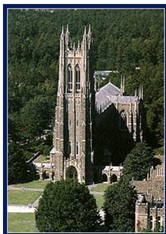

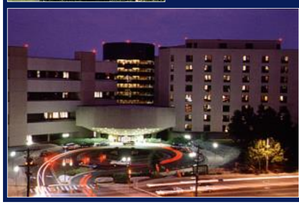

Review of PET "Physics"

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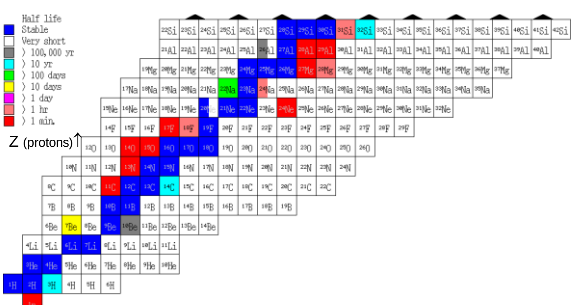
Duke University
Durham, North Carolina, USA

Disclosures

- Consultant – Data Spectrum Corporation
- Research Support – GE Healthcare

Chart of Nuclides



Nuclear Data Evaluation Lab.
Korea Atomic Energy Research Institute

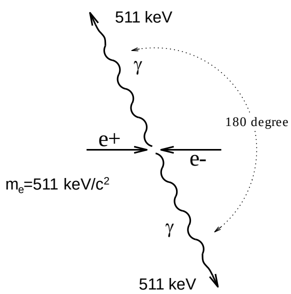
Positron Decay

$${}^{A}_{Z}X_{N} \rightarrow {}^{A}_{Z-1}Y_{N+1} + e^{+} + \upsilon$$

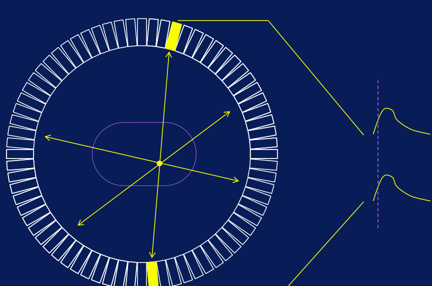
Nuclide	half-life
C-11	20.3 min
N-13	10 min
O-15	124 sec
F-18	110 min
Rb-82	*75 sec*

e.g., $^{18}F \rightarrow {}^{18}O + e^{+} + \nu$

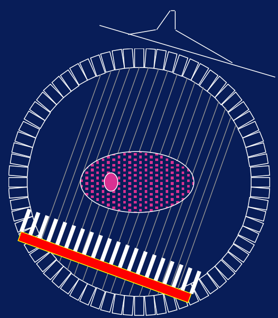
Positron Annihilation



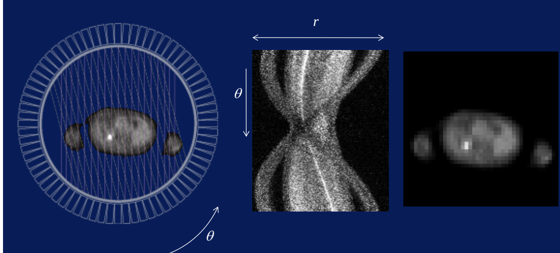
Coincidence Event



Projections



Acquisition and Reconstruction



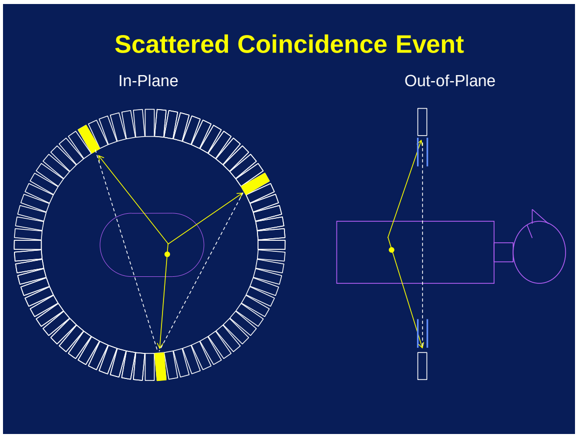
Data Acquisition

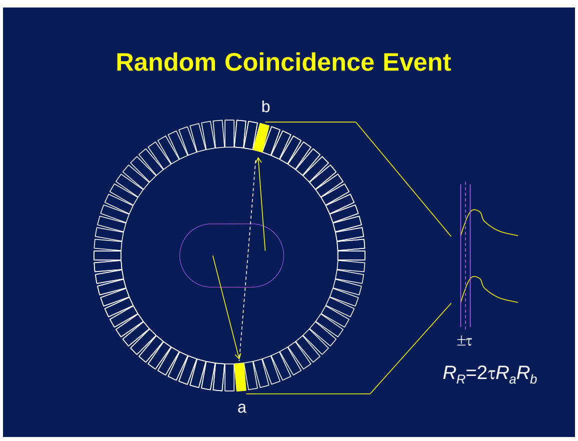
Sinogram
(raw data)

