Concepts, Applications, and Requirements for Quantitative SPECT/CT

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Conflict of Interest Disclosure

Under a licensing agreement between the GE Healthcare and the Johns Hopkins University, Eric Frey is entitled to a share of royalty received by the University on sales of iterative reconstruction software used to obtain some results in this presentation.

Eric Frey is a co-founder of Radiopharmaceutical Imaging and Dosimetry, LLC. This company was founded to provide quantitative imaging and dosimetry service to developers of radiopharmaceutical therapy agents.

These interests have been disclosed and are being managed by the Johns Hopkins University in accordance with its conflict of interest policies.

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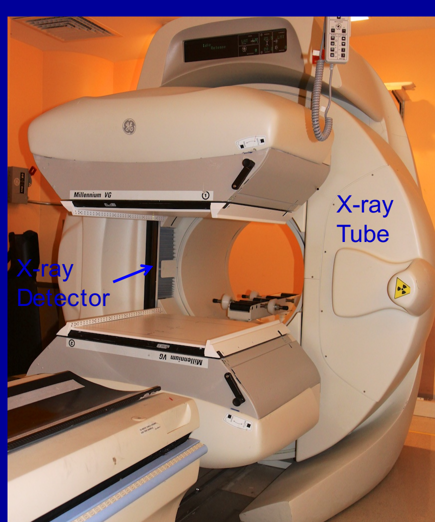
Outline

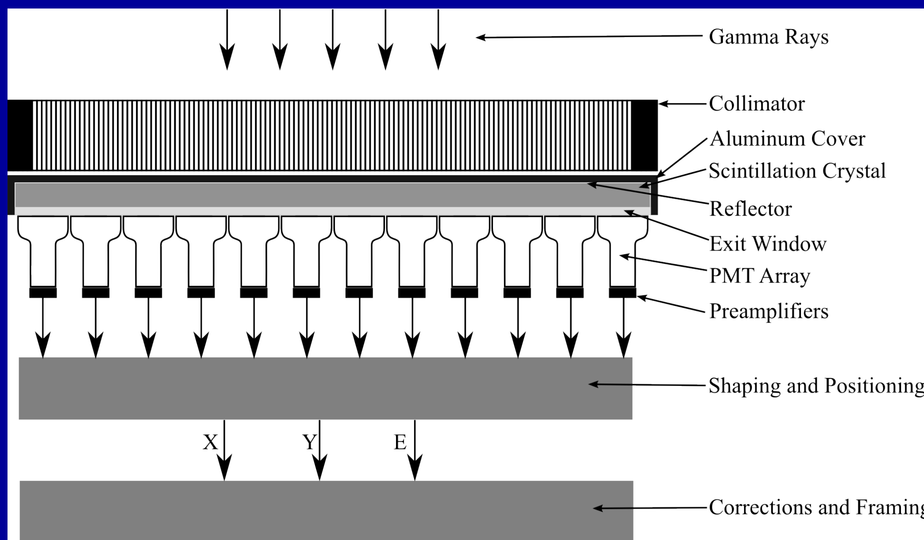
- Introduction to SPECT
- Applications of Quantitative SPECT
- Requirements for Quantitative SPECT
- Obstacles to Achieving Standardization

Single-Photon Emission Computed Tomography (SPECT)

Two-Camera SPECT/CT Systems



Gamma Cameras



Matrix Formulation of Image Reconstruction

3D Activity Distribution Image

Mean Projection Data

Projection Matrix

$$\mathbf{Ca} = \mathbf{p} + \mathbf{n}$$

Measurement Noise (Quantum, Poisson Distributed)

Reconstructed image (estimated activity distribution image)

'Inverse' of Projection Matrix

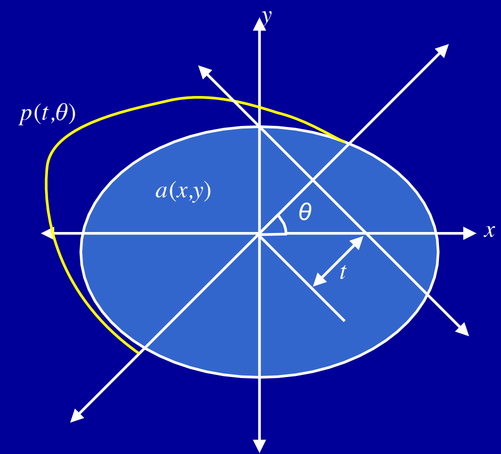
$$\tilde{\mathbf{a}} = \mathbf{C}^{\mathrm{inv}}(\mathbf{p} + \mathbf{n})$$

Projection Matrix C is

- Large (~4×10^{12} elements)
- Ill-Conditioned
- Patient-dependent

Computed Tomography

$$p(t,\theta)=\iint a(x,t)\,\delta(y\cos\theta-x\sin\theta-t)\,dx\,dy$$



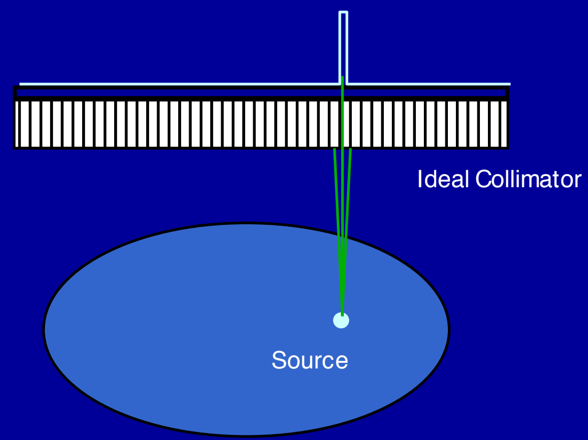
This can be inverted analytically. The solution is known as Filtered Backprojection.

