Positron Emission Tomography
Physics, Instrumentation, Data Analysis

Carl K. Hoh, MD

Department of Radiology
UCSD Medical Center

PET Radiation Detectors

- Theoretical ideal scintillation material
  - High density (Z)
  - Efficient scintillator (high & quick light output)
- Newer scintillators (more efficient)
  - Leutetium orthosilicate (LSO)
  - Gadolinium orthosilicate (GSO)
  - Use in 3D mode

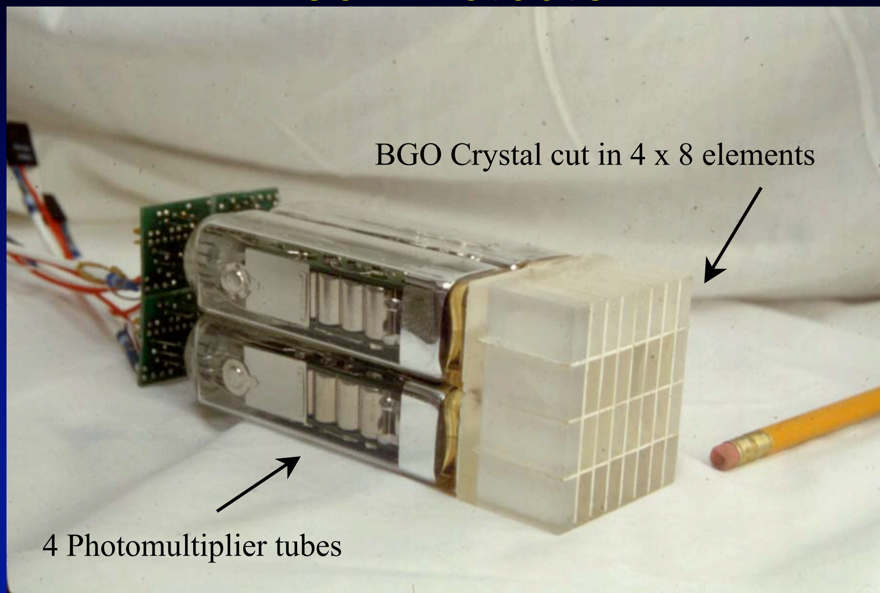
Crystals used in PET

Scintillators	Effective Z	Decay (μs)	Index of refraction	Relative light yield	Peak wavelength (nm)
Sodium iodide	50	0.23	1.85	100	410
Bismuth germanate	74	0.30	2.15	13	480
Lutetium oxyorthosilicate	66	0.04	1.82	65	420
Gadolinium oxyorthosilicate	59	0.06	1.85	25	430
Barium fluoride	52	0.62 0.0006	1.49	13 3	310 220

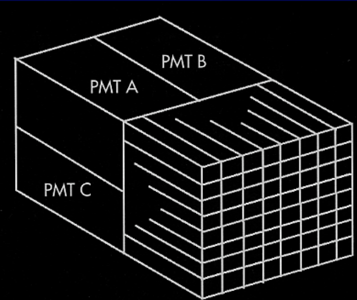
PET Scanner Design

- Smaller individual crystal size = better spatial resolution
- Physical limit to size of photomultiplier tube
- Crystal blocks
  - Cut block detector type
  - Reflector block detector type
- Buckets or modules

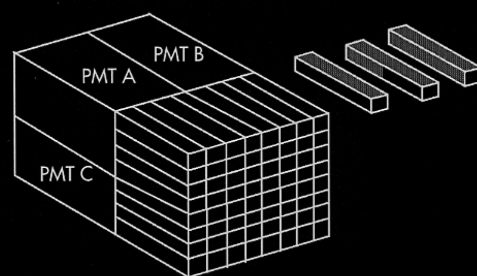
Block Detector



Block Detector Designs



BGO cut-block detector



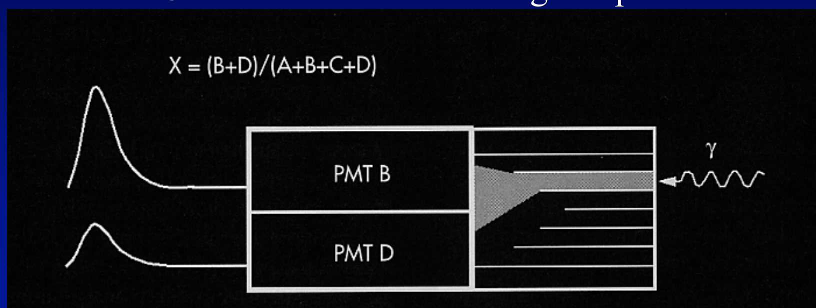
BGO reflection design block

Distribution of light from a single crystal element to 4 PMTs

Pulse strength

Light Pipe

Photon



Block Detector

Block detector with 8x8 elements and 4 photomultiplier tubes

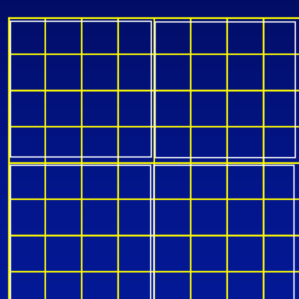
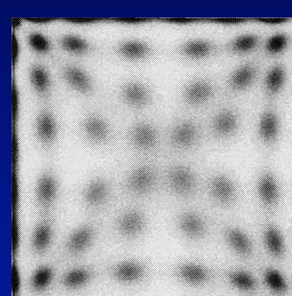
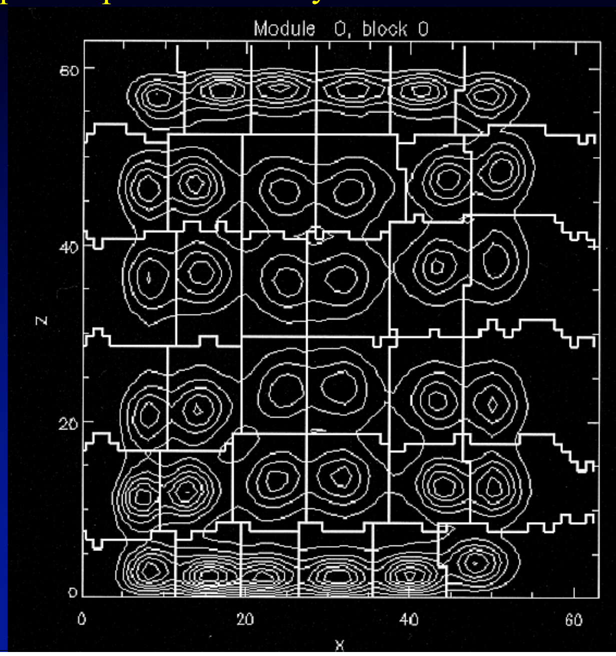


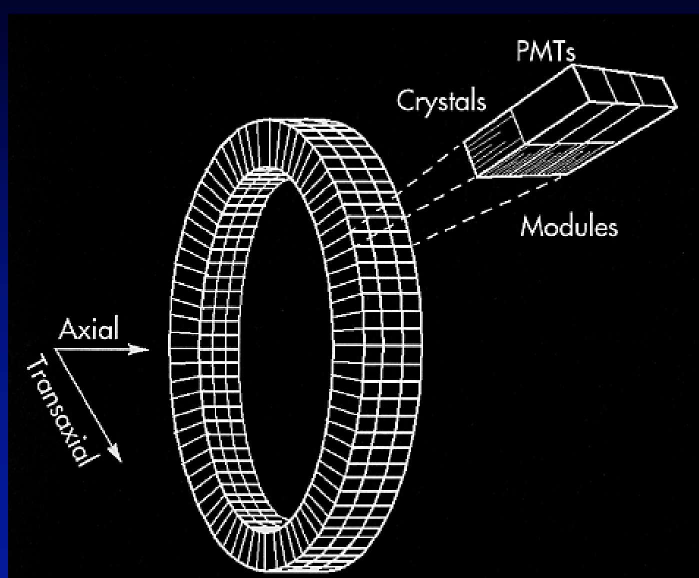
Image of the Xpos and Ypos determined from the four photomultiplier tubes outputs.



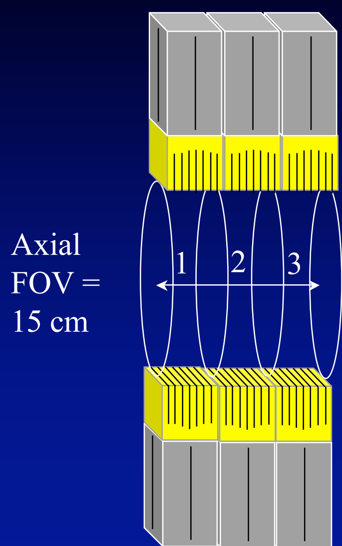
Output Map from each crystal element in a block



