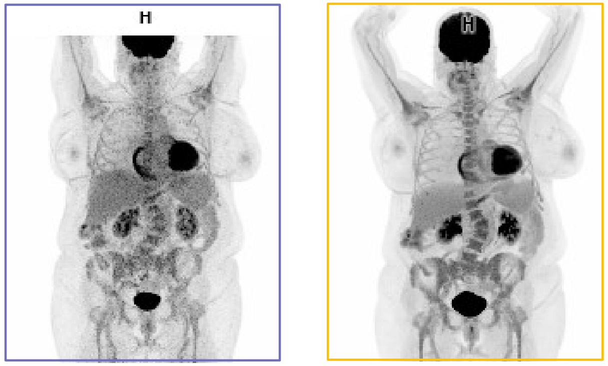
One of the first patients on på Quadra PET/CT at Rigshospitalet



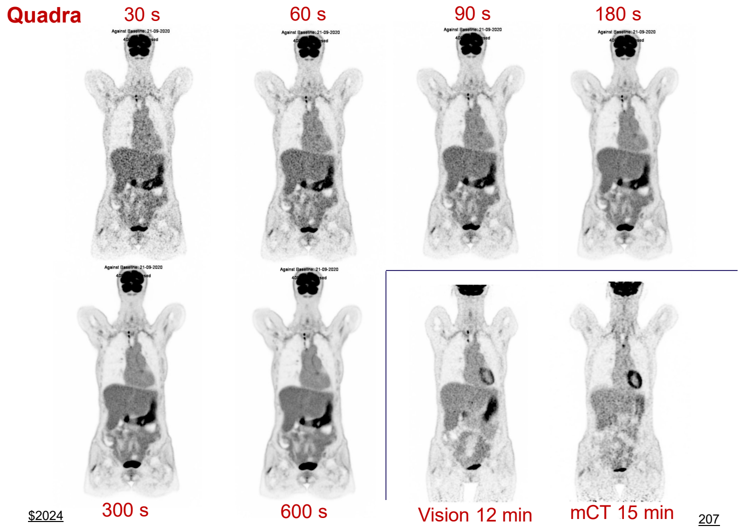

Vision, standard WB PET/CT QUADRA, 10 min recon

Activity 3 MBq/kg









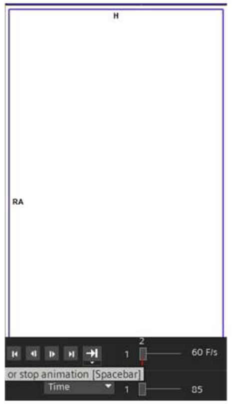







**Dynamisk FDG**

**0-60 min**




| Frame# | Starttid | Antal * Δt |
|---|---|---|
| 1 | 0 s | 30 * 1 s |
| 31 | 30 s | 15 * 2 s |
| 46 | 60 s | 12 * 5 s |
| 58 | 2 min | 6 * 10 s |
| 64 | 3 min | 6 * 20 s |
| 70 | 5 min | 5 * 1 min |
| 75 | 10 min | 5 * 2 min |
| 80 | 20 min | 4 * 5 min |
| 84 | 40 min | 2 * 10 min |

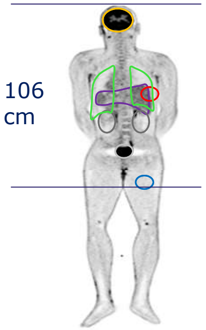


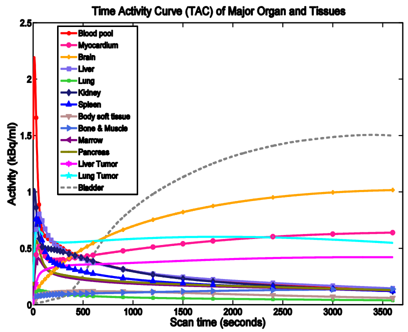




## Total-Body Tracer Kinetics

106 cm

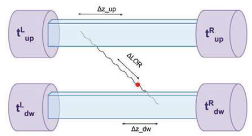


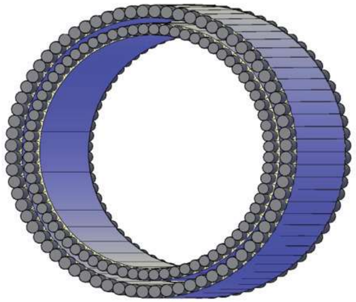



(Courtesy of Simon Cherry)

