



Imaging Refresher for Standard of Care Radiation Therapy: *Review of PET/CT Imaging*

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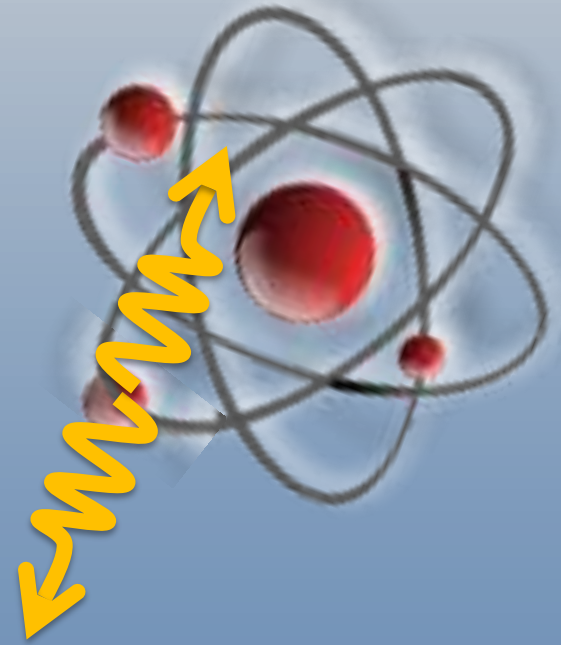
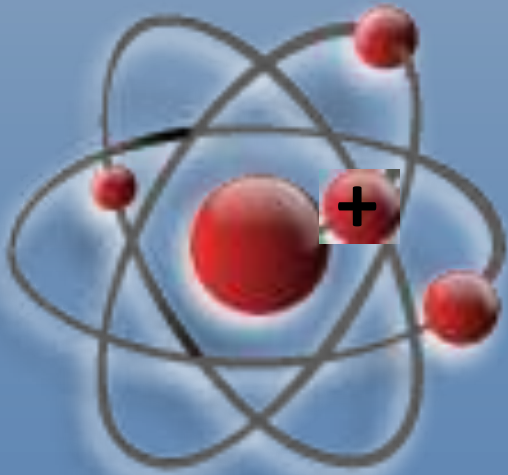
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What is not covered?

- **Does not include**
 - In-depth discussions (see references on each slide)
 - PET/MRI
 - Radiotracers other than F-18 FDG
 - Segmentation Methods
 - Registration and Respiration Control Methods
 - QA/QC
 - Reimbursement and Regulation
 - Use in specific tumor types

Isotope Physics

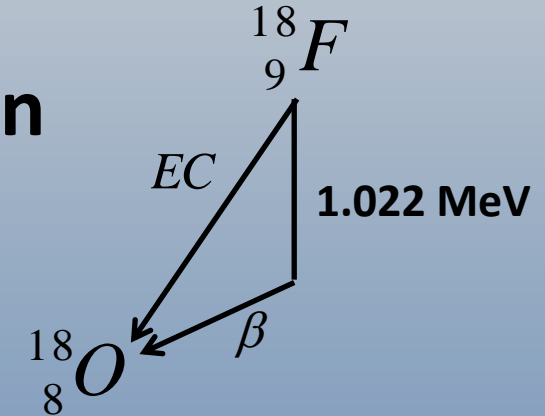
1. Positron emission
2. Annihilation



Isotope Physics: F-18 Decay

- 0.97 Positron (β^+) per Disintegration

- 634keV Maximum
- 250keV Mean

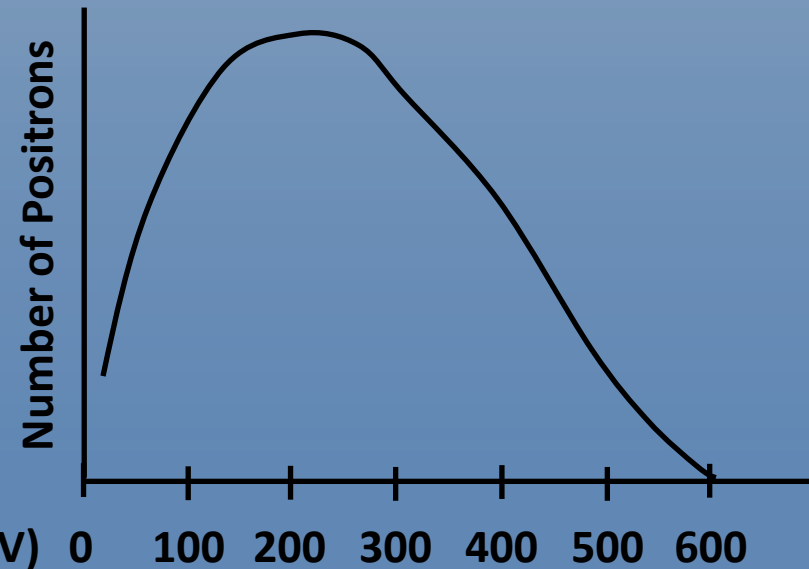


- 0.03 Electron Capture per Disintegration

- $T_{1/2}=110\text{min}$

- Range (**adds ~0.2mm blur**)

- 2.3mm mean in water
- 0.6mm max in water
- 2m max in air
(**Contamination**)