Physical Image Degrading Factors

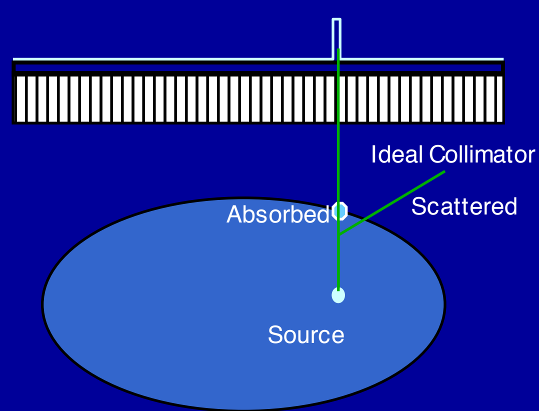
- Attenuation
- Scatter
- Collimator-Detector Response (CDR)
  - Geometric response
  - Septal penetration and scatter responses
- Partial Volume Effects
- Statistical Noise

Effects of high-energy emissions

Ideal Projection from Point Source

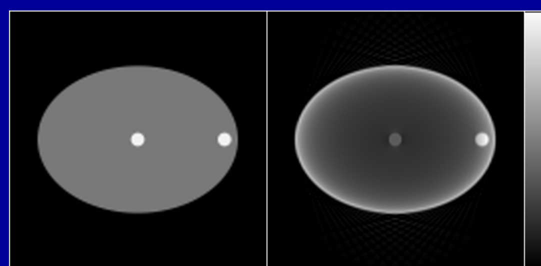


Attenuation in Patient



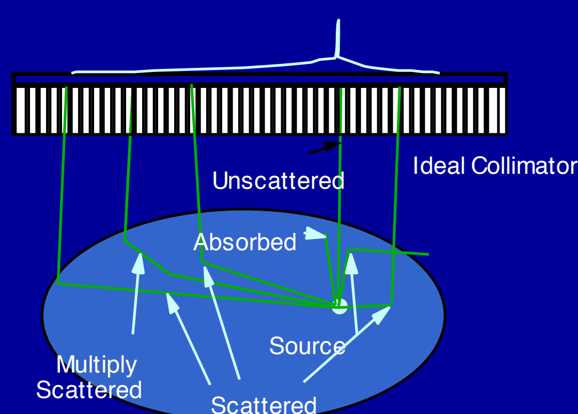
Effects of Attenuation

- Without attenuation compensation, sources at depth appear dimmer
- Reduces quantitative accuracy

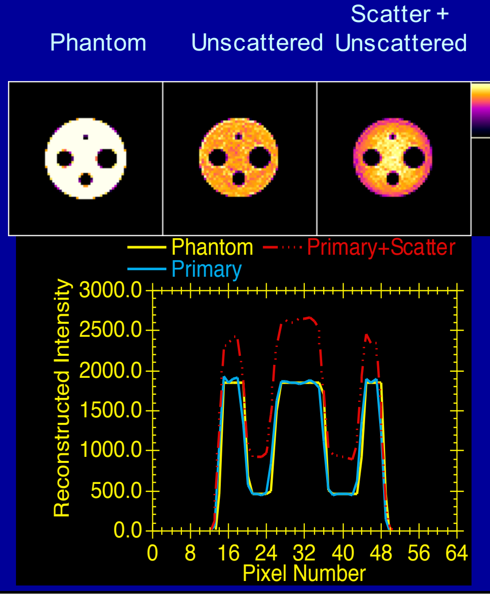


Phantom   FBP Reconstruction (no attenuation compensation)

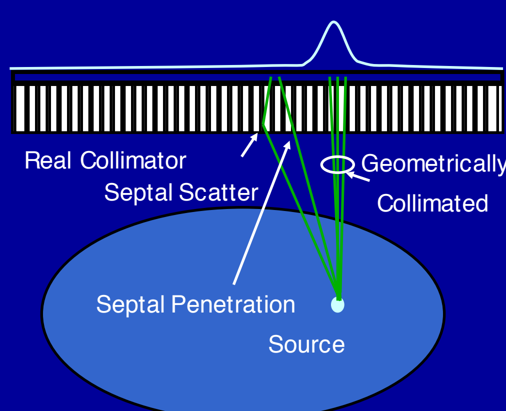
Object Scatter



Quantitative Effects of Scatter



Collimator-Detector Response (CDR)