Reconstructed Image

PET Background Events

- Scatter
- Randoms





Correcting Background; Noise Equivalent Counts

$$P_{prompts} = T_{trues} + S_{scatter} + R_{randoms}$$

$T' = P - S' - R'$ *(Estimation of true events by subtracting S and R estimates)*

$$\langle T' \rangle = \langle P \rangle + \langle S' \rangle + \langle R' \rangle = P + \begin{vmatrix} 0 \\ R \end{vmatrix} \ge P \ge T$$

(Variance propagation and Poisson properties. 0 vs. R depends on randoms correction method.)

$$SNR \equiv \frac{T'}{\sqrt{\langle T' \rangle}} \approx \frac{T}{\sqrt{P + \begin{vmatrix} 0 \\ R \end{vmatrix}}};\ NEC = \frac{T^2}{P + \begin{vmatrix} 0 \\ R \end{vmatrix}} = \frac{T}{(1 + S/T + (2?)R/T)}$$

S and R refer to scattered and random events on LORs that subtend the imaged object.

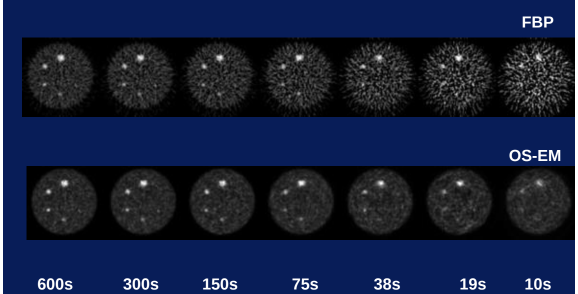
More background $\rightarrow$ more statistical image noise.

NEC Examples

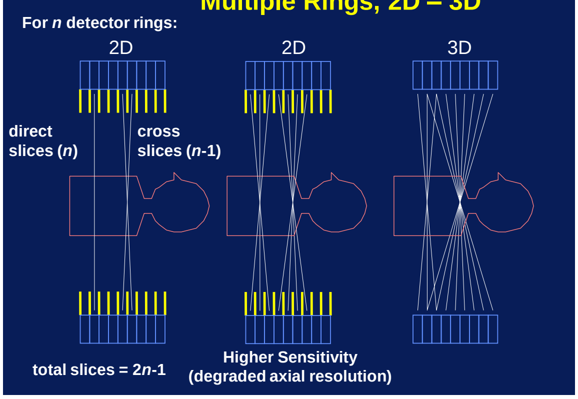
$$NEC = \frac{T}{(1 + S/T + R/T)}$$

Prompts	Trues	Scatter	SF	NEC
100	100	0	0	100
200	100	100	0.5	50
400	200	200	0.5	100

Image Noise and Lesion Detection



Multiple Rings, 2D – 3D



Time Of Flight PET: The influence of background

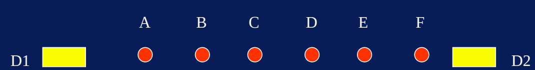
<u>How strong is source A?</u>

Detectors measure counts C_A+C_B.

S.D. of measurement is $\sqrt{C_A+C_B}$

SNR = $C_A/\sqrt{C_A+C_B}$

The influence of even more background



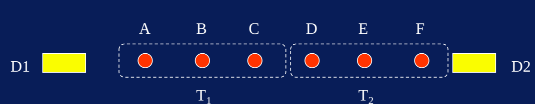
<u>SNR of measurement of A?</u>

SNR = $C_A/\sqrt{C_A+C_B+C_C+C_D+\ldots}$

If all N sources are equal,

SNR = $C_A/\sqrt{NC_A}$

Magical new detectors



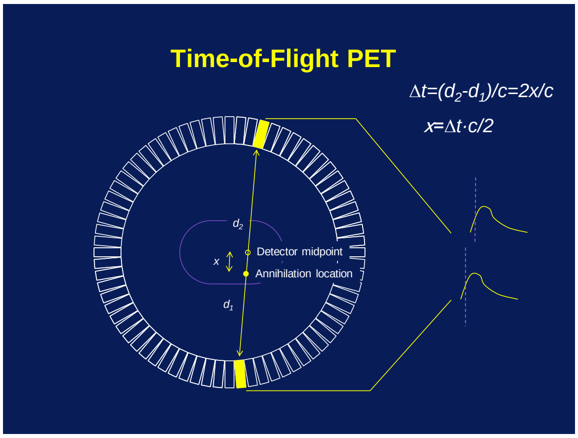
Can distinguish between counts originating in segment T_1 and counts originating in segment T_2.