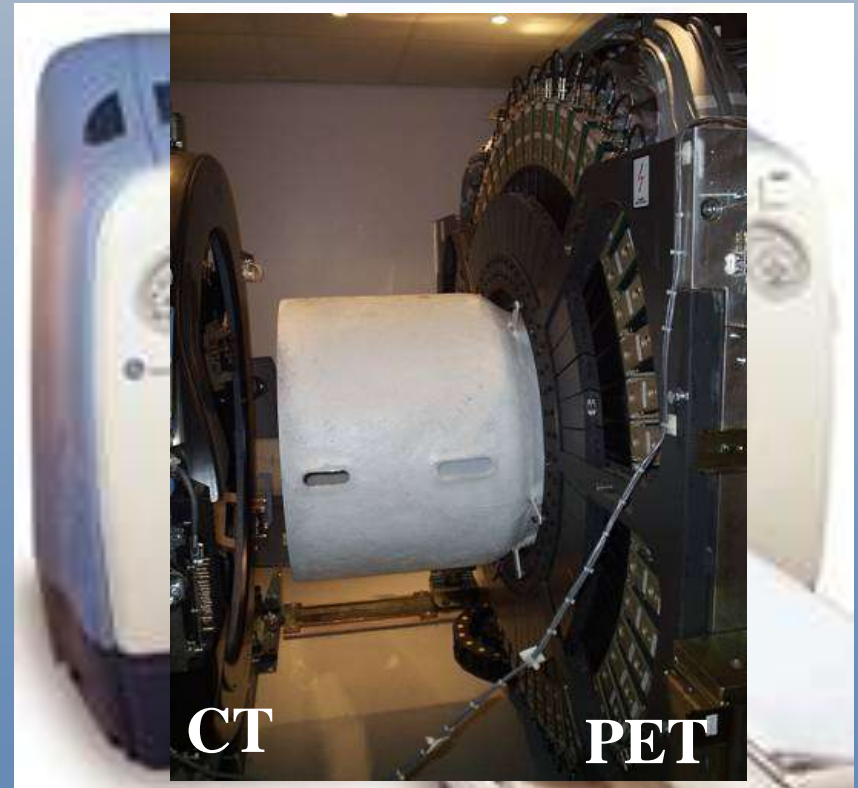


Interaction Physics: Positron Annihilation

- Positron slows to stop and forms positronium
- Annihilates creating two photons at 180° and 511keV
 - $\sim 2\%$ of the time non-zero K_{e^+}
 - Not equal energy or angle
 - $\sim \pm 0.25^\circ$ angular variation for F-18 (adds 1.75-2mm blur)
- Can have more than 2 photons, but it is rare
 - Three-photon: 0.2%
 - More than 3 photons: $\sim 0.00015\%$

System

- **CT**
 - Similar to diagnostic
 - Defer description to talk on CT simulation
- **PET**
 - 2D being phased out
 - Bore: 70-80cm
 - » Scan FOV ~10cm less
 - 170-200cm scan length
 - Scan time: 30s-3min per bed position
 - » Most are step-shoot
 - Siemens is an exception



System: Detector Ring

- Rings
 - Varies: 4-8 Block Rings
- 15-22cm axial coverage
- Detector elements
 - 12,000-30,000

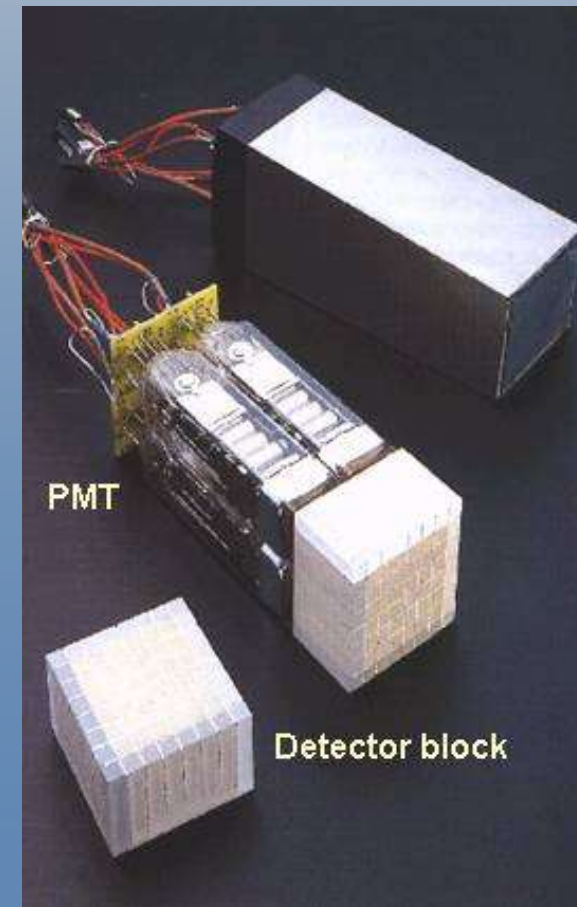
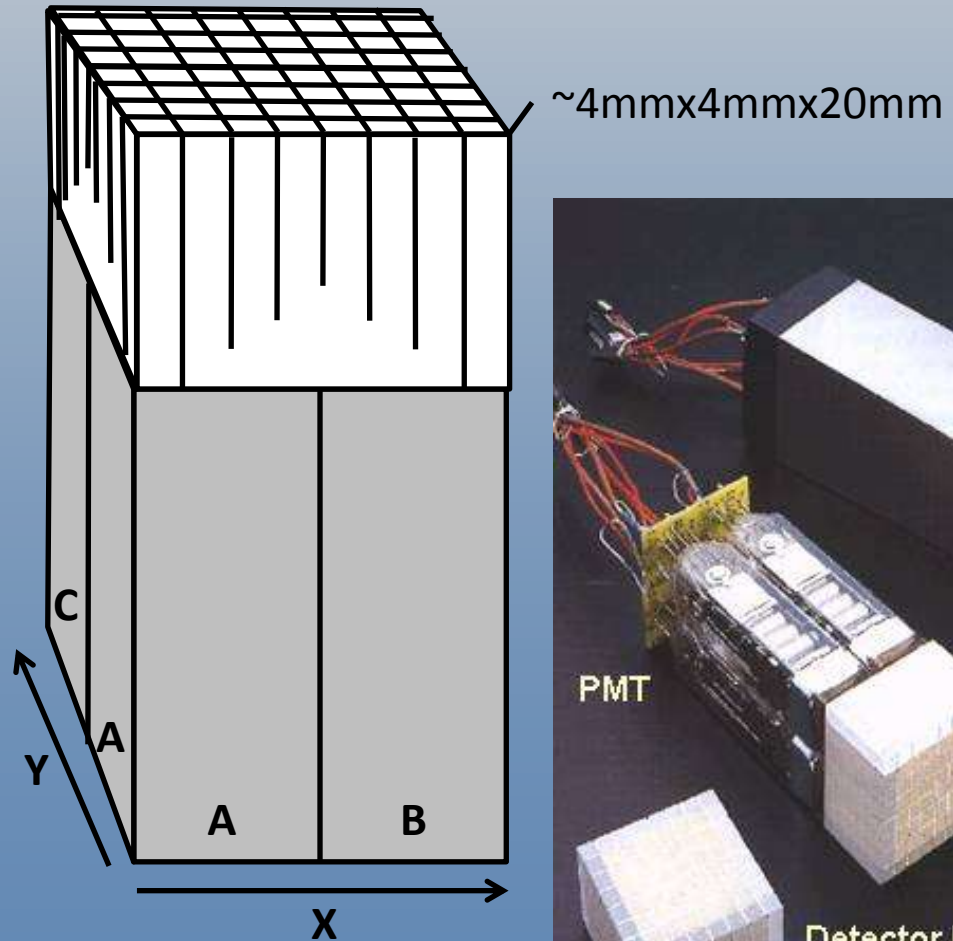