Properties of the Full CDR

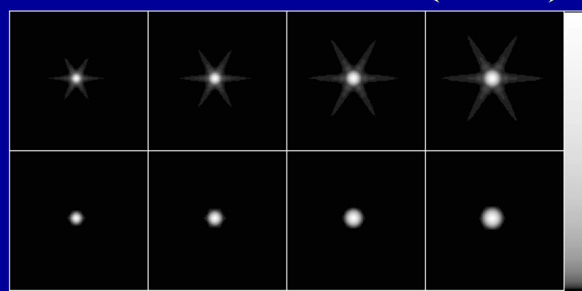
364 keV

I-131 Point Source

30 cm

MEGP Collimator

HEGP Collimator



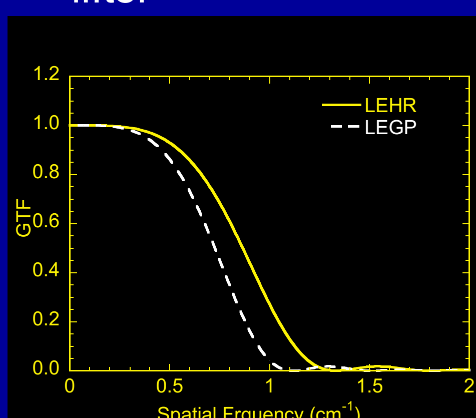
Distance from Collimator Face

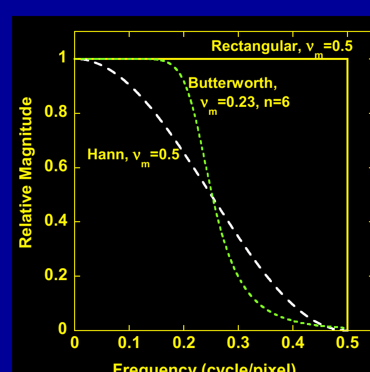
5 cm 10 cm 15 cm 20 cm

Total detected counts are a function of distance

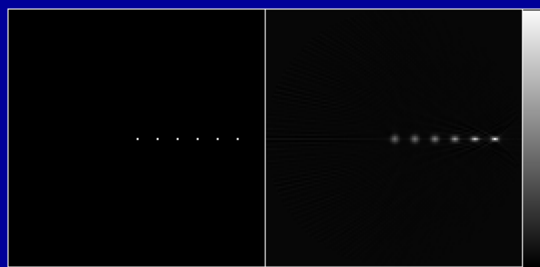
Effects of CDR on Spatial Frequencies

- Analagous to spatially varying low-pass filter





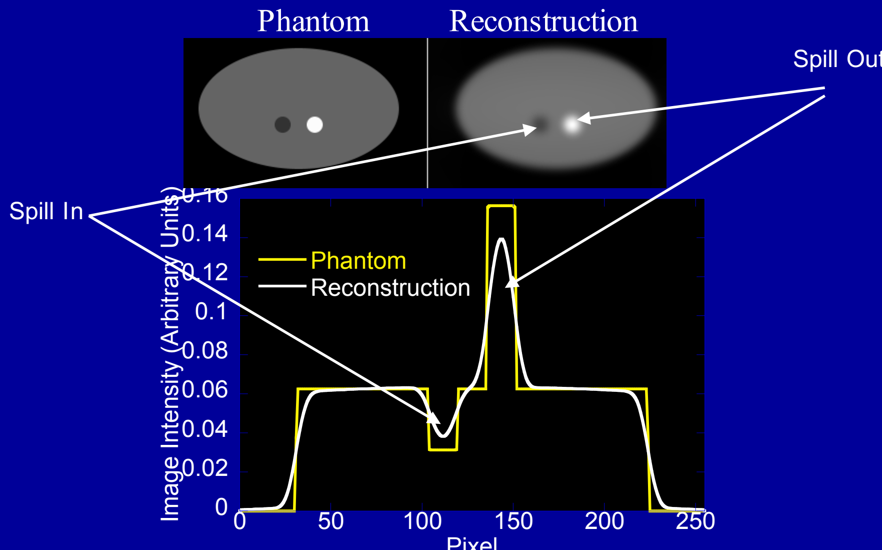
Effect of CDR on SPECT Images



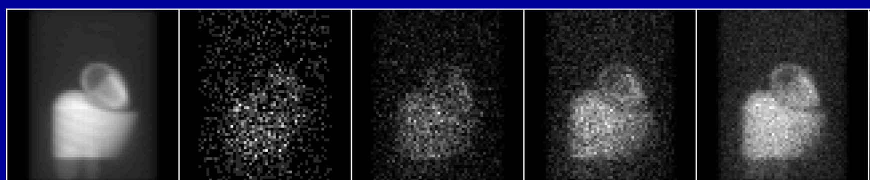
Point Source Phantom

FBP Reconstruction from Projections with LEHR Collimator

Partial Volume Effects



Statistical (Quantum) Noise

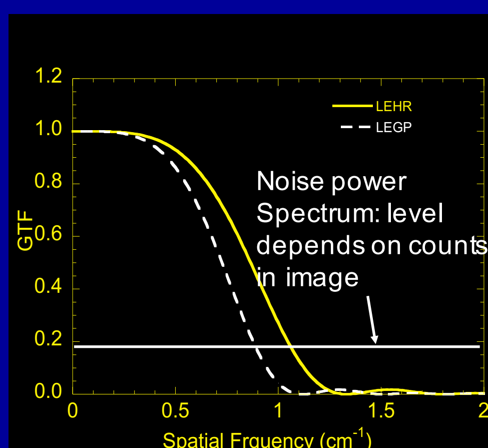


Mean | 2 kcounts | 8 kcounts | 32 kcounts | 128 kcounts

Described by Poisson Distribution

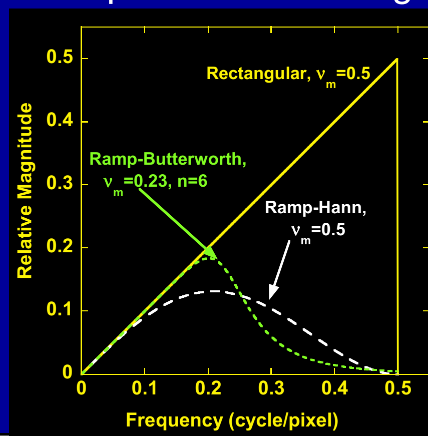
Poisson Noise

- Counts in pixels are independent random variables
- Noise has equal power at all frequencies
- Image has less information at high frequencies due to CDR



Effect of Poisson Noise on SPECT Images

- Ramp filter used in FBP amplifies high frequencies
- Combine with low-pass to reduce high this effect