Example: 3 Ring of Detector Blocks



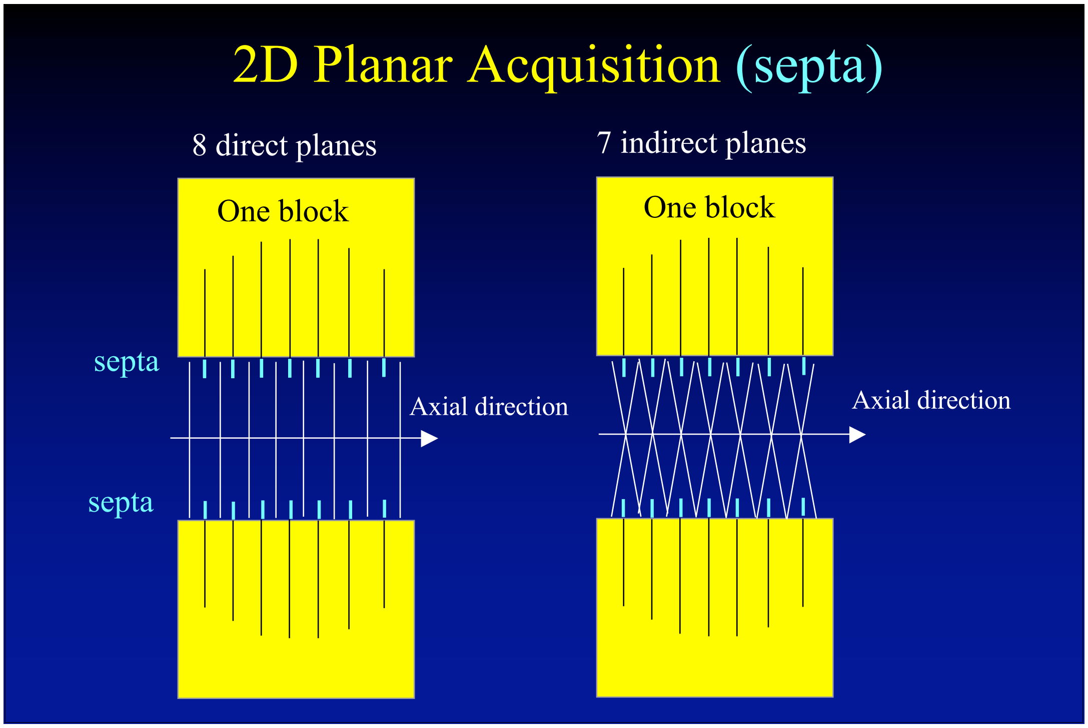
Three Rings of Detector Blocks

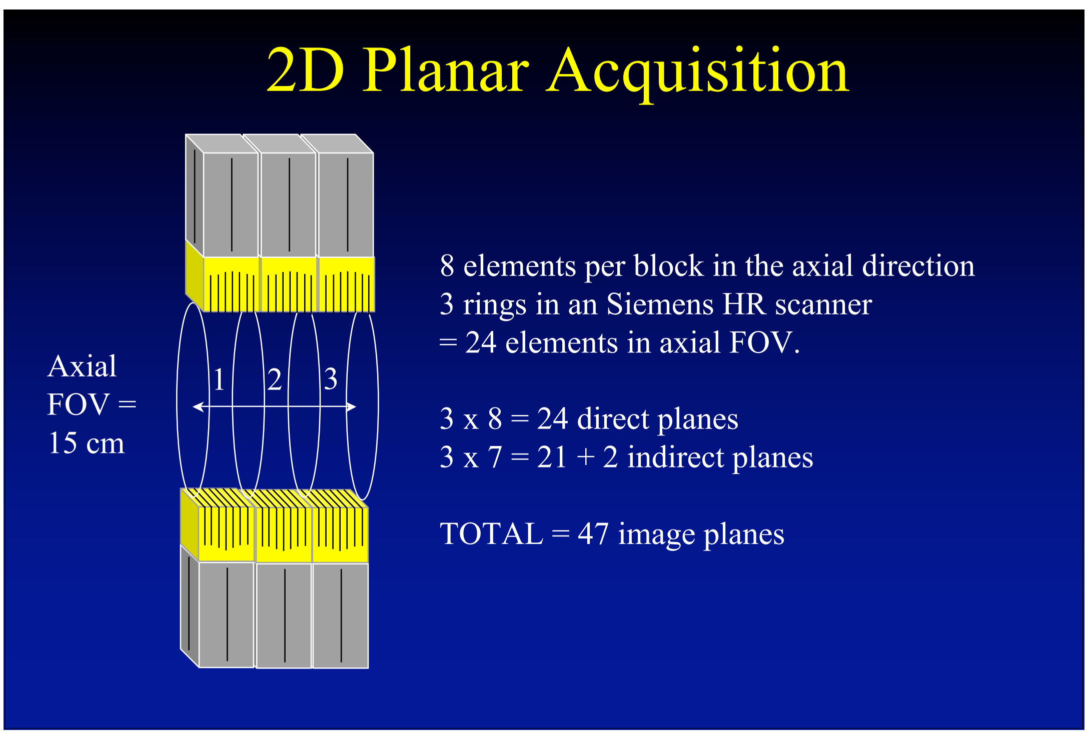


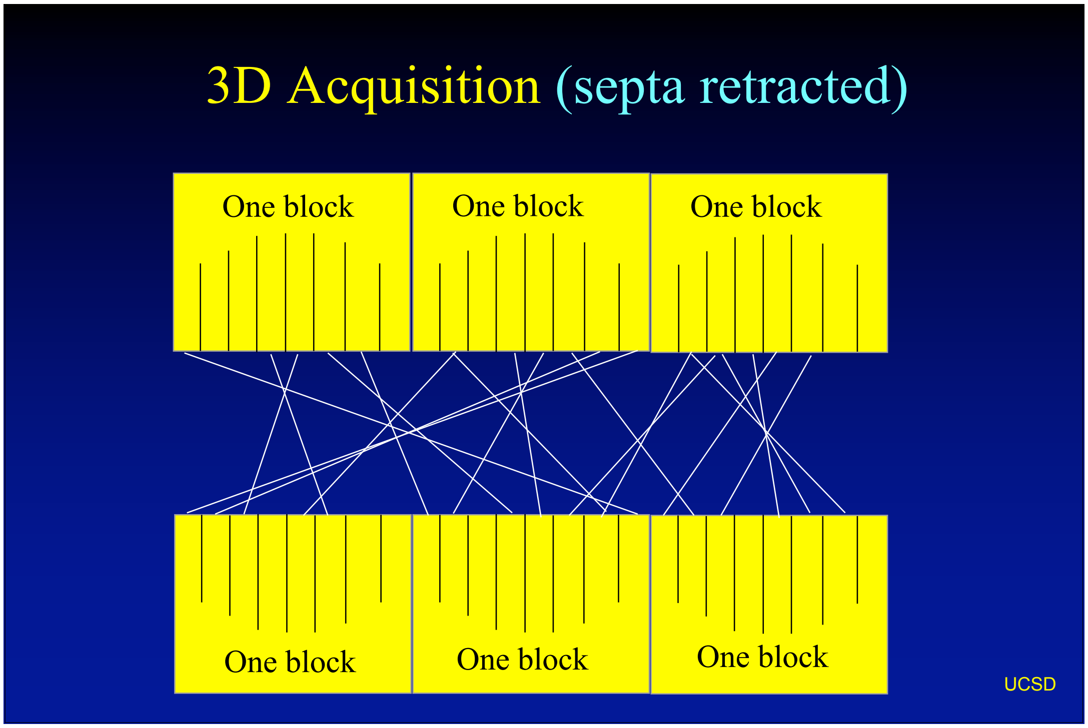
8 elements per block in the axial direction
3 rings in an Siemens HR scanner
= 24 elements in axial FOV.

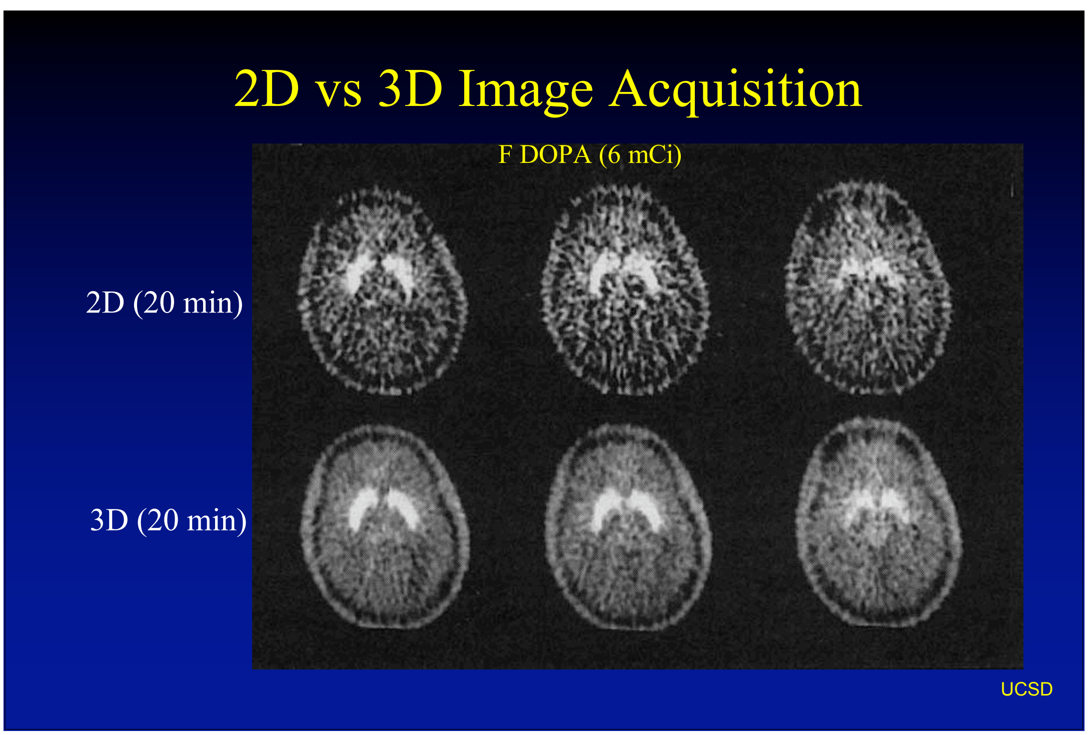
2D and 3D Detector Configurations

- 2D mode: use of septa
  - Limit axial FOV of events to 1-2 elements
  - Reduce the number of scatter
- 3D mode: retract or no septa
  - Increase sensitivity x 4-10
  - But also increase scatter and random events
  - Decreased sensitivity at end of axial FOV
  - High count rate: dead time problems
  - Huge acquired data sets


2D Planar Acquisition (septa)
8 direct planes
7 indirect planes
One block
One block
septa
septa
Axial direction
Axial direction


