# Introduction to Positron Emission Tomography


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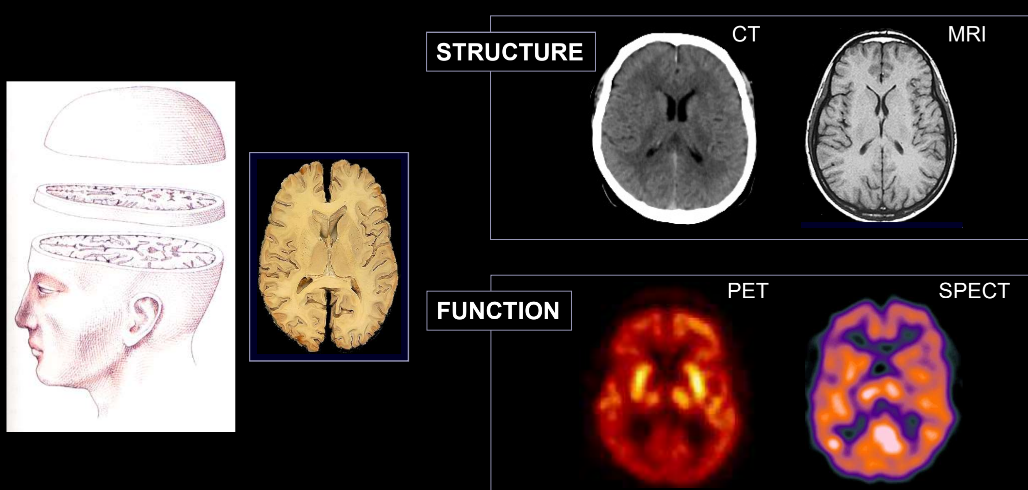
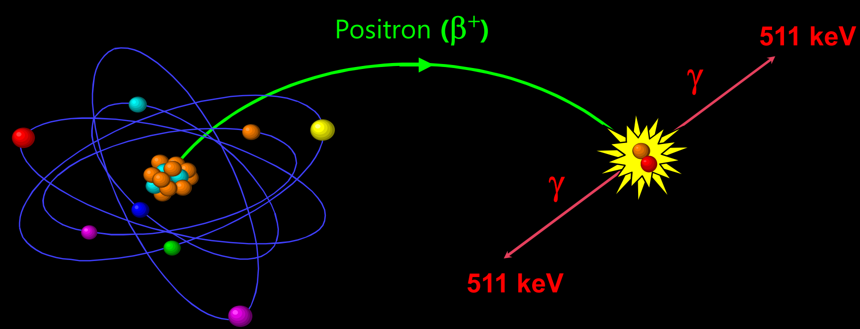
*Director of National Brain Mapping Laboratory*


## Structural & Functional Imaging



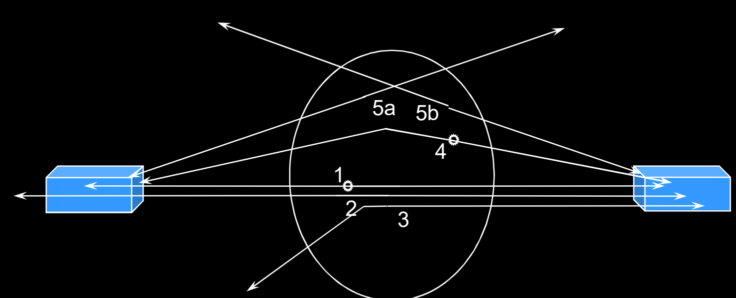

Nuclear Medicine is to physiology as Radiology is to anatomy

# PET Physics: Positron Decay




***The radioisotope emits a positron.***
***The positron produced interacts with an electron. A reaction transforms the two particles into two photons of 511 keV emitted in exactly opposite directions.***

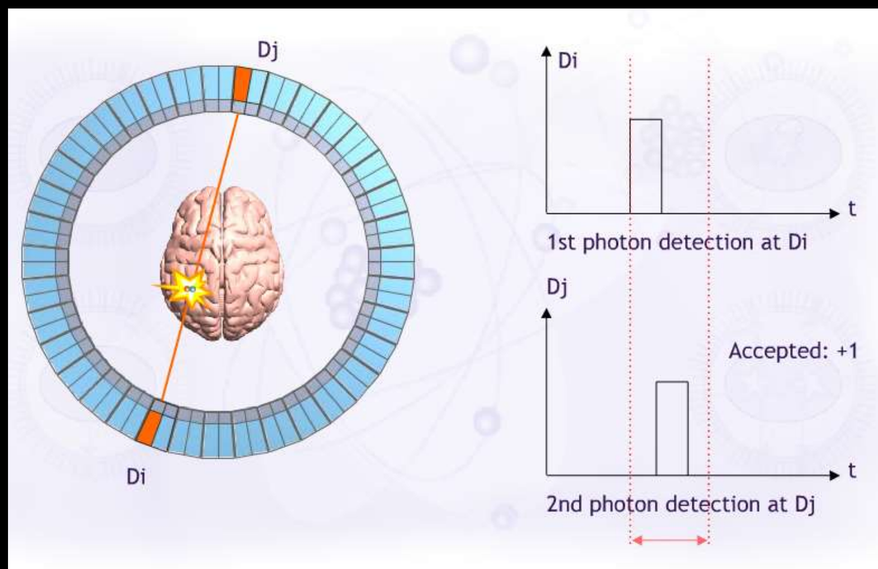
# Coincidence Events




1. **Detected True Coincidence Event**
2. **True Event Lost to Sensitivity or Deadtime**
3. **True Event Lost to Photon Attenuation**
4. **Scattered Coincidence Event**

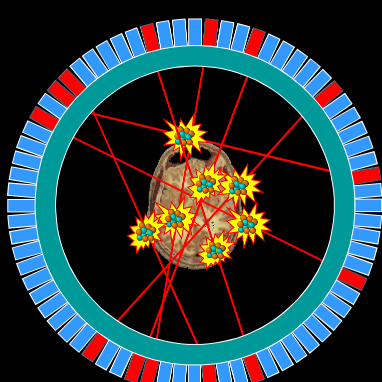
**5a,b. Random Coincidence Event**

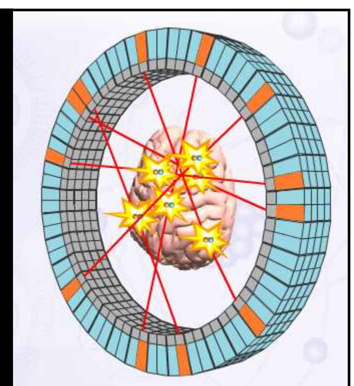
## Coincidence Detection

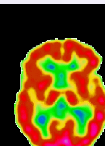



## PET data acquisition

Detector ring





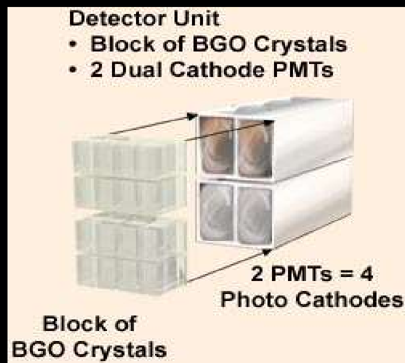


*The response lines joining the detector pairs having recorded coincidence events are used for clinical data reconstruction*

***PET = Positron Emission Tomography***

## The Block Detector

***The detector block consists of a block of BGO crystals in front of a set of PMT's***



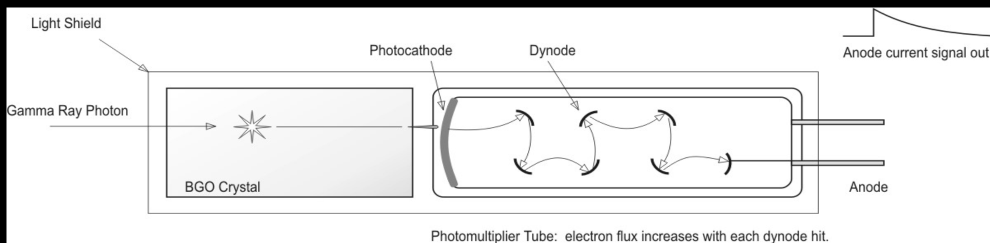

***4mm x 8mm x 30mm***

## Detectors for PET

| **Scintillator** | BGO | LSO | GSO | LuAP | $LaBr_3$ | LYSO |
|---|---|---|---|---|---|---|
| Formula | $Bi_4Ge_3O_{12}$ | $Lu_2SiO_5$:Ce | $Gd_2SiO_5$:Ce | $LuAlO_3$:Ce | $LaBr_3$:Ce | $LuYSiO_5$:Ce |
| Density (g/cc) | 7.13 | 7.4 | 6.71 | 8.34 | 5.3 | 7.1 |
| Light yield (photons/keV) | 9 | 25 | 8 | 10 | 61 | 32 |
| Effective Z | 75 | 66 | 60 | 65 | 46.9 | 64 |
| Principal decay time (ns) | 300 | 42 | 60 | 18 | 35 | 48 |
| Peak wavelength (nm) | 480 | 420 | 440 | 365 | 358 | 420 |
| Index of refraction | 2.15 | 1.82 | 1.95 | 1.95 | 1.88 | 1.8 |
| Photofraction (%)* | 41.5 | 32.5 | 25 | 30.6 | 15 | 34.4 |
| Attenuation length (cm)* | 1.04 | 1.15 | 1.42 | 1.05 | 2.13 | 1.12 |
| Energy resolution (%)* | 12 | 9.1 | 7.9 | 11.4 | 3.3 | 7.1 |
| Hygroscopic | No | No | No | No | Yes | No |

*@ 511 keV

# Crystal and Photomultiplier Tube




**Tubes?  Why are we using tubes?**

- **High Gain (>1,000,000)**
- **Low-noise signal**
- **Fast timing response**
- **Small timing variance**

