PET

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

Medical Imaging Systems
DTU, November 2018

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PET

Entrance 39

Photo: Flying Professor Andreas Kjær

Thanks to:

GE Medical Systems

CPS Innovation (Bernard Bendriem)

Siemens Medical Solutions

Philips Medico

Impact (www.impactscan.org)

UC Davis, Simon Cherry

Overview (0):

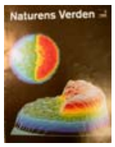
- Different kinds of tomography – PET in particular
- Reconstruction from projections, FBP vs. iterative methods
- Positron imaging history
- Raw data structure - sinograms - types of acquisition and presentation
- 2D/3D, advanced data structure – Michelogram

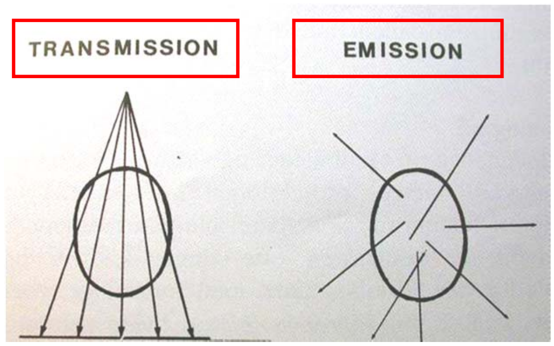
- Resolution and noise
- Scanner physics 1 – PET detectors
- Scanner physics 2 – good, bad, and noise equivalent counts (NEC)
- Attenuation and scatter correction of PET-data
- Hybrid systems – PET/CT- PET/MR - SPECT/CT… Future ideas

(T)CT ECT SPECT PET

Computer(ized)

from:

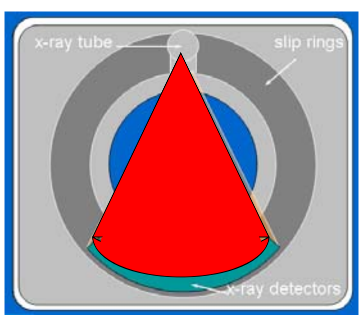


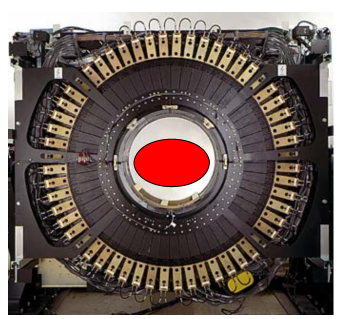


attenuation of photons
structure / anatomy

distribution of tracer
function / physiology

CT PET

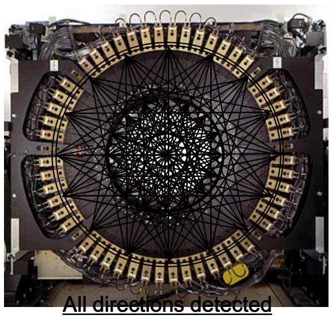




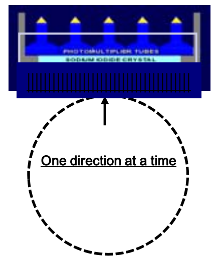
attenuation of photons
structure / anatomy

distribution of tracer
function / physiology

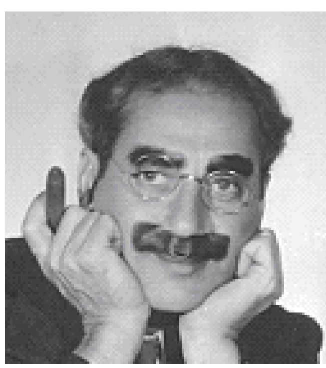
PET is stationary – SPECT rotates

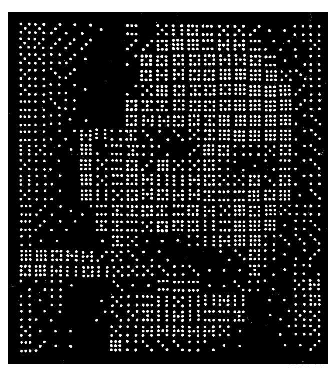


All directions detected simultaneously



Radiology Nuclear Medicine





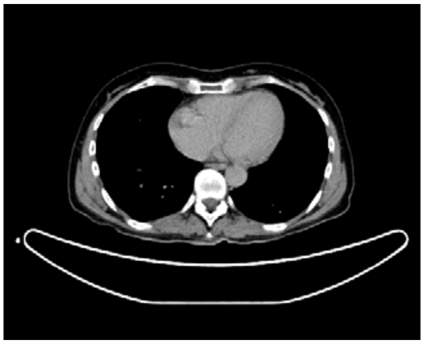
Ken Krowlton, Domino Portraits, 1982

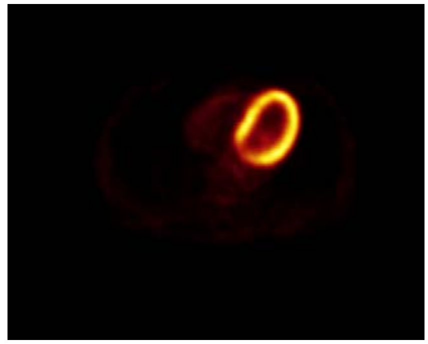
#dots recorded determine what details can be seen in image

And for those ignorants of classic entertainment : this is Groucho Marx

“I never forget a face, but in your case I'll be glad to make an exception.”

CT PET





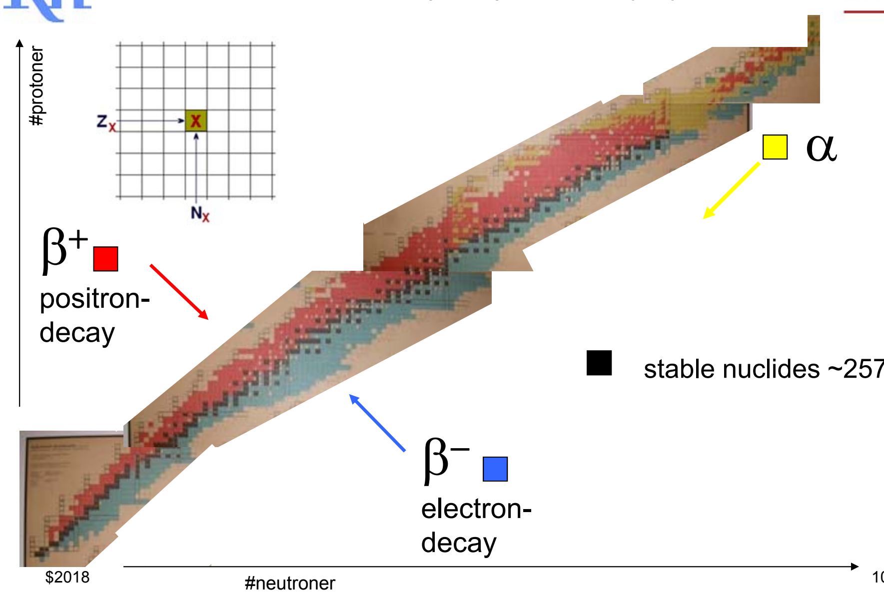
attenuation of photons

structure / anatomy

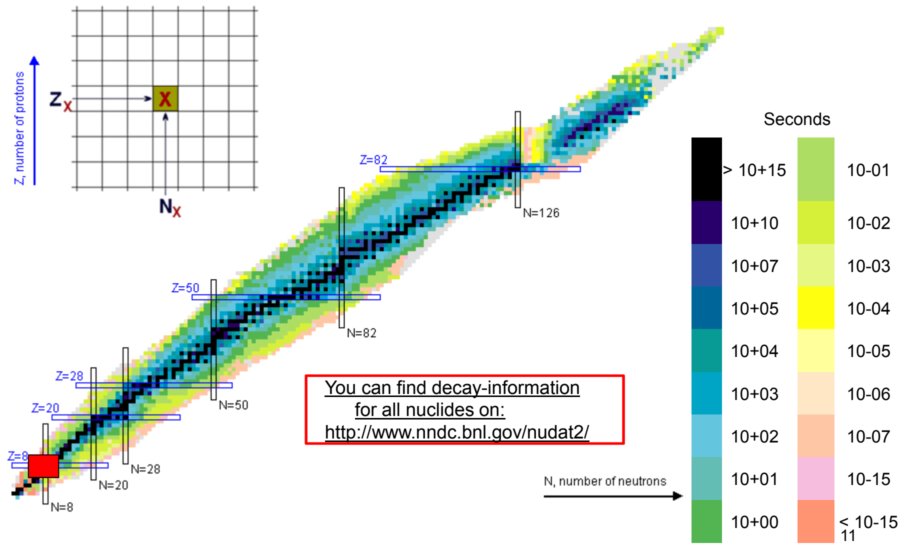
distribution of tracer

function / physiology

The nuclear chart (N,Z) – decay types



The nuclear chart (N,Z) – half lives



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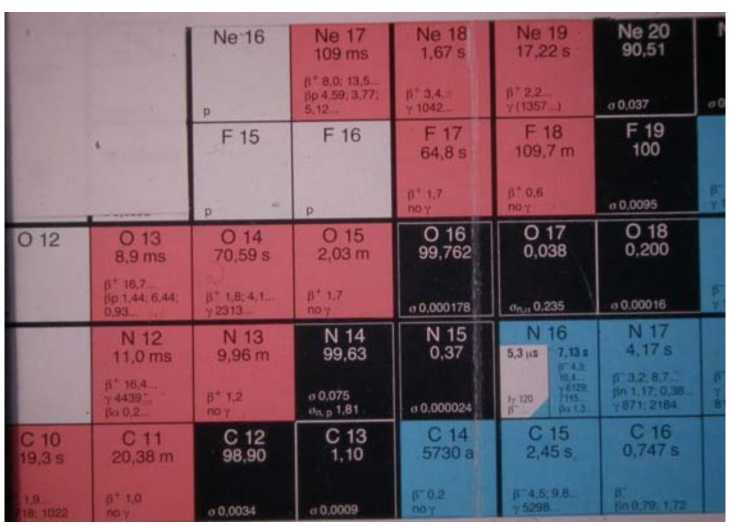
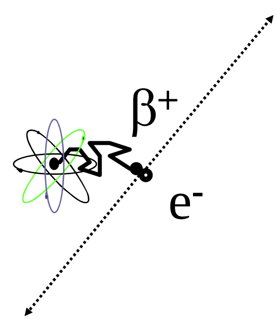
…magnified



PET *is really* ART:

Annihilation **R**adiation **T**omography



1955

E = mc²

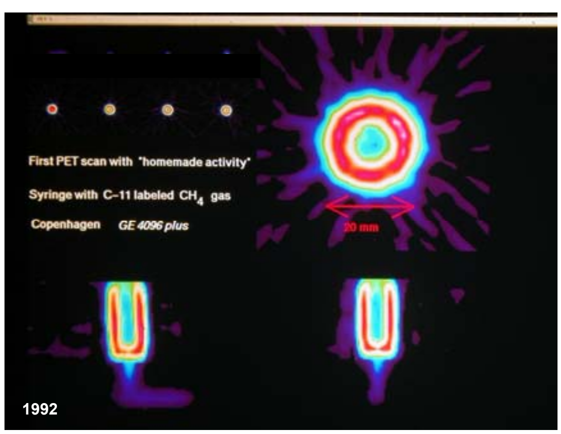
1905

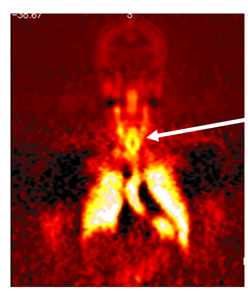
Result: Two photons on an **almost** straight line that **nearly** contains the point of decay

Positron Emission Tomography (?) or ART

We never detect the positrons directly, only the annihilation photons

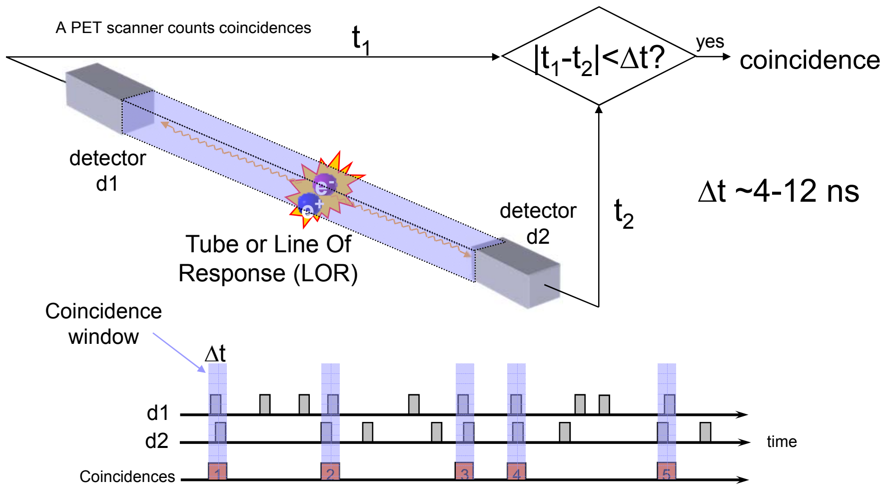
Annihilation
Radiation
Tomography



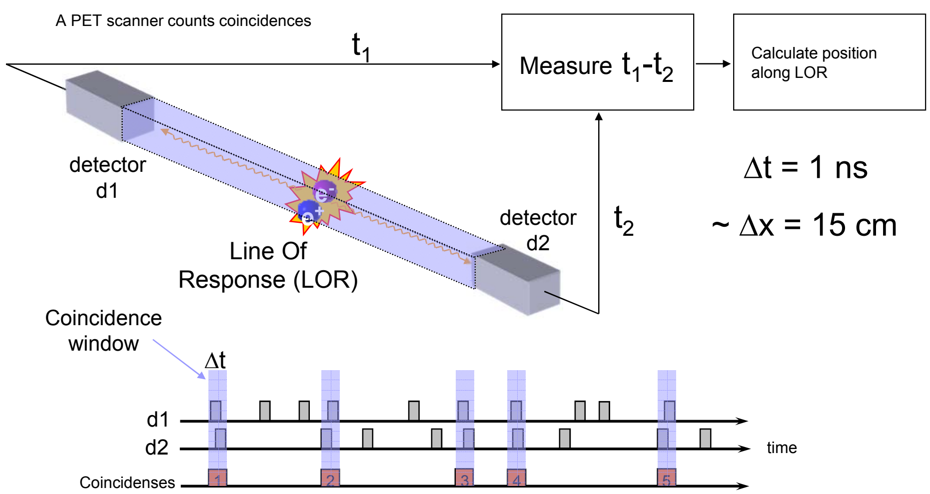


Inhalation of radioactive β^+ gas

PET radiation detection

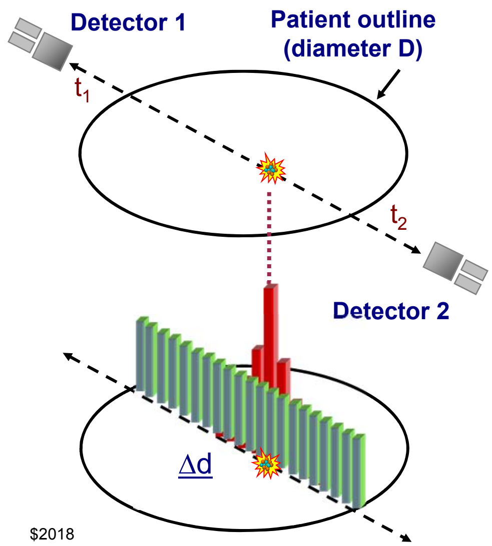


PET detection, Time-of-Flight



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
100	1.5	5.2
300	4.5	3.0
500	7.5	2.3
600	9.0	2.1

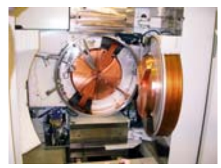
- More information available for image formation
- better image quality, or shorter scanning time, or less injected activity

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)