2D Planar Acquisition
Axial
FOV =
15 cm
1
2
3
8 elements per block in the axial direction
3 rings in an Siemens HR scanner
= 24 elements in axial FOV.
3 x 8 = 24 direct planes
3 x 7 = 21 + 2 indirect planes
TOTAL = 47 image planes


3D Acquisition (septa retracted)
One block
One block
One block
One block
One block
One block
UCSD


2D vs 3D Image Acquisition
F DOPA (6 mCi)
2D (20 min)
3D (20 min)
UCSD

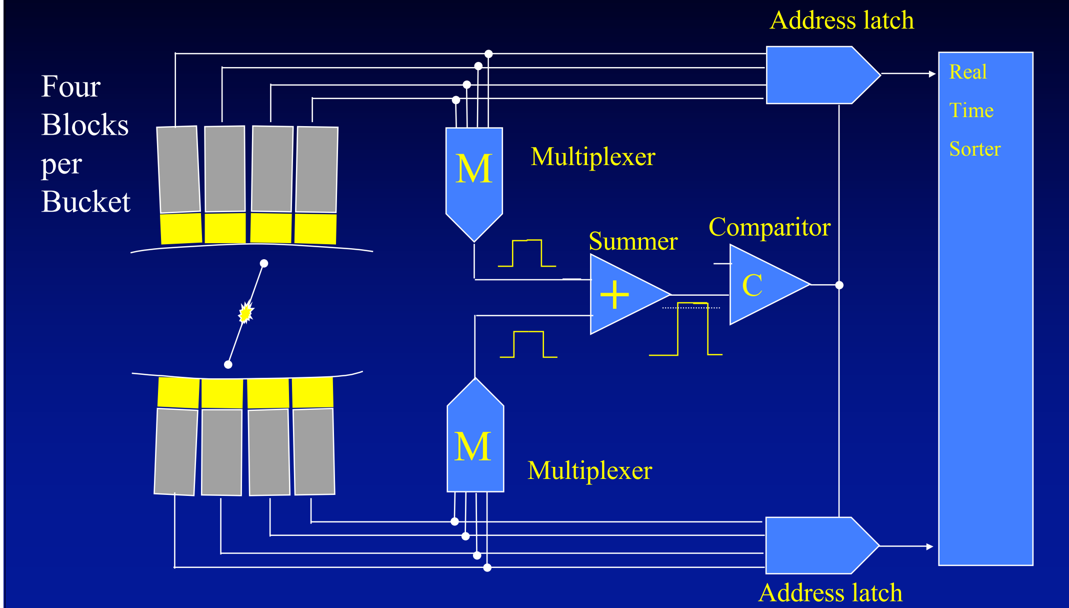
BGO systems

- Relatively poor energy resolution
- Need wide energy window: 300-650 keV
- Relatively high scatter detection
- Need for scatter correction

Coincidence Detection: Trues, Random, & Scatter Events

- True event: pair of annihilation gamma rays
  - 6-12 nanosecond event timing window
- Random event: detection of gamma rays from two different annihilation events
  - Delayed event timing window
- Scatter event: due to Compton effect in tissues
  - 15% of data in 2D mode

Bucket



PET vs SPECT Images

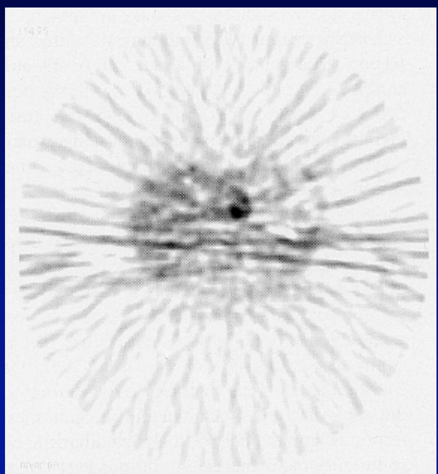
- Spacial Resolution: 4 mm vs > 12 mm
- Count Rate: 50-100 vs 1 (< 1% of pt activity)
- Acquisition: simultaneous (ring) vs rotating line profile

Reconstruction Algorithms

- Filtered Back Projection
  - Simple
  - Quick
  - Streak artifacts
- Iterative Reconstruction
  - Need fast computer

PET Image Reconstruction

Filtered Back Projection



Iterative Reconstruction

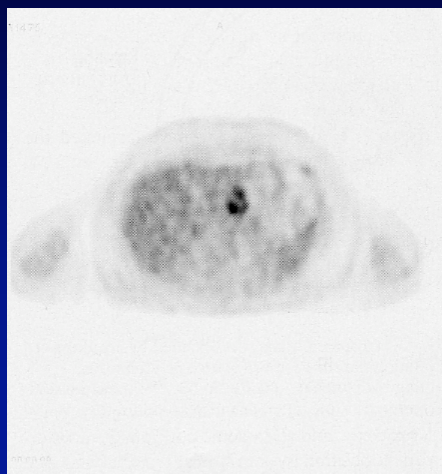
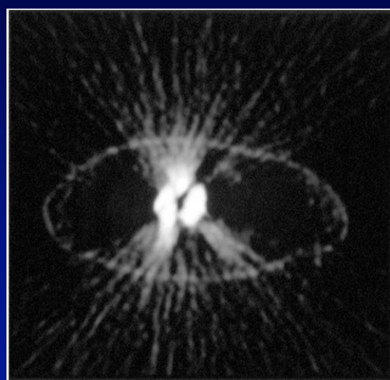


Image Reconstruction

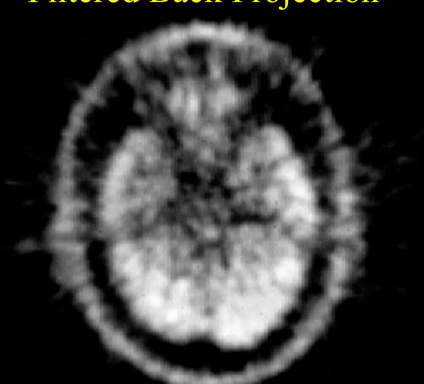
Filtered Back Projection



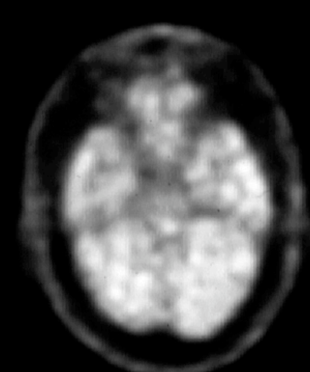
Iterative Reconstruction

Image Reconstruction

Filtered Back Projection



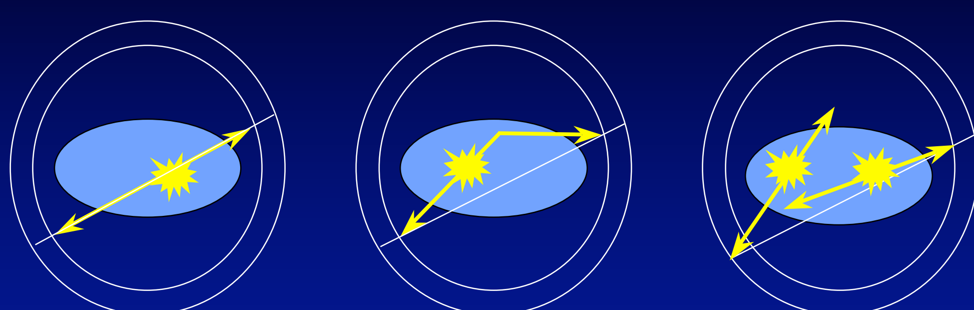
Iterative Reconstruction



Attenuation Correction by Transmission Imaging

- Tissue attenuation more visible on PET
  - Annhilation photon pairs essentially “see” full thickness of the body
- Measured Attenuation
  - By transmission imaging
- Calculated Attenuation
  - in some head/brain scans