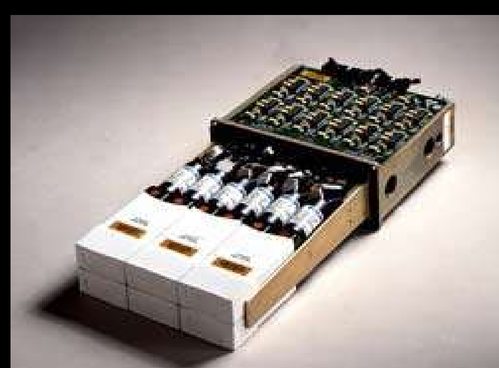
# PET DETECTOR BLOCKS

***Scintillation***

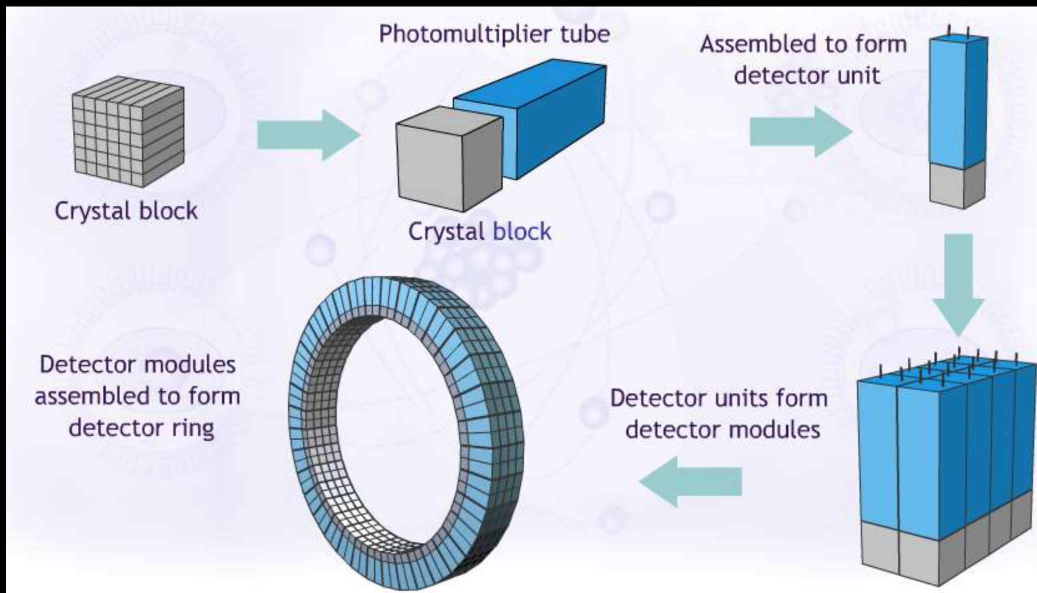
***Conversion in the PMT***

***Amplification with the dynodes***

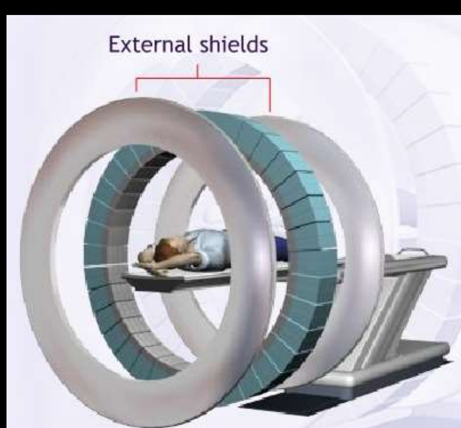
***A low level current output signal***

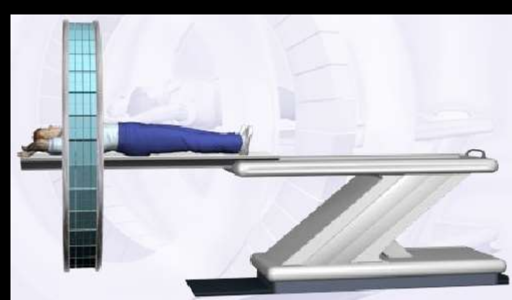


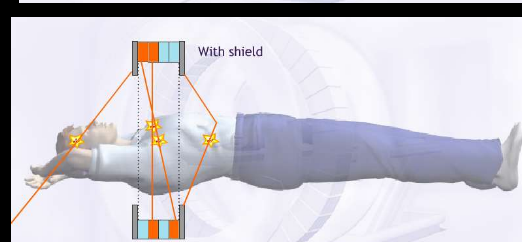
## Detector Ring



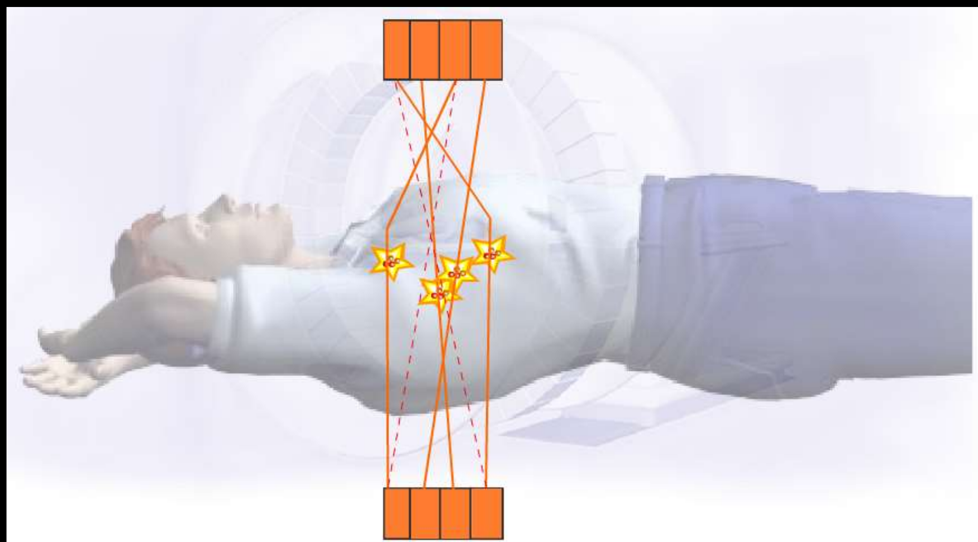

## PET Detection External Shield



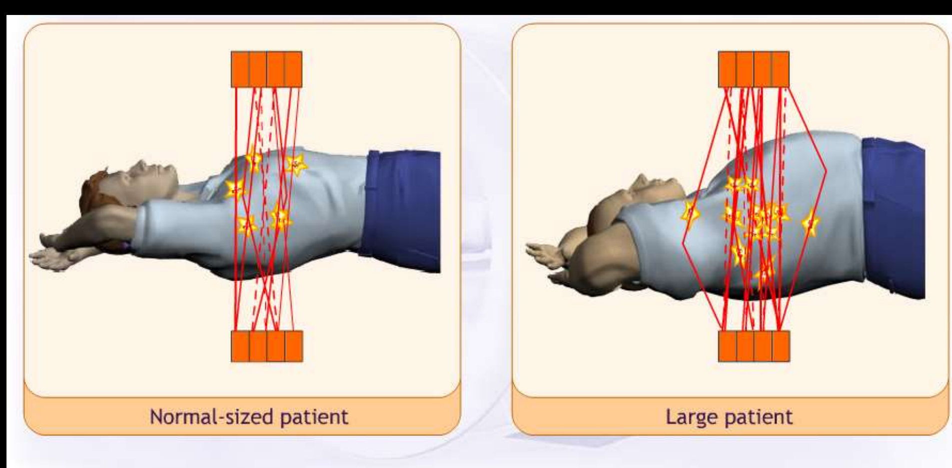





## 3D Data Acquisition

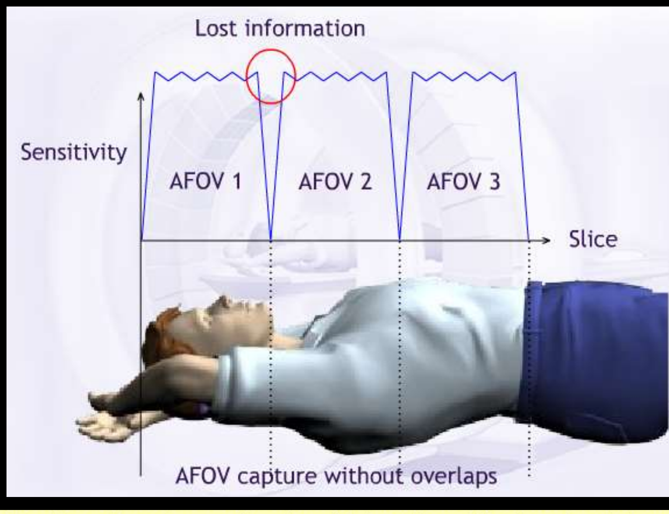


## Influence of Patient Size



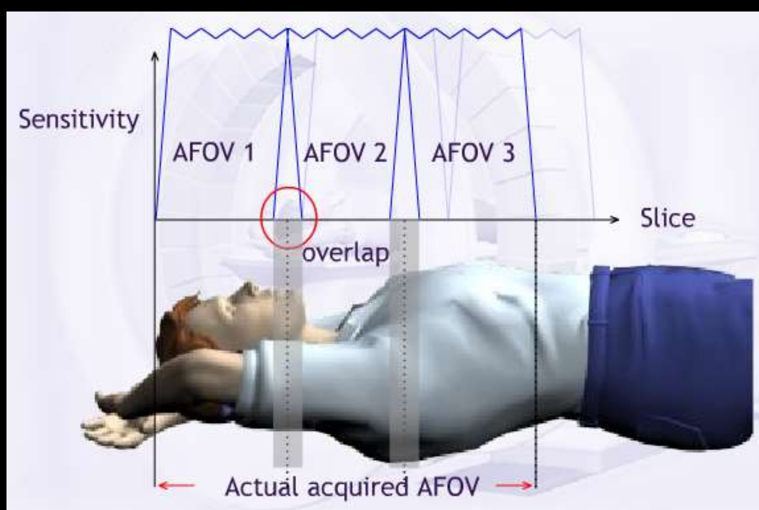

Large patients tend to have an increased number of random and scatter events due to their complex anatomical structure. This is also observed when high dose has been injected.

## Data Collection



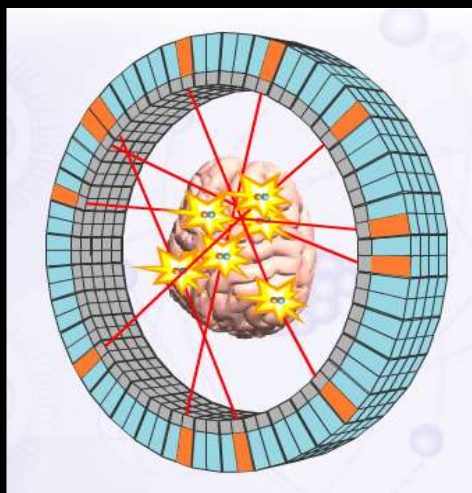

While taking slices, there is normally a loss of information at the boundary between two AFOVs. So, when scanning several AFOVs, you need to overlap them in order to have completeness and uniformity over the acquisition area.

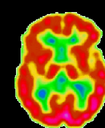
## Data Collection (Overlap Bed Position)




While taking slices, there is normally a loss of information at the boundary between two AFOVs. So, when scanning several AFOVs, you need to overlap them in order to have completeness and uniformity over the acquisition area.