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

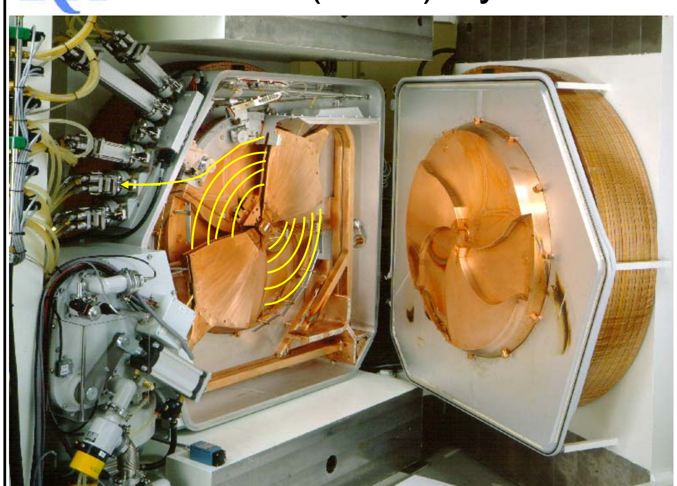
Cyclotrons



Scanditronix 32 MeV

GE Minitrace 11 MeV

(small) Cyclotron



Ion Source

Production of H^-

RF + magnetic field

Ion acceleration

Carbon foil

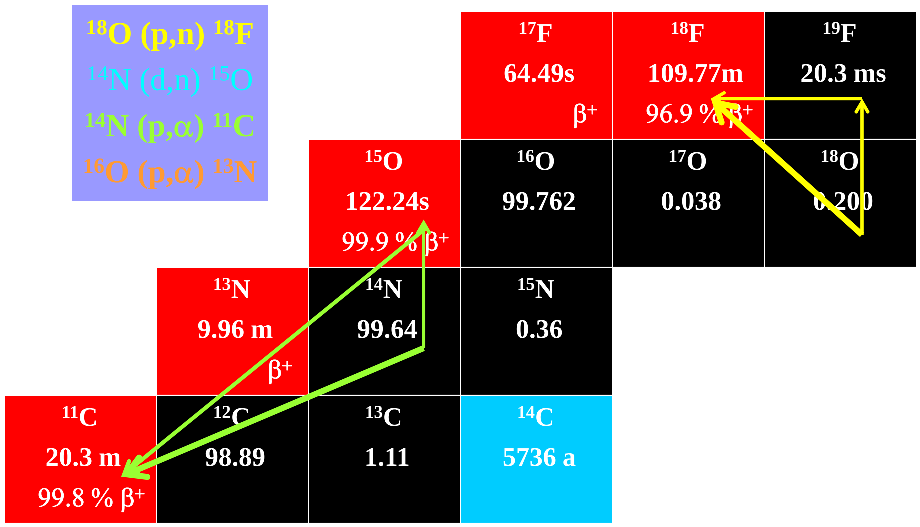
Electron stripping

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

protons do irradiate a

Target

Nuclear Reactions



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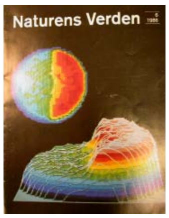
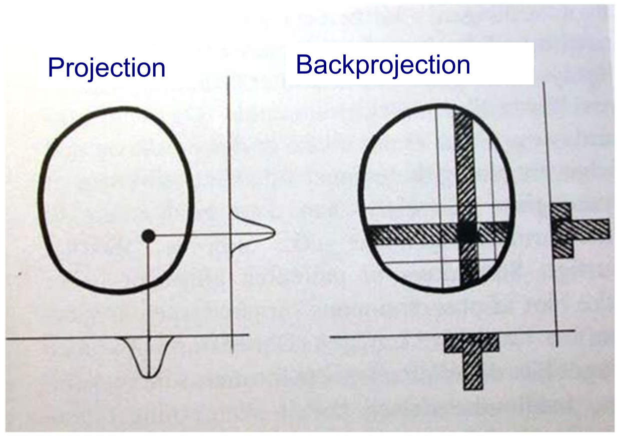
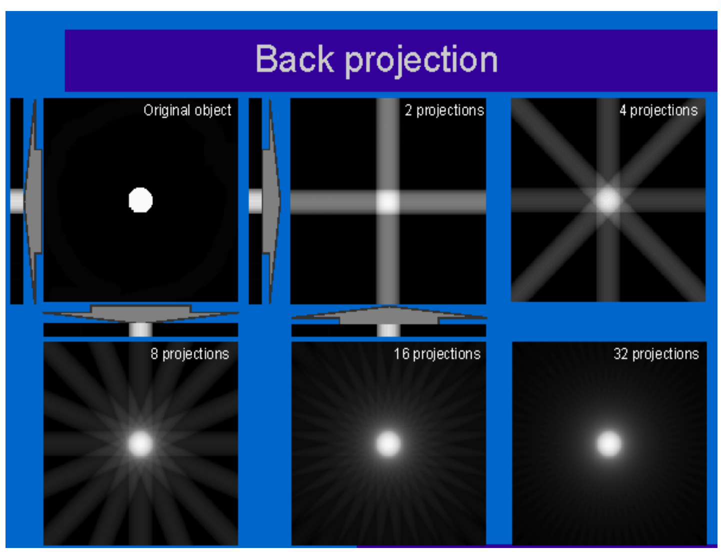
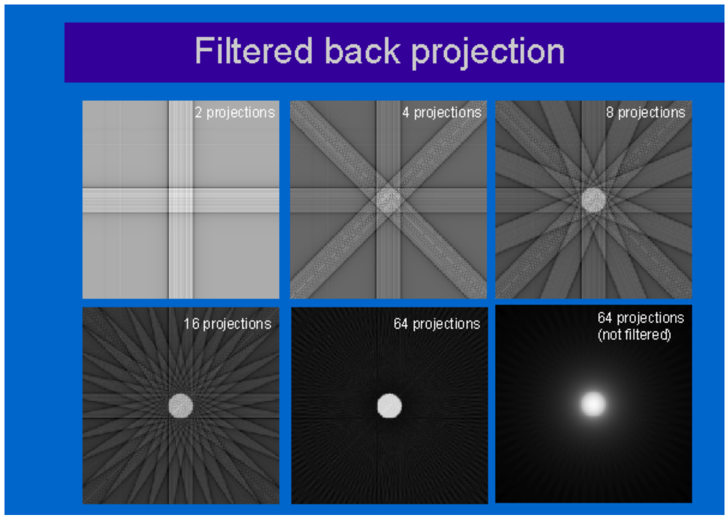
Principle of image formation!



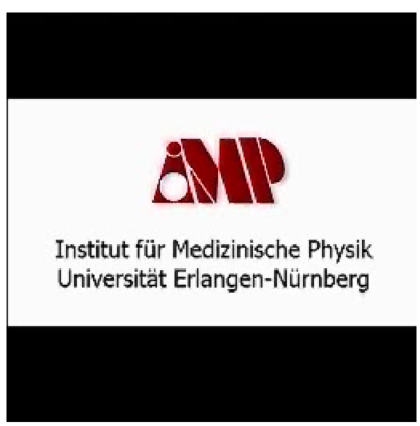




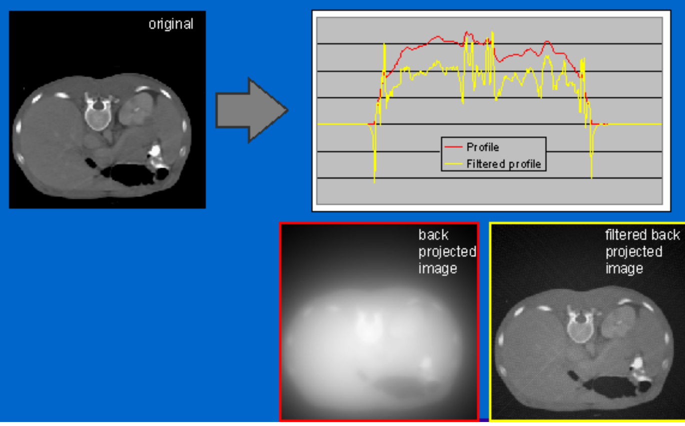


Example of FBP

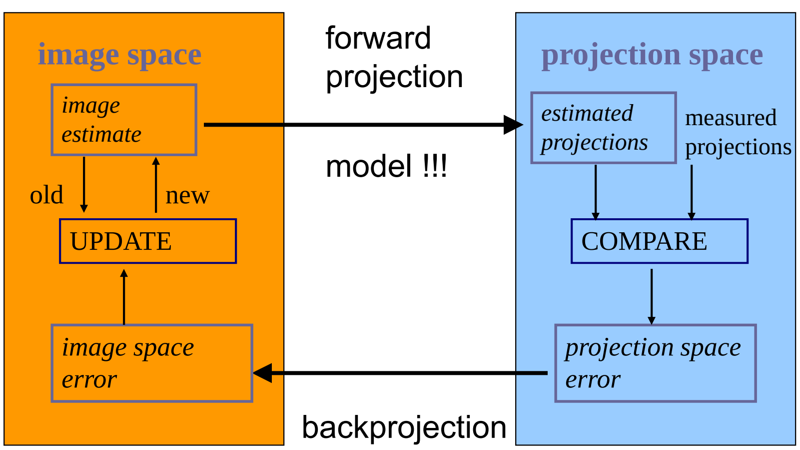
Filtered Back Projection of Xray-data (CT)



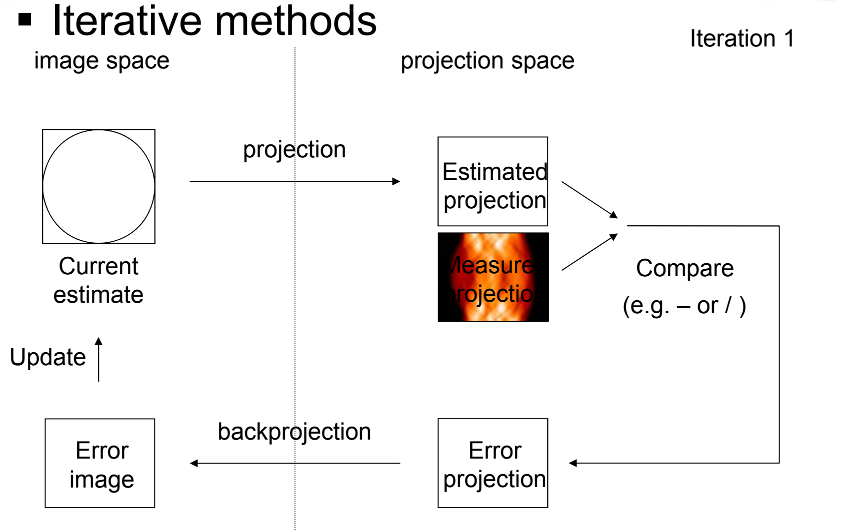
Filtered back projection



Iteration principle



- Iterative methods



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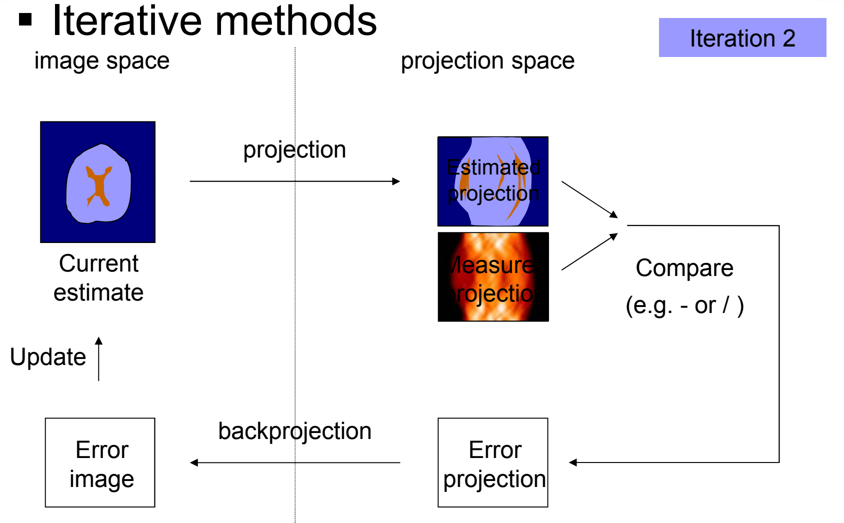
- Iterative methods



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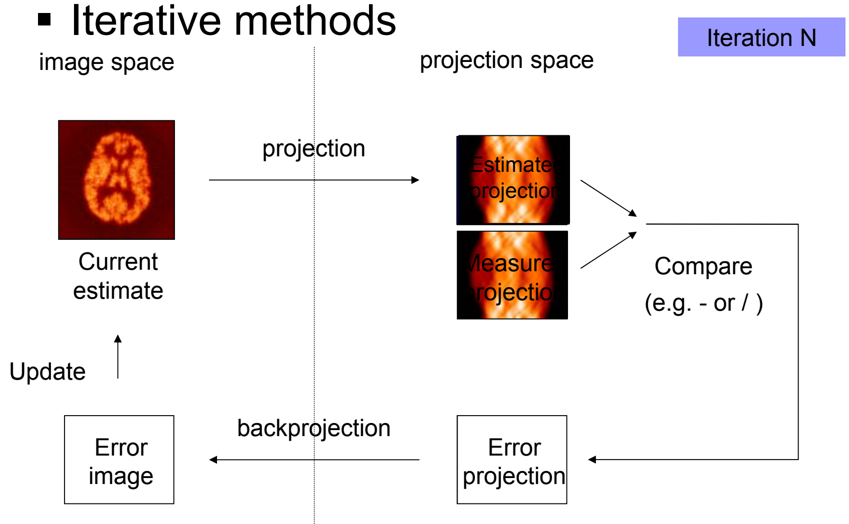
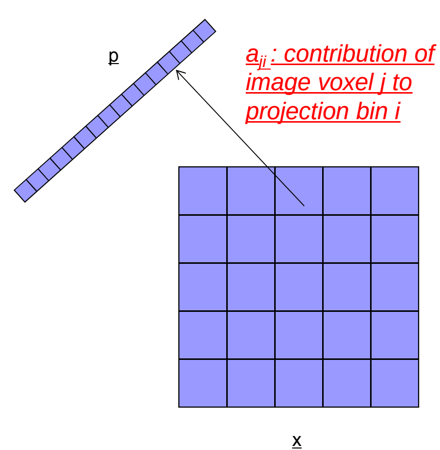
Iterative methods

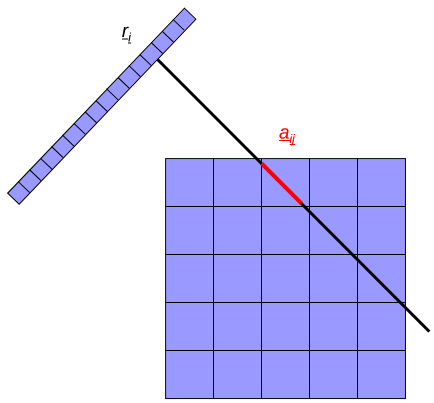


Iterative Algorithms

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



Line-Length Weighting



x

Projection (A):

$$r_j = \sum_{j=1}^{M} a_{ji} x_j$$

Backprojection (A^T):

$$x_{j,back} = \sum_{i=1}^{N} a_{ij} r_i$$

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

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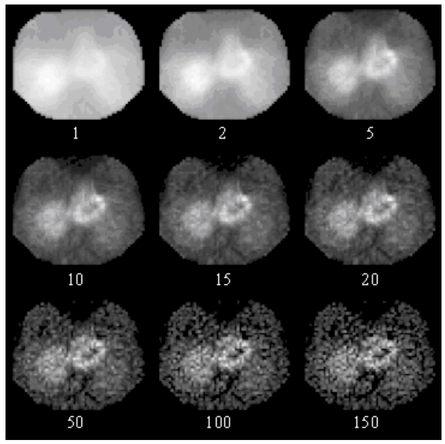
Image at different iteration numbers

Smooth
Low resolution



Noisy
High resolution

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Time to breathe…

[Reykjavik, 25. August 2011$]

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Overview (2):

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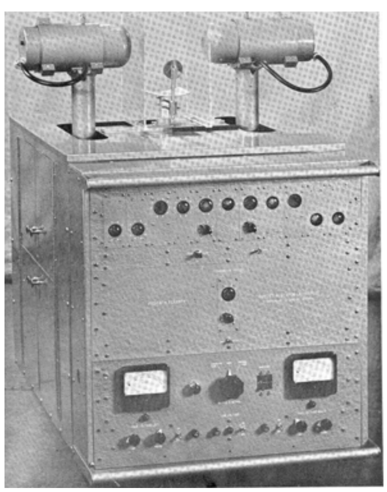
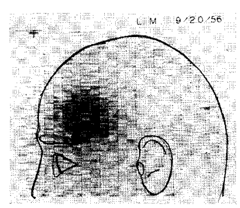
Positron scanner (*not PET*)

(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)

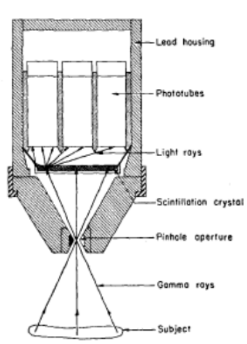

Fig. 1. Sectional drawing of scintillation camera.

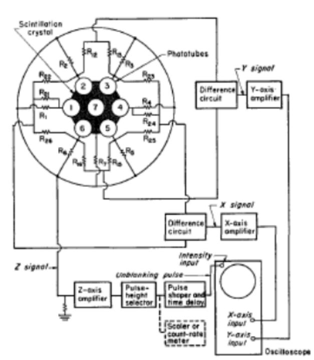

Fig. 2. Block diagram of electronic circuit.

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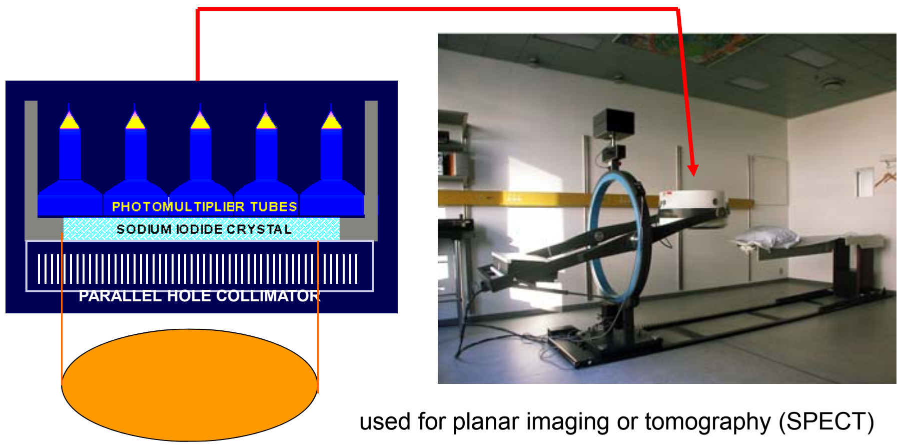
Gamma camera principle

position sensitive photon-detector



used for planar imaging or tomography (SPECT)

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

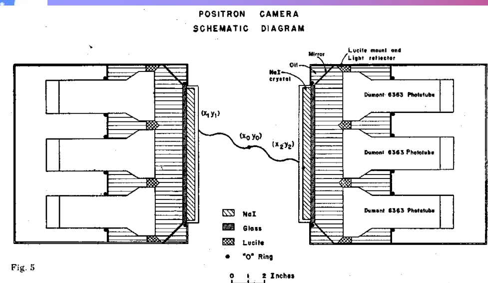
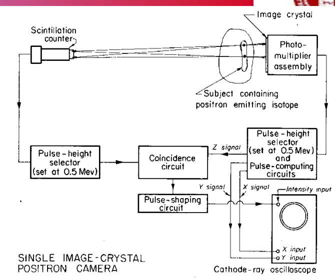


Fig. 5



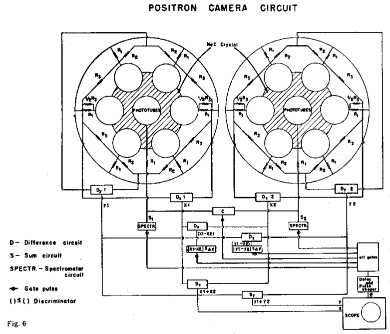
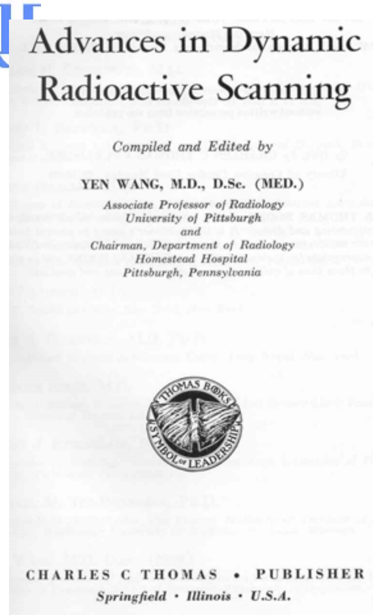


Fig. 6

Principles proposed by Hal Anger 1959



Advances in Dynamic Radioactive Scanning

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Pittsburgh, Pennsylvania

CHARLES C THOMAS • PUBLISHER
Springfield • Illinois • U.S.A.