PET: Types of Coincident Events



True event

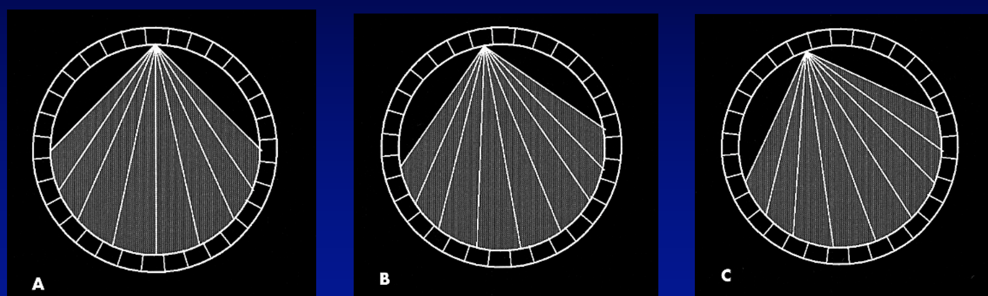
Scatter event

Random event

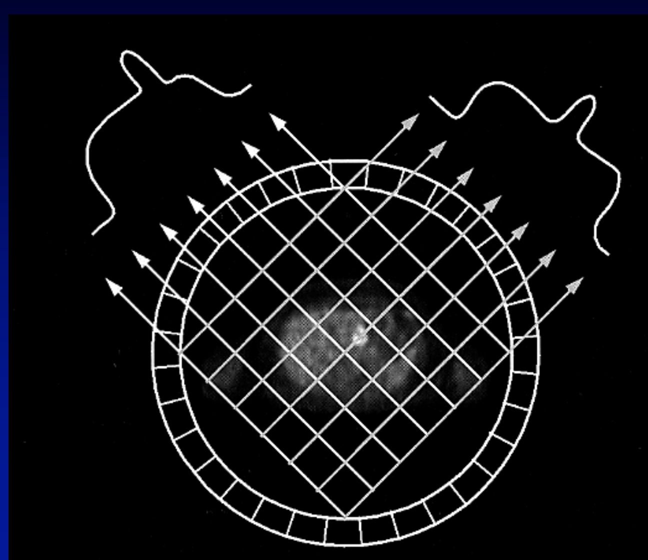
Adds low spatial frequency image noise

UCSD

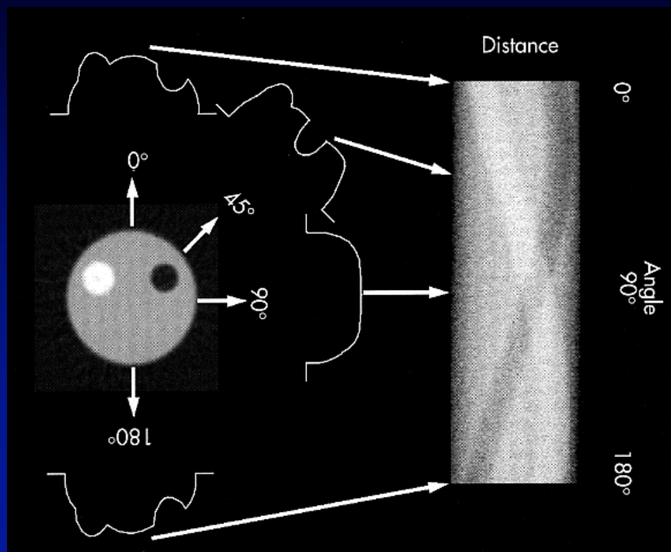
Fan Pattern of Possible Lines Of Response