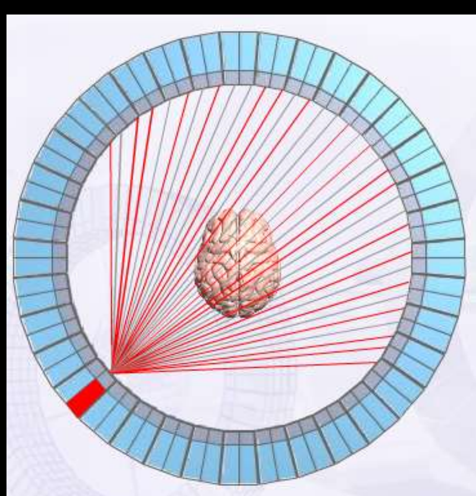
## Line of Response Concept

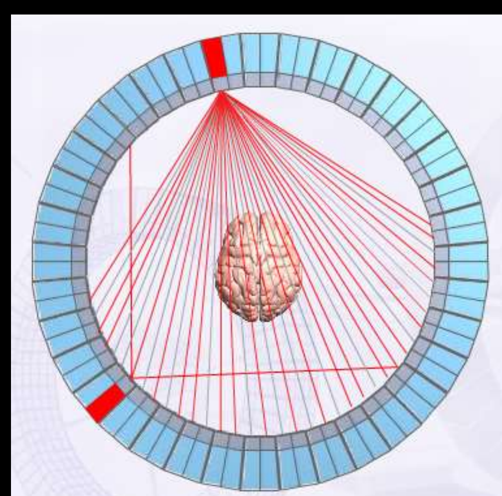




*The response lines joining the detector pairs having recorded coincidence events are used for clinical data reconstruction*

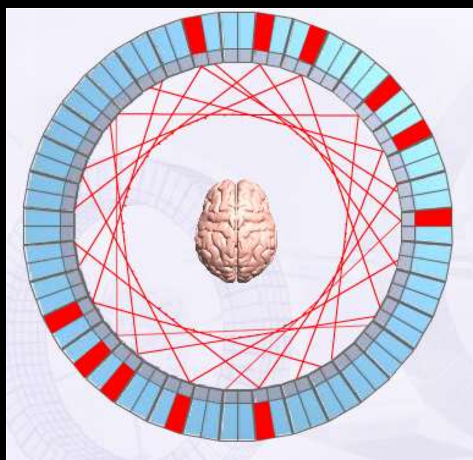
## LOR and Acceptance Angle

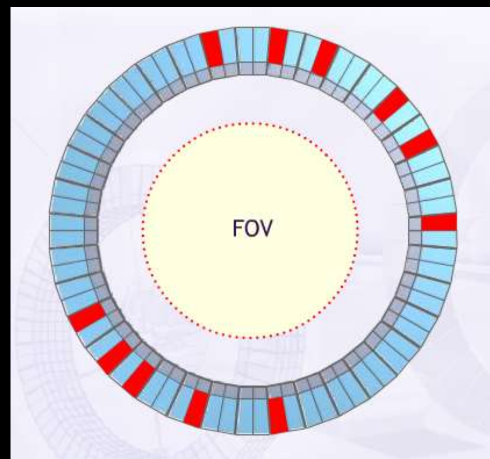




For every detector, events are searched within a range of opposite detectors.

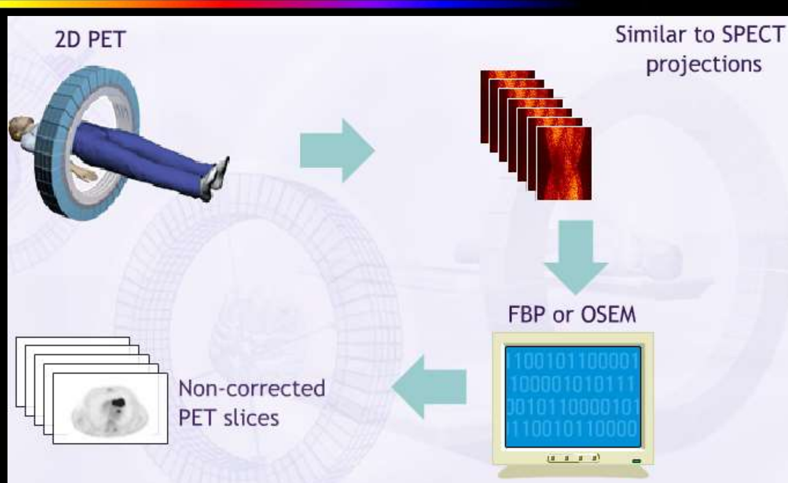
## Trans Axial FOV






The FOV results from checking the LORs in all the detectors.

## Reconstruction of 2D Acq




Because 2D sinograms are similar to SPECT projections, you can use FBP or OSEM to create PET slices. These slices can be attenuation-corrected or non-corrected. OSEM is recommended in routine oncology.

# Image Reconstruction

**PET uses a reconstructive technique, using an array processor (AP) to take the sinograms and reconstruct the image. Imagine the computer drawing all the LOR's it created, and then putting a dot at where the LOR's intersect. This is done in two steps:**

**Preprocessing**: This step makes corrections to the data for physics induced errors.

**Backprojection**: The mathematical process of estimating the distribution of the radiopharmaceutical from a set of projections.

The reconstruction process has heavy computation demands. After it's all done, the image is ready for the operator's console.

# Reconstruction Software

**There are two ways to improve the back-projected reconstruction:**

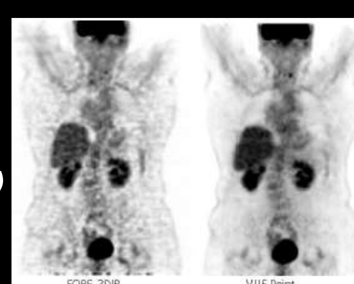
| | |
|---|---|
| - Filtering | Filtered Back-Projection (FBP) |
| - Iteration | Iterative Reconstruction |

***Iterative Reconstruction***

There are many types of Iterative Reconstruction methods. All the early CT reconstructions were iterative before Filtered Back-projection became standard. For SPECT and PET studies the most widely recommended type is the

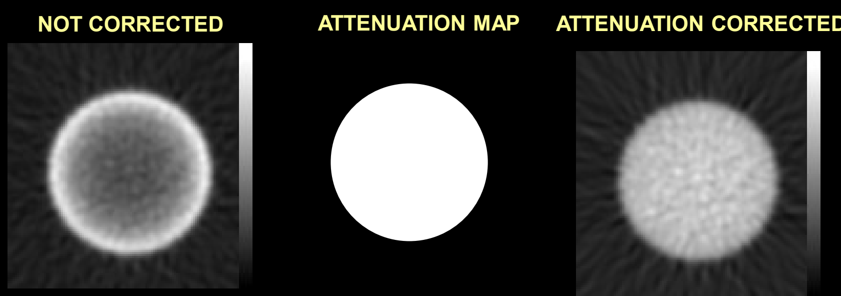
**M**aximum **L**ikelihood family, using the
**E**xpectation **M**aximization algorithm ***( ML-EM )***

*A major attraction of this algorithm is its simplicity*



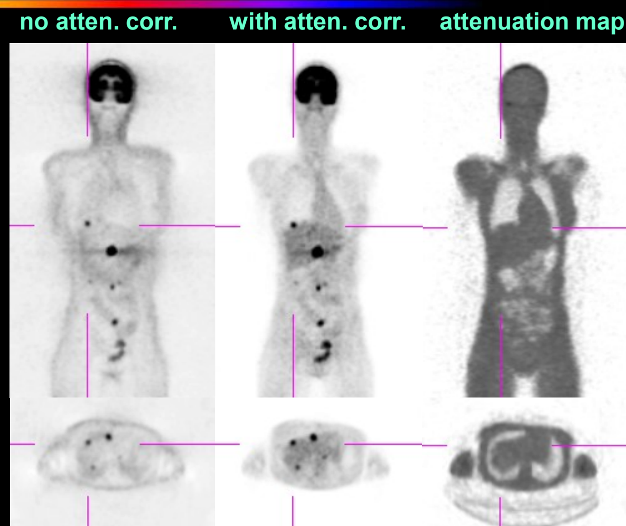
## Photon Attenuation

- Generate inaccurate Activity Distribution
- Decrease Lesion Detectability
- Produce Image Artifacts
- Decrease Image Quality



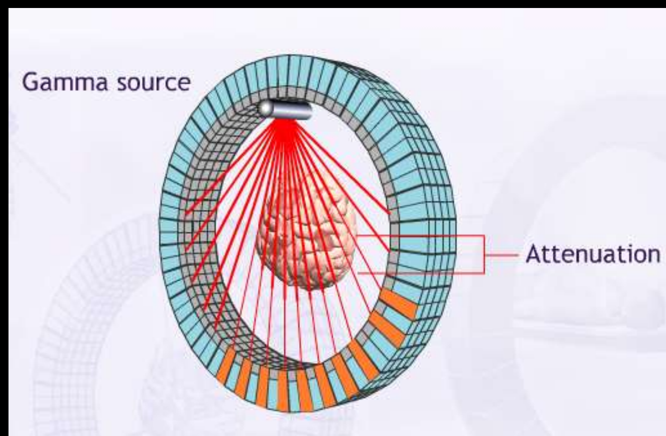

Zaidi and Hassegawa (2003) *J Nucl Med* **44:** *291-315*

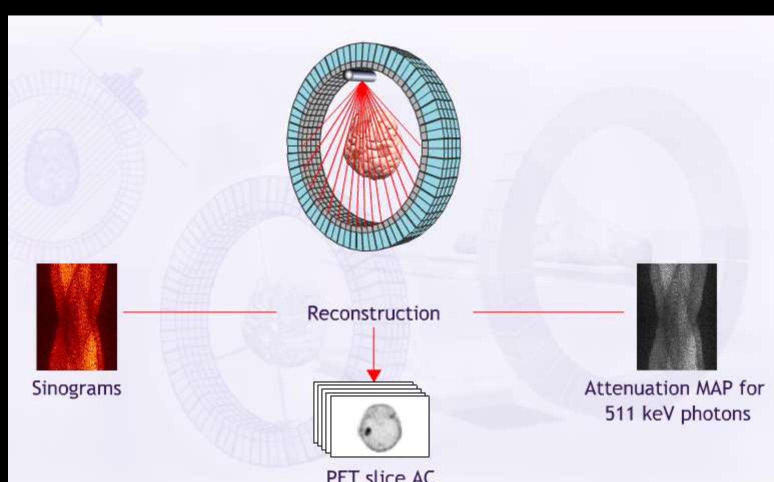
## AC or not AC?




Attenuation correction:

- improves localization
- no effect on lesion detection???