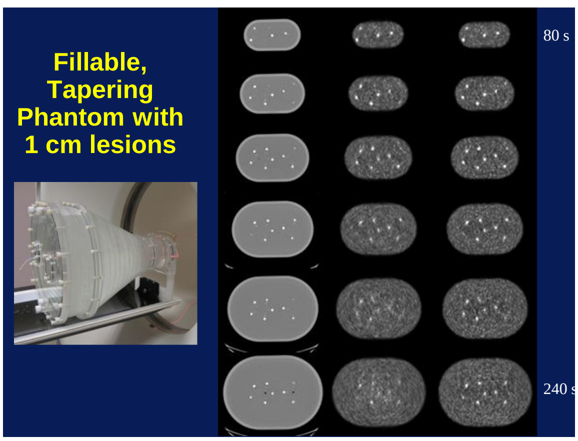
If all N sources are equal,

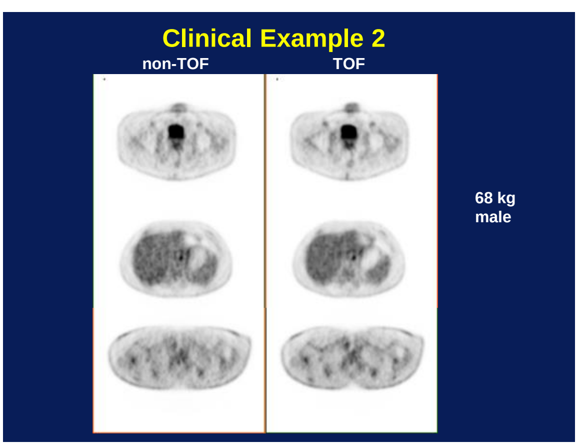
SNR = $C_A/\sqrt{nC_A}$

where n is the number of sources within zone T_1.

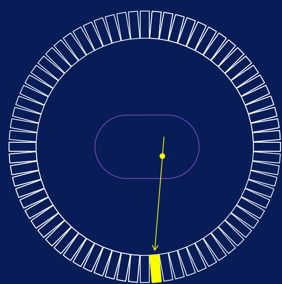
SNR improvement of sqrt(N/n); similar to counting longer by N/n.


Time-of-Flight PET
Δt=(d2-d1)/c=2x/c
x=Δt·c/2
d2
x
Detector midpoint
Annihilation location
d1

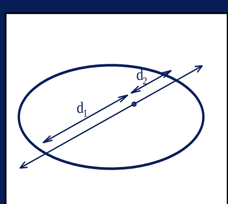

Fillable, Tapering Phantom with 1 cm lesions
80 s
240 s


Clinical Example 2
non-TOF
TOF
68 kg male

Attenuated Event



Coincidence Attenuation

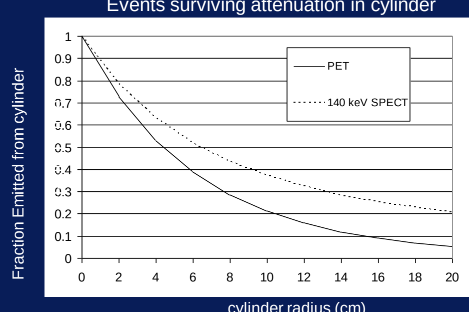


$$P_C = P_1 P_2$$
$$= e^{-\mu \cdot d_1} e^{-\mu \cdot d_2}$$
$$= e^{-\mu \cdot (d_1 + d_2)}$$

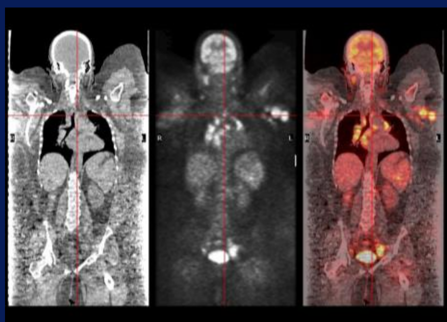
Annihilation radiation emitted along a particular line of response has the same attenuation probability, regardless of where it originated on the line.