System: Block Detectors

- **~50 blocks per ring**
 - 4 PMT
 - 1 Scintillator
 - » Cut into multiple channels (~10x10)

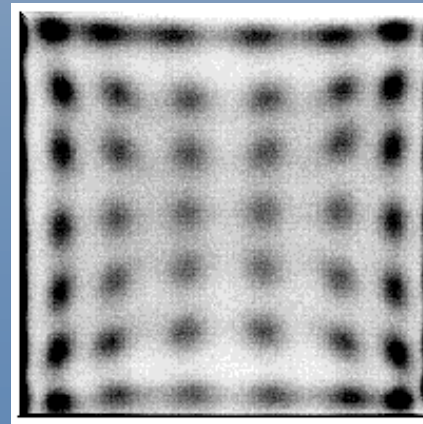
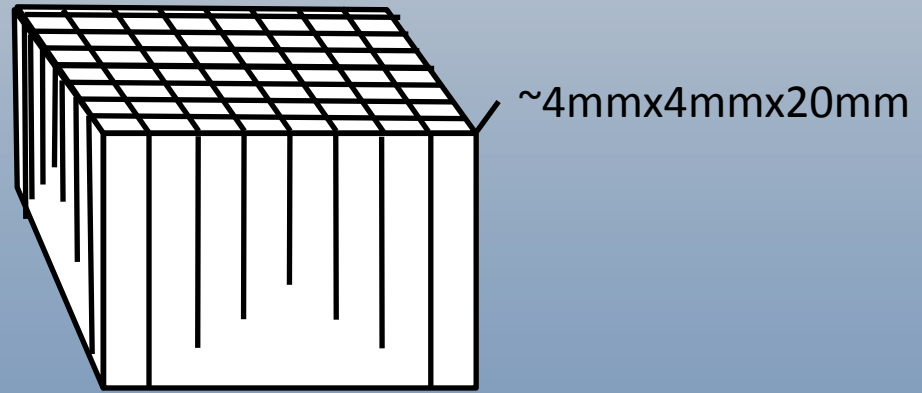
- **Anger logic**

$$X = \frac{(S_B + S_D) - (S_A + S_C)}{(S_A) + (S_B) + (S_C) + (S_D)}$$
$$Y = \frac{(S_A + S_B) - (S_C + S_D)}{(S_A) + (S_B) + (S_C) + (S_D)}$$



System: Scintillator

- **Cut to allow linear sharing of light between PMT**
 - Reflective coating in channels
- **Results in unique light patterns for each channel**



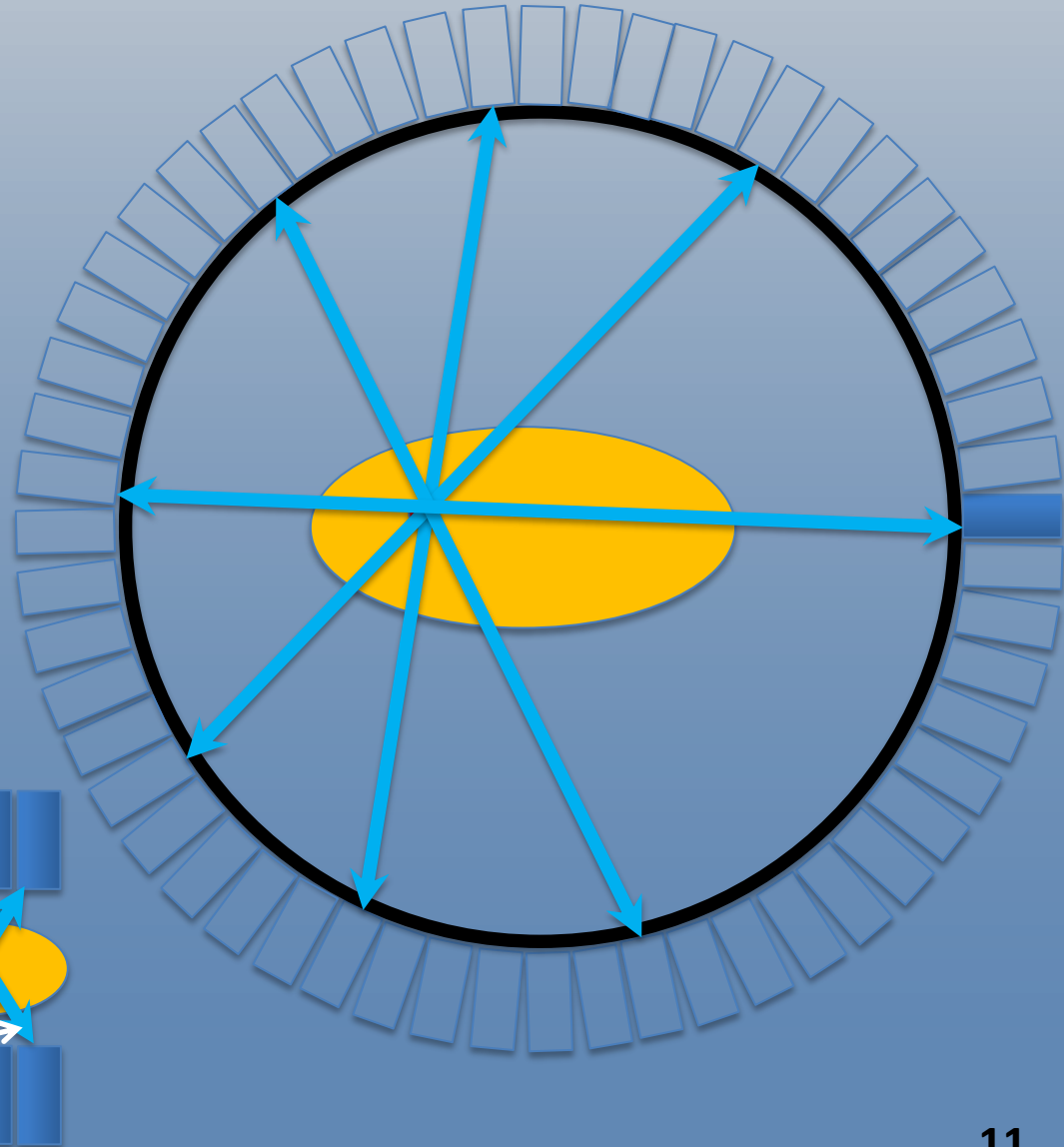
System: Scintillator

	Density (g/cc)	Z	Decay Time (ns)	Light yield (%NaI)	% PE
NaI (TI)	3.7	51	230	100	18
BGO	7.1	75	300	15	34
LSO (Ce)	7.4	66	45	80	44