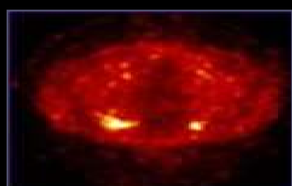


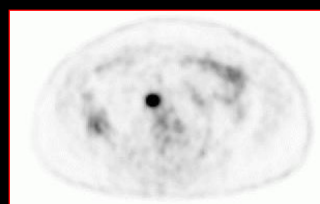



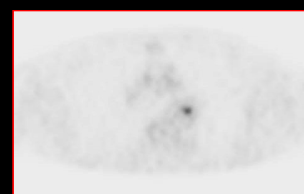

During a PET scan, you can create the attenuation map using the transmission scan. The sinograms and attenuation MAP are then used to reconstruct attenuation-corrected PET slices

## Limitation of Functional Imaging

- *LIMITED SPATIAL RESOLUTION*
- *POOR SIGNAL TO NOISE RATIO*
- *POOR UPTAKE TO THE RADIOTRACER IN THE DISEASED CONDITION*







*REGISTERATION WITH AN ANATOMICAL IMAGE CAN BE USEFUL……*

## Conventional Off-Line Image Fusion

*THE FIRST OFF LINE IMAGE FUSION IN NUCLEAR MEDICINE WAS REPORTED BY KUHL IN 1966. THEY OVERLYING GAMMA CAMERA IMAGE WITH THE CHEST X-RAY IMAGE AND DRAWING THE BOUNDARIES OF THE DIAFRAGM.*

*FUSED BY H.N. Wagner IN 1968*

# Computerized Off-Line Image Fusion

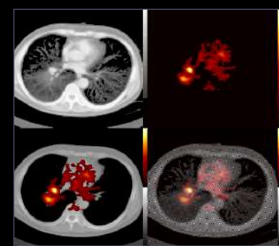
*WITH INTRODUCING THE COMPUTER IN 1970s THE OFF-LINE IMAGE FUSION DEVELOPED:*

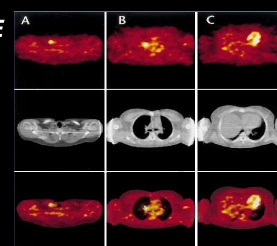
*IN THE BIGINING OF 1980s COPUTERIZED REGISTRATION ALGORITH WERE DEVISED*

*A MAJOR STEP FORWARD IN IMEGE REGISTRATION CAME IN THE FIRST HALF OF THE 1990s WITH DEVELOPMENT OF FULLY AUTOMATIC REGISTRATION ALGORITHM*

*A SIGNIFICANT BREAKTHROUGH IN THE MID 1990s WAS THE DEVELOPMENT OF IMAGE ALIGNMENT AND REGISTERATION ALGORITHMS BASED ON ENTROPY THEORY*

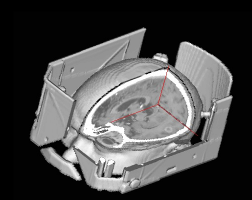
*RAPID ADVANCES IN POWER OF COMPUTER TECHNOLOGY INCREASES THE USE OF COMPUTERIZED OFF-LINE FUSION*

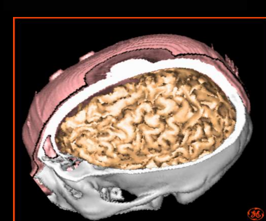





# Off-Line Fusion Disadvantage

- *IT IS VERY SENSITIVE TO PATIENT MOTION*
- *IT IS TIME CONSUMING METHOD*
- *IT IS ONLY ACCURATE FOR RIGID ORGANS SUCH AS BRAIN*
- *THIS METHOD USE ONLY FOR IMAGE REGISTRATION, NOT CORRECTION*



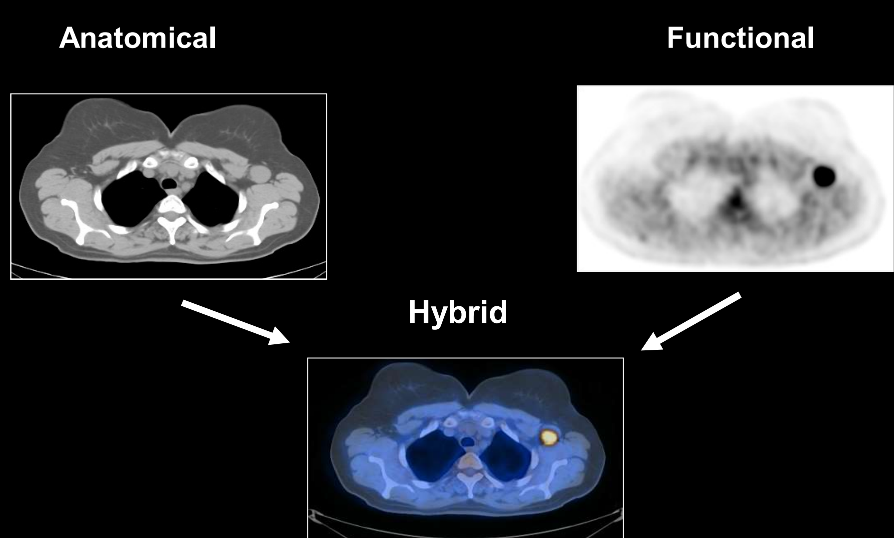


*BECAUSE OF THIS PROBLEMS THE RESERCHERS TRY TO DESIGN A SYSTEM FOR ON LINE FUSION .......*

# Outline

- PET PHYSICS & INSTRUMENTATION
- LIMITATIONS OF QUANTITATIVE 3D PET IMAGING
- OFF-LINE IMAGE FUSION
- **DUAL-MODALITY IMAGING: PHYSICS & INSTRUMENTATION**
- SOURCES OF ERROR AND ARTIFACTS IN CTAC
- FUTURE DEVELOPMENTS IN FUNCTIONAL IMAGING

# Medical imaging techniques

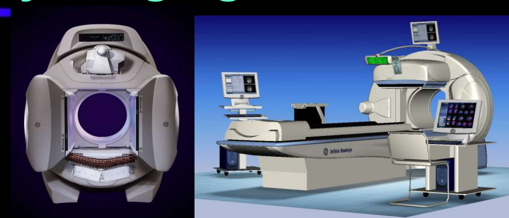


# History of dual-modality imaging

## SPECT/CT

The first prototype SPECT/CT was built by B. Hassegawa in 1990

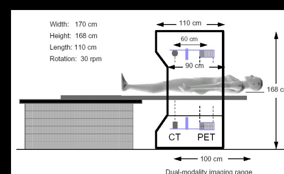
The first commercial SPECT/CT was installed in 1999

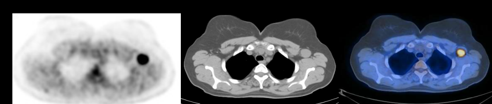


## PET/CT

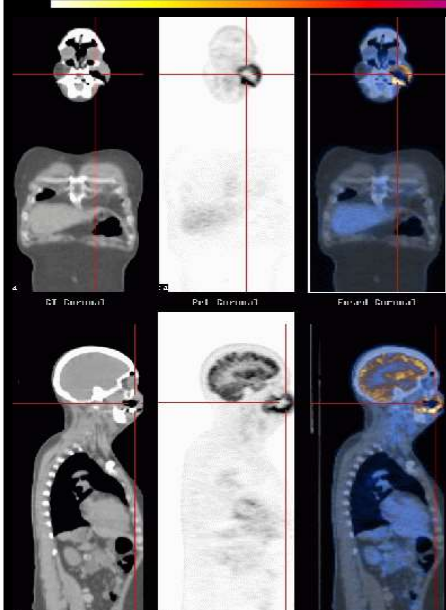
The first prototype system was built by D. W. Townsend in 1998

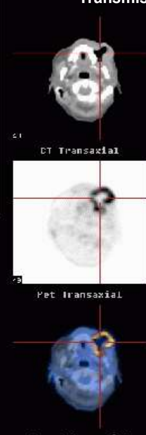
The first commercial PET/CT was installed in 2000



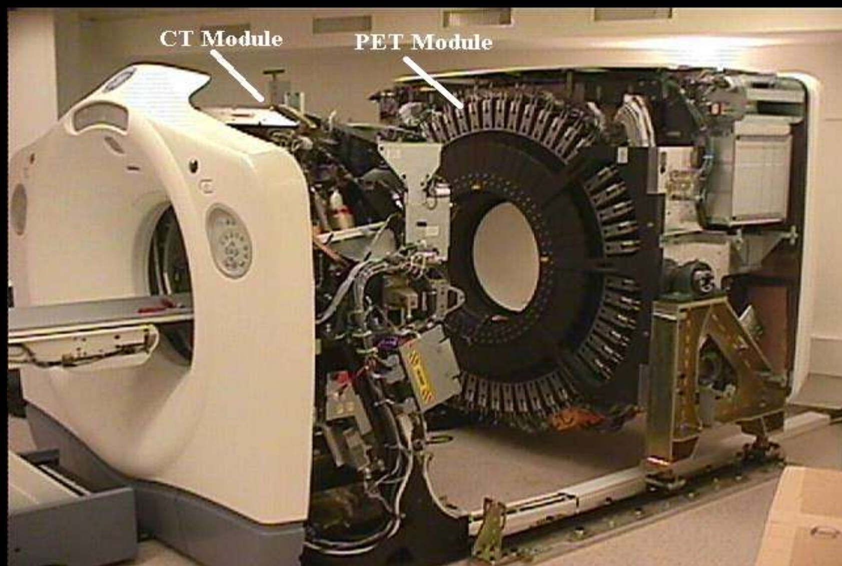
# Why PET/CT?



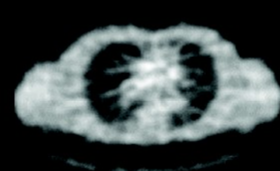

- **2x Faster exam: use CT**
  Transmission for AC
- **Increased detection & Localization accuracy**
  PET images intrinsically registered to CT images
- **Reduced operating cost**
  Faster throughput, use as stand alone CT
- **PET IQ improvement**
  Reduce contamination from scattered photons by using low-noise CT data for PET images reconstruction
- **Easier PET reading**
  Accelerates PET reading proficiency build up
- **Better RT & surgery planning**
  Direct input to RTP and surgery planning