1968 PET

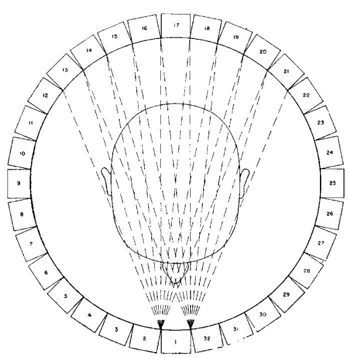
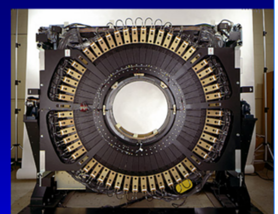


FIGURE 13. (a and b) Multicrystal positron detector of Brookhaven design. Each NaI detector and phototube feeds pulses into a coincidence matrix. Coincidences are stored in a magnetic drum memory and subsequent calculation permits the original isotope distribution to be reconstructed. (4)

PET 1966 -

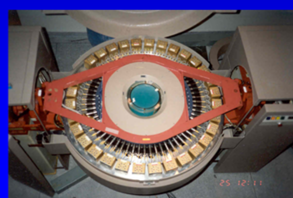
Positome I 1966

32 detectors



Advance 1993

12096 detectors



Therascan 1982

256 detectors

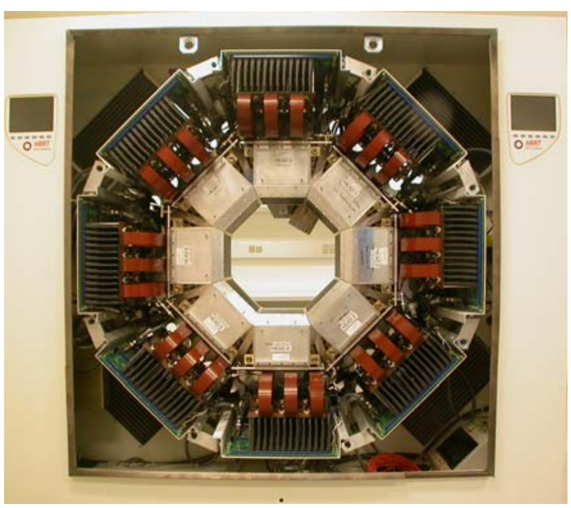
$2002

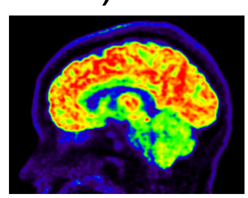
HRRT 2002

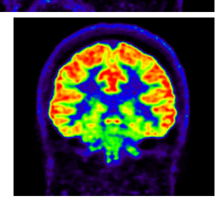
119.808 detectors

$2018

Special Brain scanner (HRRT)







119.808

Detector elements

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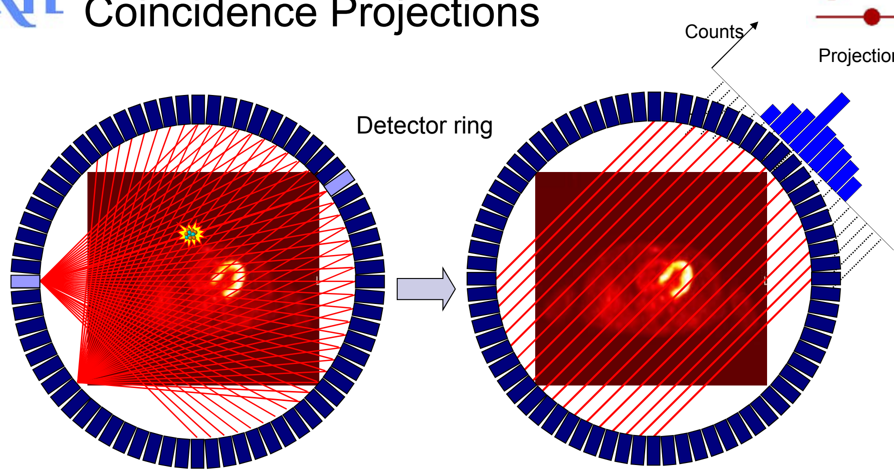
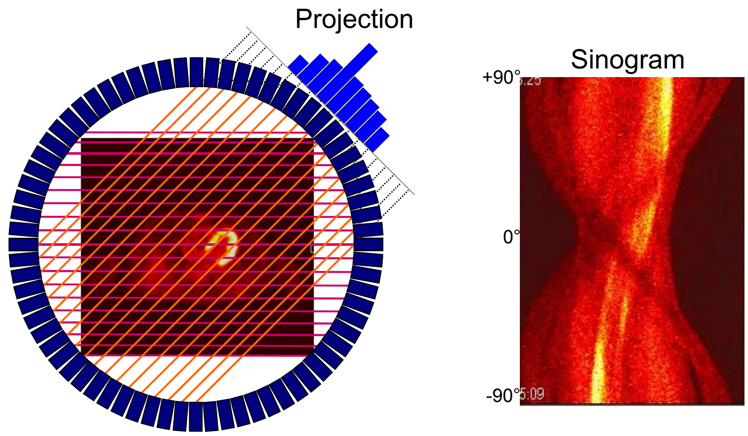
Coincidence Projections



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.

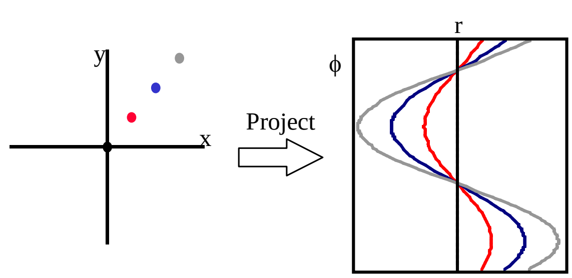
Data-Sorting Sinogram



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**.

Sinogram

Real Space

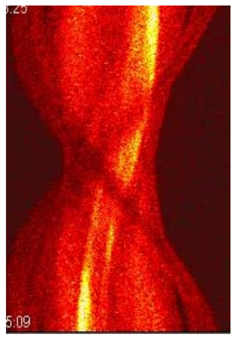


Radon transform

Point in center: straight line

Off-center: sine curve, amplitude proportional to radius

Image Reconstruction



Sinogram

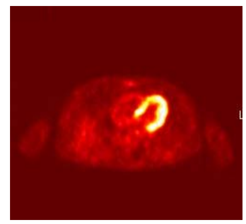
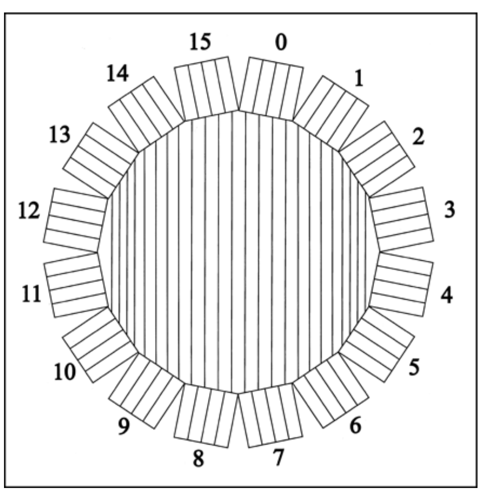


Image slice

Geometric correction

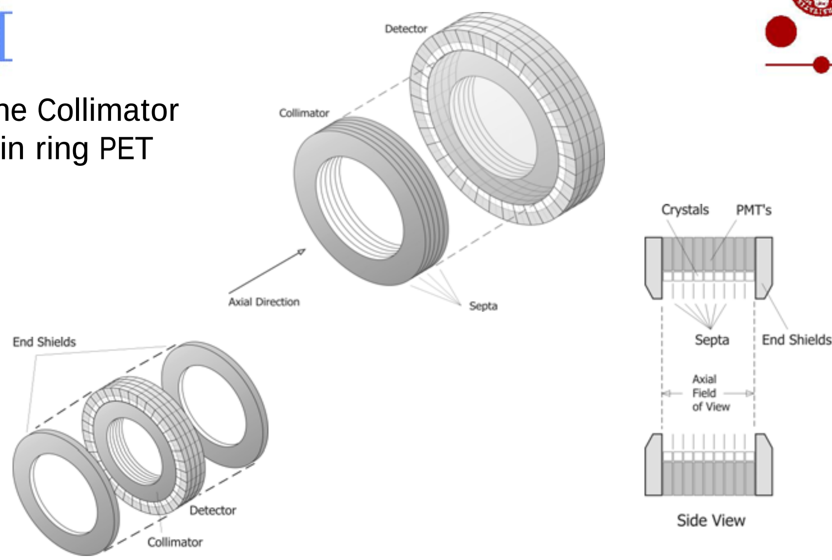
Interpolation needed before reconstruction



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



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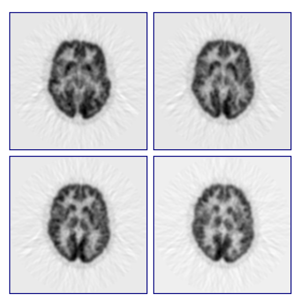
Static Frame Acquisition

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



Adjacent brain PET static slices

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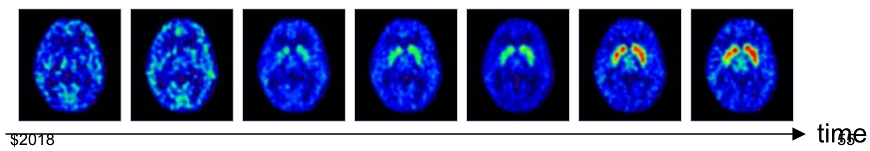
Dynamic Frame Acquisition

- 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



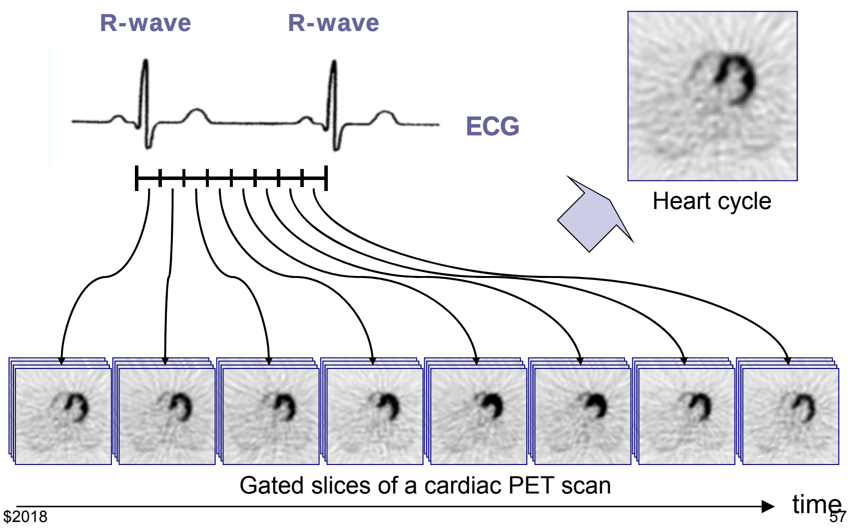
Gated Acquisition

- 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



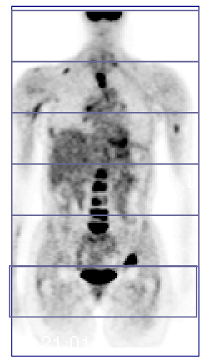
List Mode data (LM)

- 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

Whole-Body Acquisition

- Set of slices in multiple FOVs
- Step-by-step tabletop motion during acquisition
- ➢ Metastatic spread of cancer



Whole-body scan

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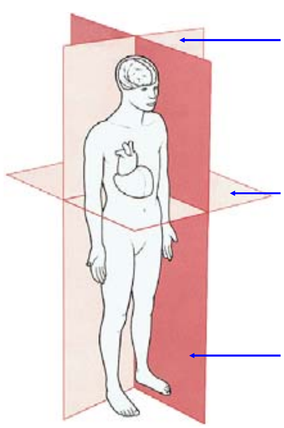
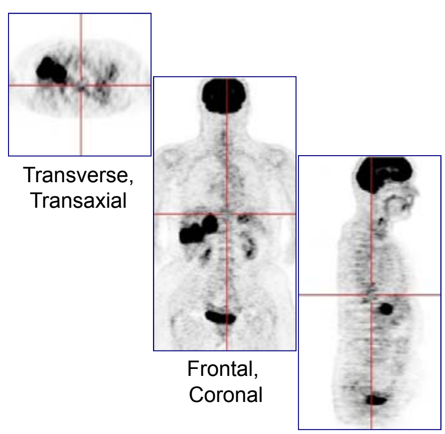
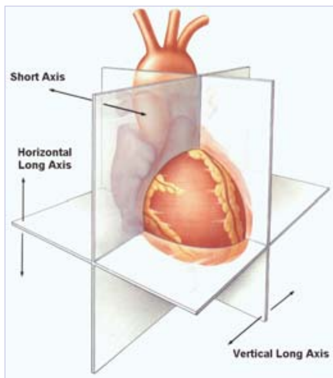
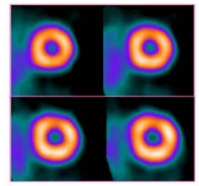
Body Tomographic Planes



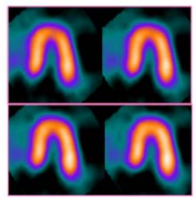


Tomographic Planes for the Heart

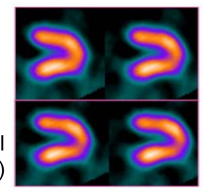




Short Axis (SA)

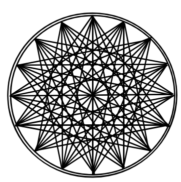


Horizontal
Long Axis (HLA)

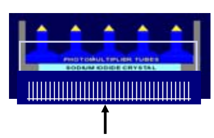


Vertical
Long Axis (VLA)

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

Overview (4):

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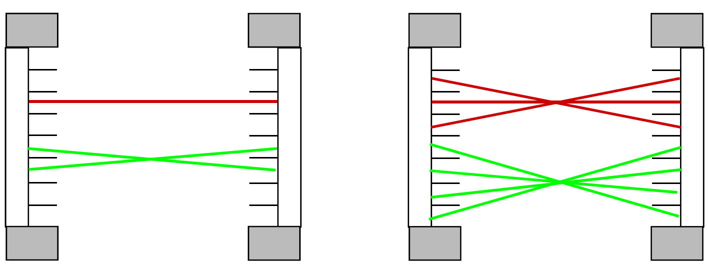
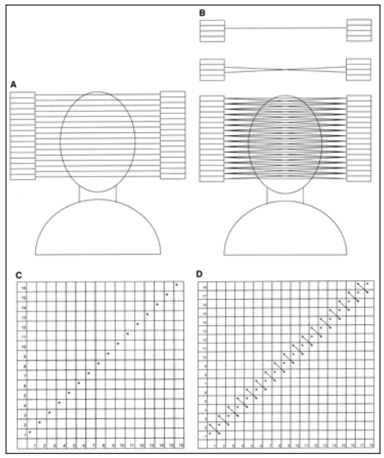
2D Imaging



High Resolution Mode
- **Direct $\Delta Z = 0$**
- **Cross $\Delta Z = \pm 1$**
- **Limited Sensitivity**

High Sensitivity Mode
- **Direct $\Delta Z = 0, \pm 2$**
- **Cross $\Delta Z = \pm 1, \pm 3$**
- **Increased Sensitivity**

Michelogram – direct and cross slices



Direct only   Direct and Cross

The diagram shows all possible combinations of two detector rings.

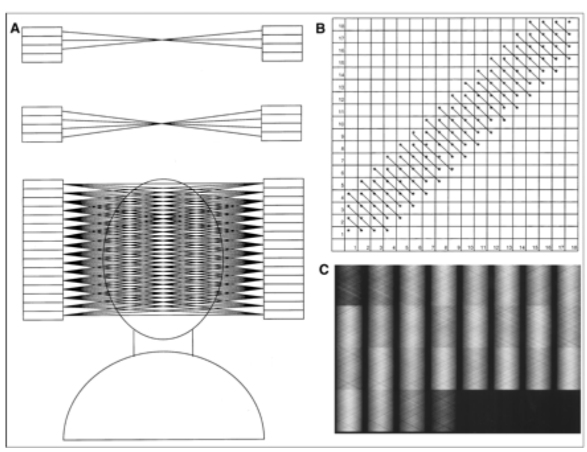
The ones ”allowed” are marked with a ”*”.