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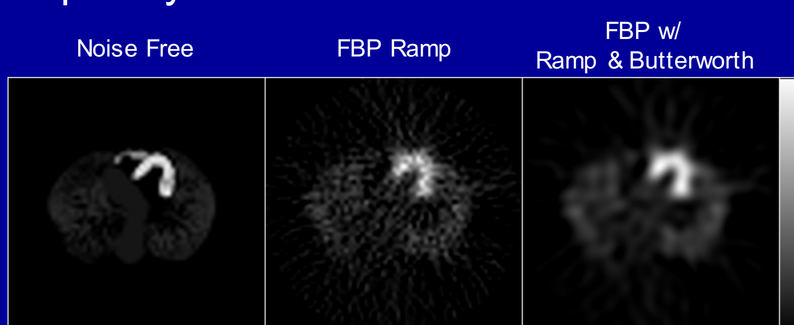
Effect of Poisson Noise FBP Reconstruction

- Ramp filter amplifies high frequencies
- Use low pass filter to reduce high frequency noise



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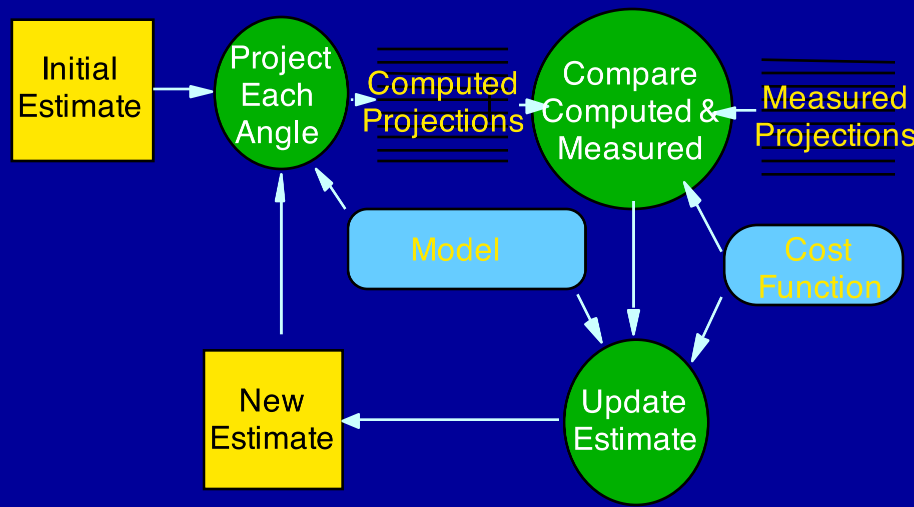
Reconstruction-Based Compensation

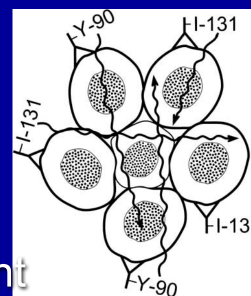


Applications of Quantitative SPEC/CT

- Radiopharmaceutical Therapy Treatment Planning (absolute, lateral)
- Diagnosis (relative, lateral)
- Response to Therapy (relative, longitudinal)

Radiopharmaceutical Therapy (RPT)

- Agents (*e.g.,* monoclonal antibodies, peptides, microspheres) that target tumors
- Bound to radionuclides whose emissions can kill tumor cells
  - Crossfire effect
  - Bystander effect
- Optimal dose is patient dependent
- Treatment planning to determine administered activity



Common Therapeutic Radionuclides for TRT

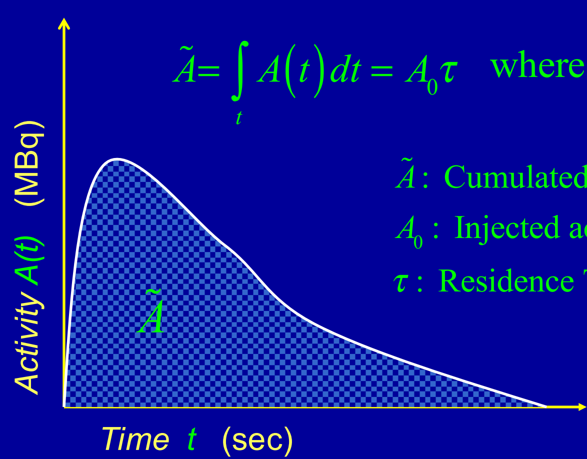
Radionuclide	Halflife (hr)	β- Energy (MeV)	γ Energy (keV) (% yield)
I-131	192.5	0.6 0	364 (82), …
Y-90	64 .0	2.28	none
Sm-153	46.3	0.81	103 (30), …
Lu-177	161.5	0.50	208 (11), …
Re-188	17.0	2.12	155 (15), …

TRT Treatment Planning Flow Chart

Administer Planning Agent → Measure Distribution over Time → Calculate Organ and Tumor Doses → Calculate Therapeutic Activity → Administer Therapeutic Quantity