- Most are LSO/LYSO, though BGO also is used
 - Testing and correction of LSO can be difficult due to natural radioactivity of Lu-176
 - 420keV β^- , and 3 γ (308keV, 202keV, and 88keV)

System: LOR

- **Line of Response**
 - No need for collimation
 - Coincident detection
 - » 5-12ns



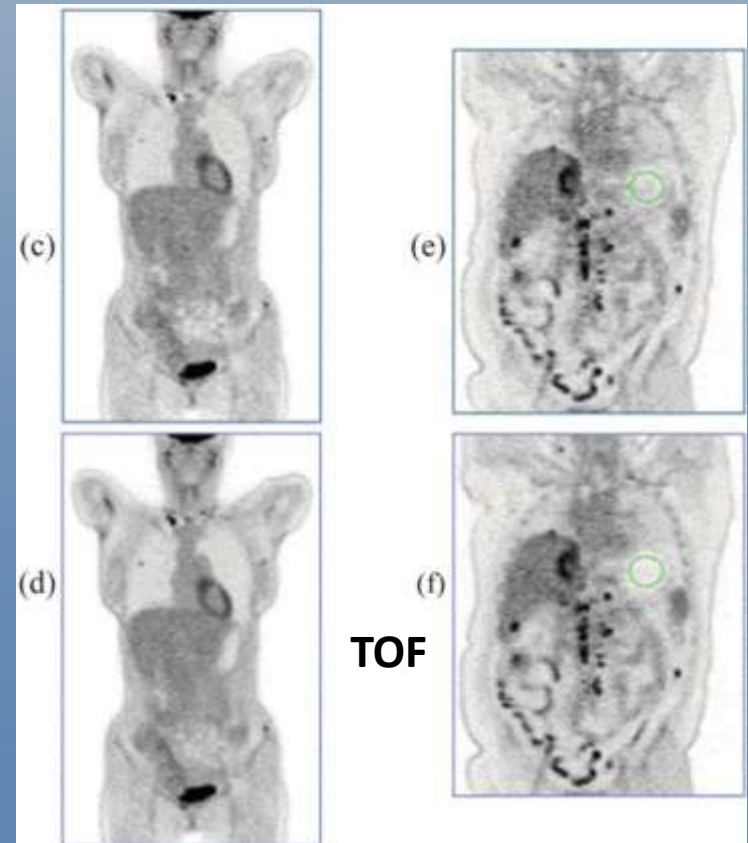
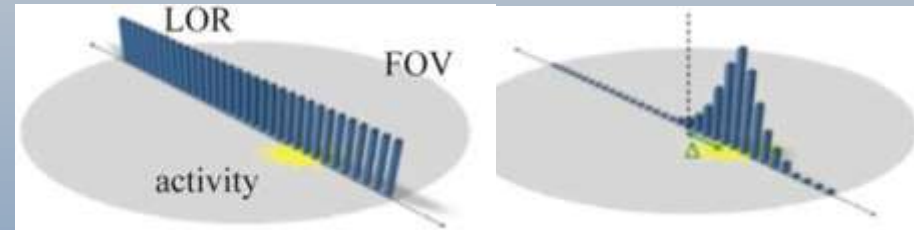
Direct Plane

Oblique Plane

System: TOF

- Time-of-Flight (TOF)
 - VUE point FX, TF, UltraHD
 - ~0.5ns coincidence timing
 - » ~7-9cm uncertainty
 - Increases SNR
 - » Better for big patient
 - D is patient size, x is signal position

$$\text{SNR}_{\text{TOF}} = \sqrt{\frac{D}{\Delta x}} \text{SNR}_{\text{non-TOF}}$$