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**

Michelogram – 2D ”span 7”

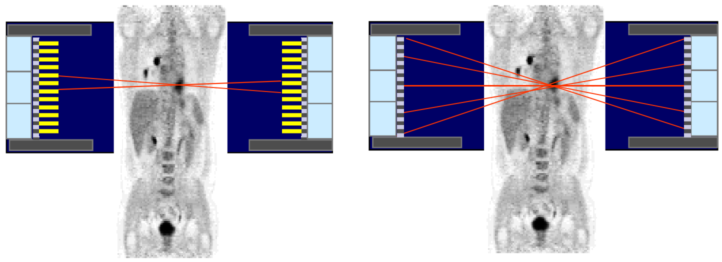


The number of combinations involved in direct and cross slices is known as the ”**SPAN**”

-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

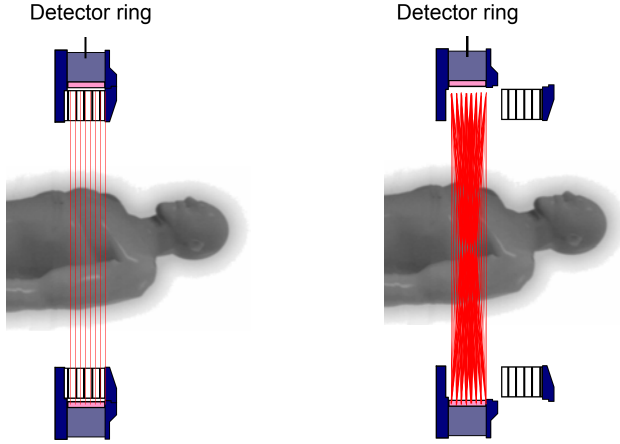
[NOT used anymore]

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

2D/3D Volume Acquisition

Detector ring

Detector ring

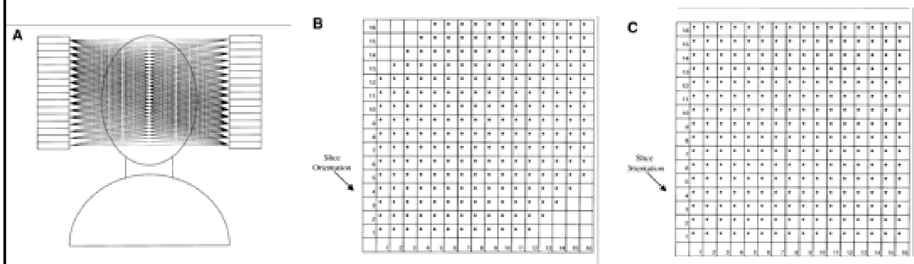


2D acquisition
(Septa installed)

3D acquisition
(Septa removed)

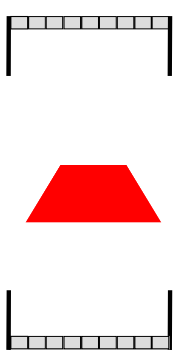
Michelogram – 3D, RD11 and RD15

RD = Ring Difference



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

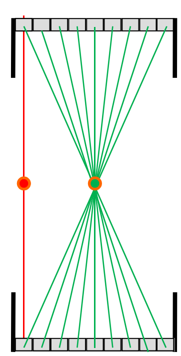
Sensitivity in ”3D” is position dependent



3D mode

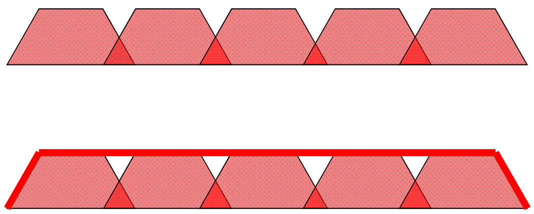
There is a large difference between center and edge slices due to the number of LORs that contribute

The ”ideal” triangle is most often truncated like this:
(we are not allowing all angles)



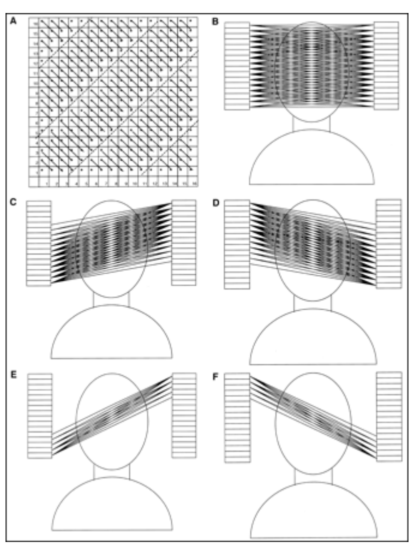
3D mode

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



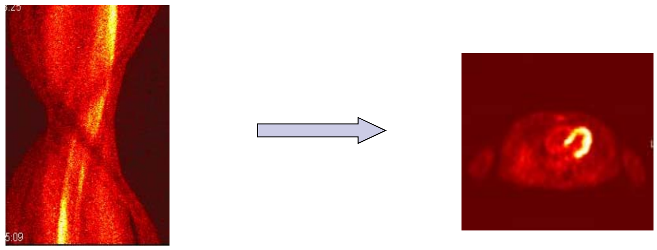
The overlapping scans add up to give a constant sensitivity and noise level (except for top and bottom)

3D data – span 7



Also for 3D, points in the michelogram may be joined, reducing the number of sinograms stored.

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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FAQ #1:

What is the smallest *[something]*

you can see in a PET scanner?

Wrong question /No simple answer

Depends on the activity concentration/contrast

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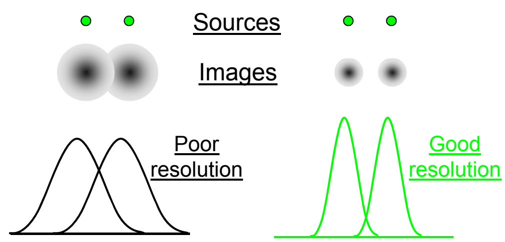
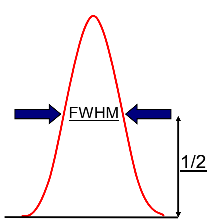
Spatial Resolution

- ~~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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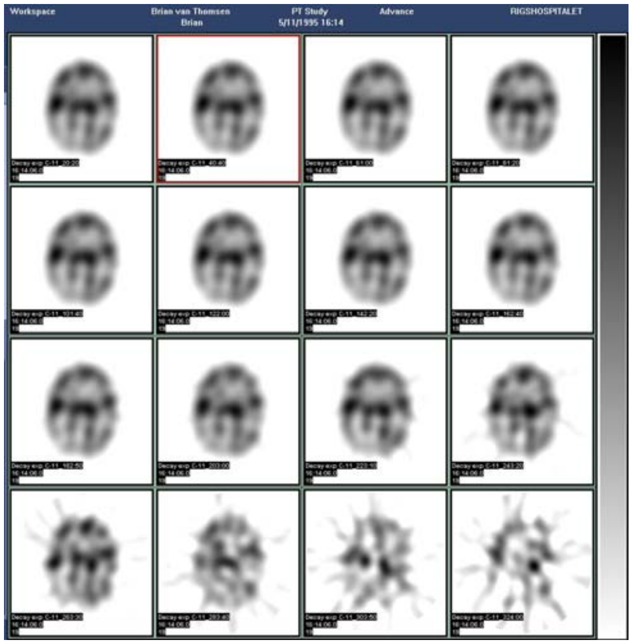
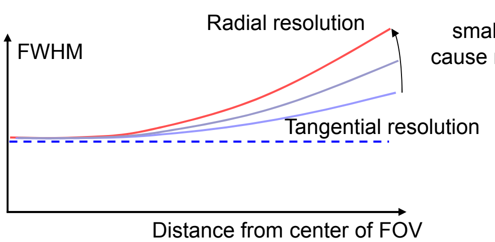
Filtering is a balance between noise and resolution (FWHM)

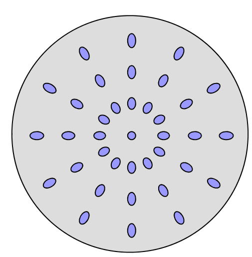


20 mm

Radial Vs Tangential Resolution



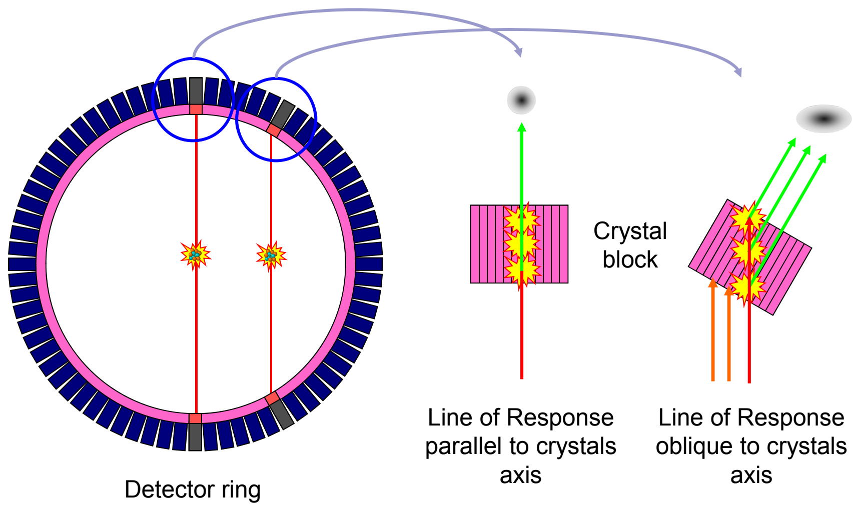
Plot of resolution versus radial position



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.

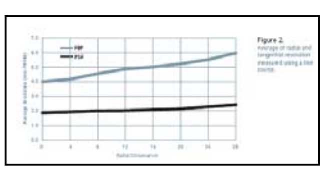
Radial Vs Tangential Resolution

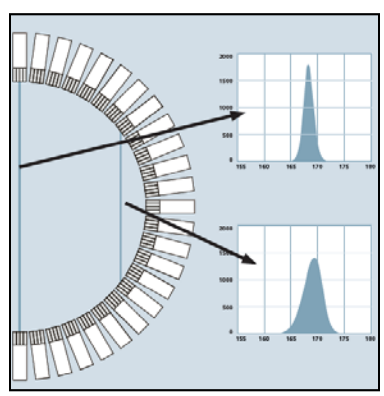


Results of modeling PSF in reconstruction

(example: Siemens "High definition" recon)

Measured PSF

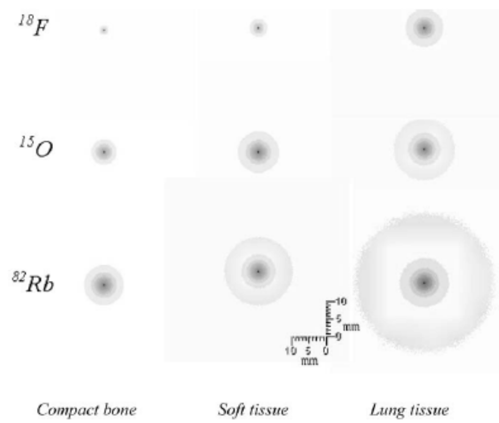




Positron flight in human tissues

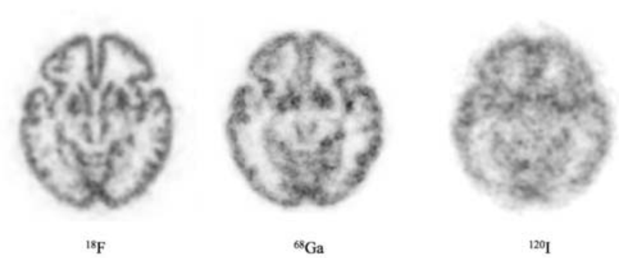
Sanchez-Crespo A et al.   Eur J Nucl Med Mol Imaging (2004)

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

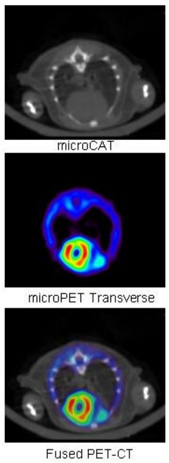
Iida-phantom



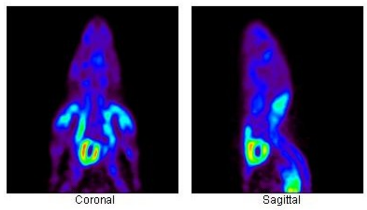
E_{max}= 0.63 Mev   1.90 Mev   4.59 Mev

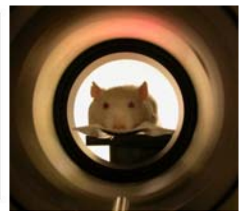
Mouse Heart PET/CT: 28g Mouse

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

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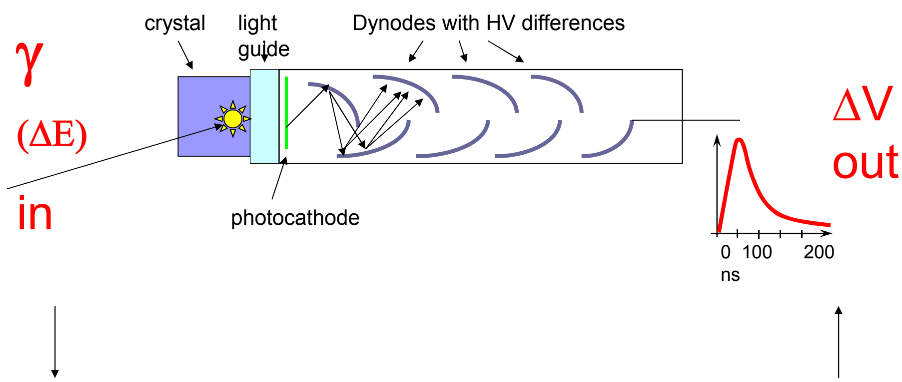
Detection of 511 keV photons

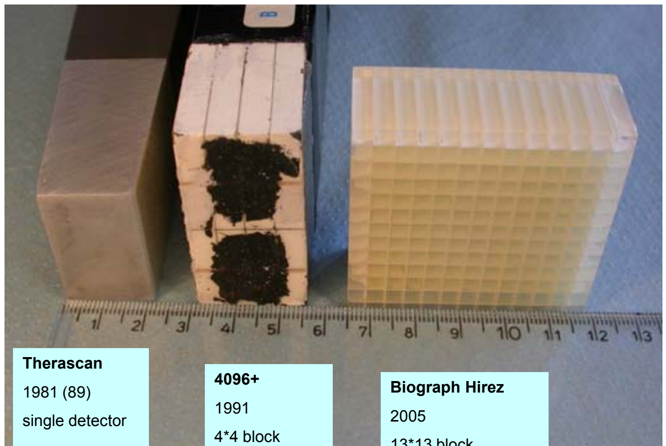
- First, we need to stop the photons
  - That requires some high Z, high density material
  - which converts the energy to low energy photons
- Then this signal must be amplied and digitized
  - Two options:
    - photo multiplier tube (PMT) or
    - solid state detectors (APD, SiPM)

Scintillation detector



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

Evolution of PET-detectors

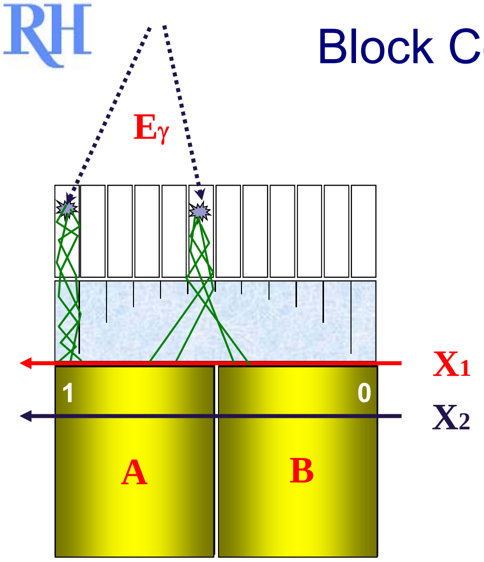


Therascan
1981 (89)
single detector
20*35 mm
total # 256

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

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

Block Concept



$X = A / (A + B)$

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

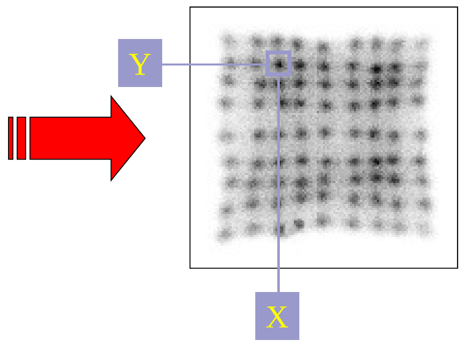
$X_2 = 55 / (55 + 45) = 0.55$

Flood Histogram / Position Map

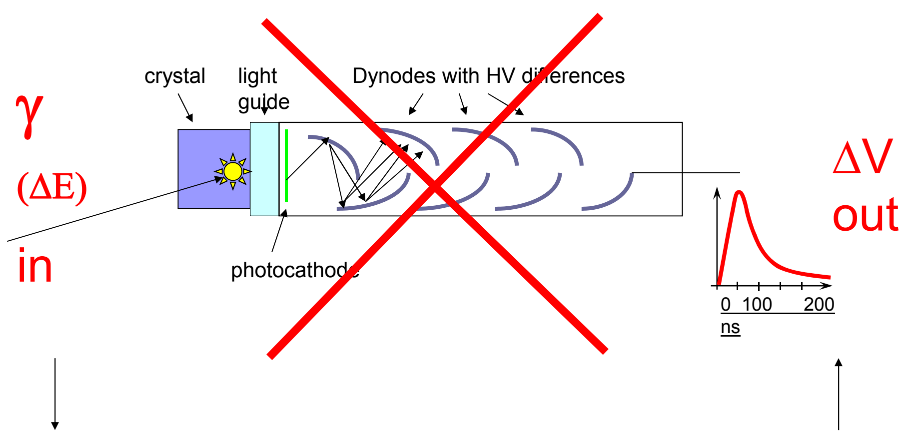
Anger Logic

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

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



Scintillation detector



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

Not effective in a MAGNETIC FIELD !

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

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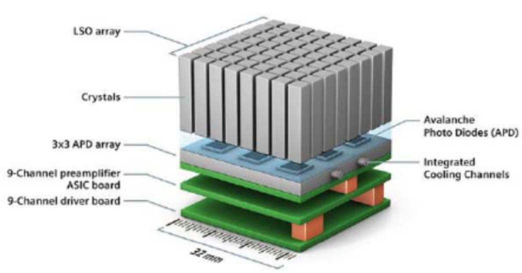
”MR-friendly PET detector”



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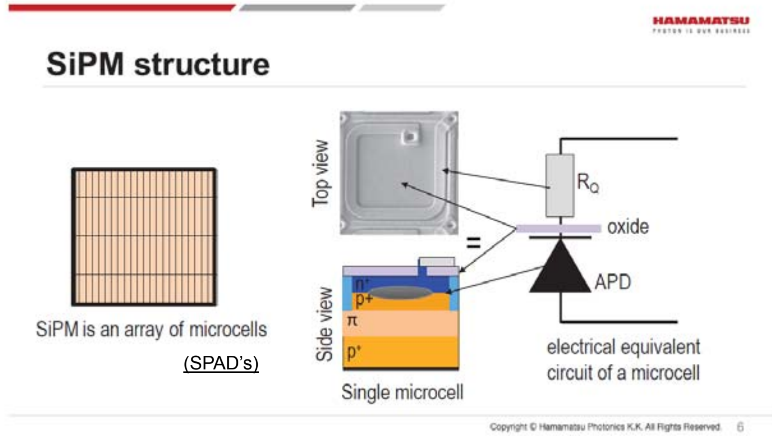
SiPM = Silicon PhotoMultiplier



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

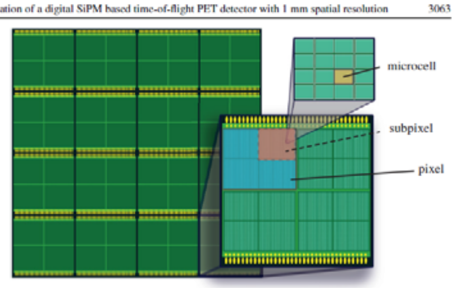
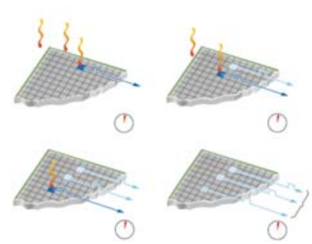


Figure 1. Schematic representation of the digital silicon photomultiplier (dSiPM) array. The larger inset depicts a zoom on a single die consisting of four pixels. Each pixel contains 6396 microcells (a number of which are shown in the smaller inset) that are arranged into 4 subpixels.