Cumulated Activity and Residence Time

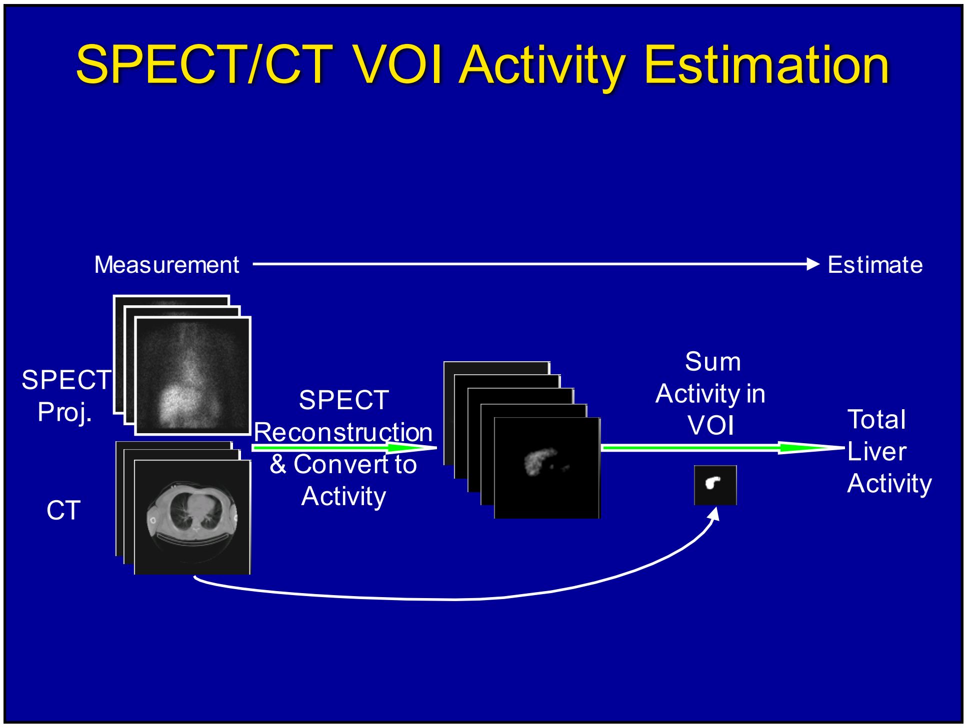
$$\tilde{A} = \int_t A(t)\,dt = A_0\tau \quad \text{where } \tau = \tilde{A} / A_0$$

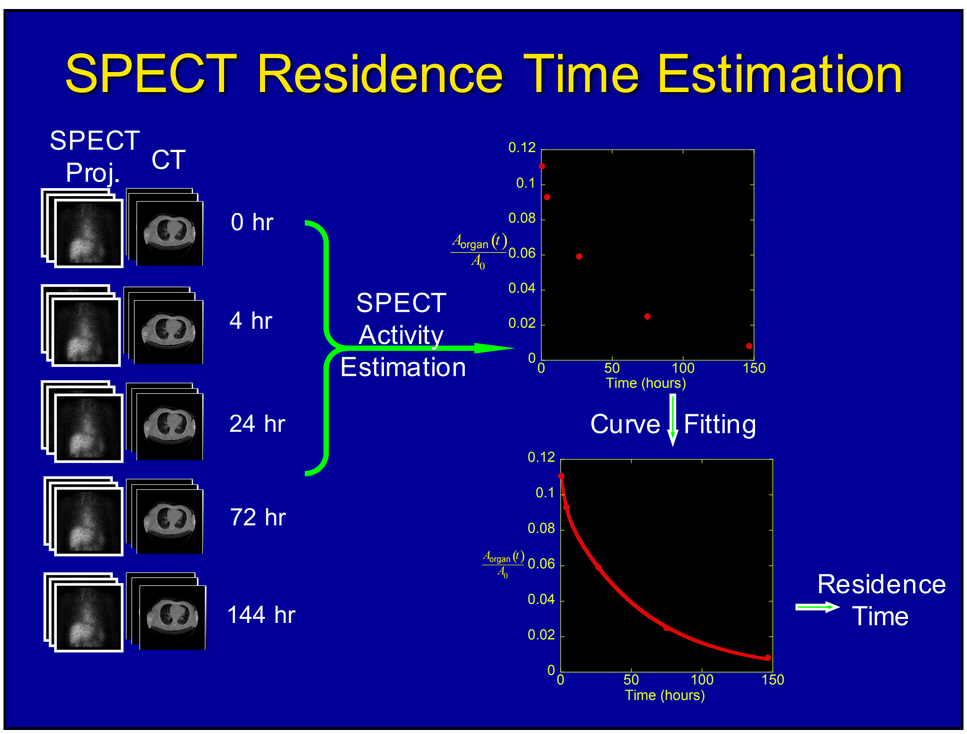


$\tilde{A}$: Cumulated activity (MBq · sec)

A_0 : Injected activity (MBq)

τ : Residence Time (sec)


SPECT/CT VOI Activity Estimation
Measurement
Estimate
SPECT Proj.
CT
SPECT Reconstruction & Convert to Activity
Sum Activity in VOI
Total Liver Activity


SPECT Residence Time Estimation
SPECT Proj.
CT
0 hr
4 hr
24 hr
72 hr
144 hr
SPECT Activity Estimation
Curve Fitting
Time (hours)
Residence Time

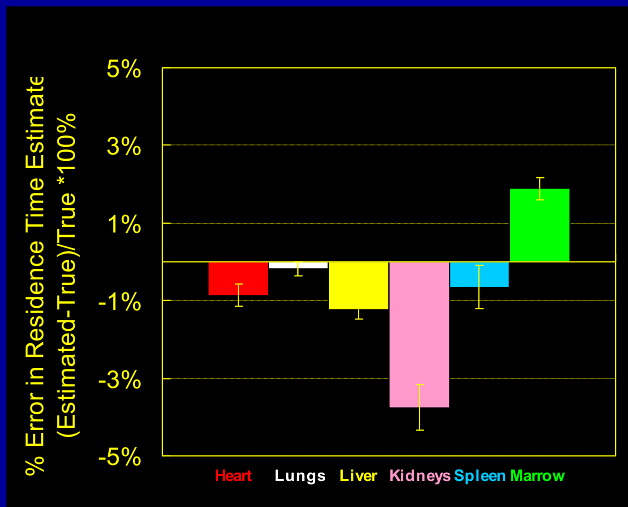
In-111 QSPECT

Reconstructed using OS-EM w/attenuation, scatter, CDR and partial volume compensation