Attenuation losses - PET and SPECT

Events surviving attenuation in cylinder



Obese Patient

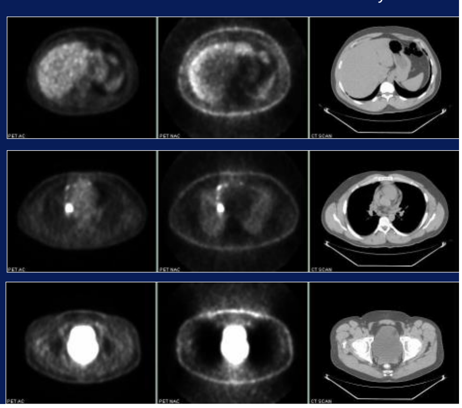


Technologist Size Variations

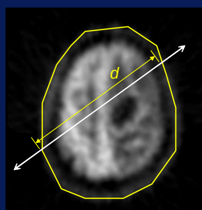
$m_b \sim 2.5 m_a$

Attenuation Effects

AC	NAC	x-ray CT

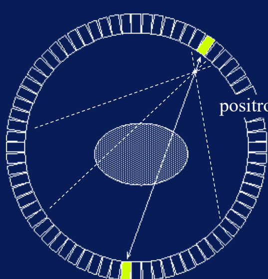


Calculated Attenuation Correction

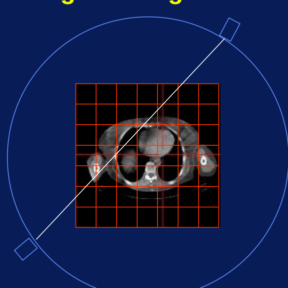


$I = I_0 e^{-\mu d}$

Transmission Attenuation Measurement



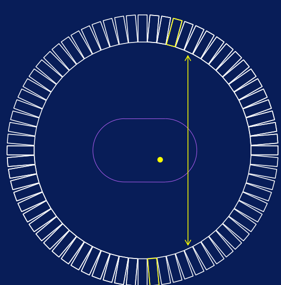
Using CT image for AC



Attenuation Correction Accuracy

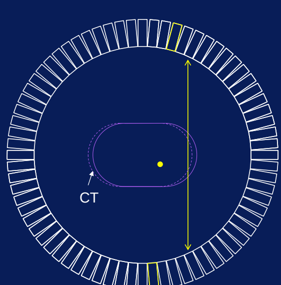
- CT-based attenuation correction is performed on almost all PET studies.
- Is it being done well?
  - Is the CT accurate (e.g., water = 0)?
  - Is the CT accurate under all relevant conditions?
  - Is the translation between CT# and 511 keV μ appropriate?
  - Patient motion between CT and PET?
  - …

Attenuation Correction



Photons emitted along this line will be attenuated by a factor that can be determined from the corresponding CT scan.

Attenuation Correction



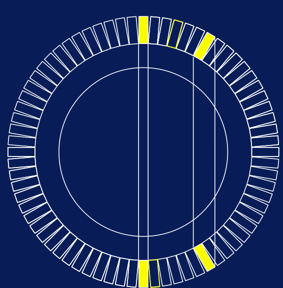
The biggest source of error in PET AC is patient motion between the CT and the PET scans.
This particular PET photon trajectory will be undercorrected. The intensity on this side of the body will be artificially low.

Spatial Resolution

$$R_{sys} = \sqrt{R_{det}^2 + R_{acol}^2 + R_{range}^2 + b^2}$$

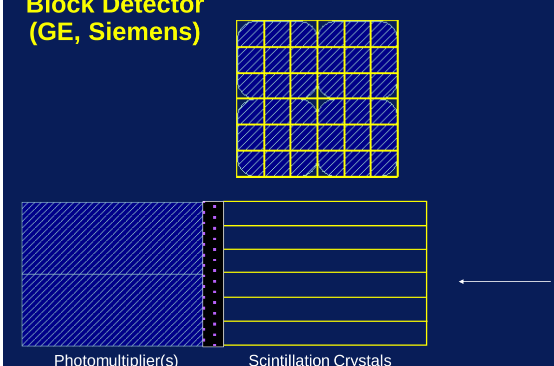
R_{det} = resolution of detectors ($\leq d$)
R_{acol} = resolution from photon acollinearity (=0.0022D)
R_{range} = resolution from positron range
b = block effect

Depth of Interaction Uncertainty

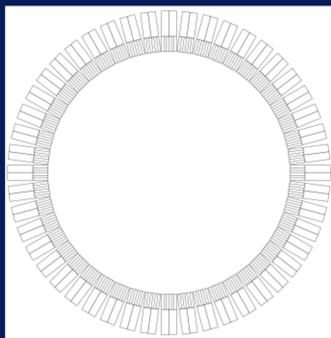


- Uncertainty in the origin of radiation when measured obliquely in a detector.
- Resolution in radial direction worsens with increasing radius.
- High stopping power helps: Interactions more likely in front of detector
- Some high resolution systems sacrifice sensitivity by shortening detectors (to mitigate DOI effects.)
- Some systems (HRRT) use two layers of detectors to lessen effect. Others propose a measurement of the DOI.

Block Detector (GE, Siemens)

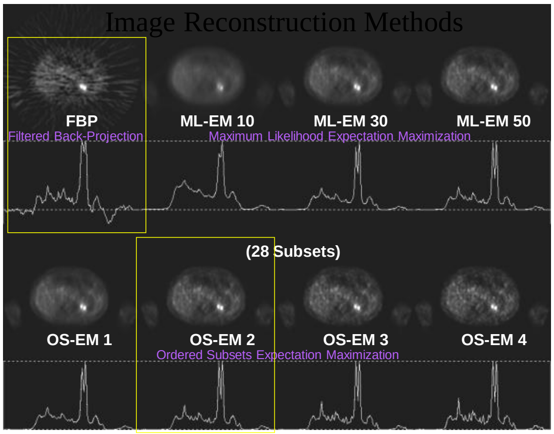


PET Ring with Block Detectors

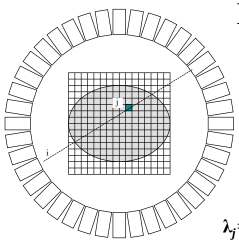


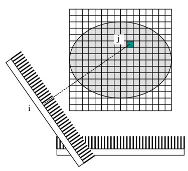
Curved Plate Pixelated Camera (Philips)