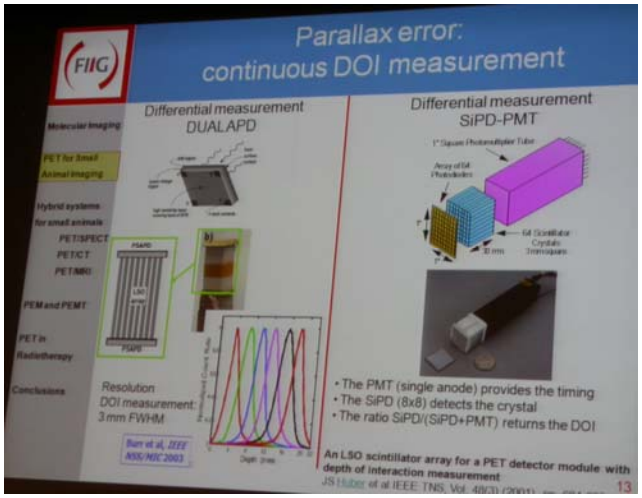
Philips Vereos Digital PET dSiPM



- 1 Tile
  - 16 dies
    - 4 pixels
      - 4 subpixels
        - ~1600 microcells

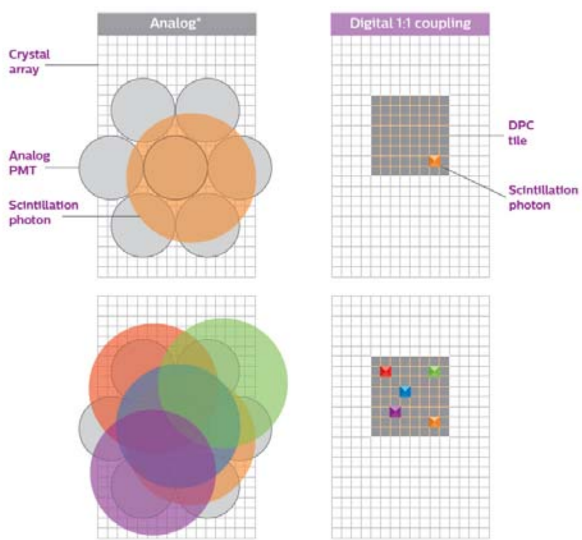
DOI measurement with APD

(Depth of Interaction – to avoid parallax-errors)



Presented at
EANM 2008 by
A. Del Guerra

Shared PMTs versus 1 to 1 coupling



PET Detector Components

Crystal elements

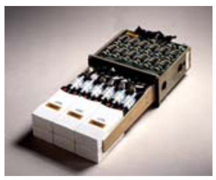
and photomultiplier tubes

Detector ring

Detector block

Module array

Detector blocks and front-end electronics



Detector module

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PET (example: GE Advance)

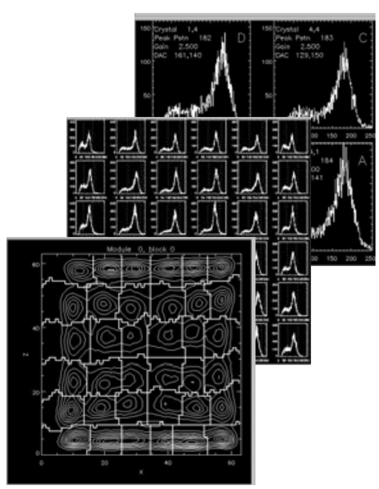
=

336 *

PMT-gain

Energy-windows

Uniformity



Every pair of blocks is tuned for coincidence timing

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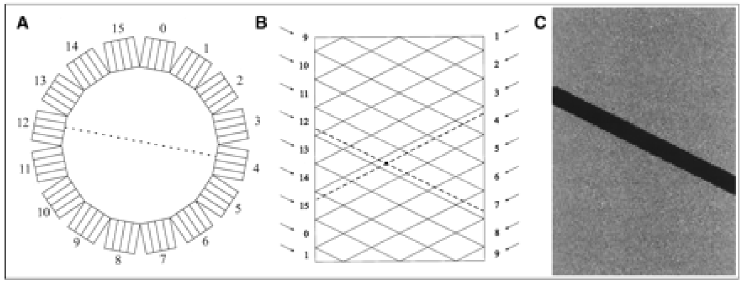
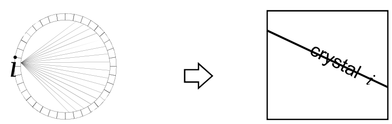
Block contribution to sinogram



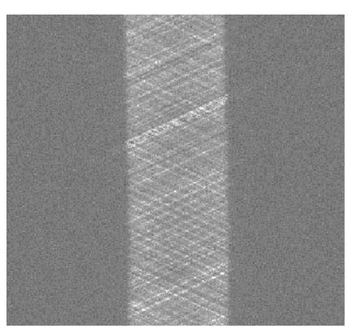
All the contributions from a single detector will be on a line, angled as shown. Due to sensitivity differences a certain "rhombic" structure will be visible in the sinogram.

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

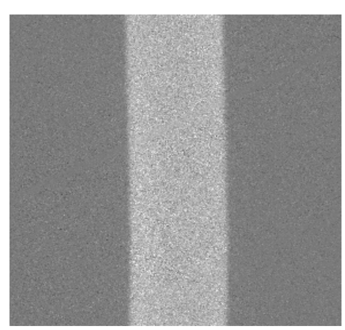


Normalisation correction

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

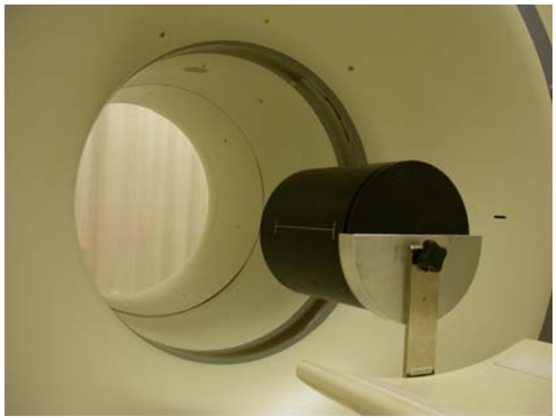


Sinogram **before** normalisation correction

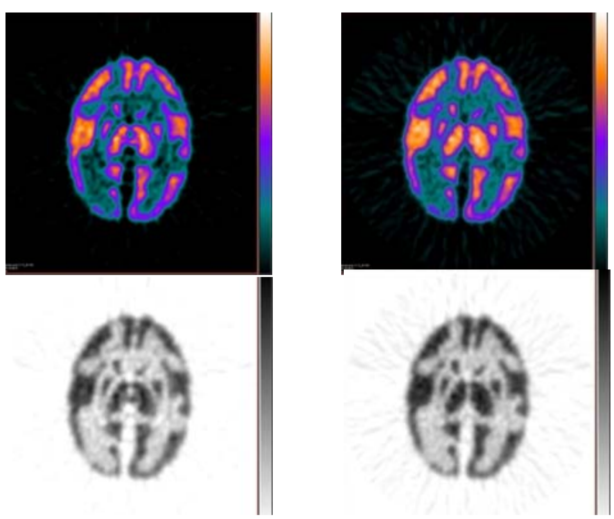


Sinogram **after** normalisation correction

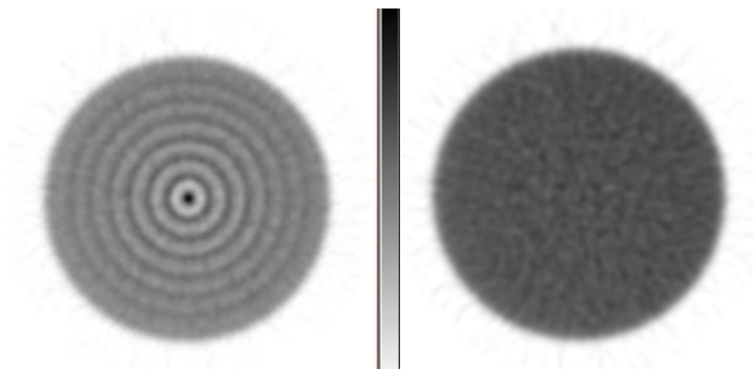
Siemens Biograph uses ^{68}Ge cylinder



Effect of Normalisation



Uniform phantom – very sensitive to NORM



without **with**

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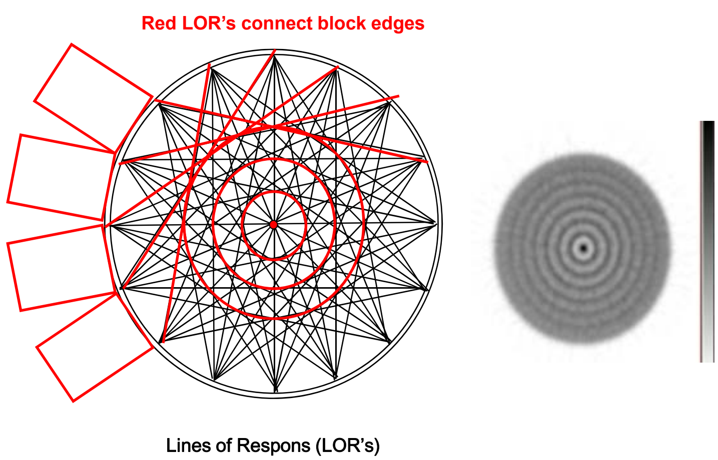
Normalisation

(digression on the origin of ring artefacts)



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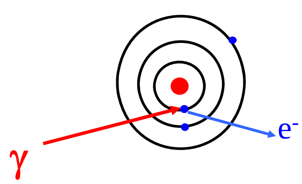
Overview (7):

- 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

Two processes stop photons in tissue:

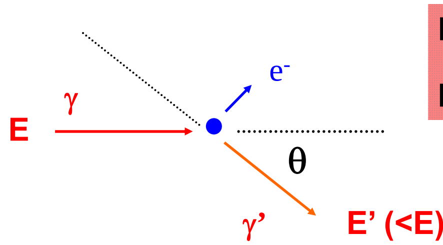
Absorption:



Simple,

no parameters

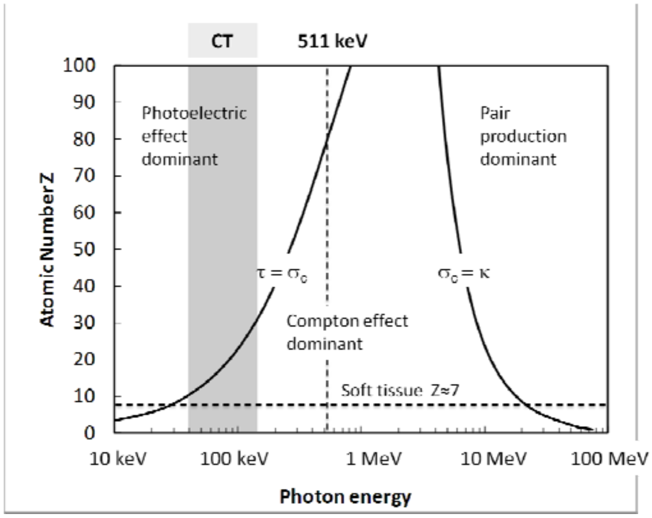
Compton scattering:



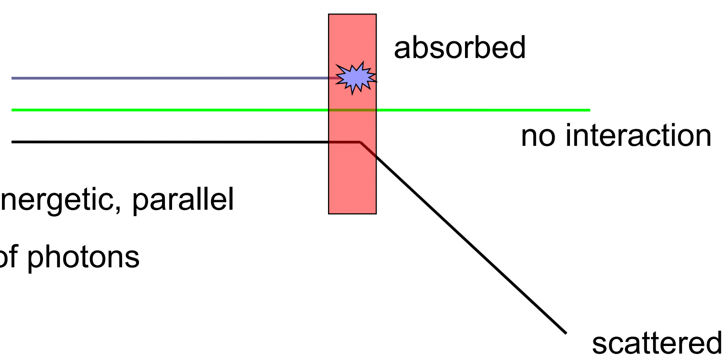
Parameters

E' and θ

Photon interactions - (E,Z) dependency



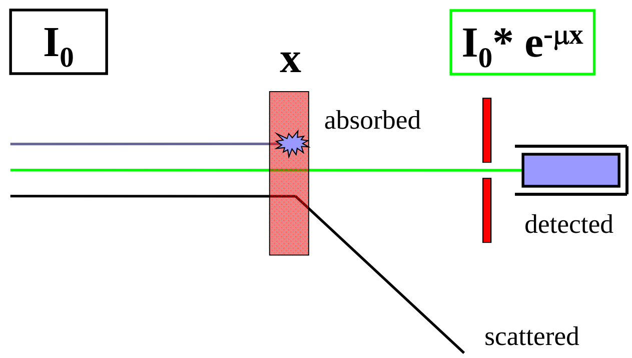
Physics: definition of attenuation



Monoenergetic, parallel beam of photons

Attenuation = Absorption + Scatter

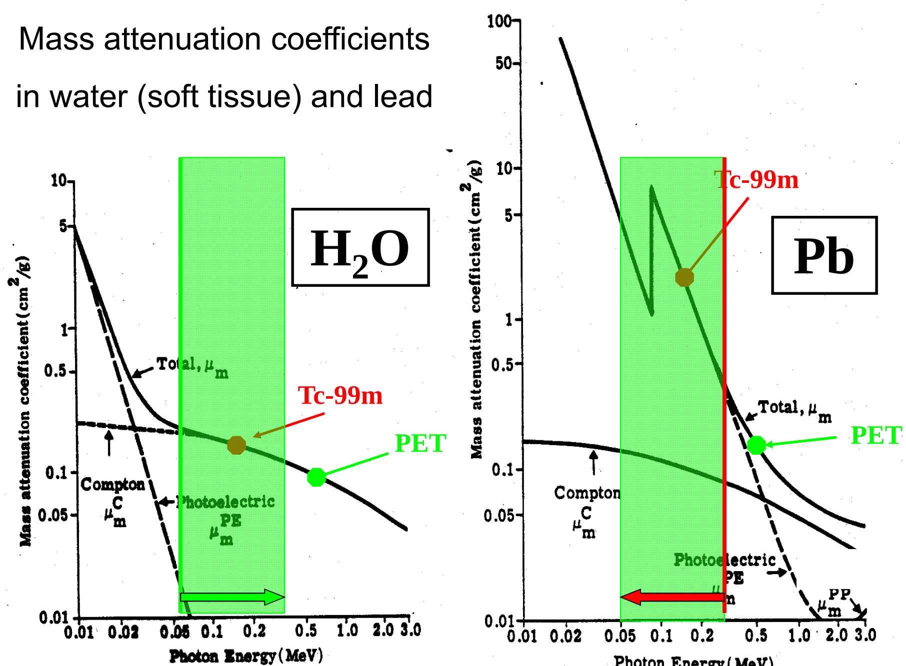
Linear attenuation coefficient: μ



Attenuation = Absorption + Scatter

$$\mu_{total} = \mu_{abs} + \mu_{scatter}$$

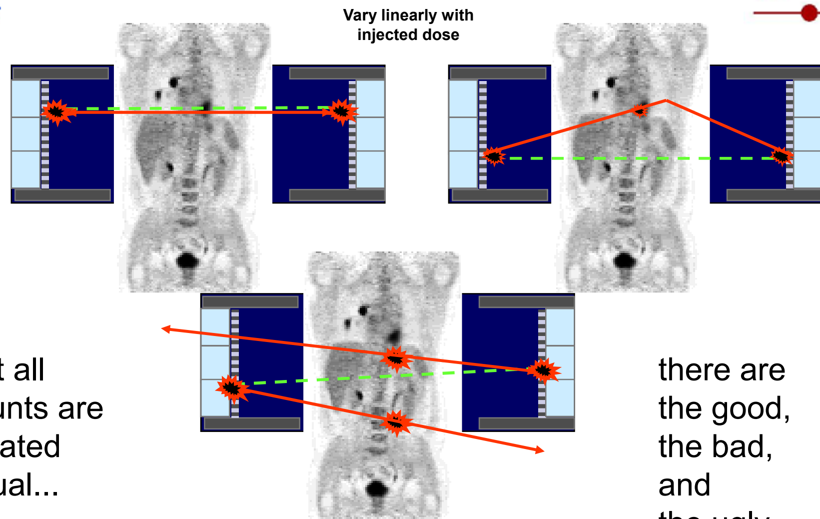
Mass attenuation coefficients in water (soft tissue) and lead



Trues Coincidence

Scatter Coincidence

Vary linearly with injected dose



Not all counts are created equal...