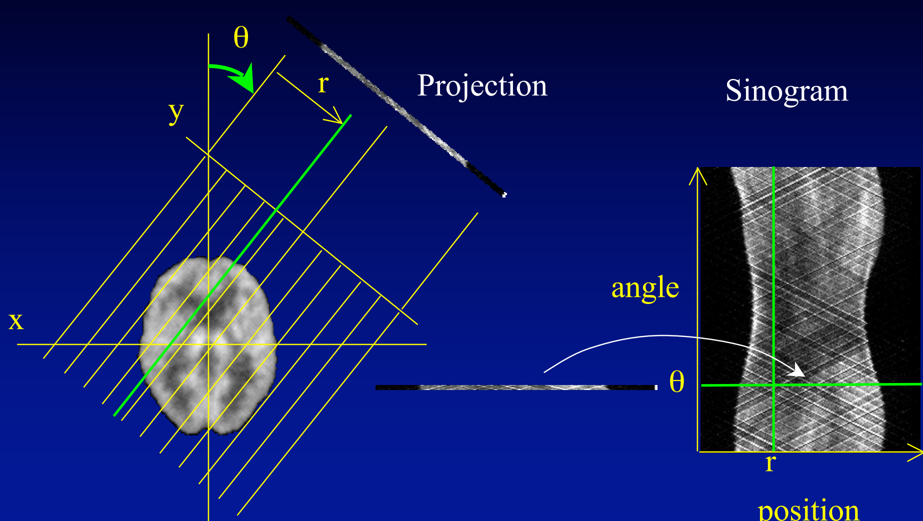
Parallel LORs form Projection Image



Projection Data in Sinogram Format



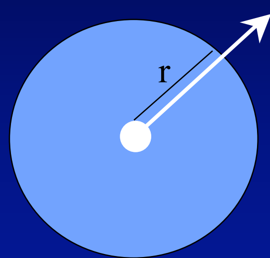
Projection Data Stored as a Sinogram



UCSD

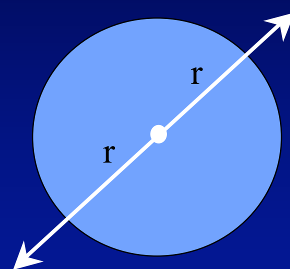
Attenuation Effects
SPECT vs PET

SPECT



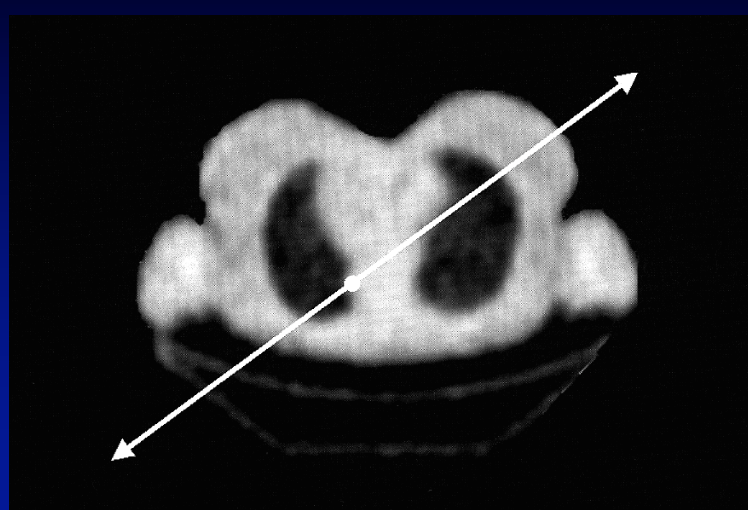
$I = I_o \, e^{-\mu r}$

PET

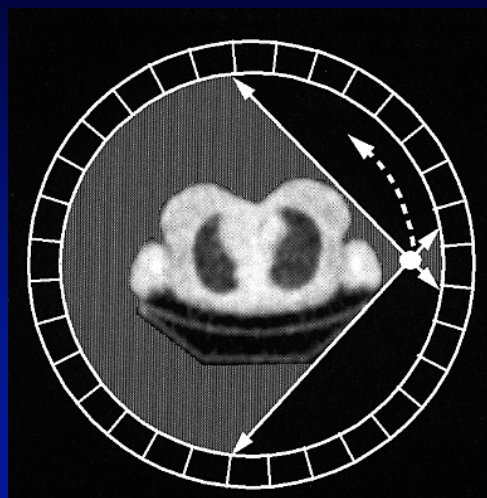


$I = I_o \, e^{-\mu 2r}$

Attenuation of a pair of annihilation photons

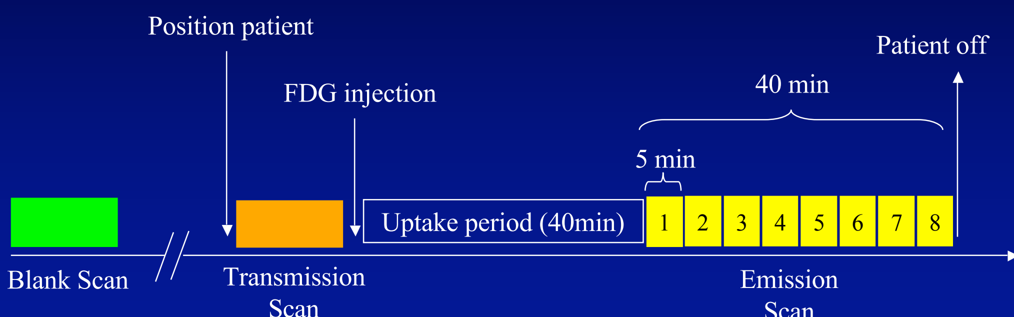


Transmission image from a Rotating Transmission Rod Source

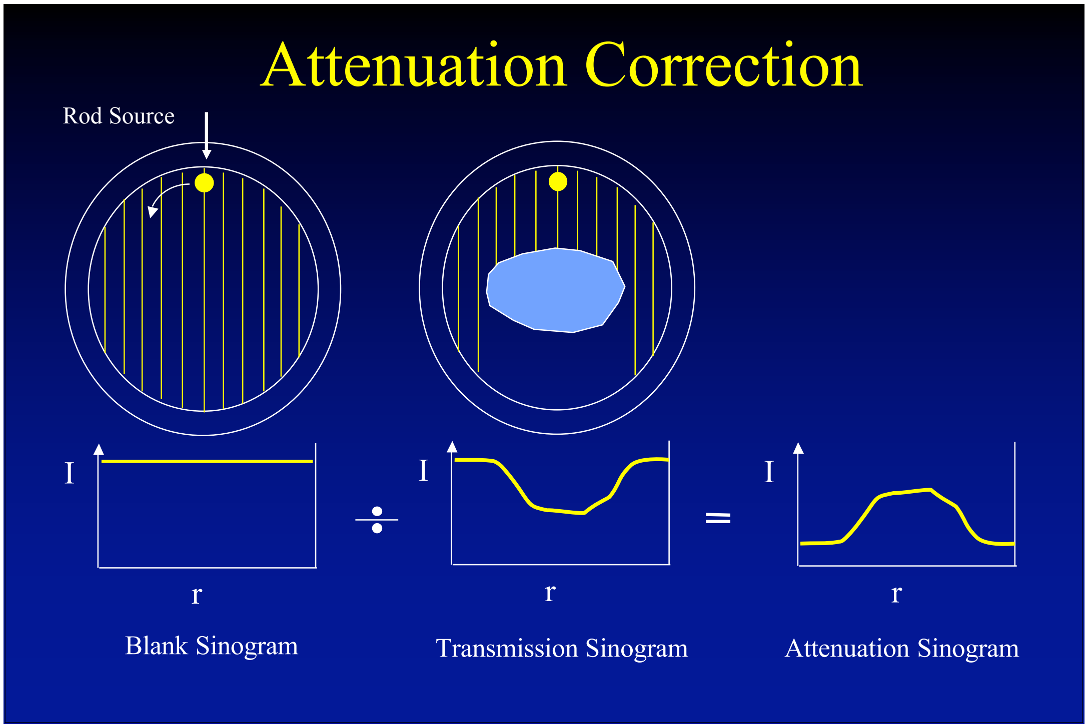


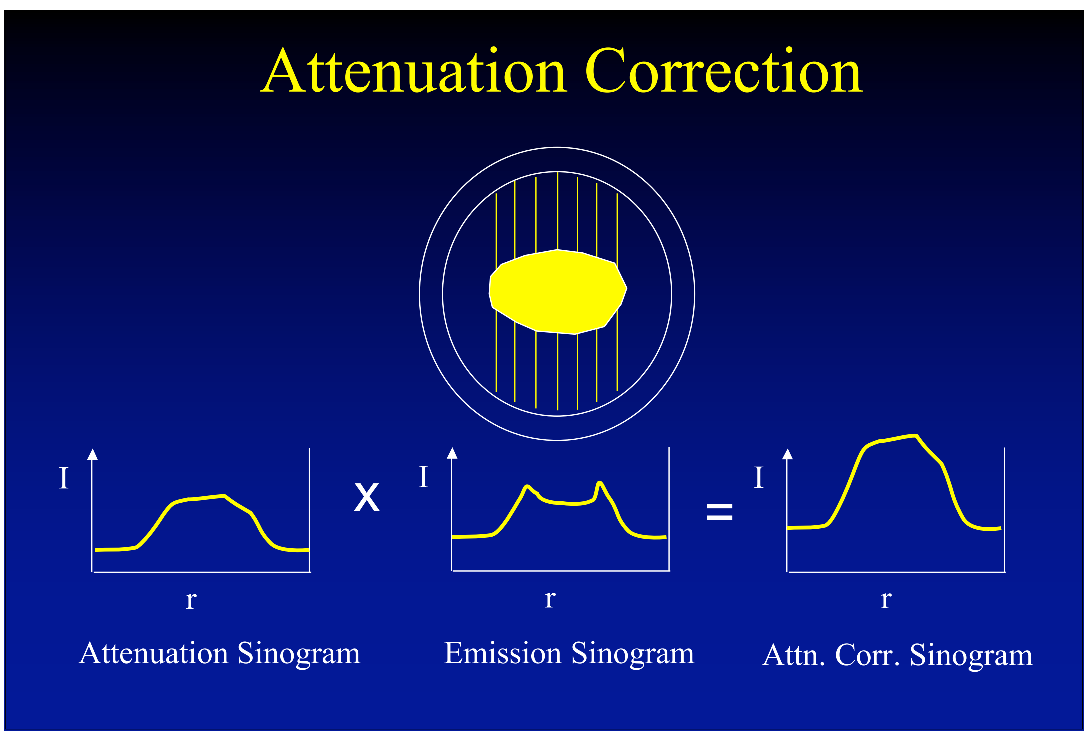
Rotating
Transmission
Source
Ge-68

Events in a Static Brain Acquisition with Measured Attenuation



UCSD


Attenuation Correction
Rod Source
I
r
Blank Sinogram
÷
I
r
Transmission Sinogram
=
I
r
Attenuation Sinogram


Attenuation Correction
I
r
Attenuation Sinogram
X
I
r
Emission Sinogram
=
I
r
Attn. Corr. Sinogram

Artifacts with Measured Attenuation Correction due to Patient Movement

Measured atten. correction

No correction applied

Attenuation artifact from motion

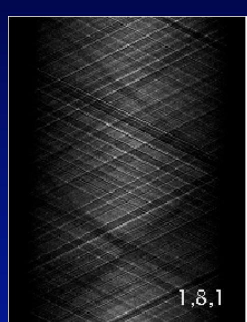
FDG Brain Scan (10 mCi)

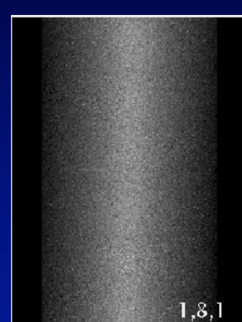
Normalization

Before Normalization

After Normalization

(rotating plane or rod source)





Normalization corrects for variations in crystal geometric and detection efficiencies

UCSD

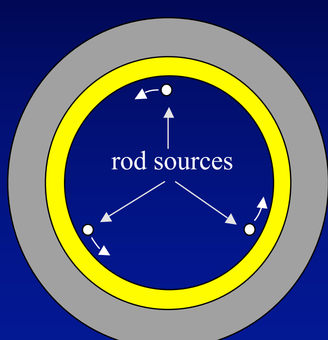
PET Quality Control

Scan Type	When to Perform
1. Daily Check Scan (blank)	Every day
2. Bucket Setup	When system is drifting
3. Normalization	Weekly to monthly, or after bucket setup
4. Phantom calibration	On a new ^{68}Ge phantom

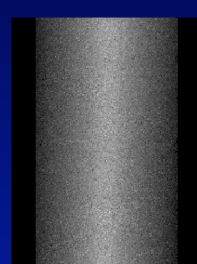
UCSD

PET Quality Control

Daily Check Scan

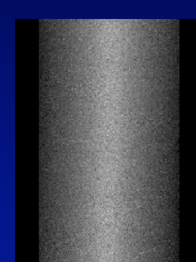


Daily
Blank Sinogram
2 hr or 200M counts



?
=

Reference
Blank Sinogram
From prior normalization

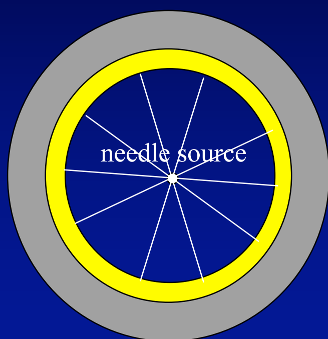


If $> \underline{+}$ 2.5 S.D. : recommend normalization
If $> \underline{+}$ 5.0 S.D. : recommend service

UCSD

PET Quality Control

Bucket Setup (2hrs)



Adjust constant fraction discriminators

Adjust x-y position of the position profile

Adjust the time alignment (electronics)

Adjusts for different type of PMTs

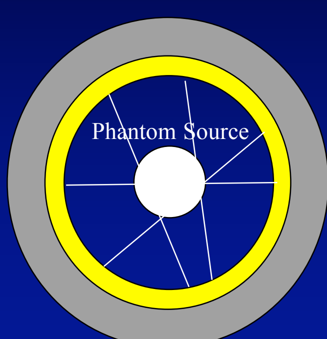
Reports bad detector blocks

UCSD

PET Quality Control

3D and 2D Normalization (~6.5 hrs)

Phantom Source: 0.5 mCi for 3D
3.0 mCi for 2D



Acquire calibration scan (30 mins)

Crystal Efficiency scan (4 hrs or 50M cnts)

Calculates Normalization file

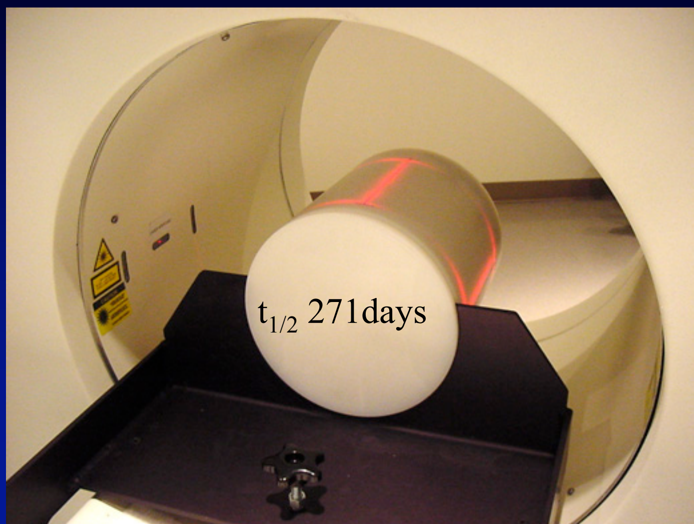
Set to the default normalization file.

Reconstructs calibration scan with attn corr

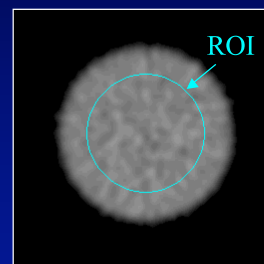
2D standard blank scan (2hrs or 200M cnts)

Computes ECF (correction factor)