Image Reconstruction



Detection Model



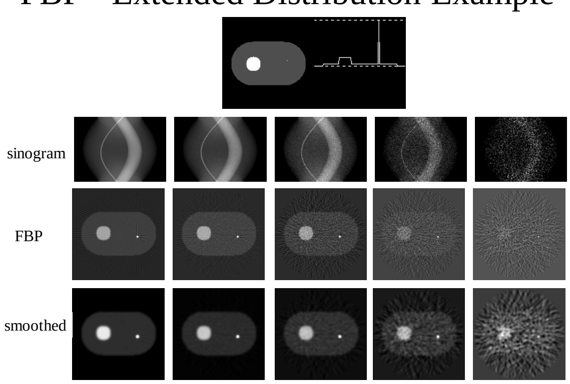


$$y_i = b_i + \sum_{j=1}^{npix} p_{ij} \lambda_j$$

$\boldsymbol{\lambda_j}$ = radioactivity at voxel ***j***
$\boldsymbol{p_{ij}}$ = probability of emission from ***j*** being measure in ***i***
$\boldsymbol{b_i}$ = background contributing to ***i***
$\boldsymbol{y_i}$ = expected counts on projection ***i***
$\boldsymbol{m_i}$ = measured counts on proj. ***i***

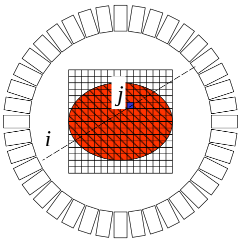
Image reconstruction: $\lambda = \boldsymbol{p}^{-1}(m_i - b_i)$ (What is $\boldsymbol{p}^{-1}$?)

FBP - Extended Distribution Example



Maximum Likelihood Expectation Maximization (ML-EM)

Shepp LA, Vardi Y., *IEEE Trans Med Imag* 1:113-121, 1982.
Lange K, Carson R., *J Comput Assist Tomo* 8:306-316, 1984.

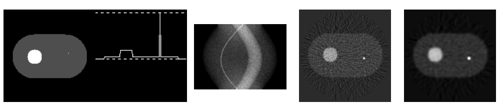


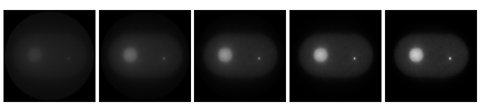
$$\lambda_j^{(n+1)} = \frac{1}{\sum_{i=1}^{nbin} p_{ij}} \sum_{i=1}^{nbin} \frac{p_{ij}\lambda_j^{(n)}}{b_i + \sum_{k=1}^{nvox} p_{ik}\lambda_k^{(n)}} m_i$$

$$y_i = b_i + \sum_{j=1}^{npix} p_{ij}\lambda_j$$

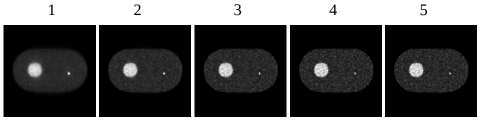
$\lambda_j^{(n)}$ is the estimated activity in voxel j at iteration n.

Extended Distribution Example



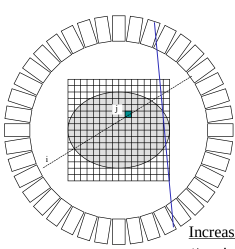


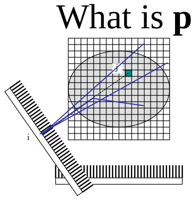
1 2 3 4 5



10 20 30 40 50

What is p?





$$y_i = b_i + \sum_{j=1}^{npix} p_{ij}\lambda_j$$

Increasing levels of complexity:

1) **p** is 1's and 0's - very sparse
2) **p** is fractional values, depending on how column intersects with voxel - still pretty sparse
3) **p** includes attenuation (lower values) – no less sparse
4) **p** includes resolution effects (collimator blurring, etc) - somewhat sparse – inherently 3D
5) **p** includes background - not sparse at all

Compensations/Corrections

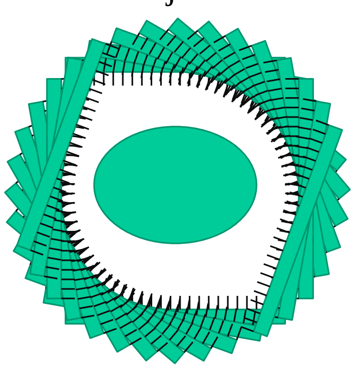
Putting physical effects into **p** allows the reconstruction to compensate for those effects.