50 noise realizations

Error bars show standard deviations of activity estimates due to quantum noise

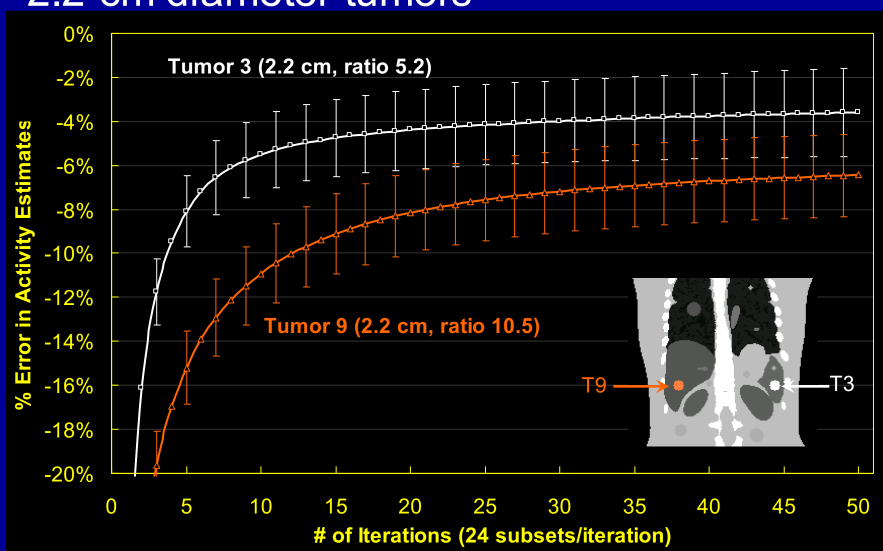
Precision better than accuracy for most organs



He B, Du Y, Song XY, Segars WP, Frey EC. A Monte Carlo and physical phantom evaluation of quantitative In-111SPECT. Phys Med Biol. 2005;50(17):4169-85.

Precision for Small Objects

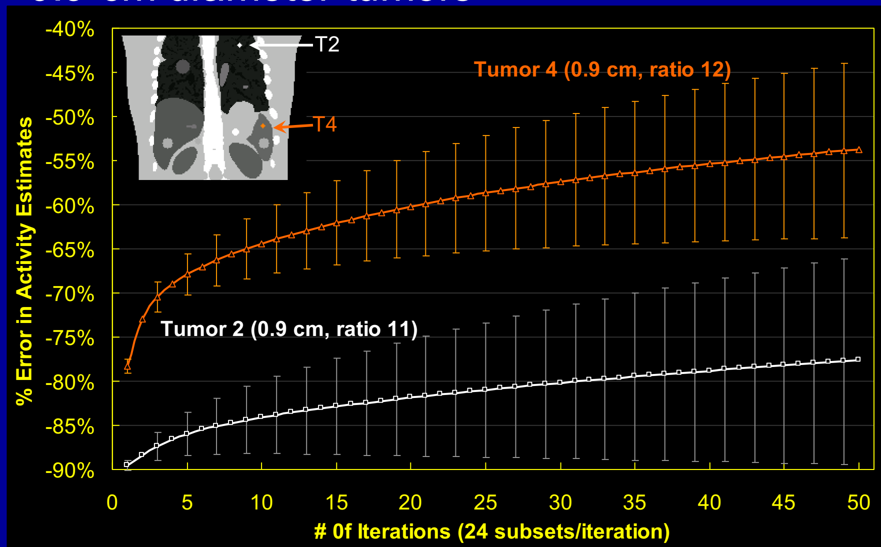
- 2.2 cm diameter tumors



OS-EM w/attenuation, CDR and scatter compensation (no PVC)

Quantification of Very Small Objects

- 0.9 cm diameter tumors



OS-EM w/attenuation, CDR and scatter compensation (no PVC)

I-131 Physical Phantom

Philips Precedence SPECT/CT system with HEGP collimator

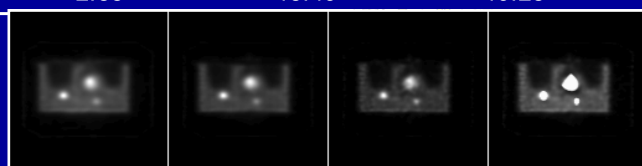
	Heart Chamber	Myocardium	Large Sphere	Small Sphere	Background
Volume (*ml*)	59.7	115.3	17.5 (r =1.61 cm)	5.7 (r =1.11 cm)	9580
Activity(*mCi*)	0.562	0.471	0.136	0.044	8.15
Activity concentration (*mCi/µl*)	9.38	4.08	7.77	7.72	0.851

- **128 projection views**
- **Acquisition time: 40s / view**

I-131 QSPECT

Percent errors of activity estimates for Anthropomorphic torso phantom

(%)	Heart	Large sphere (r = 1.61 cm 17.5 ml)	Small sphere (r = 1.11 cm 5.7 ml)
AGS	-15.21	-26.12	-32.72
ADS	4.75	-17.63	-25.77
ADS+Dwn+	-5.20	-21.10	-31.17
ADS+Dwn+PVC*	-2.88	-15.49	-19.28



50 iterations
24 subsets/iteration

+DWN=model-based downscatter compensation
*PVC=reconstruction-based PVC compensation