## Current dual-modality PET/CT systems

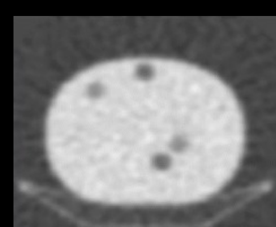



## Transmission-based attenuation correction

**Radionuclide Transmission Scanning (511 keV)**



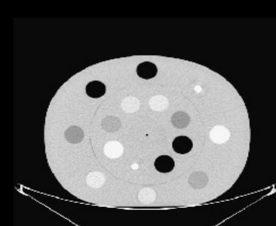
*30 min Rod Sources*



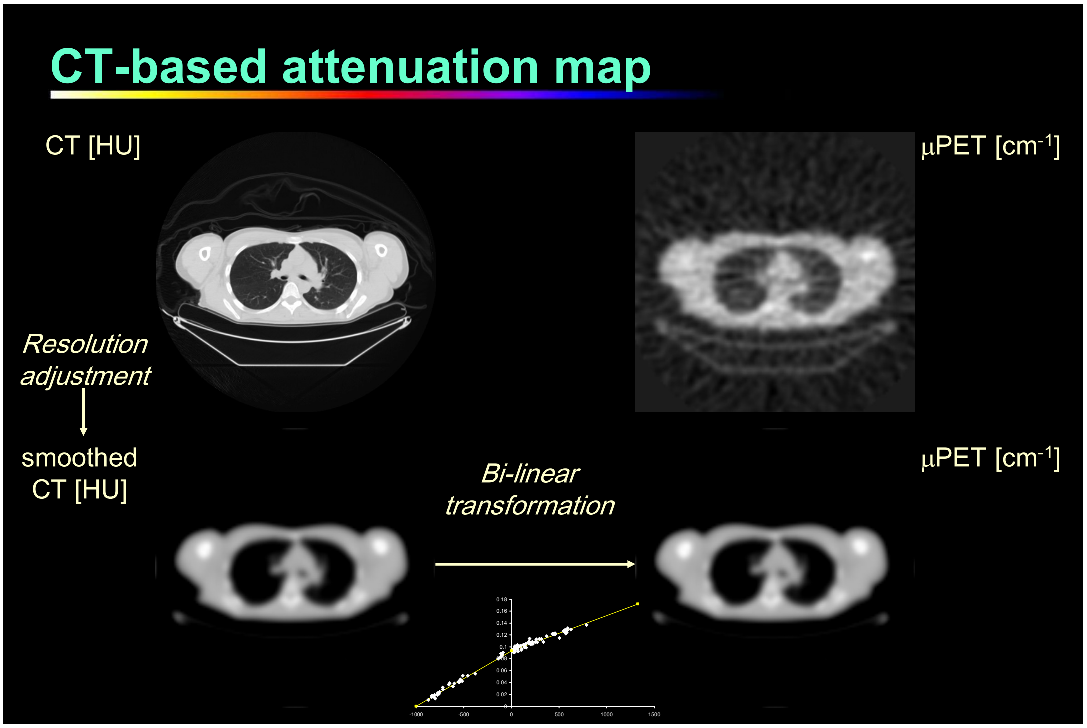
*30 min Rod Sources*

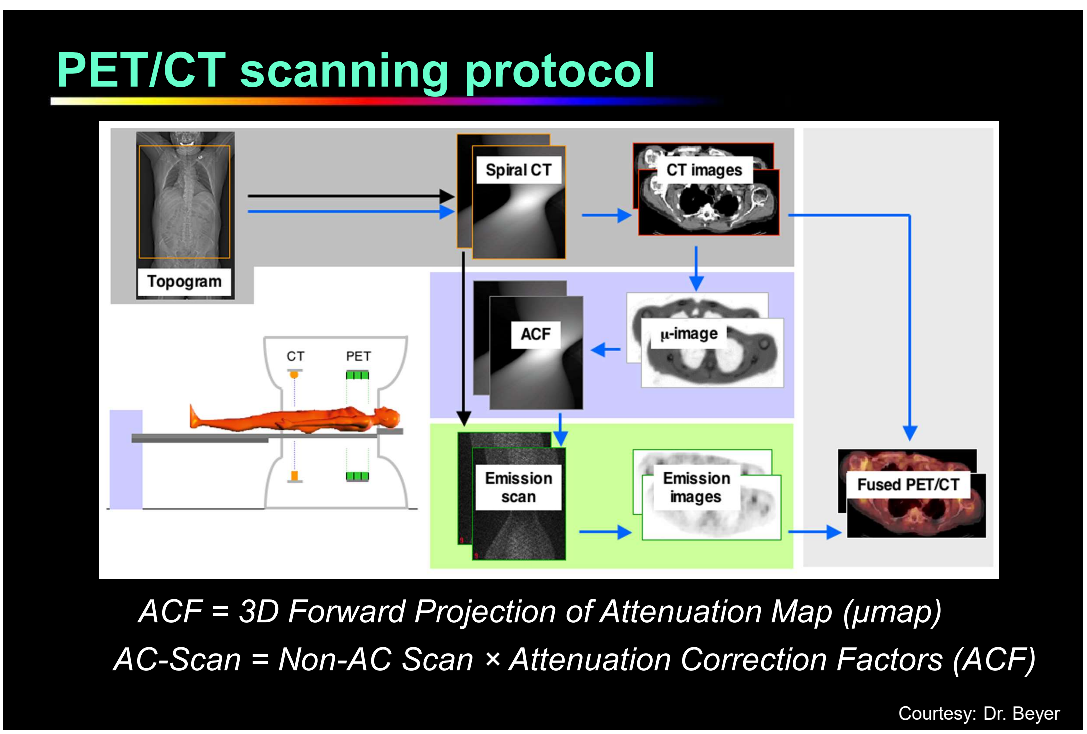
**X-ray Transmission Scanning**

*10 sec CT*



*10 sec CT*


CT-based attenuation map
CT [HU]
µPET [cm-1]
Resolution adjustment
smoothed CT [HU]
µPET [cm-1]
Bi-linear transformation


PET/CT scanning protocol
Topogram
Spiral CT
CT images
ACF
µ-image
CT
PET
Emission scan
Emission images
Fused PET/CT
ACF = 3D Forward Projection of Attenuation Map (µmap)
AC-Scan = Non-AC Scan × Attenuation Correction Factors (ACF)
Courtesy: Dr. Beyer

# Important Parameters on PET/CT

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*Division of Nuclear Medicine, Geneva University Hospital, Geneva, Switzerland*

## Detector Requirements

| *Goal* | *Requirement* |
|---|---|
| *High Spatial Resolution* | *Small Detector Elements* |
| | *High Photofraction* |
| *High Sensitivity* | *High Stopping Power* |
| | *Large Area of Crystal (angle)* |
| *Low Scatter Fraction* | *Good Energy Resolution* |
| *Low Randoms* | *Good Timing Resolution* |
| *Low Deadtime (High Livetime)* | *Fast Event Handling* |
| | *Small Channel Size* |
| | *Limited Multiplexing* |
| *Low Cost* | *None of the Above* |

## Detectors for PET

| Scintillator | BGO | LSO | GSO | LuAP | $LaBr_3$ | LYSO |
|---|---|---|---|---|---|---|
| Formula | $Bi_4Ge_3O_{12}$ | $Lu_2SiO_5$:Ce | $Gd_2SiO_5$:Ce | $LuAlO_3$:Ce | $LaBr_3$:Ce | $LuYSiO_5$:Ce |
| Density (g/cc) | 7.13 | 7.4 | 6.71 | 8.34 | 5.3 | 7.1 |
| Light yield (photons/keV) | 9 | 25 | 8 | 10 | 61 | 32 |
| Effective Z | 75 | 66 | 60 | 65 | 46.9 | 64 |
| Principal decay time (ns) | 300 | 42 | 60 | 18 | 35 | 48 |
| Peak wavelength (nm) | 480 | 420 | 440 | 365 | 358 | 420 |
| Index of refraction | 2.15 | 1.82 | 1.95 | 1.95 | 1.88 | 1.8 |
| Photofraction (%)* | 41.5 | 32.5 | 25 | 30.6 | 15 | 34.4 |
| Attenuation length (cm)* | 1.04 | 1.15 | 1.42 | 1.05 | 2.13 | 1.12 |
| Energy resolution (%)* | 12 | 9.1 | 7.9 | 11.4 | 3.3 | 7.1 |
| Hygroscopic | No | No | No | No | Yes | No |

*@ 511 keV

## What Makes a PET Scanner Better ?

***Image Quality***

- Counts - Sensitivity
- Resolution
- Low Noise (Scatter, Randoms, Lots of Counts)

***Throughput***

- Setup Time
- Sensitivity (Count/Sec)
- Transmission Scan Time
- Processing Time

***Flexibility To Perform ALL Studies***

***Cost***

- Purchase/Lease Costs
- Maintenance Costs
- FDG Dose Required

## PET Performance

**Resolution, Sensitivity, Scatter Fraction, Count-rate**

**Resolution** — **How big does a 1 mm source appear to be.**
**Limits ability to see edges. Impacts ability to detect, and define the shape of, small objects.**

**Sensitivity** — **How much information is collected per unit time from a given quantity of tracer. Primary determinant of signal-to-noise level. Principal limitation on ability to locate small foci.**

**Scatter Fraction** — **What fraction of the data collected is scatter (bad data). Degrades signal-to-noise.**

**Count Rate Performance** — **As the tracer dose is increased, how much more information is collected.**

**(Physical Performance defined by NEMA standards for PET)**

## Spatial Resolution

**Resolution, Sensitivity, Scatter Fraction, Count-rate**

**Resolution** — **How big does a 1 mm source appear to be.**
**Limits ability to see edges. Impacts ability to detect, and define the shape of, small objects.**

Spatial resolution is measured according to NEMA NU2-2007, reporting performance from data reconstructed with filtered back-projection algorithm

Transaxial Resolution

| Radial position of line source | 1cm | 10cm |
|---|---|---|
| FWHM (mm) | 4.9 | 5.5 |

Axial Resolution

| Radial position of line source | 1cm | 10cm |
|---|---|---|
| FWHM (mm) | 5.6 | 6.3 |

How Important is the Resultion?

# Respiratory Motion Challenge

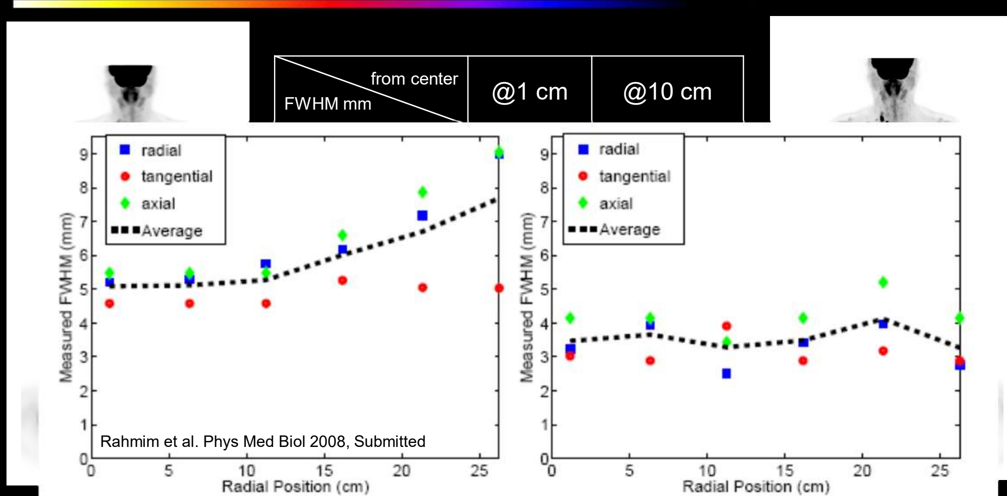
| Factor | FWHM Contribution |
|---|---|
| Positron range | 0.5 (tissue) – 1.5mm (lung)[1] |
| Positron non-collinearity | 1-2 mm |
| Detector size & sampling | 2-3 mm |
| Reconstruction filter | 2-7 mm |
| Displayed pixel size | 2-4 mm |
| **Effective Clinical Resolution + Respiratory Motion** | **4–10 mm (3 - 3.3 mm with RR) + 10-50mm** |

1. Sánchez-Crespo, et al. "Positron flight in human tissues and its influence on PET image spatial resolution", Eur J Nucl Med, Vol 31, Iss 1, Jan 2004, pp 44-51.