For example, including attenuation in the model leads to attenuation correction in the final image. Putting system blurring (imperfect spatial resolution) can improve the final image resolution (and/or noise).

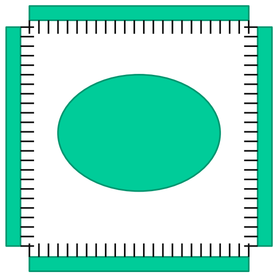
ML-EM Characteristics

- Not Fast
- Non-negative pixel values - can lead to biases
- Noise is greatest in areas of high activity
- Can compensate for physical effects
- Allows image reconstruction from limited projections.

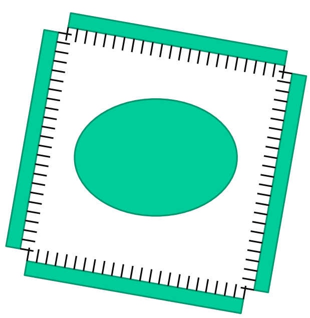
All Projections



Subset 1



Subset 2



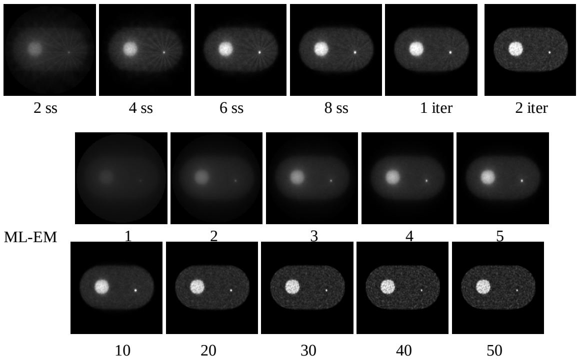
Ordered Subsets Expectation Maximization (OS-EM)

Hudson HM, Larkin RS . *IEEE Trans Med Imag* 13:601-609, 1994.

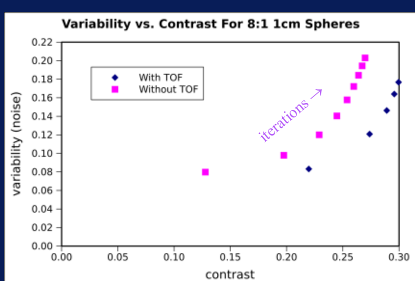
$$\lambda_j^{(n+1)} = \frac{1}{\sum_{i=1}^{nbin} p_{ij}} \sum_{i=1}^{nbin} \frac{p_{ij}\lambda_j^{(n)}}{b_i + \sum_{k=1}^{nvox} p_{ik}\lambda_k^{(n)}} m_i$$

Instead of processing all projection for each image update, projections are divided into subsets, and the image is updated after processing each subset.

OS-EM 10 subsets



TOF vs NTOF : 1 Hot Spheres



Regularization in iterative reconstruction

Is it possible to control noise during the iterations so that resolution improves but noise doesn't increase?

Regularized Reon (Q.Clear)

$$\sum_{j=1}^{n}\sum\nolimits_{k\in N_j} w_j\, w_k \frac{(x_j - x_k)^2}{(x_j - x_k) + \gamma|x_j - x_k|}$$

Regularized Recon (“Q.Clear”)

4min 2min 1min 30s

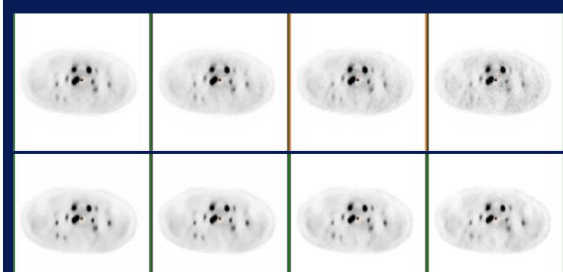


Image Quantitation

What is Image Quantitation?

- Generally - Deriving numbers from images
- Volume measurement
- Motion measurements (e.g., ejection fraction)
- Distributions of radiotracers, and, under the right circumstances, the underlying physiological processes.

What Factors Affect Quantitation of Radionuclide Distributions?

- Successful calibration of scanning system (counts/s to activity)
- Accurate corrections for
  - attenuation
  - scatter
  - randoms
  - dead time
    (the bigger the effect, the more accurate the correction must be)
- Quantitative reconstruction algorithm
- Resolution effects (degradation of small structures)
- ROI (Region Of Interest) Analysis

Standardized Uptake Value (SUV)

- The SUV radioactivity concentration (what the scanner measures) normalized to injected dose and body mass:

$$SUV = \frac{radioactivity\ concentration}{injected\ dose / body\ mass}$$

- Local concentration divided by the body mean concentration
- Dimensions are mass/volume (e.g. g/ml). A*lmost* dimensionless.
- This is sometimes referred to as a semi-quantitative measure (compared to kinetic modeling.)