Y-90 QSPECT

- Physical phantom experiment
  - Elliptical phantom with 3 spheres
  - Philips Precedence SPECT/CT: HEGP
  - Acquisition time per view: 45s/view
  - Crystal thickness: 9.525 mm
  - 128 projection views over 360°
  - Matrix size per view: 128*128
  - Pixel size: 4.664mm
  - VOIs defined from CT

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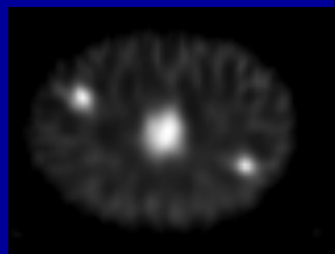
Y-90 Physical Phantom Study



	5.5 cm diameter sphere	3.3 cm diameter sphere	1.5 cm diameter sphere
% Error	-7.0%	-9.7%	-10.2%

$$\text{Error} = (\text{Estimated Activity} - \text{True Activity}) / \text{True Activity} \times 100\%$$

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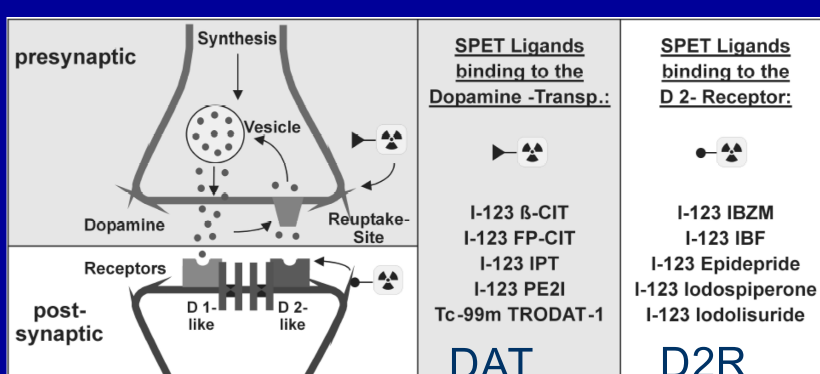
Quantitative SPECT Imaging in Diagnosis and Monitoring of Parkinsonism

- Neurotransmission in dopaminergic system
  - Commercially available agent for SPECT (I-123 FP-CIT)



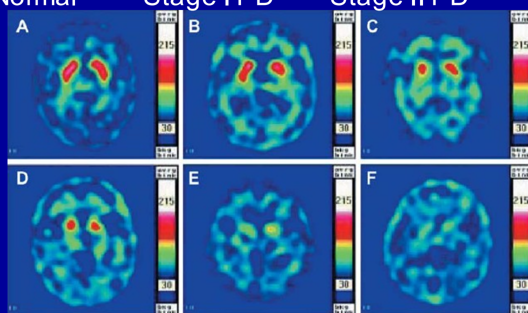
Tatsch, Nucl. Med. Commun. (2001) 22, p819-827.

SPECT Imaging in Parkinsonism

Imaging assessment:

- Visual inspection
- Quantitative studies
  - ✓ Disease degree, progression, etc.

Normal　Stage I PD　Stage II PD



Stage III PD　Stage IV PD　Stage V PD

Huang, et. al, Euro. J. Nucl. Med. (2004) 31, p155-161.

Quantitative brain SPECT Imaging

Tc99m-TRODAT imaging of Parkinson's disease in different HYS stages

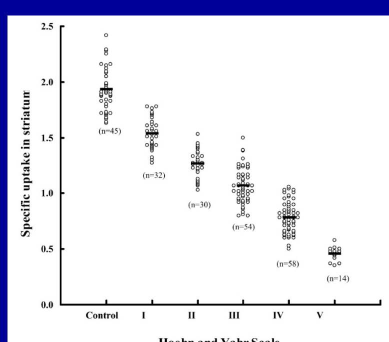


Table 1. The specific uptake in the striatum and putamen in patients with PD

	No.	Age (yr)	Specific uptake	
			Striatum	Putamen
Controls	45	66±10	1.92±0.23	1.74±0.24
HYS				
I	32	64±9	1.53±0.14[a]	1.26±0.16[a]
Ipsilateral[b]				1.51±0.22[a]
Contralateral[c]				1.00±0.20[a]
II	30	67±8	1.26±0.13[a]	1.00±0.18[a]
III	54	64±9	1.07±0.16[a]	0.71±0.25[a]
IV	58	67±8	0.78±0.14[a]	0.50±0.17[a]
V	14	69±6	0.46±0.06[a]	0.26±0.09[a]

Age and specific uptake data are expressed as mean ± standard derivation

HYS, Hoehn and Yahr scale

[a] $P<0.01$ compared with controls or adjacent HYS groups

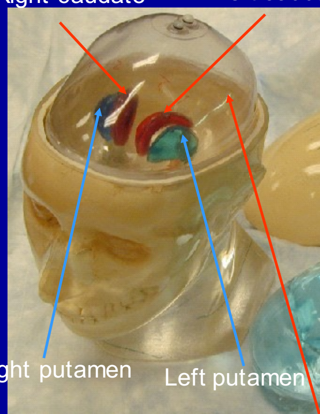
[b] Ipsilateral: side of symptoms or more affected limbs

[c] Contralateral: side opposite to symptoms or more affected limbs

Huang, et. al, Euro. J. Nucl. Med. (2004) 31, p155-161.