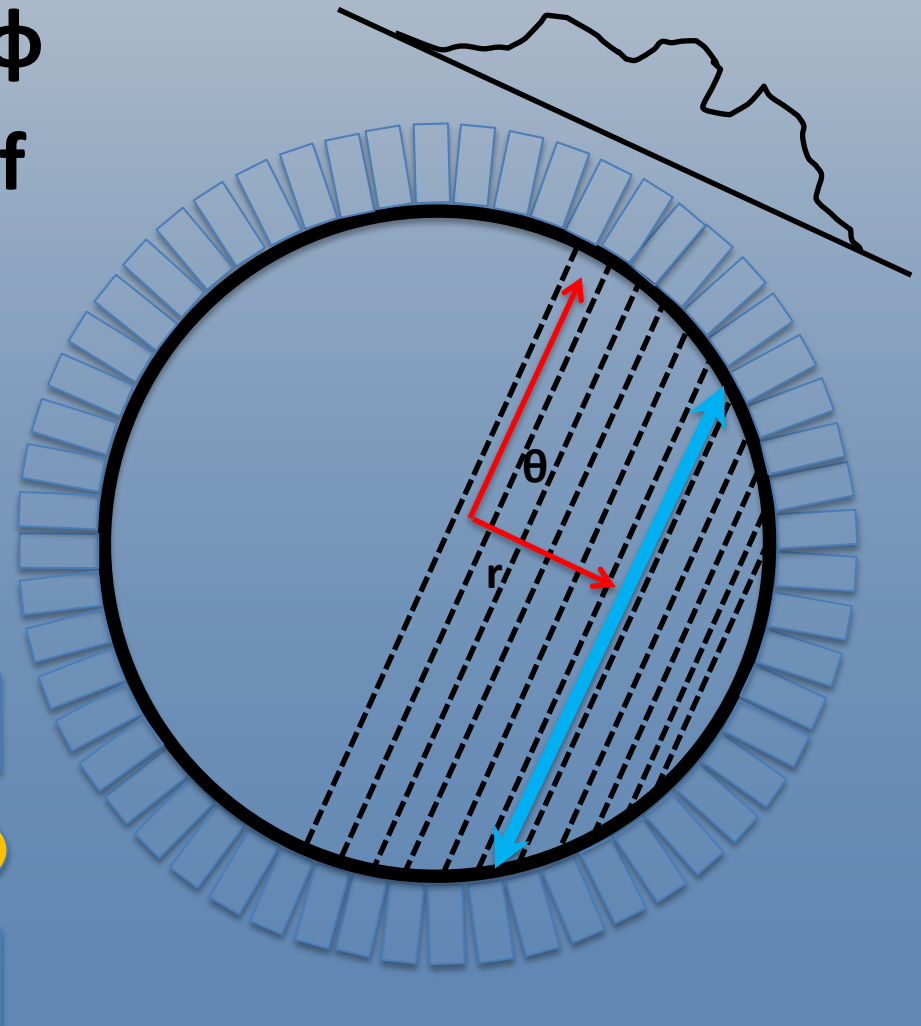


System: Sinogram

- Three coordinates: r , θ , ϕ
- May rebin to get stack of 2D sinograms (r , θ)
 - SSRB, MSRB, or FORE

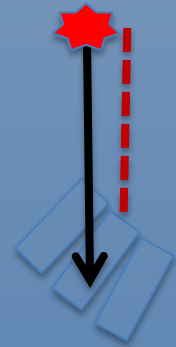
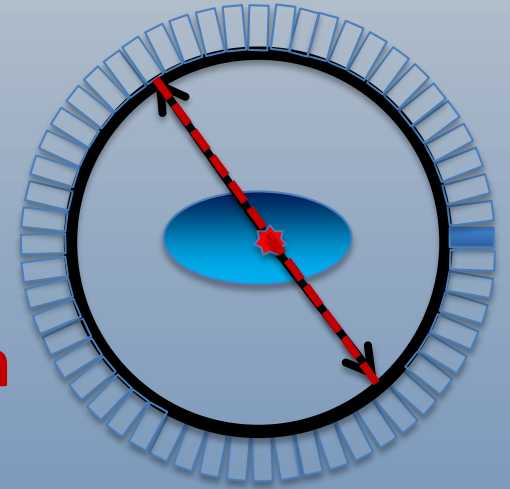


Oblique Plane



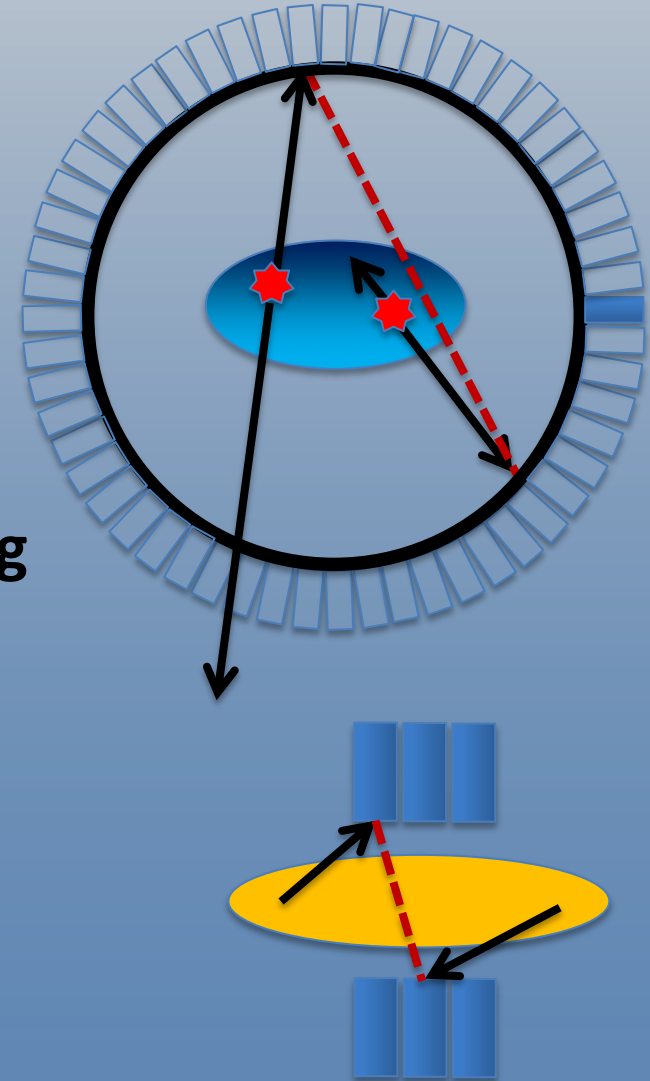
System: Depth of Interaction

- HVL in crystal $\sim 1\text{cm}$
- System displaces LOR
 - 10cm off-center: 40% worse resolution
 - Center target in scanner
- Correction
 - Layered detector to determine depth of interaction (not clinically available)
 - PSF reconstruction



System: Randoms

- Random
 - Random Fraction: 35-65%
- Corrections
 - Delayed coincidence subtraction
 - Best for 2D, worst SNR (high noise)
 - Delayed subtraction with smoothing
 - Singles estimate for each LOR
 - $R_{Random} = T_{Coinc.} * R_{Single1} * R_{Single2}$
 - Reduce $T_{coinc.}$
 - Note: No perceptual difference between correction methods



System: Scatter

- Scatter

- 50% scatter in the scintillator
 - Generally left uncorrected
- Scatter Fraction 30-70% (body)
- Most probable scatter is 35° (433keV) by Klein-Nishina

- Corrections

- Energy Window
 - 380-640keV, 400-600keV
- Single Scatter Simulation (standard)
- Tail fitting
- Monte Carlo