# J-PET

Longitudinal plast-scintillators



P Moskal *et al*

Phys. Med. Biol. **61 (2016)** 2025

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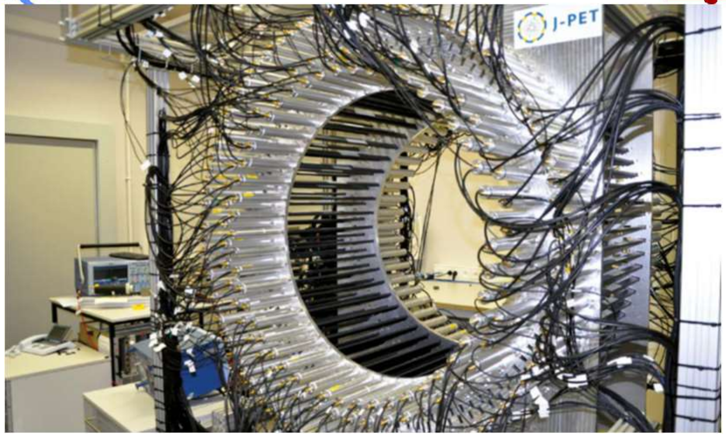
## J-PET Prototype (50 cm)




$2024 Kilde: CERN Courier November 2018 212

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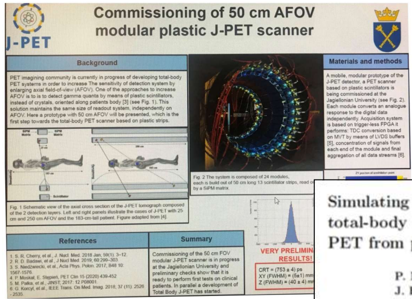
## Screenshot fra ECMP2021




Phys Med Biol 66 (2021)

Simulating NEMA characteristics of the modular total-body J-PET scanner - an economic total-body PET from plastic scintillators

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Though the whole-body sensitivity increase of the TB-J-PET is less than the one of uExplorer it is still a significant improvement with respect to the current 16-26 cm long PET systems (and can still be increased by adding a third detection layer). This makes J-PET an economic and alternative technology for the construction of the total-body PET systems. The cost of the TB-J-PET is expected to be a factor of 5 lower with

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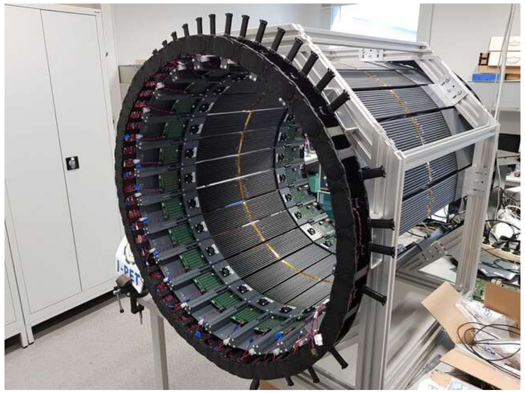
## J-PET

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## J-PET

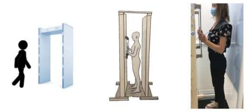


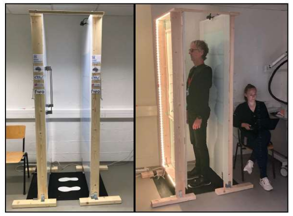




**Walk-Through TB-PET**
Patient in upright position

*Walk and stand in the scanner*





*Our mock-up at the Infinity lab*

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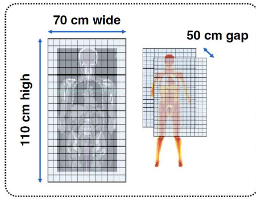