Patient Motion is
The Resolution limiting factor in PET

# Resolution Recovery Reconstruction

| FWHM mm / from center | @1 cm | @10 cm |
|---|---|---|




**Conventional** **Resolution Recovery**

Precise system modeling providing optimum image resolution

Image courtesy of Mayo Clinic

## Sensitivity

**Resolution, Sensitivity, Scatter Fraction, Count-rate**

**Sensitivity** **How much information is collected per unit time from a given quantity of tracer. Primary determinant of signal-to-noise level. Principal limitation on ability to locate small foci.**

| | |
|---|---|
| System Sensitivity (Trues[3]) | 7.0 cps/kBq |
| Peak NECR | 130 kcps @27 KBq/ml |

[3] Using ring difference of +23. Average of 0 cm and 10cm off Axis.

## *Noise Equivalent Count Rate (NECR)*

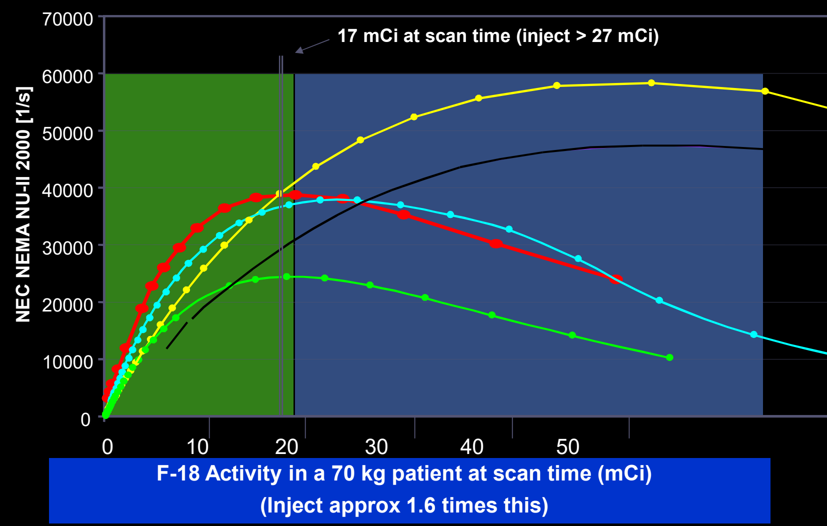
***NECR is computed from count rate data as:***

$$\mathbf{NECR} = \frac{\mathbf{T}^2}{\mathbf{T} + \mathbf{S} + \mathbf{kR}}$$

- ***T is trues***
- ***S is scatter***
- ***"k" represents the means of randoms correction***
  - ***k=2 for randoms by delayed event channel***
  - ***k=1 for randoms from singles***

***NECR is the closest numerical measure for image quality***

# *Noise Equivalent Count Rate (NECR)*




# PET Performance

**Resolution, Sensitivity, Scatter Fraction, Count-rate**

**Scatter Fraction** **What fraction of the data collected is scatter (bad data).** **Degrades signal-to-noise.**

| | |
|---|---|
| Scatter fraction | 37% |

## What Factors Make a Great PET Scanner?

*Detector / System Geometry*
*Detector Scintillator Material*
*Detector Light Conversion Devices*
*Front End Electronics*
} **PET Detector**
*Data Processing Algorithms*
*Applications capability*
*System Reliability*
*System Cost*

**No One Single Component Determines Overall System Performance…It's the overall recipe!**

## Image Quality

| RADIOLOGY (CT or MR) | PET or PET-CT |
|---|---|
| Signal | True Coincidences (T) |
| Noise | Scatter (S) + Randoms (R) |
| Signal to noise ratio<br>SNR= S / N | Noise Effective Count Rate<br>NECR = $T^2/(T+S+R)$ |
| Resolution<br>• (CT – Defined by detector and acq technique<br>• MR –performance of gradient ) | Resolution<br>• Defined by detector geomety |

**NECR and Sensitivity => Better IQ and Faster Acquisition**

## Optimizing on the right parameter(s)

| Scanner Design Considerations | Sensitivity | Resolution | Resolution Uniformity | Contrast | Scatter Fraction | NECR |
|---|---|---|---|---|---|---|
| Crystal Size | Moderate | Strong | | | | |
| Crystal Material | Strong | | | Strong | Moderate | Strong |
| Crystal Spacing | Strong | | | | | |
| Ring Diameter | Strong | Moderate | Strong | Moderate | Moderate | Strong |
| Collimation | Strong | | Moderate | | Strong | Strong |
| Shielding | | | | Moderate | Strong | Strong |
| Light Collection System | Strong | weak | | weak | | Strong |
| Front-End Electronics | weak | weak | | | | Strong |
| Data Pipeline | | | | | | Strong |
| Pre-Processing | | Strong | | Moderate | | |
| Reconstruction | | | | Moderate | | |

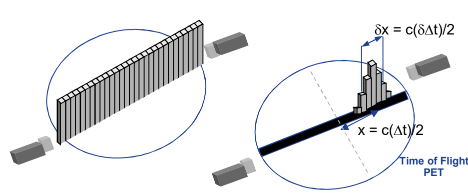
Strong influence | Moderate | weak | none

# Time of Flight PET

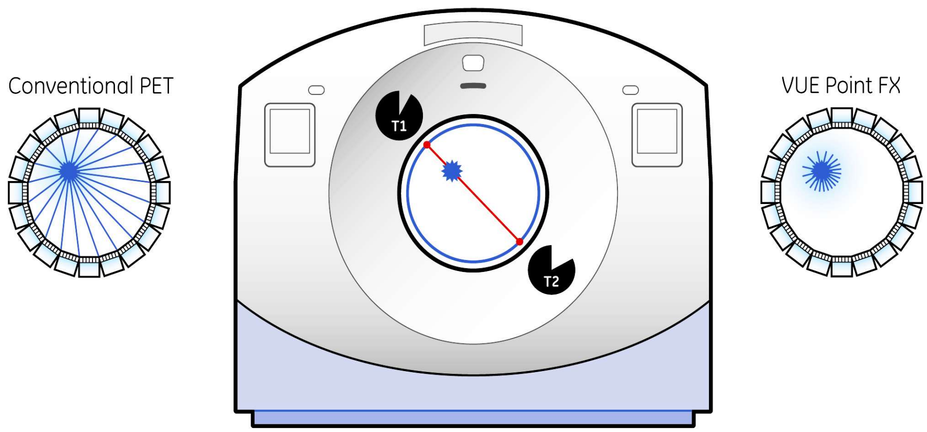
## Improve confidence in diagnostic reads with Time of Flight

- Improve lesion localization
- Improve quantitative accuracy
- Enhance contrast to noise

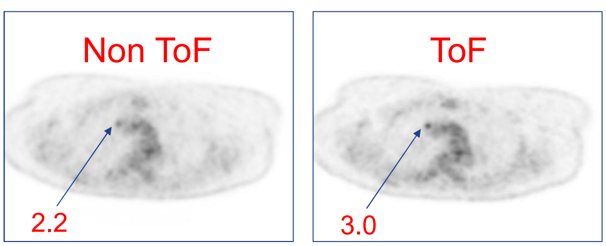
$$I_n^{i+1} = \frac{I^i_{(x,y,z)}}{\sum_{(u,v,\theta,\phi,\Delta t)} A_{(u,v,\theta,\phi,\Delta t)} H_{(u,v,\theta,\phi,\Delta t),(x,y,z)}} \sum_{(u,v,\theta,\phi,\Delta t)} A_{(u,v,\theta,\phi,\Delta t)} H_{(u,v,\theta,\phi,\Delta t),(x,y,z)} \frac{P_{(u,v,\theta,\phi,\Delta t)}}{A_{(u,v,\theta,\phi,\Delta t)} \sum_{(x,y,z)'} I^i_{(x,y,z)'} H_{(u,v,\theta,\phi,\Delta t),(x,y,z)'} + \left(S_{(u,v,\theta,\phi,\Delta t)} + R_{(u,v,\theta,\phi,\Delta t)}\right)}$$



## Improve confidence in diagnostic reads with Time of Flight

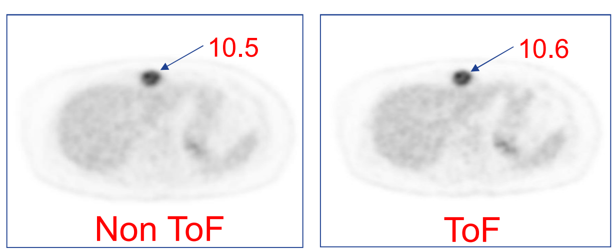



## Time of Flight Clinical Images

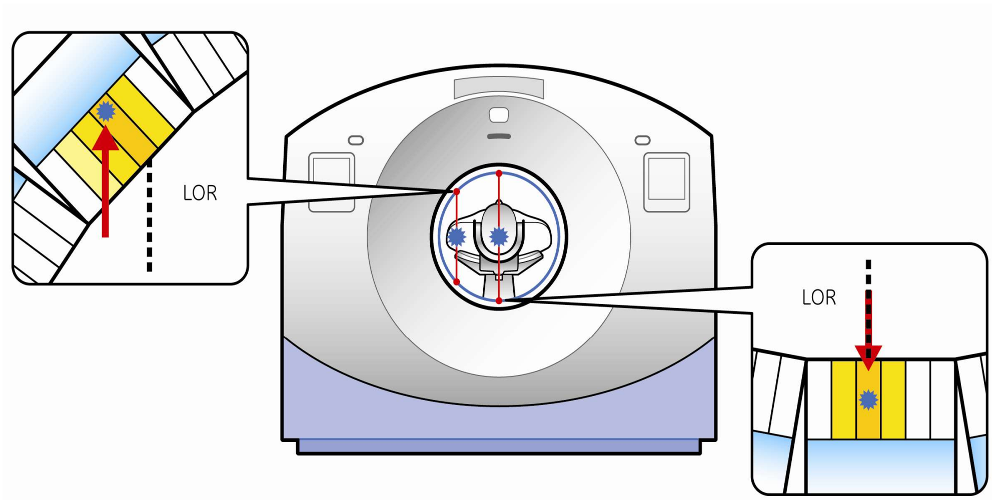



Impact on small lesions

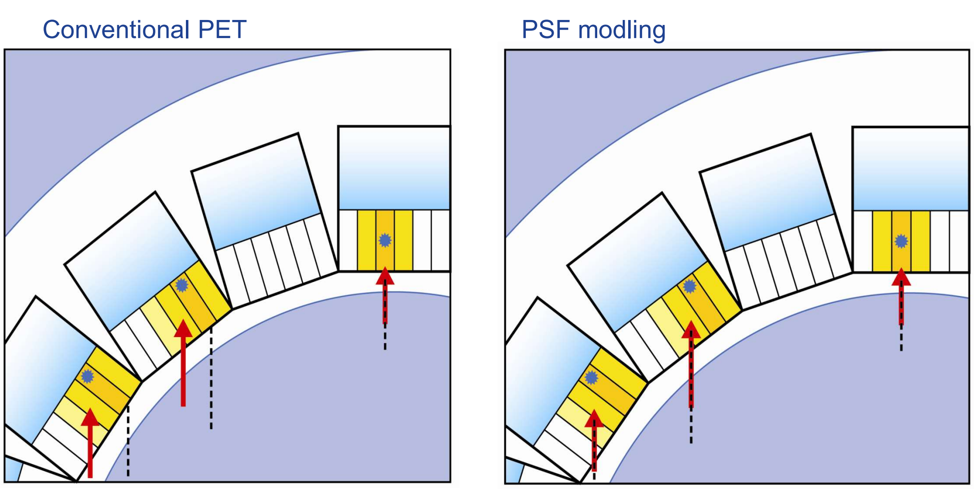
Impact on larger lesions



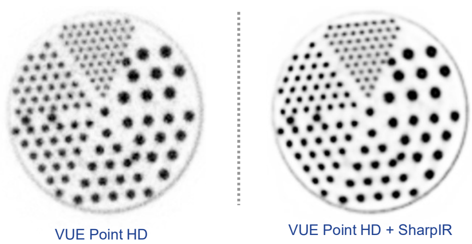
## PSF modeling Improve image quality with a new detector response model