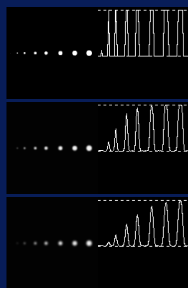
Sphere Size vs. Spatial Resolution

"Full Recovery":
When at least some pixels in a region retain full intensity

"Recovery coefficient":
Ratio between measured and actual values (due to resolution effects only)
RC $\leq$ 1

Sphere diameter $\geq$ 3X FWHM resolution $\rightarrow$ full recovery (for 3D blurring)
(Not so bad if non-spherical, or non-3D blurring)

Sphere diameters:
"1", 2, 3, 4, 5, 6, 7, 8 pixels



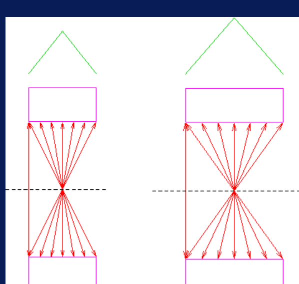
no smoothing

2 pixel FWHM 3D smoothing

3 pixel FWHM 3D smoothing

Some New Developments

3D Sensitivity vs. axial FOV



Sens $\propto$ (FOV)^2

GE Discovery IQ

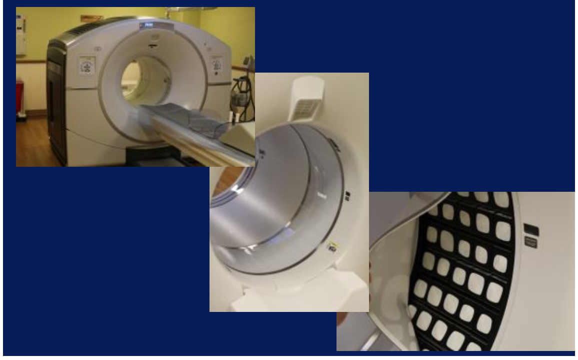
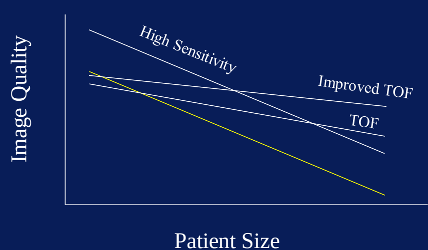


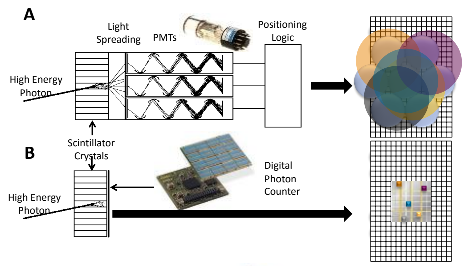
Image Quality vs. Size



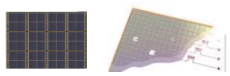
Digital PET (Philips)

(Thanks to Jun Zhang, PhD, Ohio State University)

PMT detector approach versus SiPM DPC detector approach



array of 64 pixels DPC detector element. each pixel couples directly to a single scintillation crystal.



thousands of microcells / pixel -> direct detection of single photons -> a pure binary output signal.

Jun Zhang, PhD DABR; Michael V Knopp, MD, PhD; WCIBMI, Radiology at The Ohio State University

Continuous Bed Motion (Siemens)

(Thanks to John Sunderland, PhD, University of Iowa)

FlowMotion: Engineering

Non-Trivial Implementation!

Mechanical
- Magnetically driven bed with 0.25mm positioning accuracy
- Speeds of 0.1mm/sec – 20mm/sec
- Cantilevered bed – no differential deflection

Acquisition Electronics
- Position recorded real-time in list mode data
- SSD RAID system continuously collects list mode data independently of acquisition computer
- RAID continuously streams output to sinograms in real time (uses stored list-mode position data)

Normalization is non-trivial and scan dependent
- Events accumulate in *virtual* Lines of Response (*vLOR*). The final efficiency (normalization coefficient) is a combination individual efficiencies of detectors as the patient moves through the gantry.

Randoms correction is similarly complex
- Because singles rate not constant over time as patient flows through gantry

FlowMotion: How it works: Equivalency Table

Equivalency Table

Legs for melanoma patients

3 Ring Scanner

Stop and Go Acquisition Time (min/bed)	Flow Bed Velocity (mm/s)
1:00	1.5
1:48	0.8
2:00	0.7
2:30	0.6
3:00	0.5
4:00	0.4
5:00	0.3
6:00	0.2
10:00	0.1

Table 1. *Stop and go min/bed acquisition times mapped to FlowMotion bed velocity to achieve equivalent image quality for the Biograph mCT Flow.*

4 Ring Scanner
"TrueV" Option

Stop and Go Acquisition Time (min/bed)	Flow Bed Velocity (mm/s)
1:00	2.1
1:48	1.2
2:00	1.1
2:48	0.8
3:00	0.7
4:00	0.5
5:00	0.4
8:00	0.3
10:00	0.2

Table 2. *Stop and go min/bed acquisition times mapped to FlowMotion bed velocity to achieve equivalent image quality for the Biograph mCT Flow with TrueV option*

Body, depending upon BMI

Cardiac Sarcoidosis Protocol

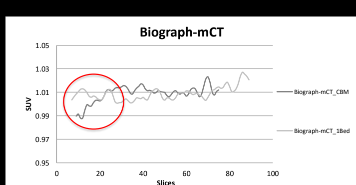
FlowMotion: Why Yes?