Advances in Dynamic Radioactive Scanning

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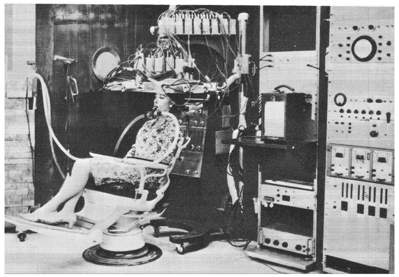
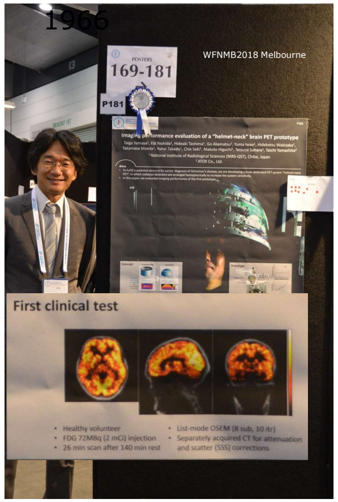
## 1968 PET












## 2015

Development of the Helmet-Chin PET Prototype

Hideaki Tashima, Eiji Yoshida, Fumihiko Nishikido, Hidekatsu Wakizaka, Munetaka Nitta, Abdella M. Ahmed, Akram Mohammadi, Shusaku Tazawa, Yasuyuki Kimura, Tetsuya Suhara, Yasuhisa Fujibayashi, and Taiga Yamaya, *Member, IEEE*

Chiba, Japan [Poster M3CP-97 at MIC2015]

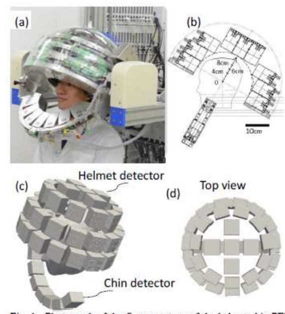



Fig. 1. Photograph of the first prototype of the helmet-chin PET (a), design sketch (b), and geometry of the crystals (c), (d)

## 2019: Commercial product (Korea)

$2024 (exhibition at EANM 2022, Barcelona) 219

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## 2023: Commercial product (Switzerland)


$2024 (exhibition at EANM 2023, Vienna) 220

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## Could this become a sales success" ?

**IF** a cure for, e.g. Alzheimer's disease is found

**AND**

**IF** we have a PET-tracer that can tell if that cure works for YOU

**AND**

**IF** attenuation correction can be made from PET data with AI

**AND**

**IF** this device can be manufactured for ¼ of the price of WB PET/CT

**THEN** it is likely to.

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Time to press…


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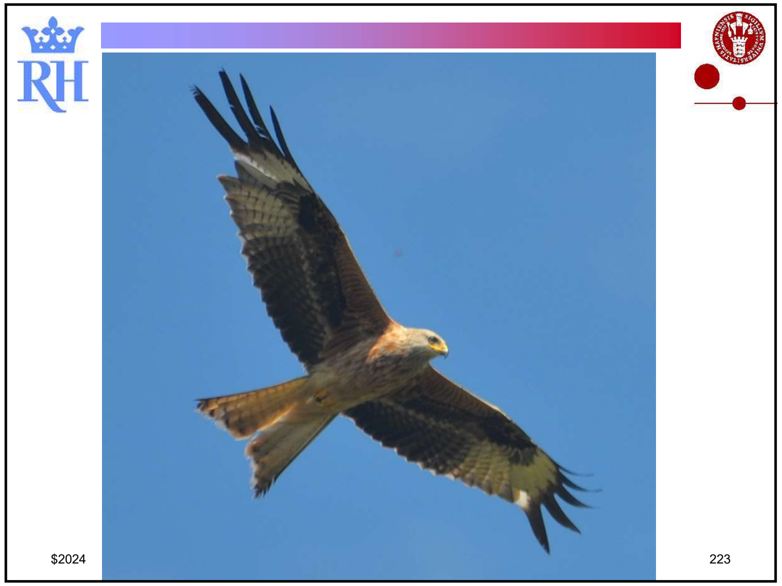


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