Accuracy of Activity Quantitation: I-123 Brain SPECT

RSD Striatal Phantom

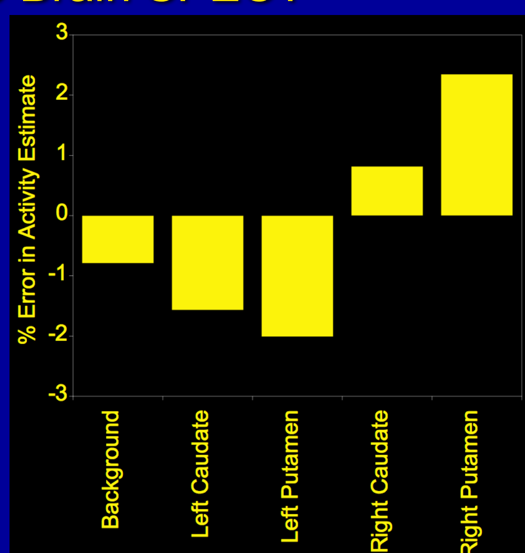


- GE Millennium VG/Hawkeye (5/8" thick crystal)
- LEHR Collimator
- 128 views/360°, 128*128 projection w/ 0.24 cm pixels
- CT attenuation maps
- Manually defined VOIs using registered MR Images
- Activity concentrations:
  - Bkg: 110 kBq/ml
  - Left Caudate: 212 kBq/ml
  - Left Putamen: 154 kBq/ml
  - Right Caudate: 1770 kBq/ml
  - Right Putamen: 222 kBq/ml

Y. Du, B.M.W. Tsui, and E.C. Frey, "Model-based compensation for quantitative I-123 brain SPECT imaging," *Phys Med Biol*, 51(5): 1269-1282, 2006

Accuracy of Activity Quantitation: I-123 Brain SPECT

OS-EM w/
Attenuation
Scatter &
CDRF Compensation
Post-Reconstruction
pGTM PVC



Requirements for Quantitative SPECT/CT

- Quality Control/Calibration
- Acquisition
- Reconstruction/Processing

Quality Control & Calibration

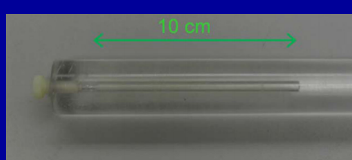
- Activity meter calibration and QC
- Routine Camera and CT QC
- Registration of SPECT and CT
- Calibration of QSPECT imaging

Calibration Factor Measurement

- Planar calibration (sensitivity)
  - Static image of standard source in air at known distance from camera
  - Sensitivity = std. counts/(std. activity * acq. time)
- Phantom-based Calibration
  - Acquire SPECT study of object with known activity
  - Reconstruct and compute counts
  - Scale factor is true phantom activity/image counts
  - Should be consistent with planar calibration for "ideal" reconstruction/compensation

Limitations of Planar Calibration Quantitative Y-90 SPECT

- Planar Calibration



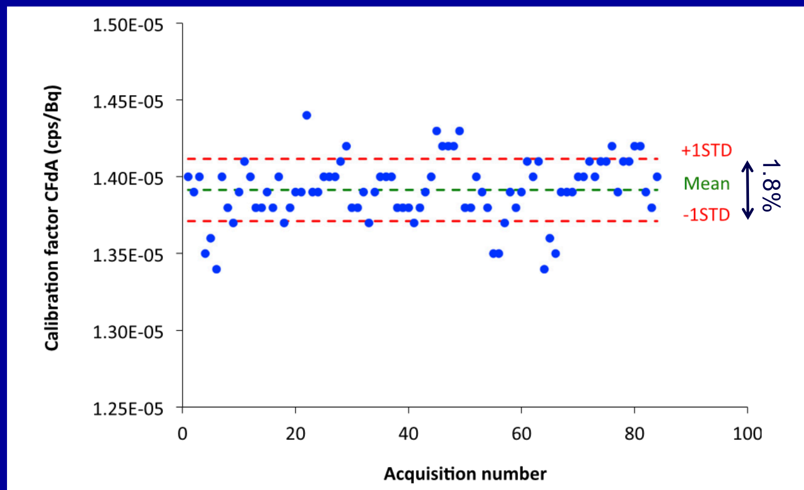
Scanner	Calibration Factor
GE Discovery 670	1.14
Siemens Symbia	1.08

- SPECT Calibration

Phantom	Dimensions
Large Uniform Cylinder	20 cm diameter
Small Uniform Cylinder	4.6 cm diameter
Sphere in cold Elliptical Phantom	5.5 cm diameter sphere in 32x20 phantom

Scanner	Calibration Factor
GE Discovery 670	1.21-1.23
Siemens Symbia	1.15-1.18

Variations in Calibration Factor



- Largest source of variation (77% of variance) was due to inter-source effects
- Suggests that consistent preparation and measurement of source activity is key

Acquisition Parameters

- Collimator selection
- Injected activity/acquisition time
- Voxel size
- Number of views
- Energy windows

Reconstruction/Compensation

Factor	Large Object	Small Object	Commercially Available
Attenuation	Yes	Yes	Yes
Scatter	Yes	Yes	Energy-based: yes Model-based: limited
Geometric Response Compensation	No	Yes	Yes
Full CDR Compensation (High Energy)	Desirable for HE, ME radionuclides	Desirable for HE, ME radionuclides	No
Partial volume compensation	No	Yes	No
Noise Regularization	No	Yes?	Filtering

Obstacles to Standardization

- Radioactivity measurement
  - Variety of devices
  - Variety of radionuclides
- Compensation Methods
  - Many systems are SPECT-only
  - Variety of imaging hardware
  - Variety of image reconstruction and compensation methods
- Clinical Practice
  - Variation in protocols
  - Habits

Summary

- Quantitative SPECT/CT is achievable now
- There are a number of emerging clinical applications
- Limited commercial availability of state-of-the-art reconstruction and compensation methods
- There is a need for standardization of protocols and methods