Advantages:

1. Nearly uniform efficiency across the field of view
   - Step and Shoot overlap <50% results in non-uniform efficiency.
   - Physicians don't notice. I appreciate. Have not measured though.
2. Better end plane statistics due to "overscanning"
   - FlowMotion purposely overscans at endplanes to get additional statistics. End-planes no longer "unusable".
   - Nice feature but not a difference-maker.
3. Up to 4 regions can be defined with different bed speeds.
   - Can tune acquisitions to meet specific patient body habitus.
   - Use this capability ALL THE TIME (although most protocols 2-3 regions)
4. 2 meter bed throw for head to toe melanoma acquisitions
   - Can't live without. All melanomas on mCT, Not FlowMotion specific. mCT bed, too
5. Flexibility to perform "whole-body" dynamic protocols.
   - Several research protocols use this capability
6. Patient experience.
7. Technologists seem to like the implementation

FlowMotion: Why Not?

- $$$ Bang for the Buck?
- Non Uniformity? 3% directional bias in uniform phantom studies. Fixed in newest software release.

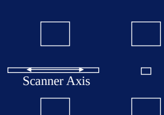


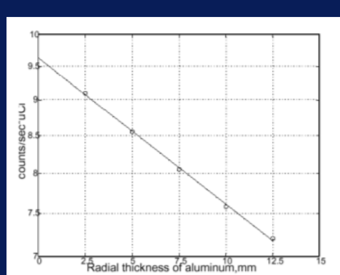
NEMA NU-2 Performance Tests

- Spatial Resolution
- Sensitivity
- Count Rate and Scatter Fraction
- Image Quality

PET Performance - Sensitivity

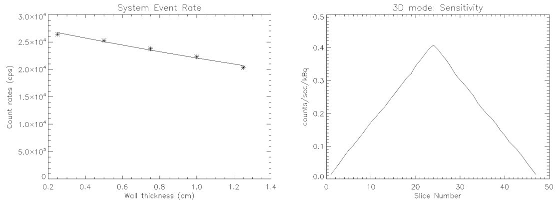
Five Concentric 70 cm long aluminum tubes surrounding source





Why long line source? Whole body sensitivity.

Sensitivity - 3D, r=0



System sensitivity: 9.75084 (counts/sec/kBq)

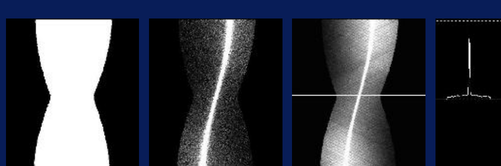
Attenuation Coef. for sleeves: 0.127310 (1/cm)

Results generated from scan with NU2−2001 3D Sens R0 sleeve 5

Scatter Fraction and Count Rate

Scatter Fraction

- S/(S+T) --- low is good
- reflects energy resolution and geometry
- Method:
  - Axial low-intensity line source in phantom
  - Mask out LORs not subtending phantom
  - Line source makes sinusoid in each slice's sinogram
  - Pixels off the sinusoid measure background (scatter and random)
  - At very low rates, no randoms.

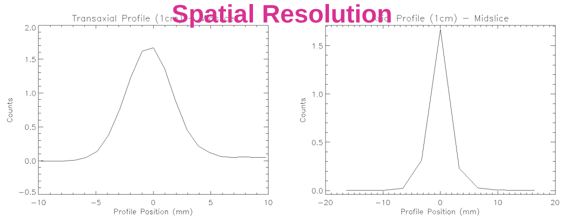


Spatial Resolution

- Small (< 1 mm) point sources placed in several locations within FOV
- Scan, reconstruct with very small (< 1/10 expected FWHM) pixels.
- Measure FWHM of resulting profiles in all three directions

Generally, pixels should be 1/3 the expected FWHM or smaller, for any NM application. Combination of recon FOV and image matrix.

Spatial Resolution



Results for 1 cm source

Trans FWHM:	5.11617 (mm)
Trans FWTM:	10.0089 (mm)
Axial FWHM:	5.03312 (mm)
Axial FWTM:	10.7149 (mm)

Results for 10 cm source

Radial FWHM:	5.91931 (mm)
Radial FWTM:	12.9862 (mm)
Tang. FWHM:	6.72302 (mm)
Tang. FWTM:	32.1492 (mm)
Axial FWHM:	5.99356 (mm)
Axial FWTM:	11.4418 (mm)