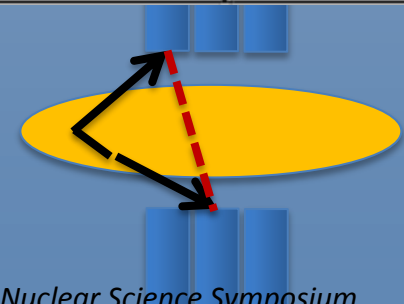
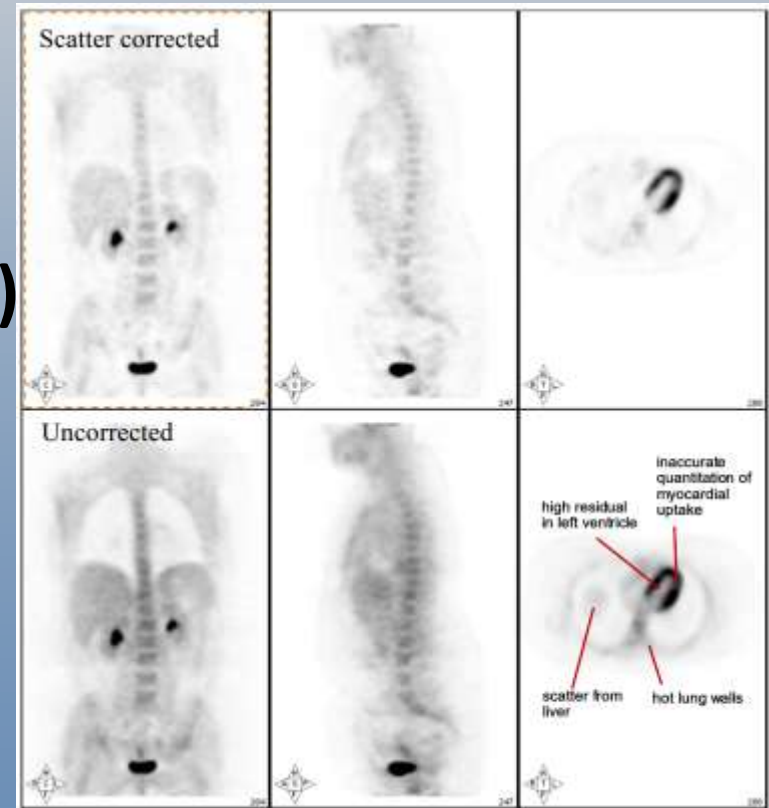


Image: Watson, C.C.; Casey, M.E.; Michel, C.; Bendriem, B., "Advances in scatter correction for 3D PET/CT," *Nuclear Science Symposium Conference Record, 2004 IEEE*, vol.5, no., pp.3008,3012, 16-22 Oct. 2004

Figure: William F. Sensakovic, PhD

System: Some Scatter Physics

- Klein-Nishina Electronic Cross-section

$$- \frac{d_e \sigma_c^{KN}}{d\Omega} = \frac{r_e^2}{2} (1 + \cos^2 \theta) F_{KN}$$

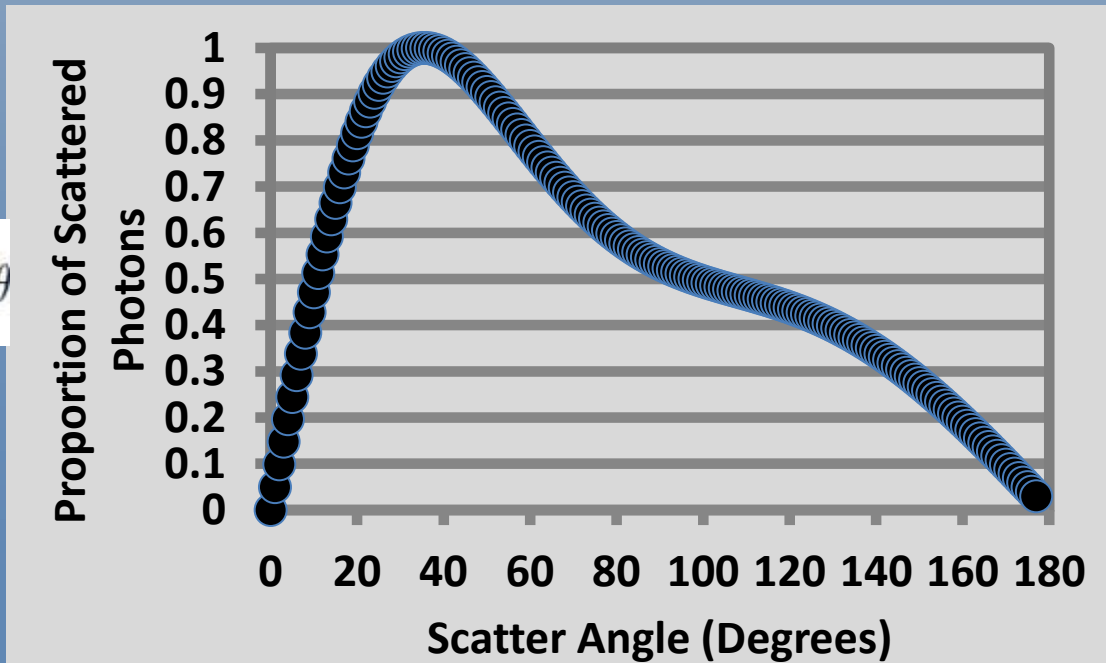
- Klein-Nishina Form Factor (F_{KN})

$$F_{KN}(h\nu, \theta) = \frac{1}{[1 + \epsilon(1 - \cos \theta)]^2} \left\{ 1 + \frac{\epsilon^2 (1 - \cos \theta)^2}{[1 + \epsilon(1 - \cos \theta)] (1 + \cos^2 \theta)} \right\}$$