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

Random Coincidence

Vary quadratically with injected dose 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

⇒ Less Deadtime, fast counting

⇒ Narrow coincidence window

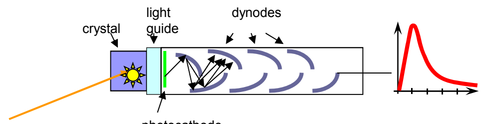
⇒ less Randoms

- High ligth output

⇒ Good energy resolution

⇒ Scatter rejection

- Low price



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PET Detector Scintillator Materials

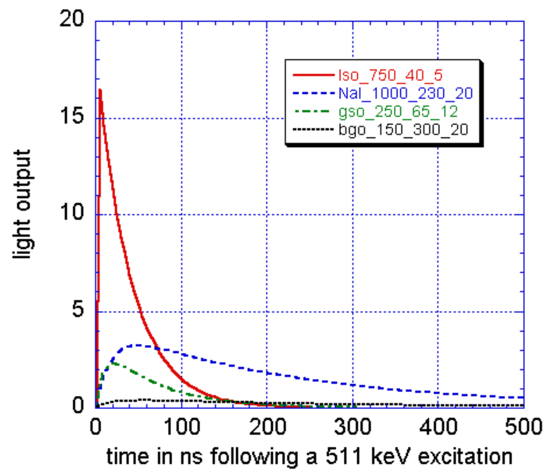
Crystal material	max Z	effective Z	density g/cm^3	output photons/keV	decay time ns
NaI:Tl	53	51	3.7	**40**	230
BGO	**83**	**73**	7.1	8	300
LSO:Ce	71	66	**7.4**	28	**40**
LYSO	71	54	5.4	28	53
GSO:Ce	64	59	6.7	7.5	56
BaF_2	55	54	4.1	2	**0.8**

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

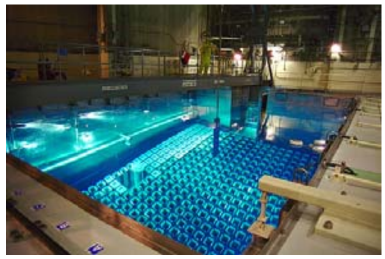
BGO may have a come-back

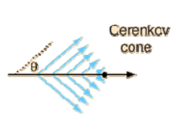
Scintillator Light Output

Light fractions emitted during the first 100 ns:
LSO 92%; NaI 35%; GSO 79%; BGO 28%



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:

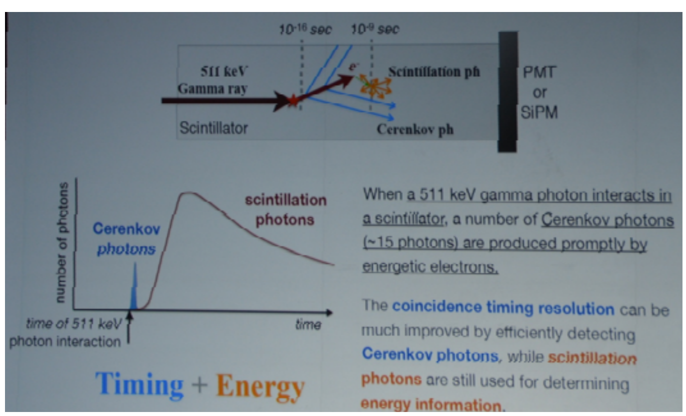
$$\theta = \cos^{-1}\frac{1}{1.33} = 41.2°$$

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

Timing with Cerenkov



Kwon et al, MIC 2016

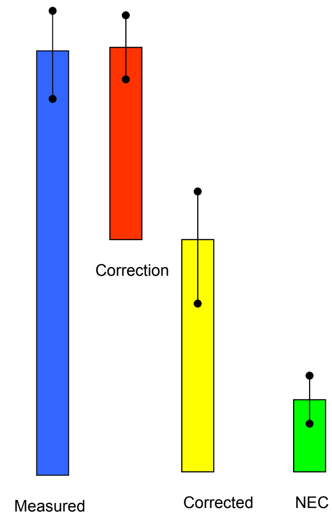
Noise Equivalent Counts (NEC)

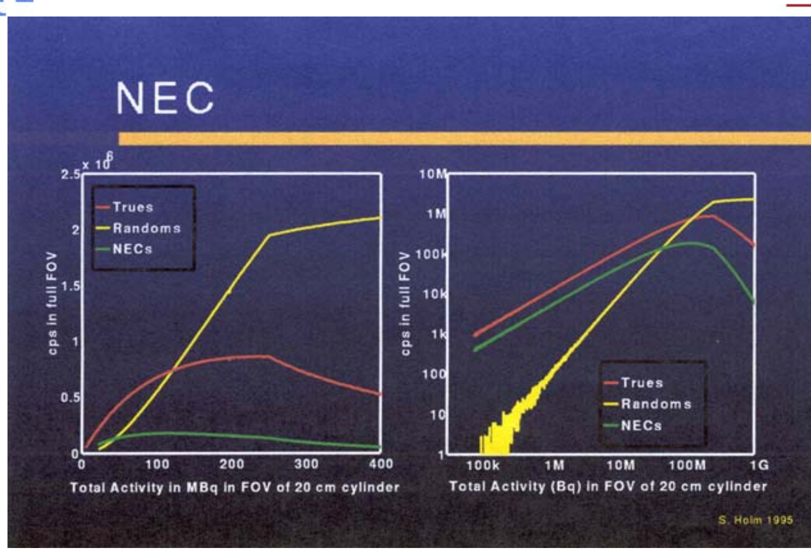
When correcting for randoms and scatter, counts are subtracted

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)

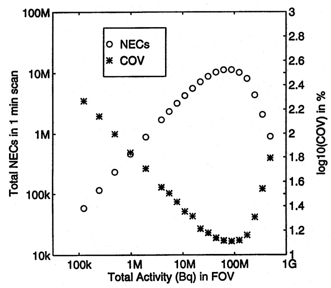


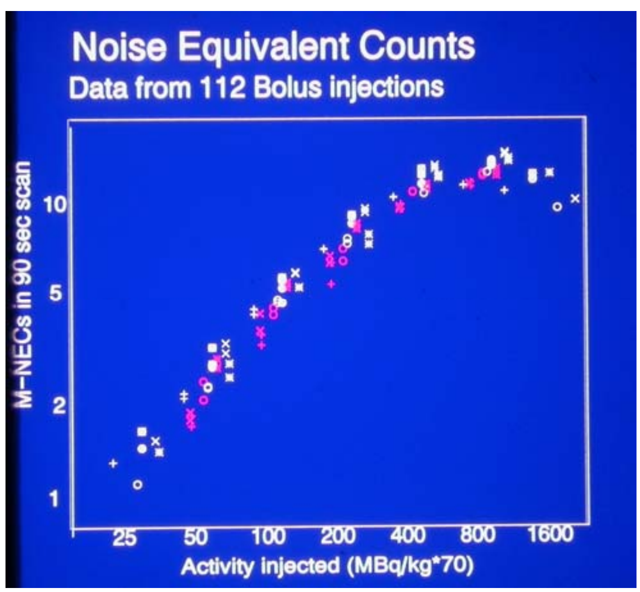


Noise Equivalent Counts (or count rate)

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

- k = 0 (R is estimated from singles)
- K = 1 (R measured in delayed window)
- NEC actually "reflects" the noise!

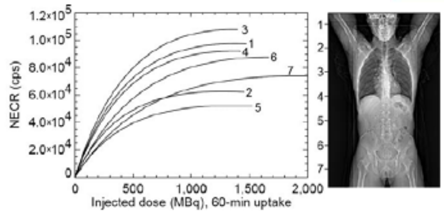


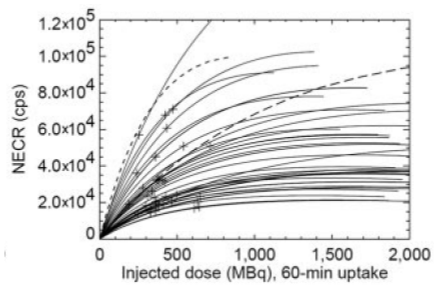


Optimizing Injected Dose in Clinical PET by Accurately Modeling the Counting-Rate Response Functions Specific to Individual Patient Scans

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





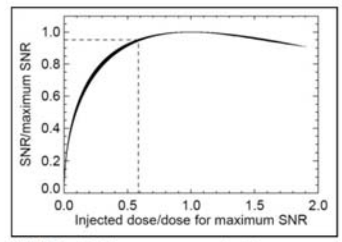


FIGURE 3. Relative response curves for 163 scans on conventional LSO PET/CT scanner, obtained by scaling SNR (1R case) and D_{inj} by their values at peak response.

Time to breath…

[Reykjavik, 25. August 2011$]

Overview (8):

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- 2D/3D, advanced data structure – Michelogram

- Resolution and noise
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- Hybrid systems – PET/CT- PET/MR - SPECT/CT…   Future ideas

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
- …

Attenuation and Scatter

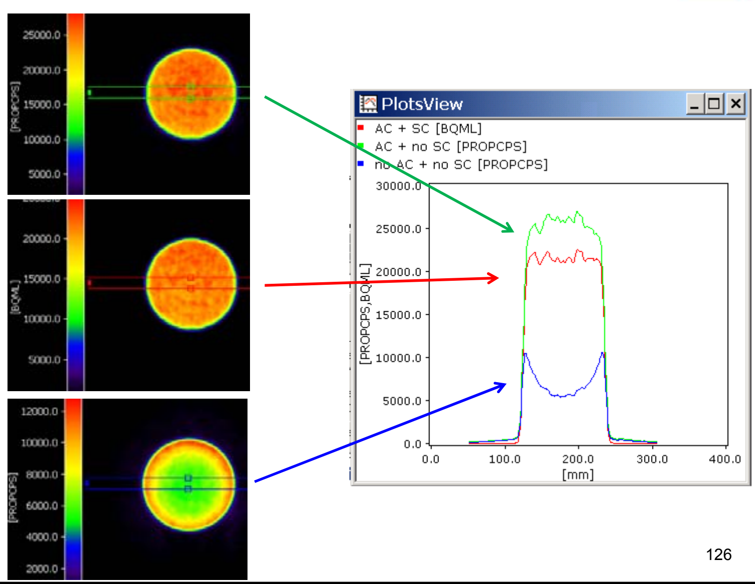
- It is a paradox in our terminology that from a *physics* point of view, attenuation (in NM) is caused mainly by scattering processes (and only partly by absorption)
- but in our *correction* procedures:
  - Attenuation is ”lack of counts” that we must restore while
  - Scatter is a surplus of counts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

Attenuation and Scatter

Attenuation correction

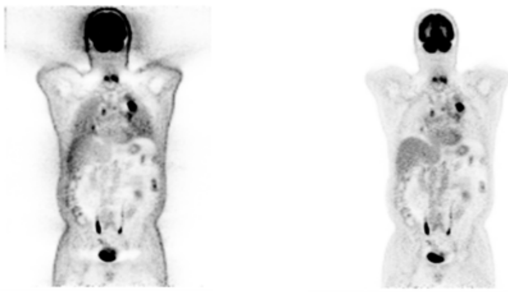
Attenuation + Scatter correction

No correction



Attenuation correction

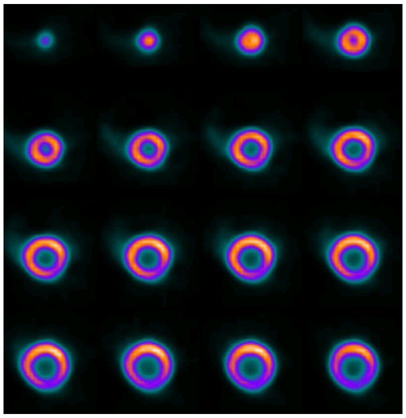
- Provides PET images closer to real radiotracer distribution
- Corrects attenuation-introduced geometric artifacts
- Improves lesion detection in deep organs
- Allows absolute quantitative PET studies

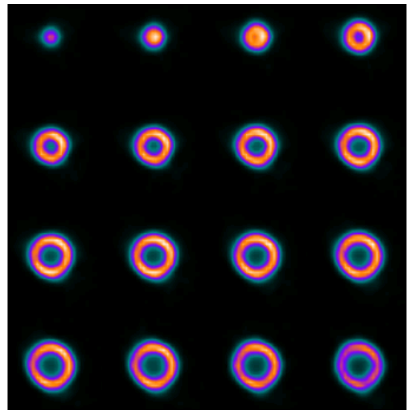


Without attenuation correction   With attenuation correction

Anthropomorphic phantom

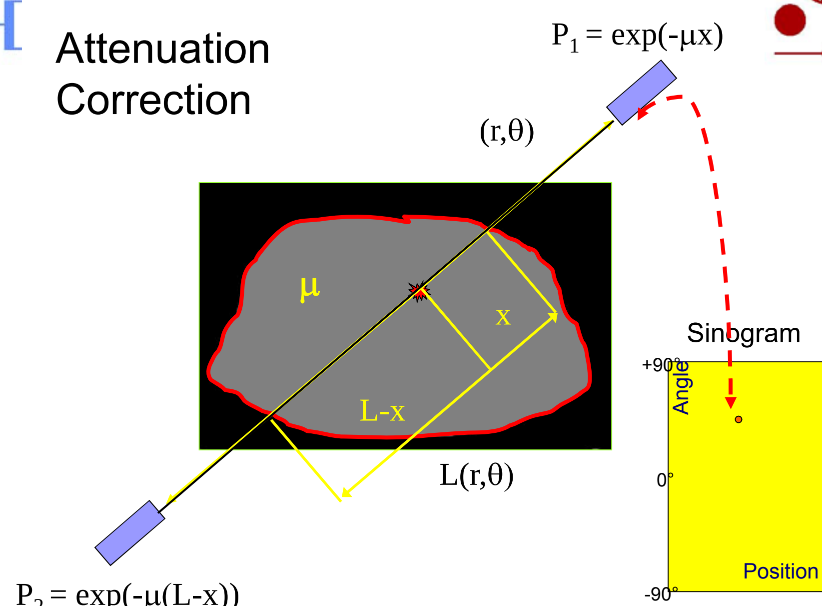
BEFORE Correction | AFTER Correction





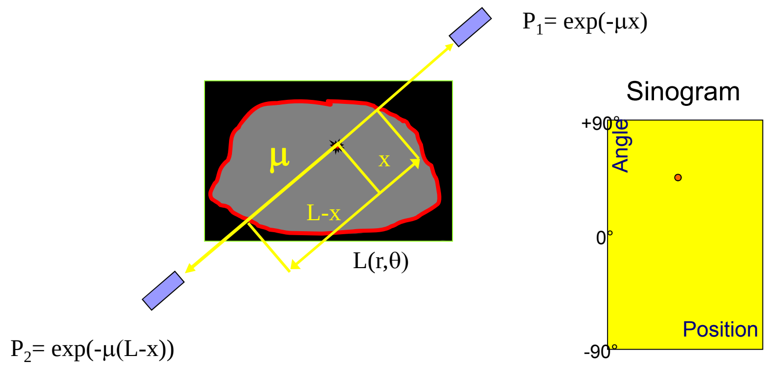
Conclusion: Correction may cure the patients…(?)

Attenuation Correction



Probability of a coincidence:

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



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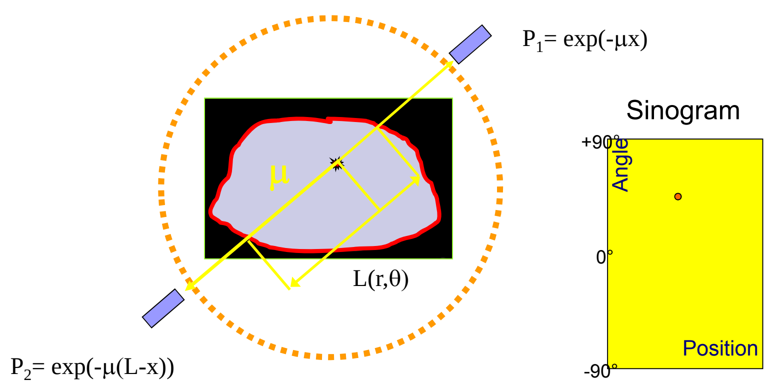
Probability of a coincidence:

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

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



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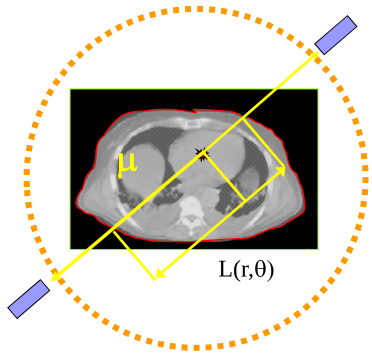
If μ is not a constant (and it IS NOT):

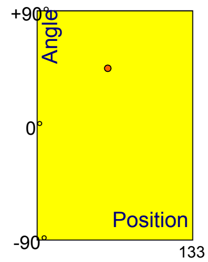
$$P_1 * P_2 = \exp\left(-\int_0^x \mu(x)dx\right) * \exp\left(-\int_x^L \mu(x)dx\right) = \exp\left(-\int_0^L \mu(x)dx\right)$$

still independent of the source position

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



Transmission Sinogram



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

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)

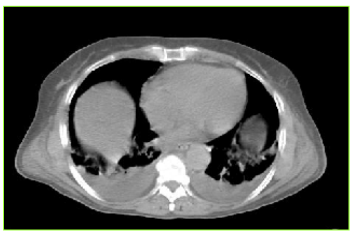
CT scans are μ-maps (in HU)

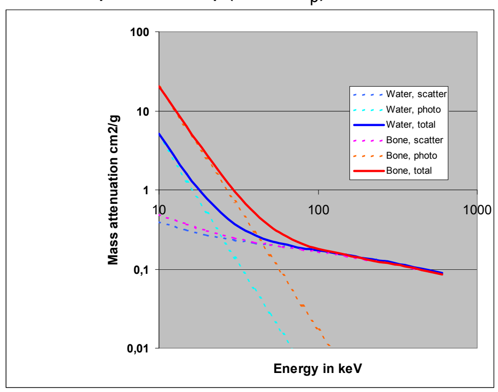
They can be used for attenuation correction – essentially noise free

But: $\mu(511\ \text{keV}) \neq \mu(80\ \text{keV})$, therefore a scaling is required

Soft tissue and bone (and contrast) scale differently

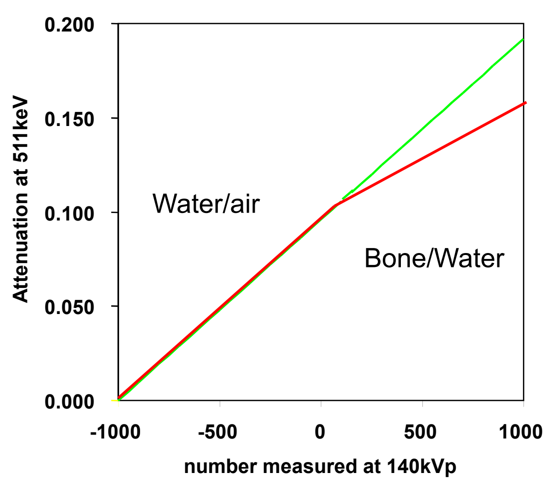
Not one simple scaling factor, but a lookup table for $\mu(\text{HU}; kV_p)$





Conversion of CT Numbers to μ_{PET}

- For CT values < 100 , materials are assumed to have an energy dependence similar to water
- For CT values > 100, material is assumed to have an energy dependence similar to a mixture of bone and water
- The green line shows the effect of using water scaling for all materials

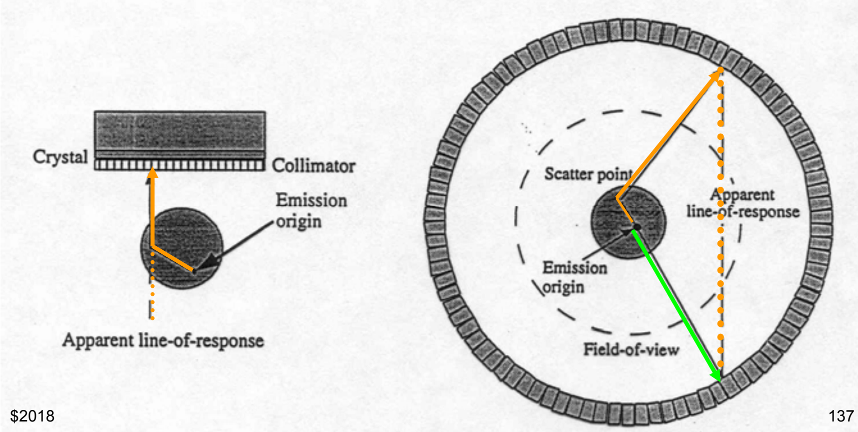


Scatter in

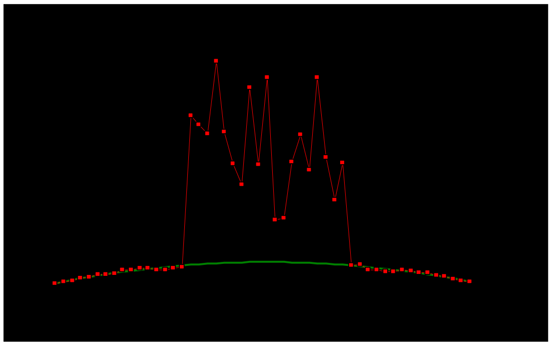
SPECT PET

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 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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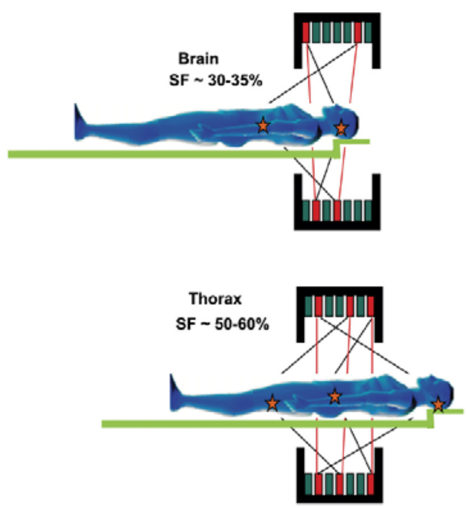
Scatter fractions in 3D PET