^{68}Ge Cylinder Phantom

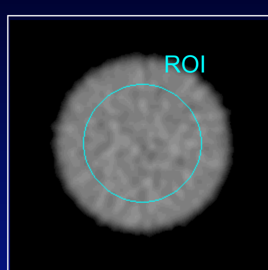


Transaxial Image of Phantom



Determination of Calibration Factor

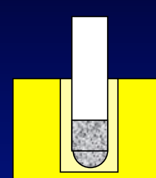
Image of ^{68}Ge cylinder fluid



cylinder filled with water and 68Ge activity
$T_{1/2}$ = 271 days

Cylinder ROI counts $\left[\frac{\text{image-cnts}}{\text{pixel sec}}\right]$

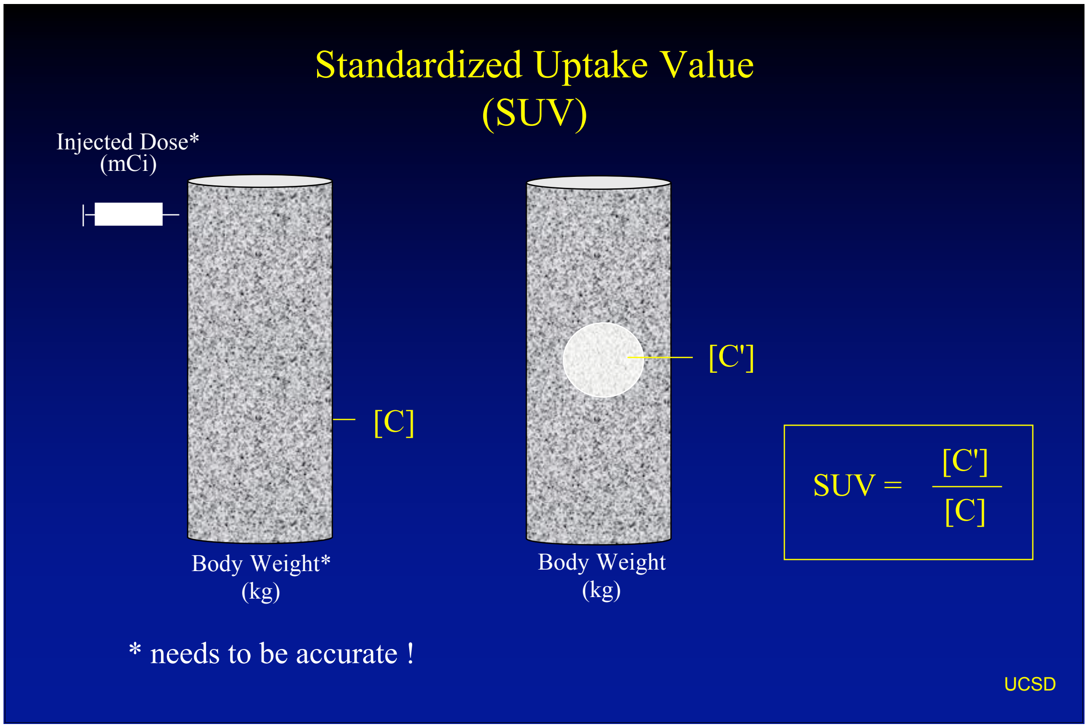
Well Counter measure of ^{68}Ge cylinder fluid

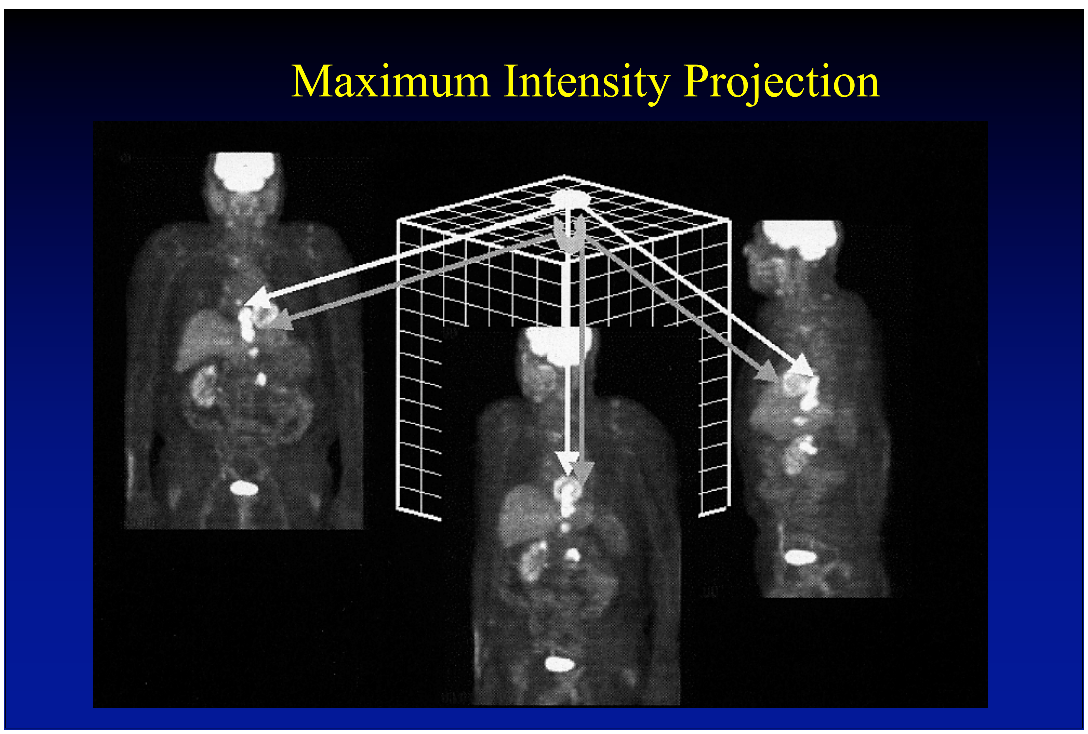


Cylinder well counts $\left[\frac{\text{well-cnts}}{\text{cc sec}}\right]$

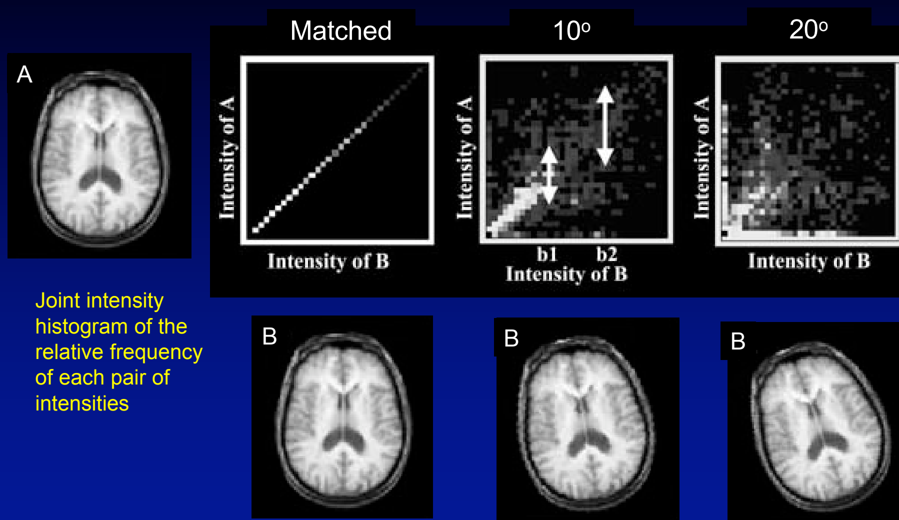
$$\text{Calibration } \textbf{Factor} = \frac{\text{Cylinder well counts}}{\text{Cylinder ROI counts}} \quad \left[\frac{\text{well-cnts}}{\text{cc }\cancel{\text{sec}}}\right]\left[\frac{\text{pixel }\cancel{\text{sec}}}{\text{image-cnts}}\right]$$

UCSD


Standardized Uptake Value
(SUV)
Injected Dose*
(mCi)
[C]
[C']
Body Weight*
(kg)
Body Weight
(kg)
SUV = [C'] / [C]
* needs to be accurate !
UCSD

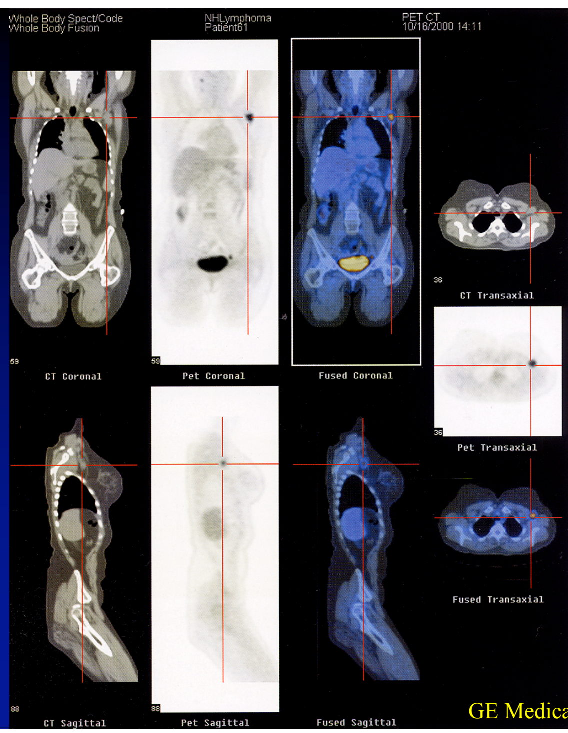

Maximum Intensity Projection

Registration by Maximization of Mutual Information

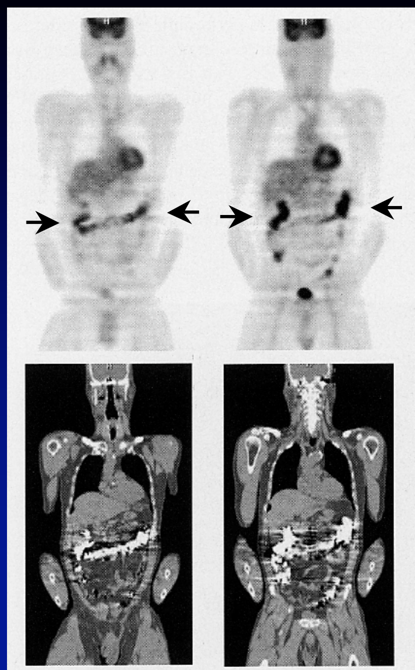


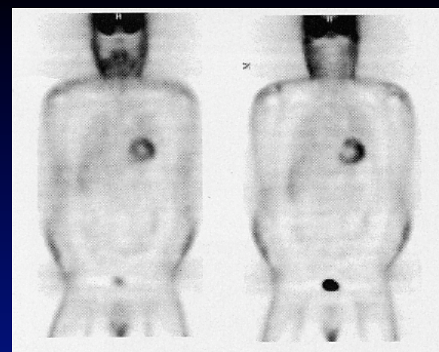
Joint intensity histogram of the relative frequency of each pair of intensities

Hutton EF, Braun M. Sem Nucl Med 2003, 28: 180-192.
Maes F, et al. IEEE Trans Med Imag 1997, 16: 187-198.