- $d\Omega = 2\pi \sin \theta d\theta$

- So,

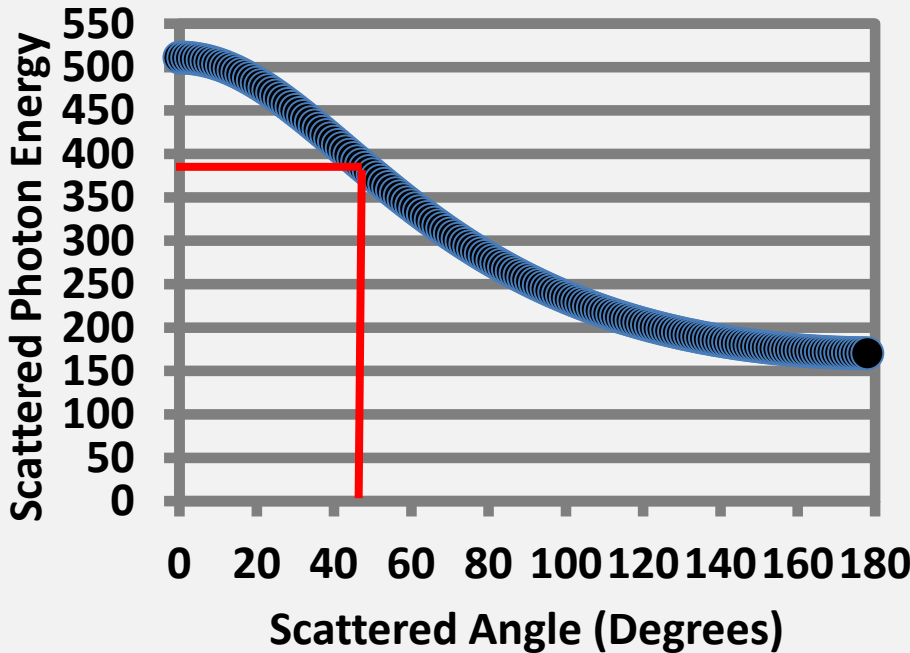
$$\frac{d_e \sigma_C^{KN}}{d\theta} = \frac{d_e \sigma_C^{KN}}{d\Omega} \frac{d\Omega}{d\theta} = \pi r_e^2 F_{KN} (1 + \cos^2 \theta) \sin \theta$$



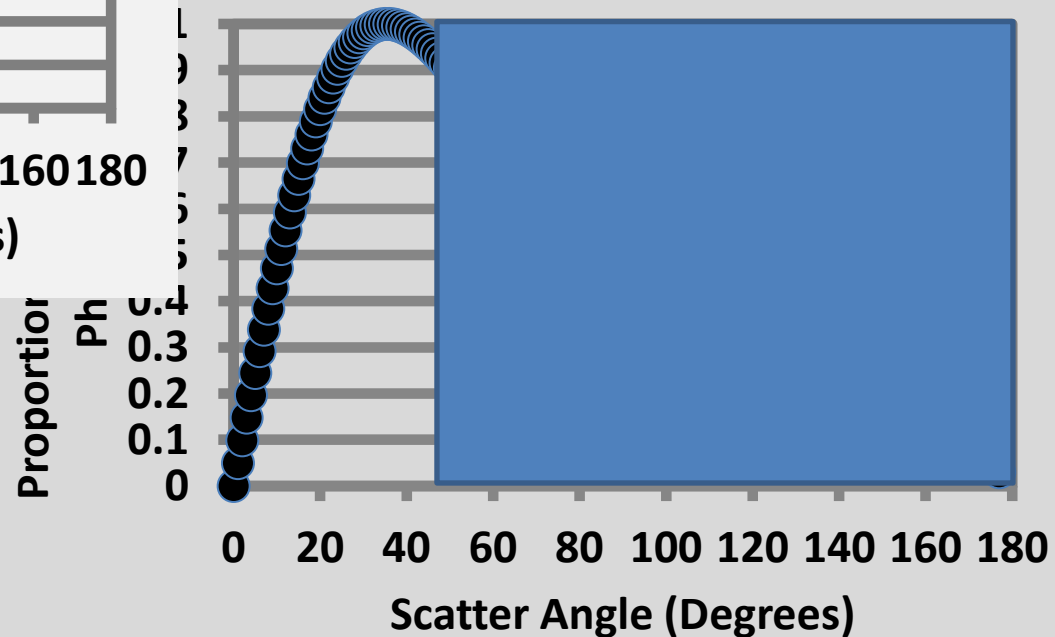
System: Some Scatter Physics

- Scattered photon energy

$$E_s = \frac{E}{1 + \frac{E}{m_0 c^2} (1 - \cos\theta)}$$



400keV accepts up to 44° scatter
 380keV accepts up to 49° scatter



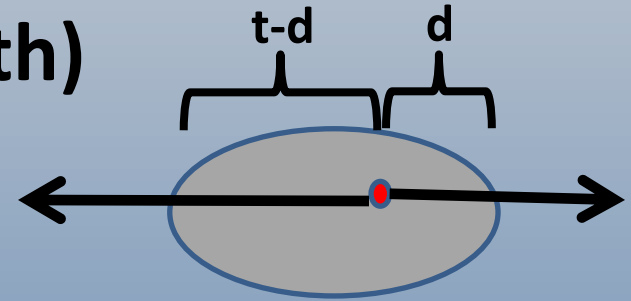
- Low energy thresh
 – 380keV

ref: Podgorsak, Radiation Physics for Medical Physicists 2nd ed. Springer Heidelberg, 2010.
 Figures: William F. Sensakovic, PhD

System: Attenuation Correction

- Depends on thickness (not depth)

- Muscle: 97%@35cm 86%@20cm
- Bone: 16%@1cm 29%@2cm



- Correction

- Bilinear Map HU to $\mu(511)$

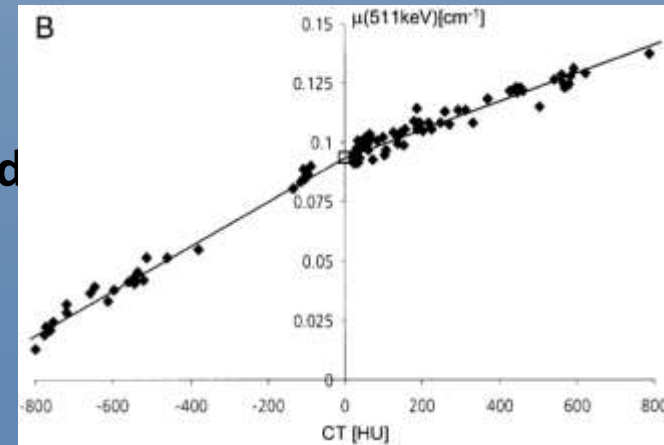
- CT energy compensation (70keV vs. 511keV)

- PE contribution in CT for high Z (bone and iodine contrast media)

$$\mu^{\text{PET}} = \begin{cases} \mu_{\text{H}_2\text{O}}^{\text{PET}} (\text{CT} + 1000) / 1000 & \text{CT} \leq 0 \text{ HU} \\ \mu_{\text{H}_2\text{O}}^{\text{PET}} + \text{CT} \frac{\mu_{\text{H}_2\text{O}}^{\text{CT}} (\mu_{\text{Bone}}^{\text{PET}} - \mu_{\text{H}_2\text{O}}^{\text{PET}})}{1000 (\mu_{\text{Bone}}^{\text{CT}} - \mu_{\text{H}_2\text{O}}^{\text{CT}})} & \text{CT} > 0 \text{ HU} \end{cases}$$