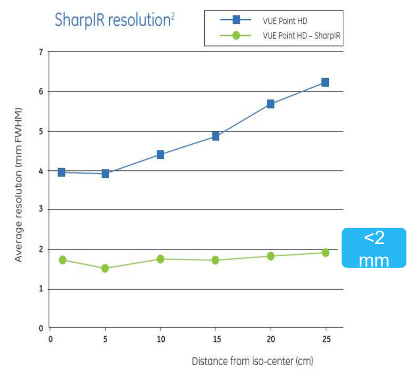



## PSF Improve image quality with a new detector response model



## SharpIR Improve image quality with a new detector response model






Contrast Recovery

Resolution Recovery

! 2mm resolution over entire FOV

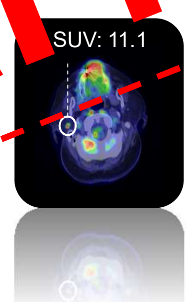
## What is more important in PET imaging?

Image Quality

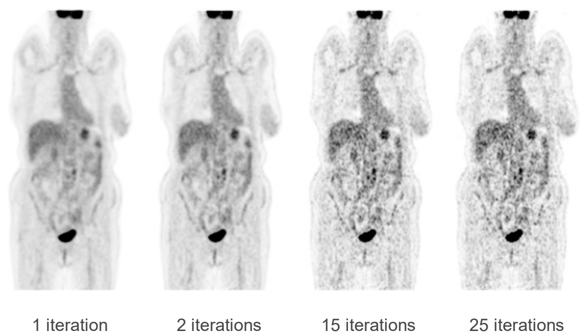
or

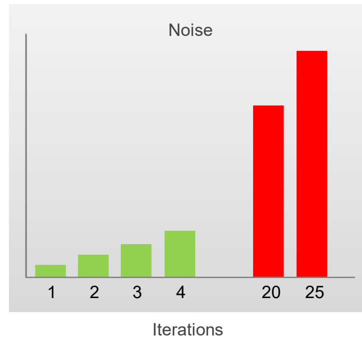
Accurate Quantitation

Both

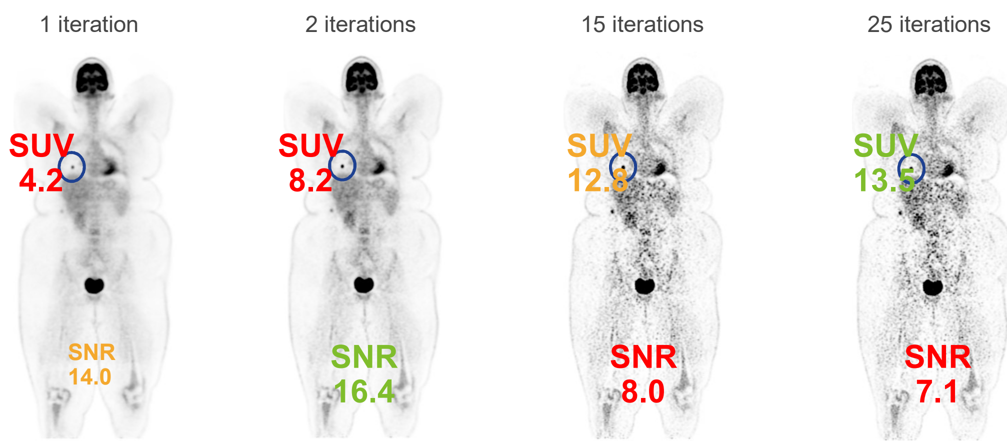


## Conventional Iterative Reconstruction
Image quality deteriorates with more than a few iterations



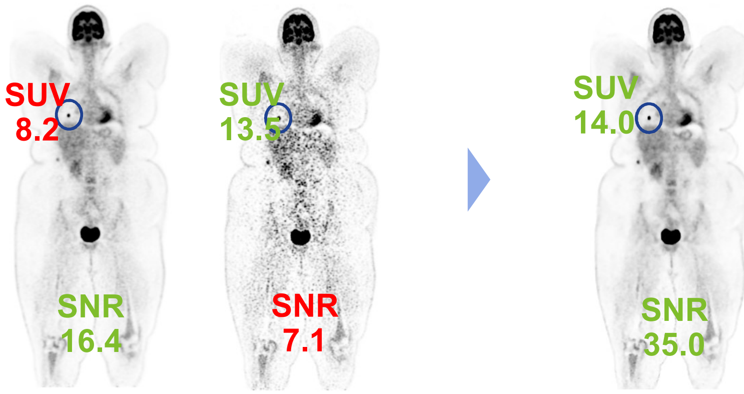

## Conventional Iterative Reconstruction
Significant compromise between image quality and quantitation




BMI : 52.5 | ROI : 15mm | OSEM: 6.4mm, TOF, PSF

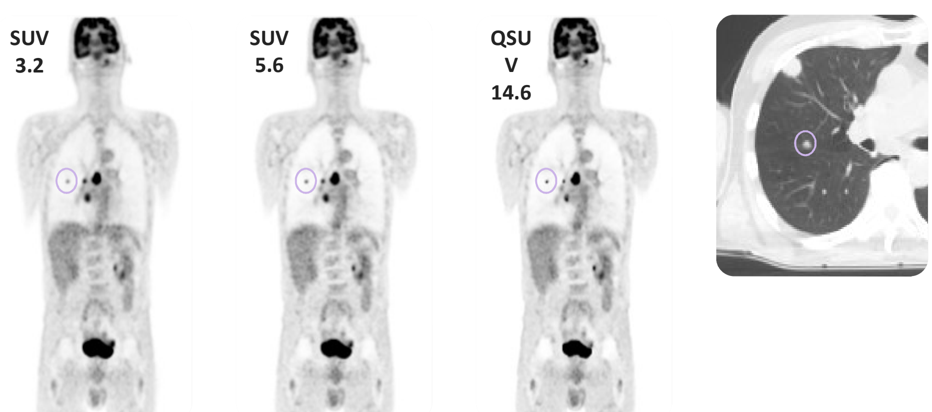
# Full Convergence with No Compromise

2 iterations | 25 iterations | 25 iterations




BMI : 52.5 | ROI : 15mm | OSEM: 6.4mm, TOF, PSF

# Improved Visualization and Quantitation of Small Lesions




Discovery PET/CT 710 $F^{18}$-FDG scan – Quantitation SUVmax (g/ml)

# The Value of Quantitation for Referring Physicians

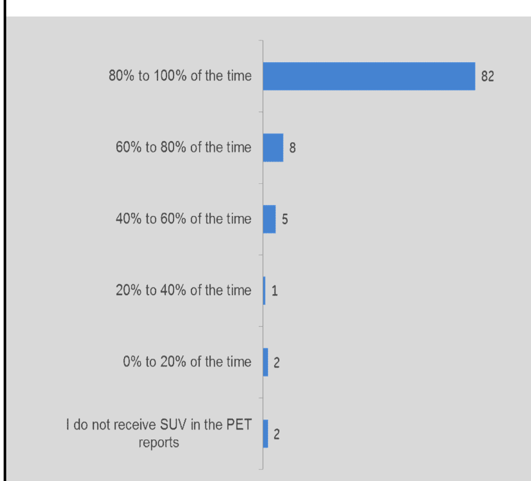
## FDG uptake is now routinely reported, and is asked for by referring physicians

Paul Kinahan, PhD
Professor or Radiology, University of Washington

Abstract: PET/CT imaging for response monitoring in multicenter studies: an update and future challenges
http://amos3.aapm.org/abstracts/pdf/77-22625-310436-90874.pdf

We've asked 100 medical oncologists…

How often do you review SUV numerical data provided in PET the report?

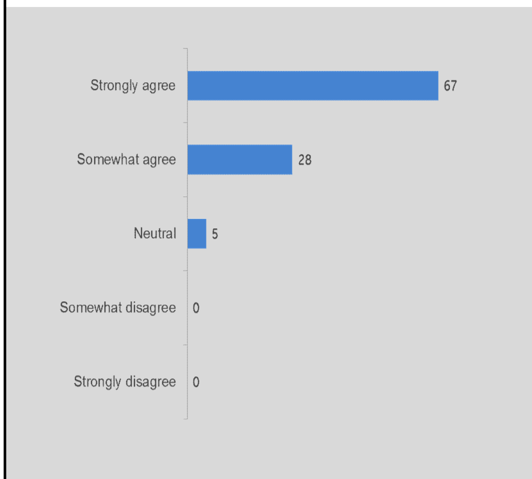



**90%**

60% or more of the time

Double-blinded survey with 100 medical oncologists in the U.S.

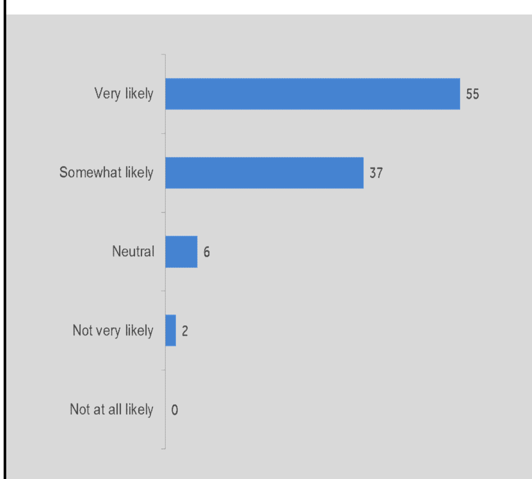
## PET SUV helps me to better understand the PET findings, impressions, disease state, or disease progression




**95%**
agree

Double-blinded survey with 100 medical oncologists in the U.S.

## If SUVs could be more accurately measured and understood, how likely this would improve clarity and conclusiveness of the PET scan?




**92%**
likely

Double-blinded survey with 100 medical oncologists in the U.S.