GE Medical Systems, Waukesha, WI





Attenuation artifact from barium

Data Analysis: Tracer Kinetic Modeling

- PET can image [radiotracer] in tissue
  - Calibration factor
  - Tomograpic technique
  - Accurate tissue attenuation correction
- Accurate time activity curves
  - Dynamic acquisitions
  - Fine temporal framing resolution

Tracer Kinetic Modeling

Assumptions

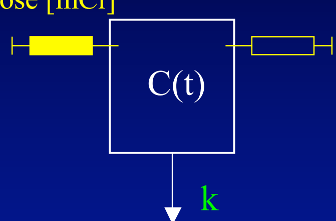
1. The tracer is structurally related to the natural substance in the dynamic process.
2. The tracer is measurable and distinguishable from the natural substance that it intends to trace.
3. The tracer is used in “trace” amounts; does not perturb the original metabolic state or physiologic condition.
4. The process being measured has “steady state” kinetics; the reaction rates are constants.

Tracer Kinetic Modeling

Example of Absolute Quantitation: Renal Clearance

One Compartment Model

Dose [mCi]



Monoexponential kinetics

$$\frac{d\,C(t)}{dt} = -k\,C(t)$$

$$\int \frac{d\,C(t)}{C(t)} = -k \int dt$$

$$\ln[C(t_2)] - \ln[C(t_1)] = -k\,(t_2 - t_1)$$

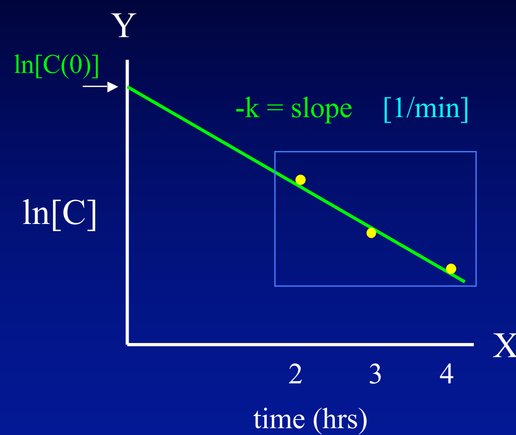
$$\ln[C(t_2)] = -k\,t_2 - \ln[C(0)]$$

Tracer Kinetic Modeling

Example of Absolute Quantitation: Renal Clearance

$$\ln[C(t_2)] = -k\, t_2 + \ln[C(0)]$$

$$Y = \text{slope}\ X + B$$

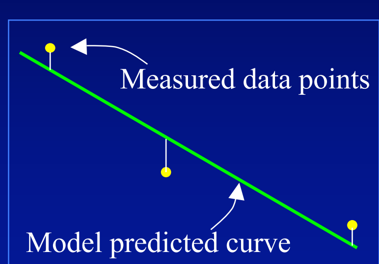


Tracer Kinetic Modeling

Example of Absolute Quantitation: Renal Clearance

Linear Least Squares Regression

Fitting the data to a straight line



$$\text{slope} = \frac{\Sigma XY - n\bar{X}\bar{Y}}{\Sigma X^2 - n\bar{X}^2}$$

$$B = \bar{Y} - \text{slope}\ \bar{X}$$

Tracer Kinetic Modeling

Example of Absolute Quantitation: Renal Clearance

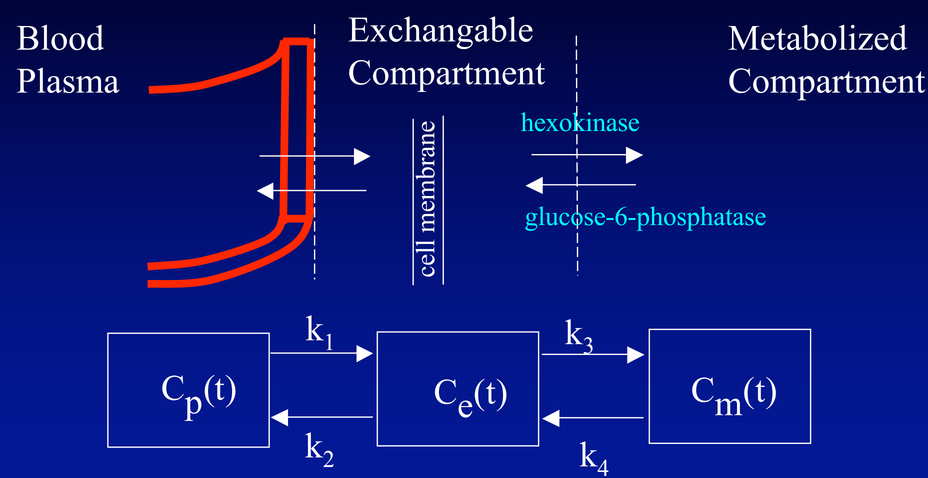
Renal Clearance Formula

$$\text{Clearance} = \frac{k * \text{Dose}}{C(0)}$$

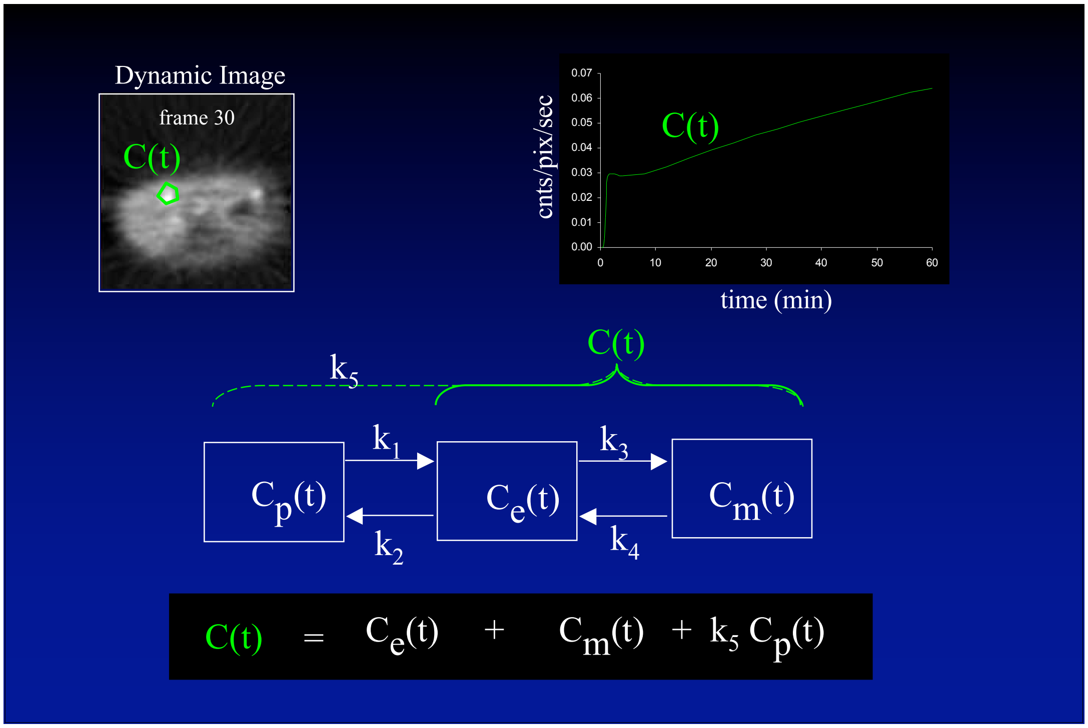
Units

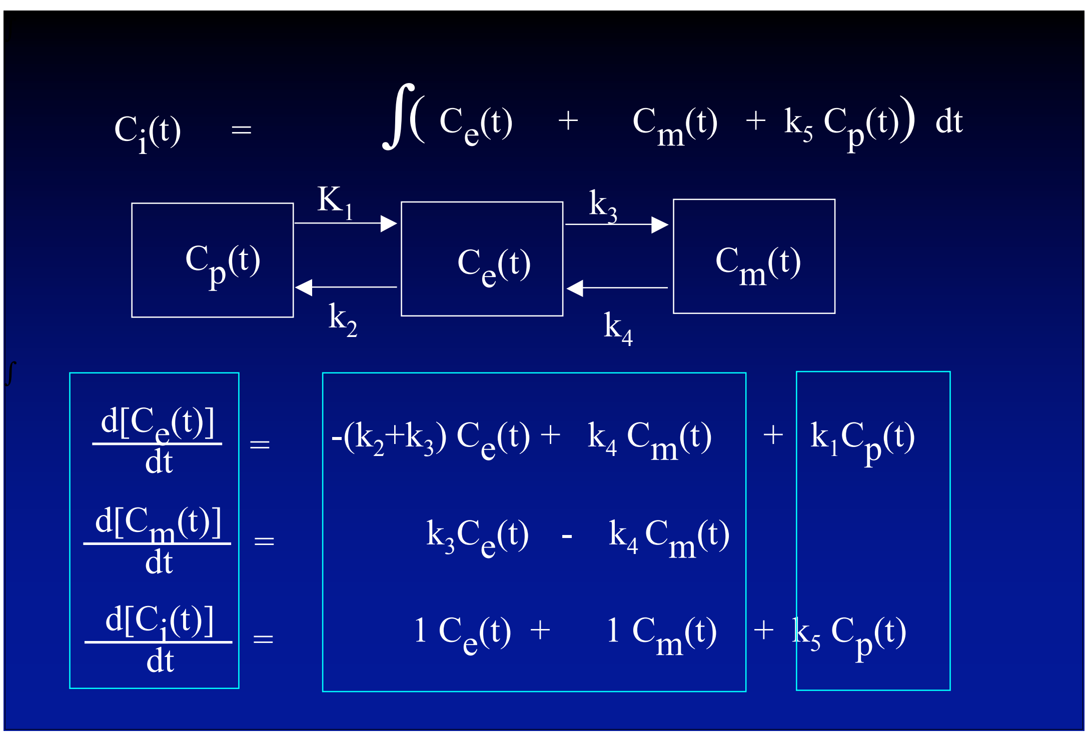
$$\left[\frac{\text{ml}}{\text{min}}\right] = \frac{\left[\frac{1}{\text{min}}\right][\cancel{\text{mCi}}]}{\left[\frac{\cancel{\text{mCi}}}{\text{ml}}\right]}$$