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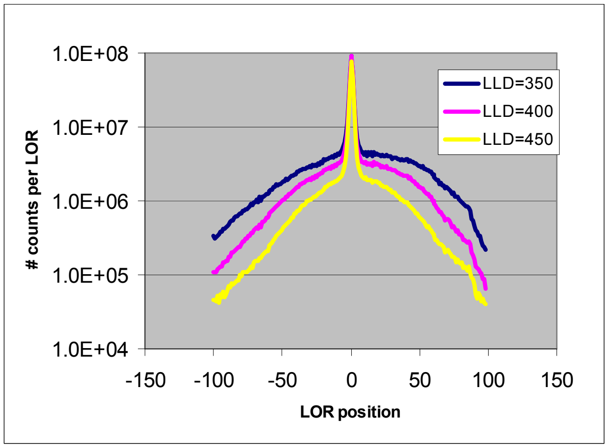
Scatter removal by energy discrimination



(keV)

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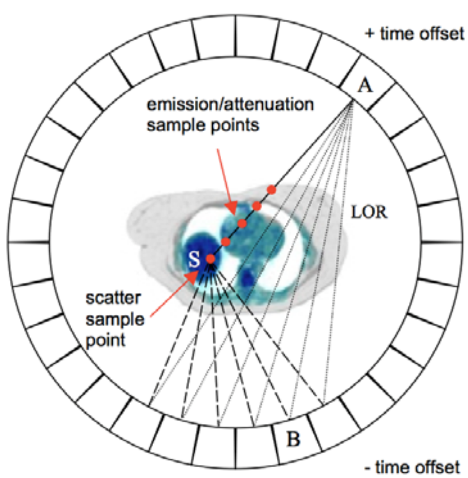
Scatter correction



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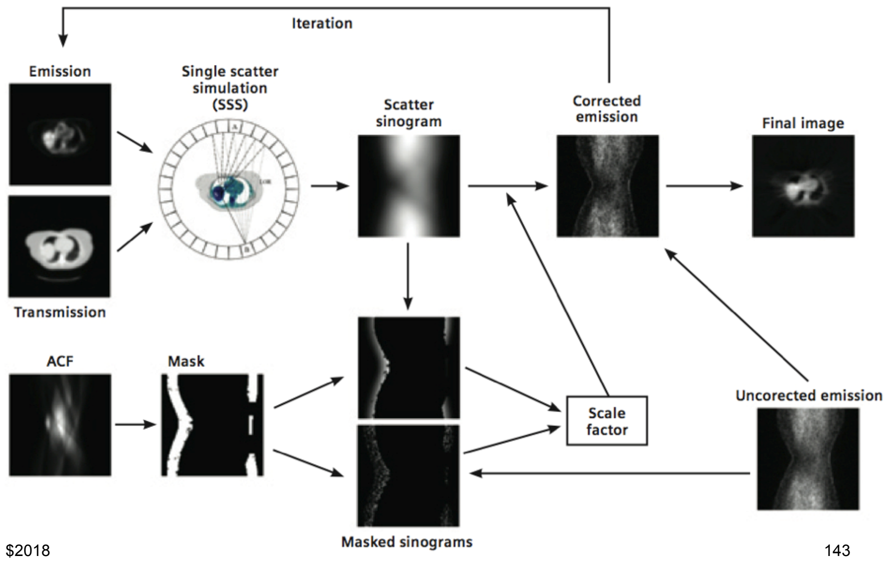
Scatter correction



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

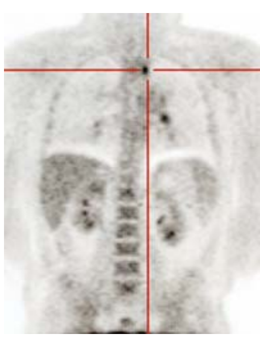
- Resolution and noise
- Scanner physics 1 – PET detectors
- Scanner physics 2 – good, bad, and noise equivalent counts (NEC)
- Attenuation and scatter correction of PET-data
- Hybrid systems – PET/CT- PET/MR - SPECT/CT… Future ideas

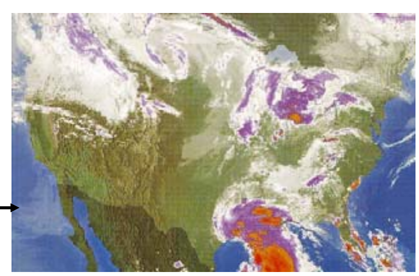
Good reasons to combine PET and CT:

- 0: Because it was possible *(MR more difficult)*
- 1: Complementary information
  - structure + function
  - anatomy + physiologi/biochemistry
- 2: Exact localization (”free” coregistration)
- 3: Improved attenuation correction in PET

Functional Images

PET Images
“abnormal activity”

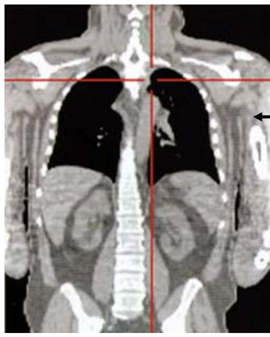




Weather Patterns
“weather activity”

GE imagination at work

Structural Images



CT Images

"precise body's anatomy"

Geographic Map

"precise outlines of the states"

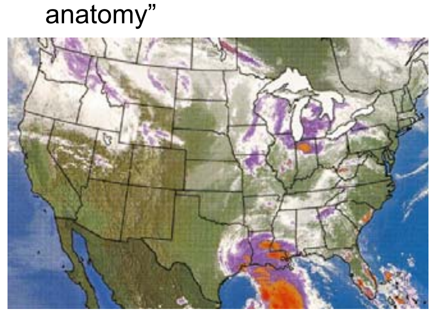
GE imagination at work

$2018 147

Fusion Images

Discovery PET/CT Images

"abnormal activity **and** precise body's anatomy"



USA Weather Map

"intense weather **and** precise outlines of the states"

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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
  and a few others
- \- with more than 5000 installations worldwide

- Since 2005, almost NO stand-alone PETs have been installed

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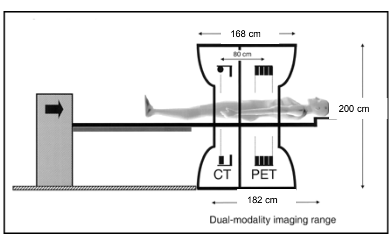
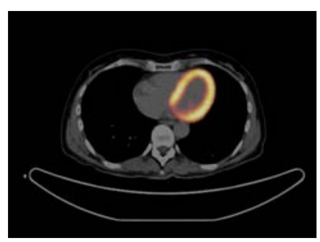
PET/CT (or SPECT/CT) scanner:





(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

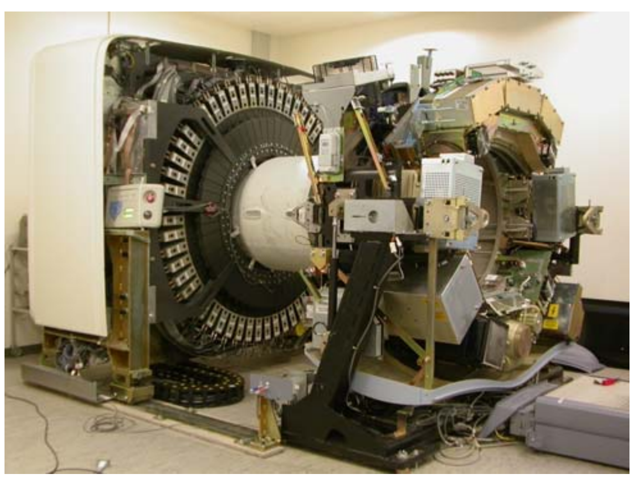
Advance NXI + Lightspeed plus

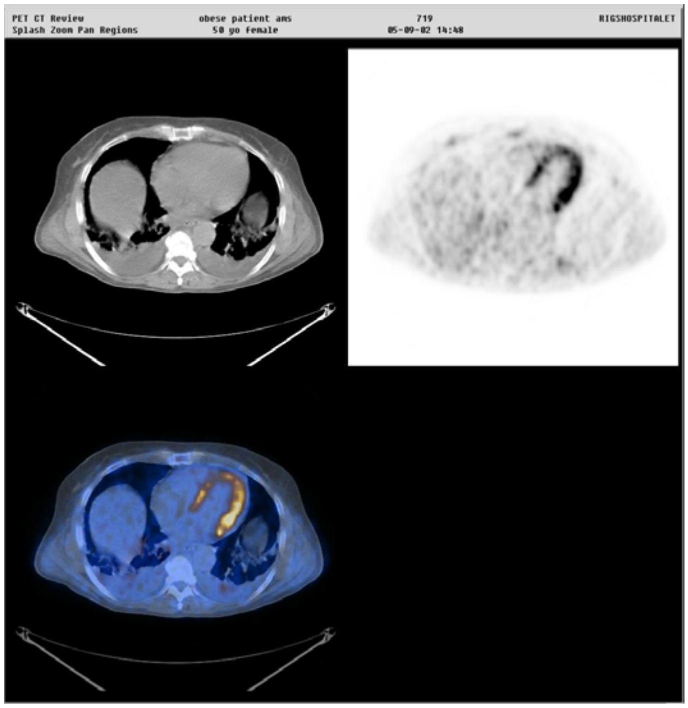
Detector

material

BGO

Inside Discovery LS





PET/CT (images from around 2005)

Herlev
Hillerød
Vejle (2)
Århus Skejby RT

Philips Gemini (KAS Herlev)

Siemens Biograph (RH)

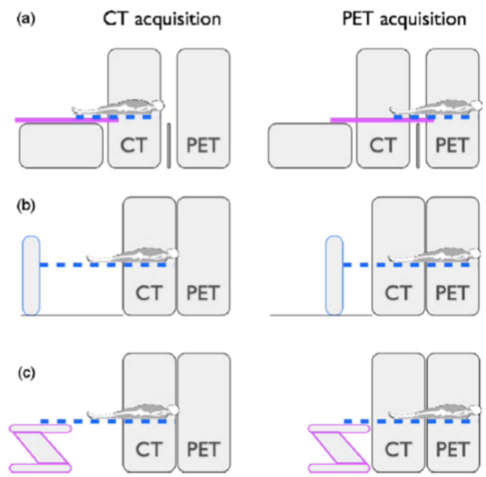
RH (5)
Næstved (2)
Århus PET (2)
Århus NUK
Herning
Herlev (3)
Glostrup

GE Discovery (Milano San Raffaele)

Odense (5)
Ålborg (2)
Køge (2)
Århus Skejby
Hvidovre
Gentofte
Bispebjerg (3)

PET/CT instrumentation: adding CT

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



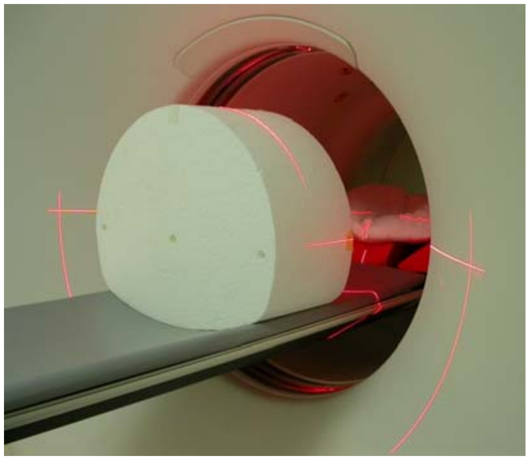
PET –CT alignment /registration

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

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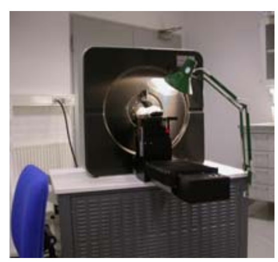
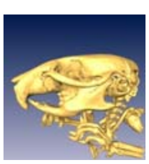
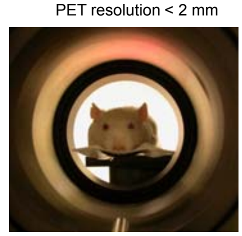
Small Animal PET-CT



CT resolution down to 15 μ



PET resolution < 2 mm



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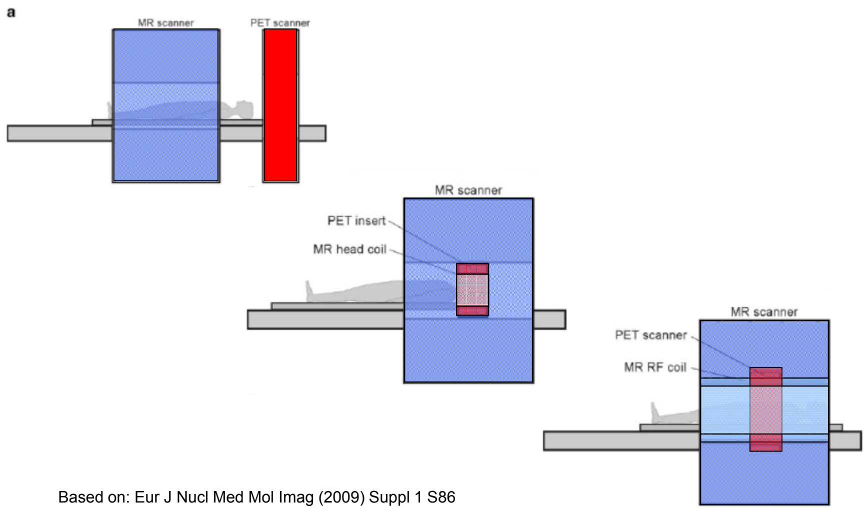
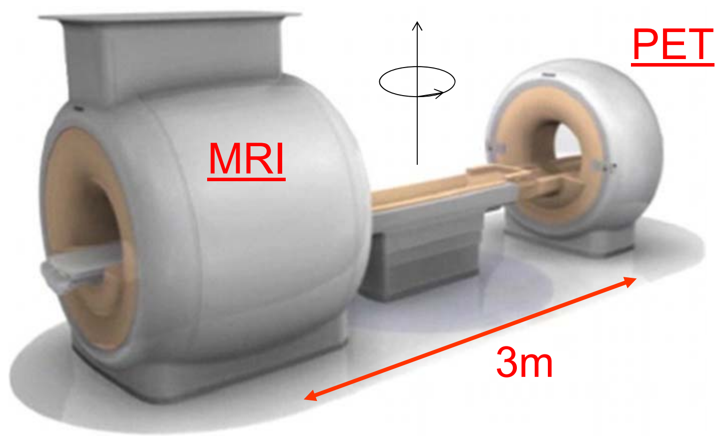
Potential PET-MR configurations



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 is now available

- 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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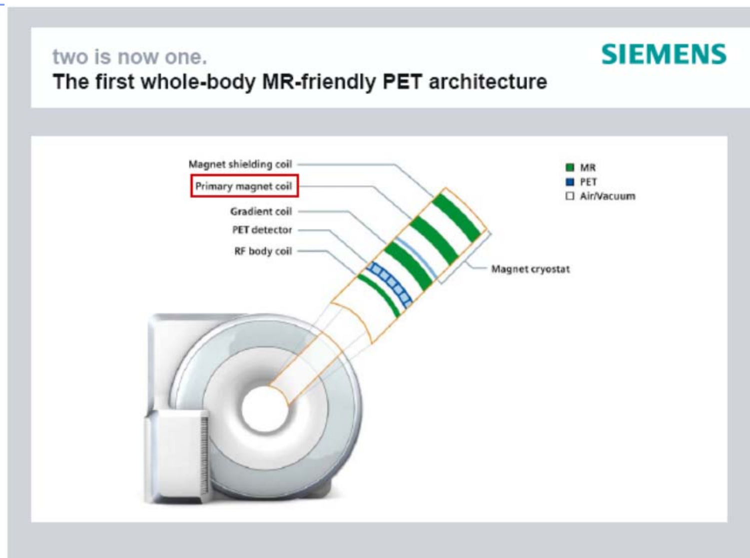
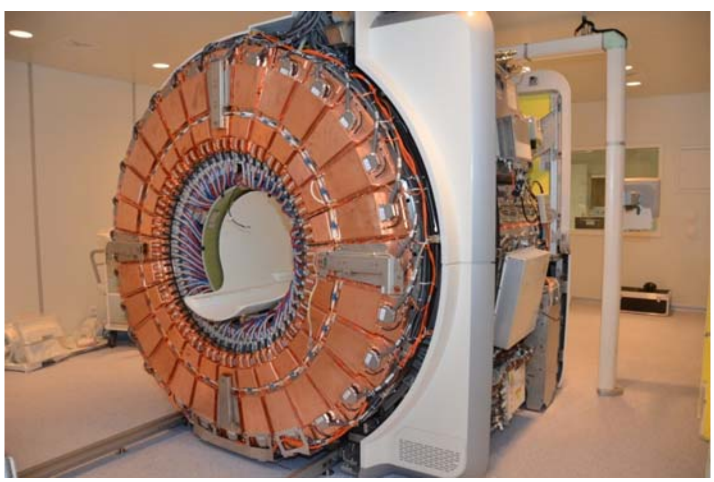
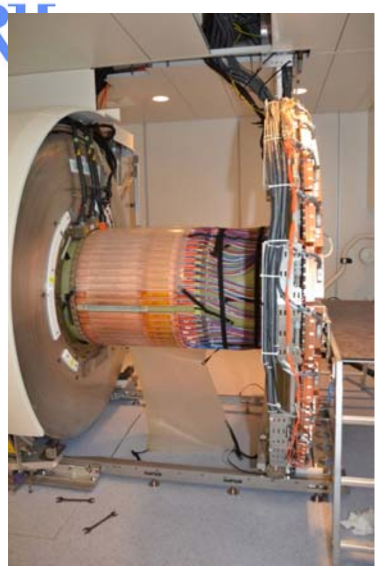


PET/MR



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



PET(/MR) service (PET module exchange)