If you received a PET report without SUV information, would you contact the radiologist/NM?

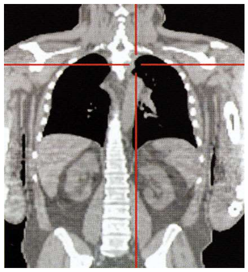
"I would think it was strange if the report did not mention metabolic uptake"

"Yes, this would be a bad report"

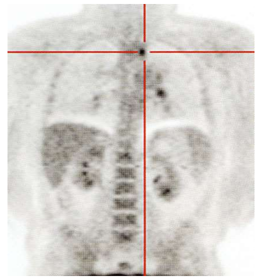
"Yes, this would concern me only since we are used to having the SUV value"


## Building a PET/CT Center Starting From Zero...

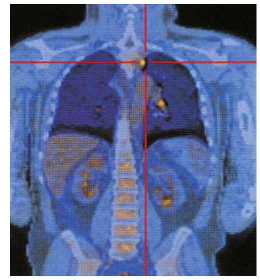
Mohammad Reza Ay, PhD



CT Image
« Precise Body Anatomy »

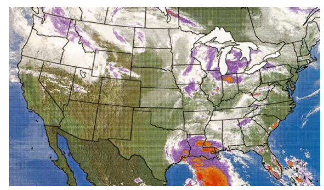


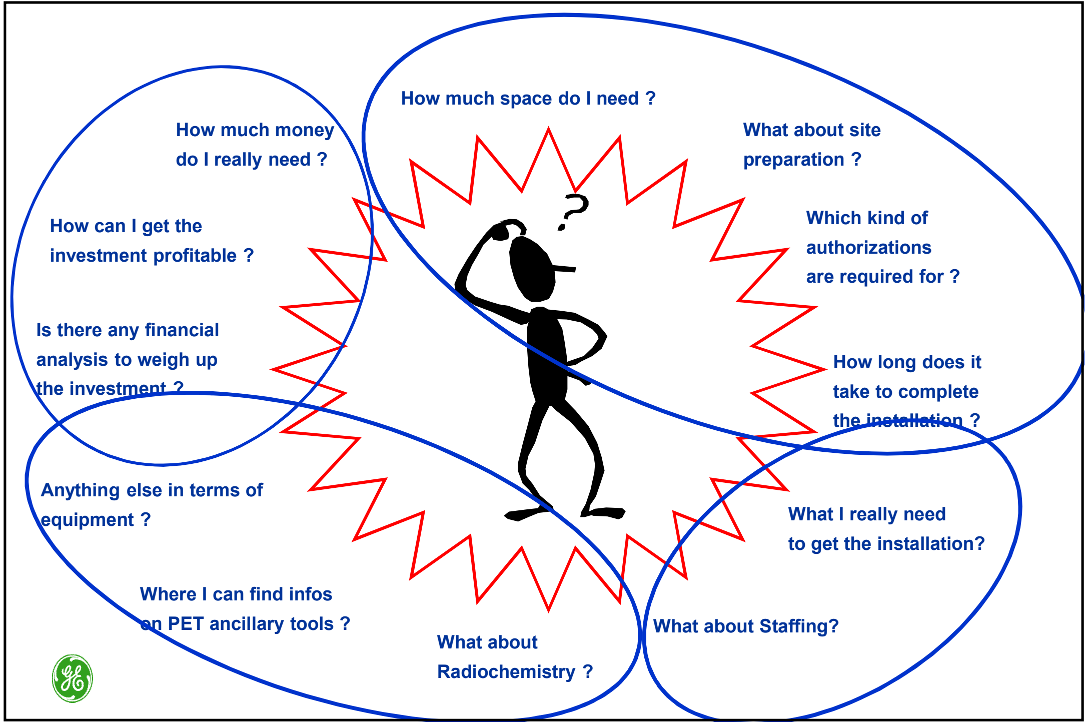
PET Images
« abnormal activity »



PET-CT Images
Abnormal activity and
precise localization

| Structural Images | Functional Images | Hybrid Images |
|---|---|---|
| Geographic Map<br>"precise outlines of the states" | Weather Patterns<br>"intense weather activity" | Weather MAP |





# Voice of the Customer:

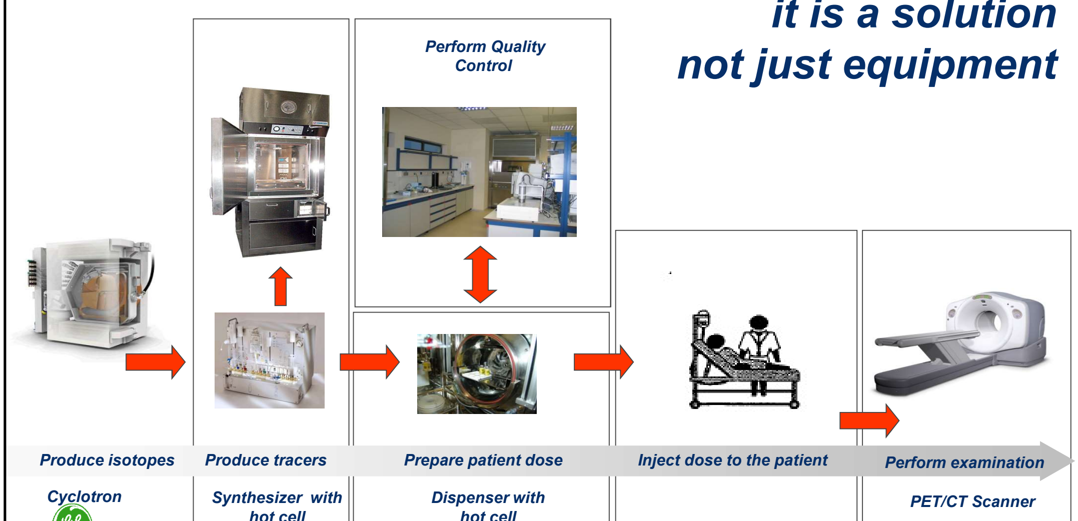
'As starting point, we must avoid clinical awareness ….'

| General Requirements | Site Planning | Regulatory | Economic/ Finance | Equipment | Ordering |
|---|---|---|---|---|---|

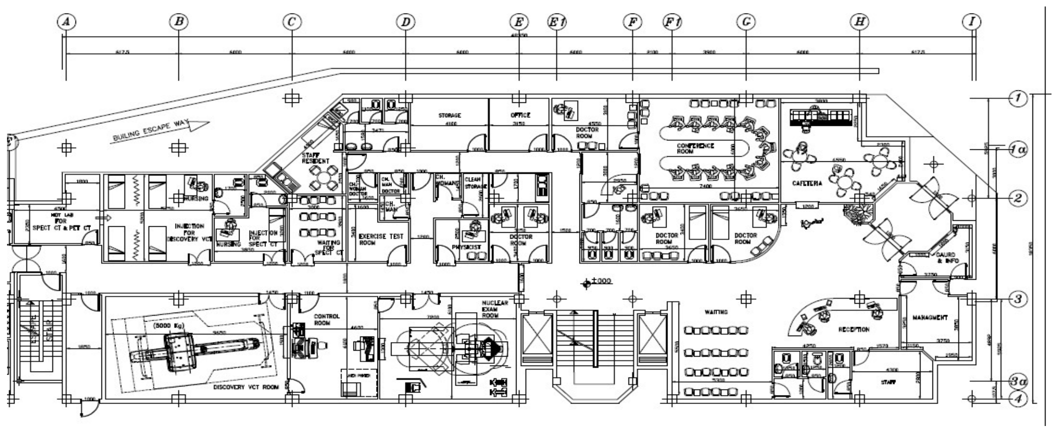
**Clinical Benefit > Improved Patient Management** (JNM, may01, scientific papers…)
**Cost/Benefit Analysis > Reimbursement & Health Care Cost Savings** (Feasibility Studies, meta-analysis, Reports,…)
**Staffing Organization** (Local Regulatory, Competencies & Training )
**Evolution program** (Growth Plan)

# PET/CT Radiopharmacy today

*it is a solution not just equipment*



## Typical PETCT Site



## PET/CT Shielding Documentation

**AAPM Task Group 108: PET and PET/CT Shielding Requirements**

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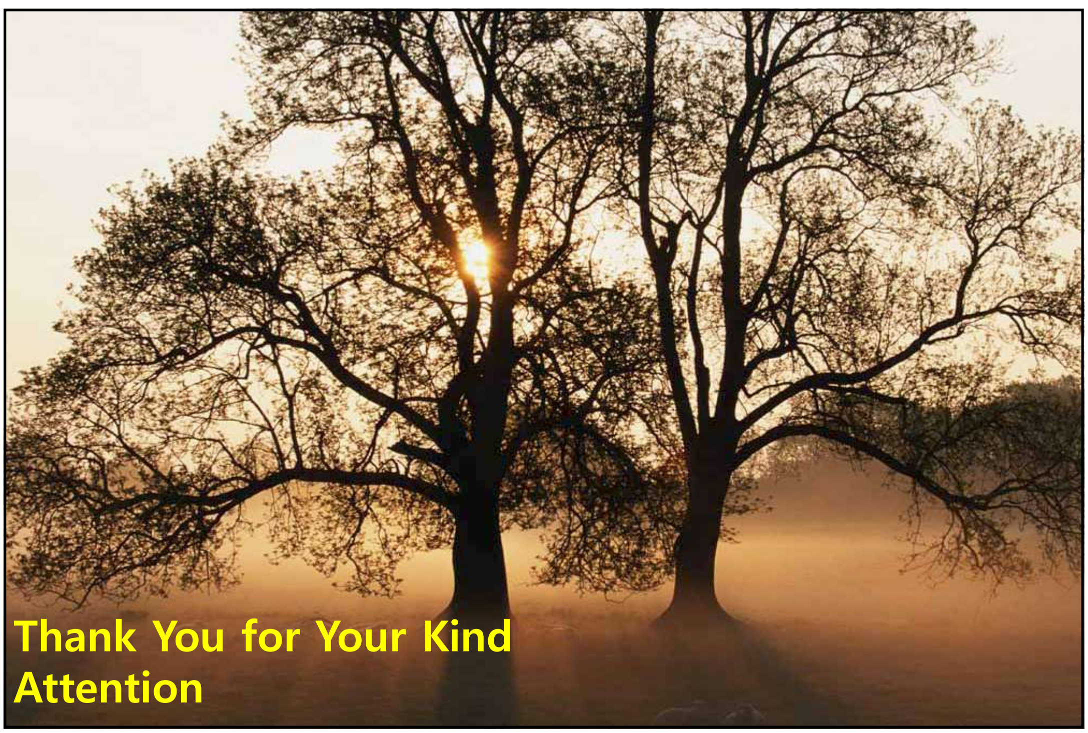
(Received 21 July 2005; revised 17 October 2005; accepted for publication 18 October 2005; published 19 December 2005)


Thank You
Iran, Persepolis (500 Years B.C.)


Thank You for Your Kind Attention