Three compartment model of 18F-fluoro-2-deoxyglucose (FDG)



Phelps ME, Positron Emission Tomography and Autoradiography, Raven Press, New York 1986


Dynamic Image
frame 30
C(t)
cnts/pix/sec
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0.00
0
10
20
30
40
50
60
time (min)
C(t)
C(t)
k_5
k_1
k_2
k_3
k_4
$C_p(t)$
$C_e(t)$
$C_m(t)$
$C(t) = C_e(t) + C_m(t) + k_5 C_p(t)$


$C_i(t) = \int (C_e(t) + C_m(t) + k_5 C_p(t)) \, dt$
K_1
k_2
k_3
k_4
$C_p(t)$
$C_e(t)$
$C_m(t)$
$\frac{d[C_e(t)]}{dt} = -(k_2+k_3) C_e(t) + k_4 C_m(t) + k_1 C_p(t)$
$\frac{d[C_m(t)]}{dt} = k_3 C_e(t) - k_4 C_m(t)$
$\frac{d[C_i(t)]}{dt} = 1 C_e(t) + 1 C_m(t) + k_5 C_p(t)$

Arrange into State Space Equations

$$\dot{X}(t) = A \; X(t) + B \; C_p(t)$$

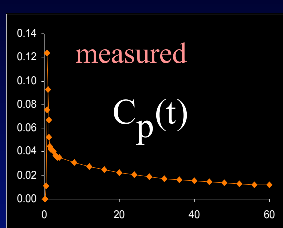
$$Y(t) = C \; X(t) + D \; C_p(t)$$

$$\begin{bmatrix} \dot{C}_e(t) \\ \dot{C}_m(t) \\ \dot{C}_i(t) \end{bmatrix} = \begin{bmatrix} -(k_2+k_3) & k_4 & 0 \\ k_3 & -k_4 & 0 \\ 1 & 1 & 0 \end{bmatrix} \begin{bmatrix} C_e(t) \\ C_m(t) \\ C_i(t) \end{bmatrix} + \begin{bmatrix} k_1 \\ 0 \\ k_5 \end{bmatrix} C_p(t)$$

$$\begin{bmatrix} C_i(t) \end{bmatrix} = \begin{bmatrix} 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} C_e(t) \\ C_m(t) \\ C_i(t) \end{bmatrix} + \begin{bmatrix} 0 \end{bmatrix} C_p(t)$$

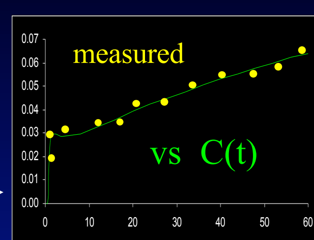
Raven FH, Automatic Control Engineering, McGraw-Hill, New York, 1978

Non-linear Regression Analysis



Solve State Space Equations

$C(t)$

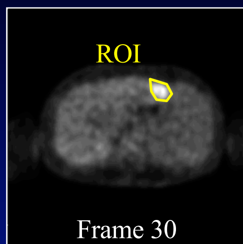


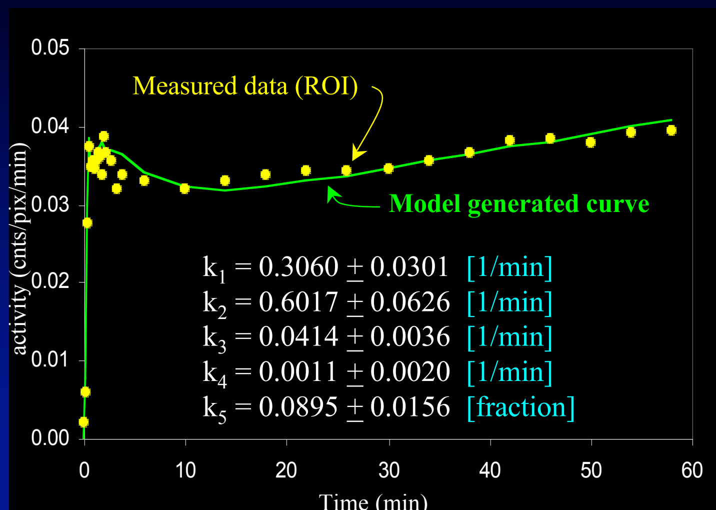
$k_1 \;\; k_2 \;\; k_3 \;\; k_4 \;\; k_5$ function $\Rightarrow$ Error = Σ (measured – $C(t))^2$

Error = function(k_1, k_2, k_3, k_4, k_5)

Bate DM, Nonlinear Regression Analysis and its Applications, Wiley & Sons, New York, 1988

FDG Tracer Kinetic Analysis: Final Results





K_{NLR} = 0.0197 [1/min]
Stnd. Error = 0.0008

Luc_10de_bb_20_de10tumor.cpt

Net Uptake Rate Constant of FDG: K_{NLR}

$$\frac{d[C_m(t)]}{dt} = \boxed{\frac{k_1 * k_3}{k_2 + k_3}} C_p(t) + \frac{k_2 * k_4}{k_2 + k_3} C_m(t)$$

$$\text{Net FDG Uptake} = \boxed{\frac{k_1 * k_3}{k_2 + k_3}} C_p(t) = \boxed{K_{NLR}} C_p(t)$$

$$\text{Net Glucose Uptake} = \boxed{\frac{k_1 * k_3}{k_2 + k_3}} \frac{[\text{Glucose}]}{LC} = \frac{\boxed{K_{NLR}}}{LC} [\text{Glucose}]$$

NLR = non-linear regression
LC = lumped constant

Patlak Graphical Analysis

$$\frac{C_i(t)}{C_p(t)} = K_{PAT} \frac{\Sigma C_p(t)\ dt}{C_p(t)} + V_d$$

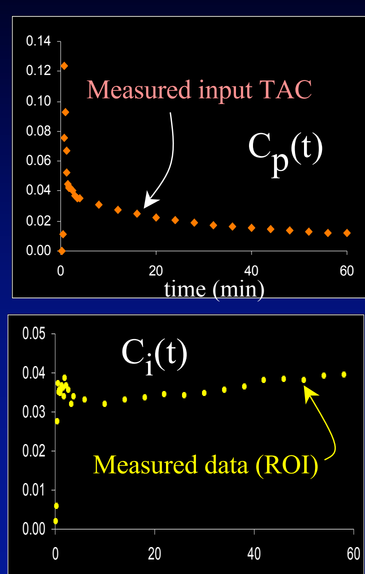
$$Y = \text{slope} \quad X \quad + \quad B$$

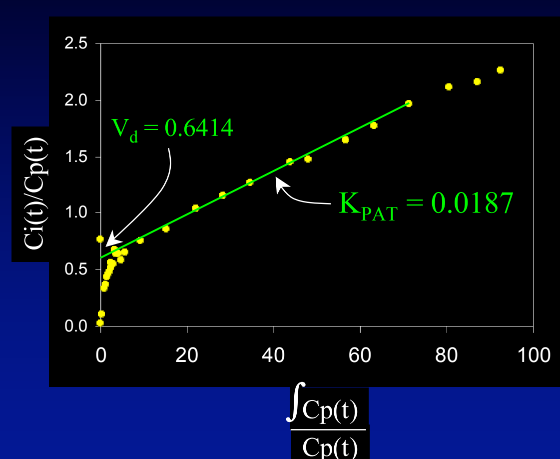
$$K_{PAT} = \text{slope} = \frac{\Sigma Y X - n X Y}{\Sigma X^2 - n X^2}$$

least squares
linear regression

Patlak CS J Cereb Blood Flow Metab 1983; 3: 1-7.

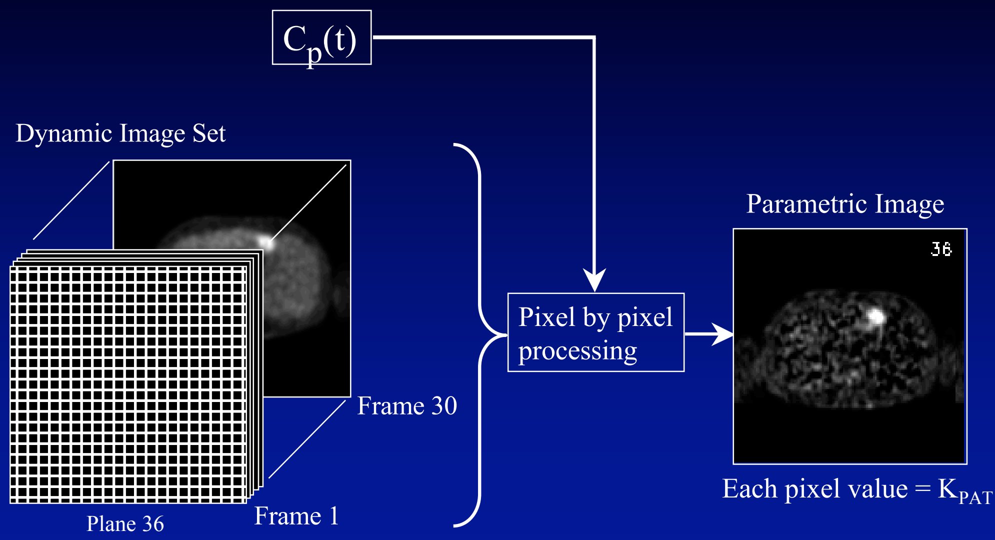
Patlak Graphical Analysis





Luc_10de_bb_20_de10tumor.cpt

Patlak Graphical Analysis



Future of PET technology

1. New detector technology: crystals & electronics.
2. Iterative image reconstruction modeling in scanner characteristics.
3. Quantitative image in whole body acquisition mode.
4. PET/CT, PET/MRI?