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Arrival: 29.November 2011

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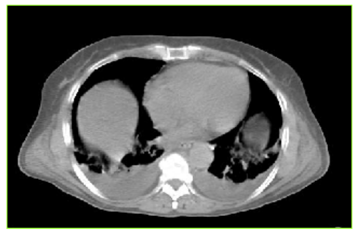
Arrival: 29.November 2011

Inauguration 14.December 2011

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)



In PET/MR:

Attenuation correction is a challenge (and a current 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

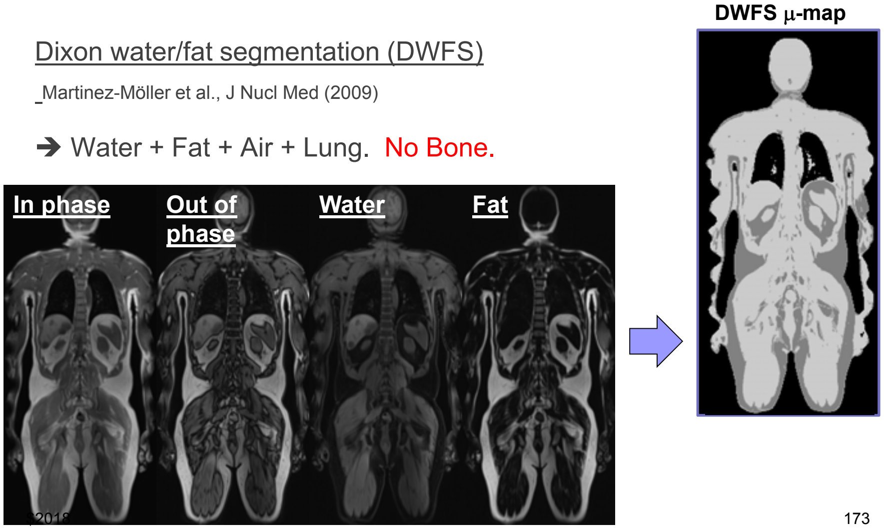
MR-based attenuation correction

Dixon water/fat segmentation (DWFS)

_Martinez-Möller et al., J Nucl Med (2009)

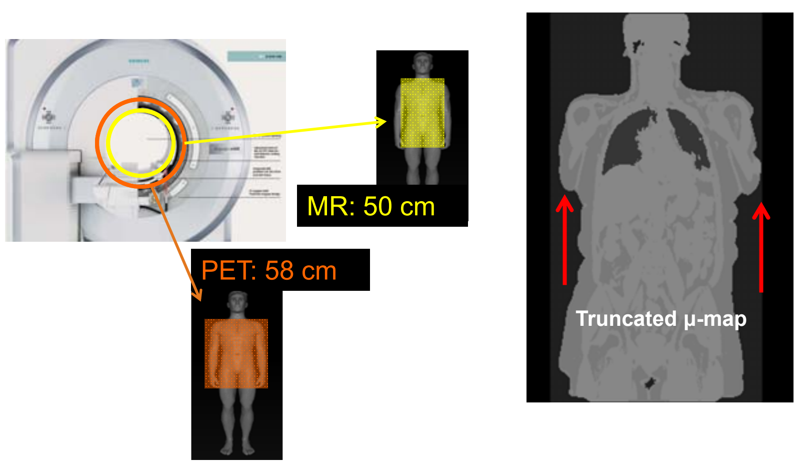
➔ Water + Fat + Air + Lung. No Bone.

DWFS μ-map

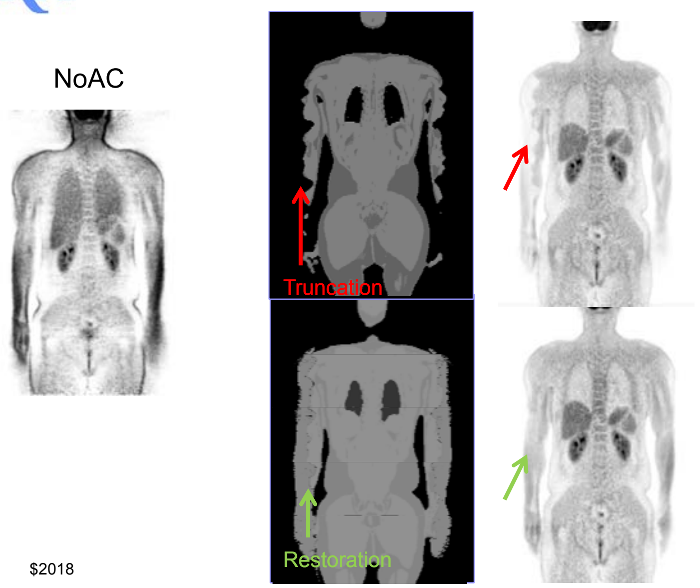


Truncation = Mismatch of transverse field-of-view

”Arms down” is standard position in PET/MR



Keller et al, Magnet Reson Mater Phys (2012)



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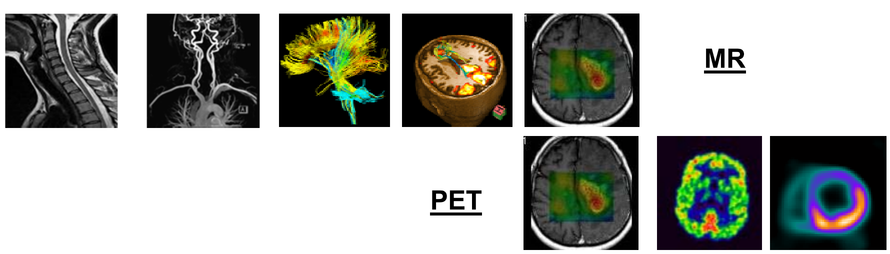
Vision:

Morphology, physiology & molecular imaging
……….in one scanner …simultaneously



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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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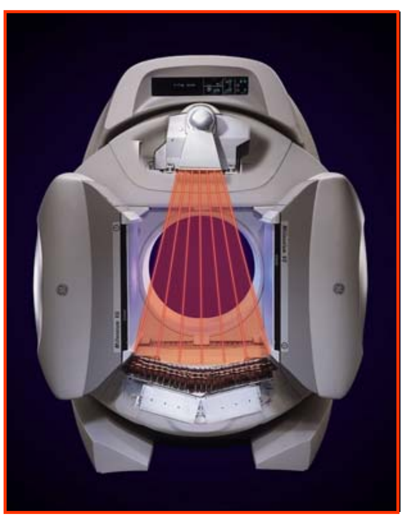
SPECT/CT (GE Hawkeye)



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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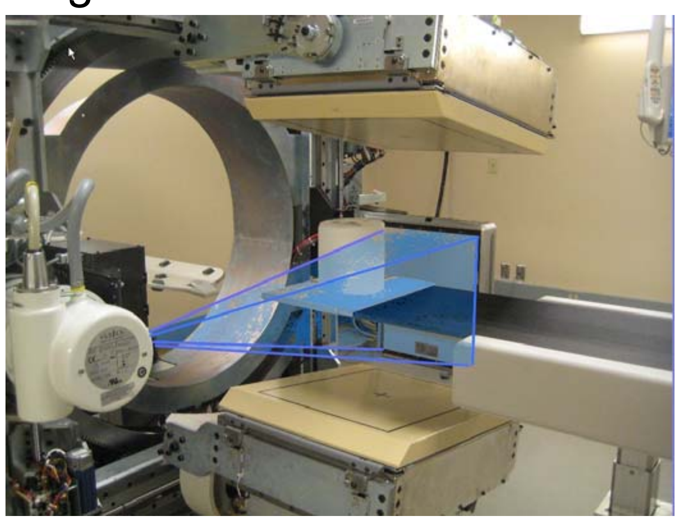
BrightView XCT SPECT/CT



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Combinations...

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

$2018 Exhibition EANM October 2012 181

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

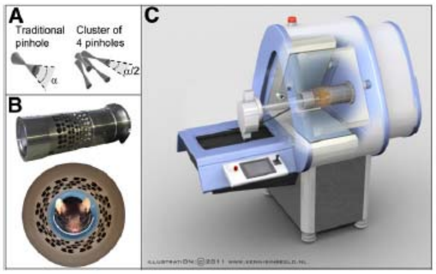

FIGURE 1. Integration of clustered-pinhole collimator into existing SPECT/CT platform. (A) Traditional pinhole with opening angle α and cluster of 4 pinholes with approximately same field of view and opening angle α/2. (B) Clustered-pinhole collimator optimized for imaging SPECT and PET tracers, into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

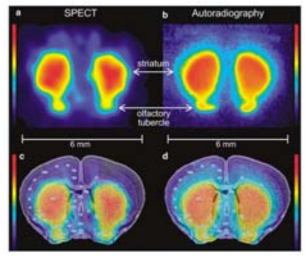

Figure 2 High resolution *in vivo* imaging of striatal DAT (left) compared with DAT autoradiography (right).

MILabs G-SPECT

• Game-Changing SPECT

Spectrum Dynamics D-SPECT

CZT

= CdZnTe

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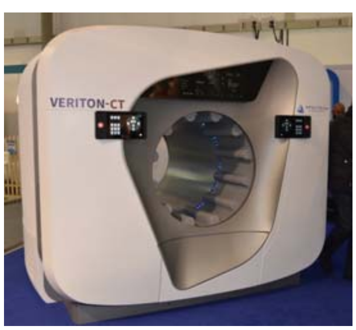
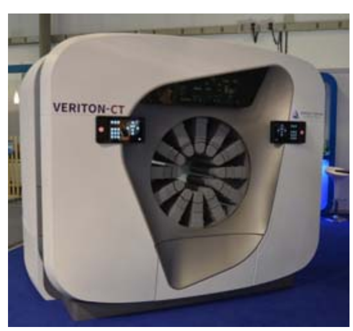
Spectrum Dynamics Veriton-CT

CZT = CdZnTe





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PET / SPECT / CT

AnyScan

Mediso
Budapest

Exhibition at
EANM 2008

Still marketed

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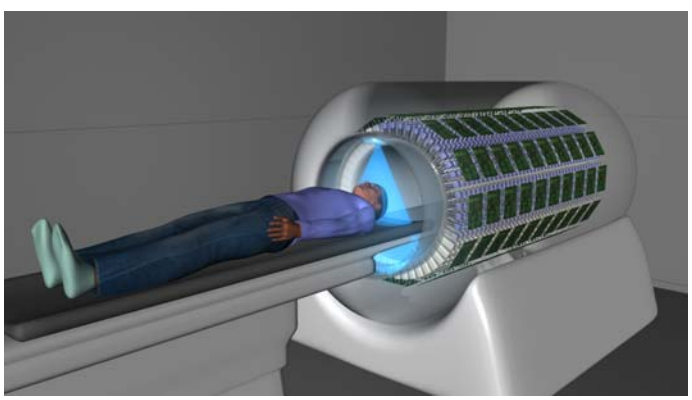
EXPLORER



UCDAVIS
UNIVERSITY OF CALIFORNIA

BERKELEY LAB

Penn
UNIVERSITY of PENNSYLVANIA

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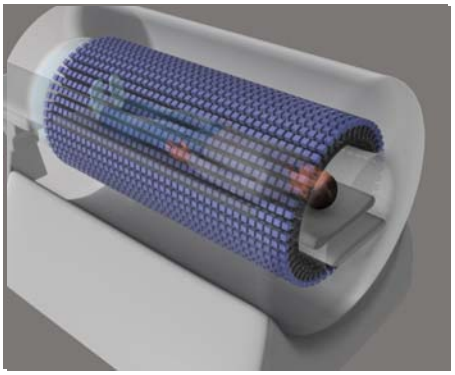
Maximizing Sensitivity by Total-Body PET



~40-fold increase
for adult total-body imaging

~20-fold increase
for pediatric total-body imaging

~4-fold increase
for single organ imaging

Applications

Systemic disease and therapies:
- Cancer: Ultra-staging and micrometastasis
- Inflammation
- Infection
- Cellular therapy and trafficking
- Mind-body interactions

Total body pharmacokinetics
- Drug development
- Toxicology
- Biomarker discovery

Low dose opens up new populations:
- Expanded use in pediatrics
- Use in chronic disease
- Studies of normal biology

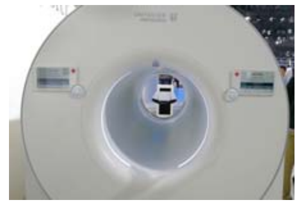
Completed EXPLORER Scanner

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

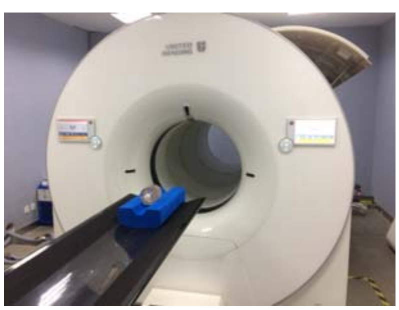
# of crystals: 564,480
crystal blocks: 13,440
of SiPMs: 53,760

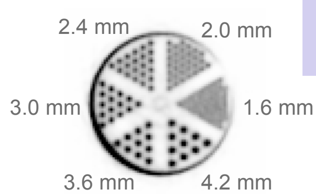
80 detector row CT

UNITED IMAGING

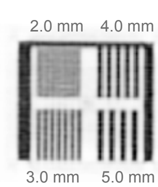




Preliminary Resolution Tests





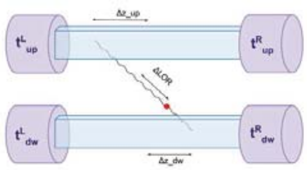
mini Derenzo:
8 billion prompts
transaxial slice

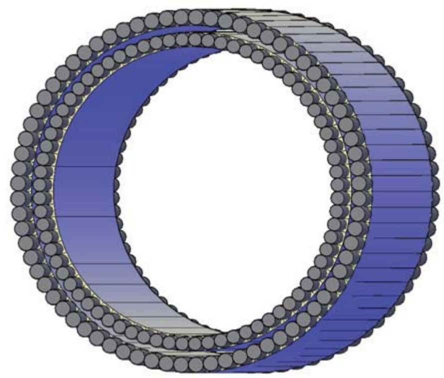


axial bar:
12 billion prompts
sagittal slice

J-PET

Longitudinal plast-scintillators

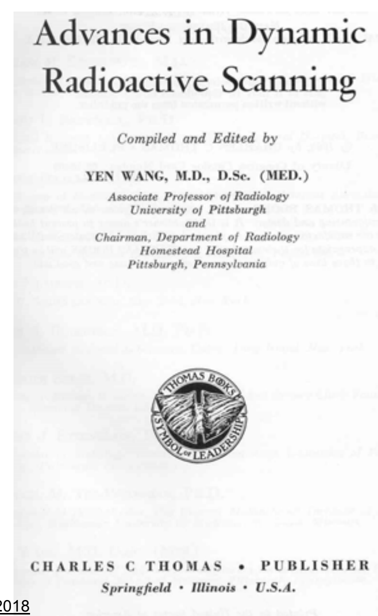




P Moskal *et al*

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

1968 PET


Advances in Dynamic Radioactive Scanning

Compiled and Edited by

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

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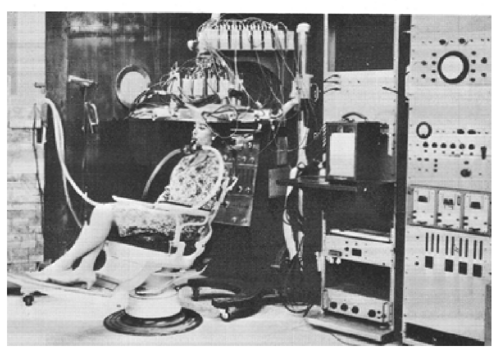
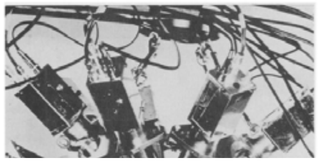
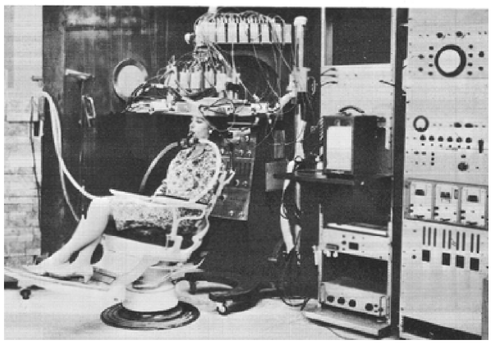


1966 **2015**





Development of the Helmet-Chin PET Prototype

Chiba, Japan [Poster M3CP-97 at MIC2015]

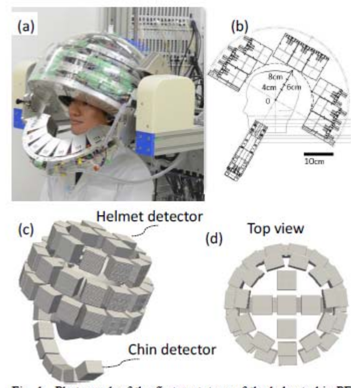
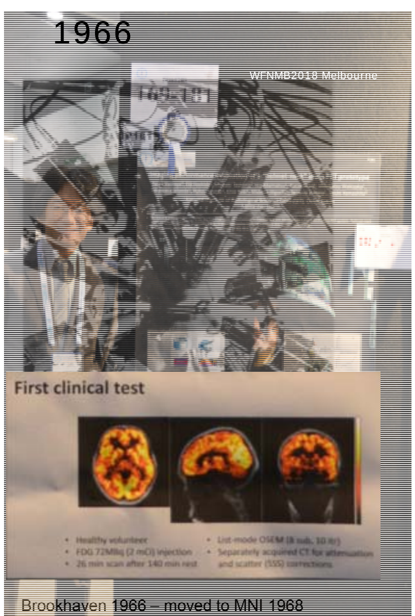


Fig. 1. Photograph of the first prototype of the helmet-chin PET (a), design sketch (b), and geometry of the crystals (c), (d).

 Brookhaven 1966 – moved to MNI 1968



2015

Development of the Helmet-Chin PET Prototype

Chiba, Japan [Poster M3CP-97 at MIC2015]

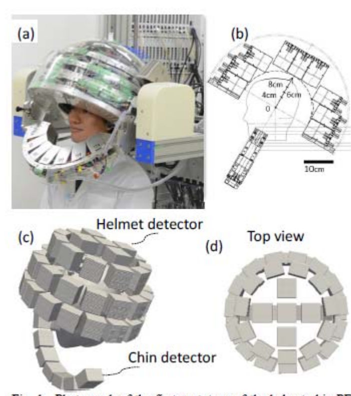


Fig. 1. Photograph of the first prototype of the helmet-chin PET (a), design sketch (b), and geometry of the crystals (c), (d).

$2018 Brookhaven 1966 – moved to MNI 1968

Could this become a ”trend” ?

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

THEN it is likely to.

Time to press…