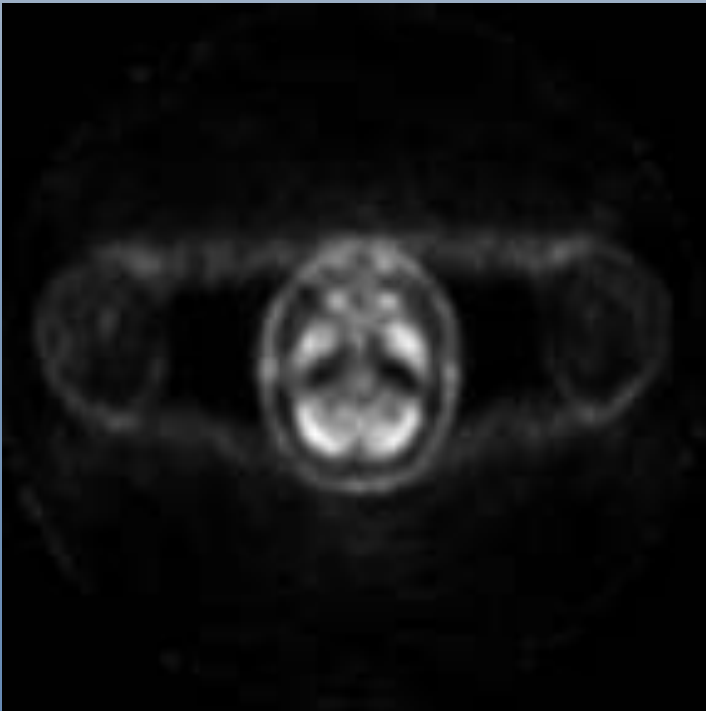
$$e^{-\mu(t-d)} e^{-\mu d} = e^{-\mu t} \quad \text{In } \left[\frac{1}{\text{cm}} \right] \text{ units:}$$

$$\mu_{\text{skelmusc}} = 0.099; \mu_{\text{corbone}} = 0.172$$

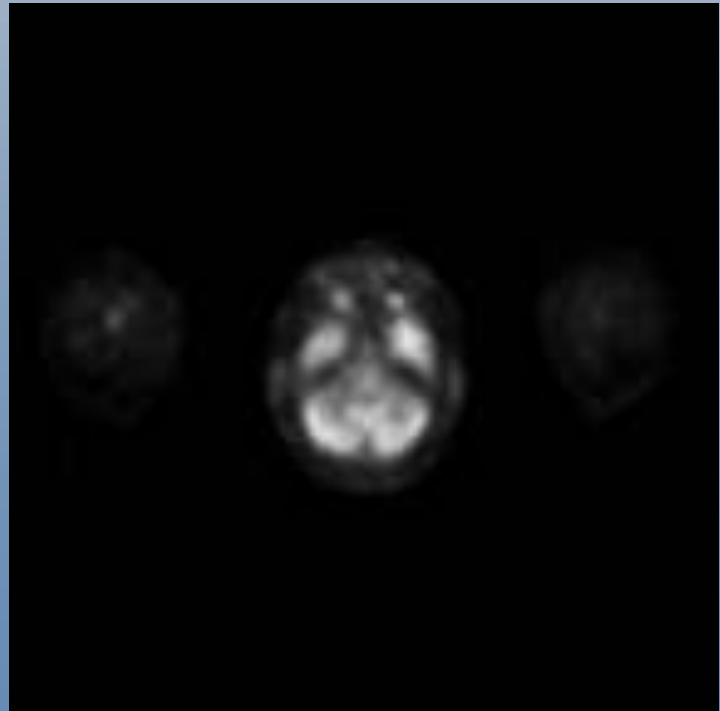


System: Attenuation Correction

Uncorrected

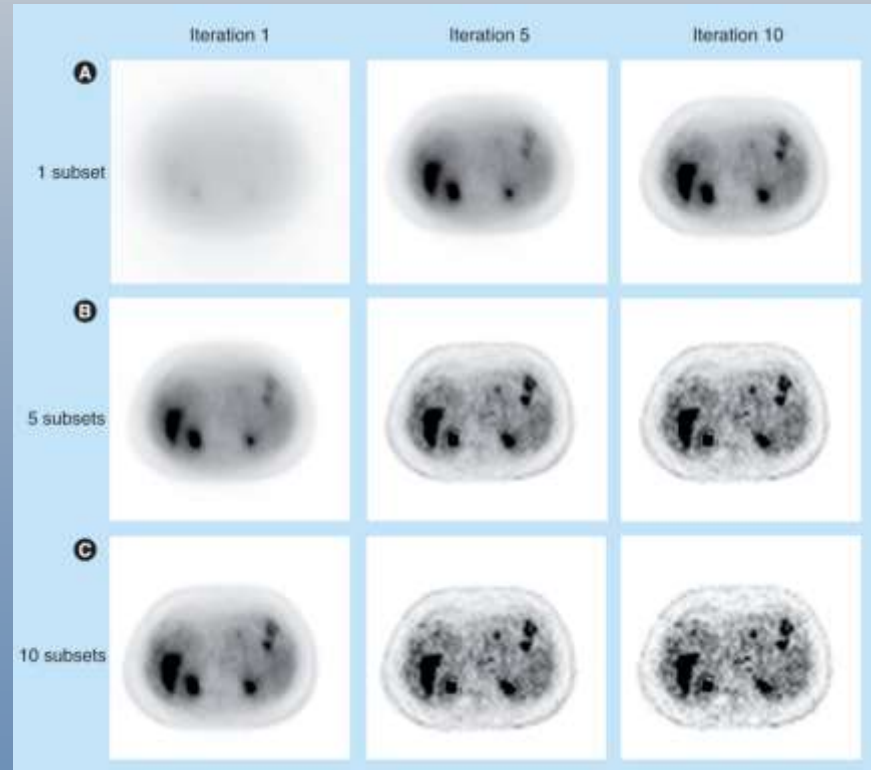


Corrected



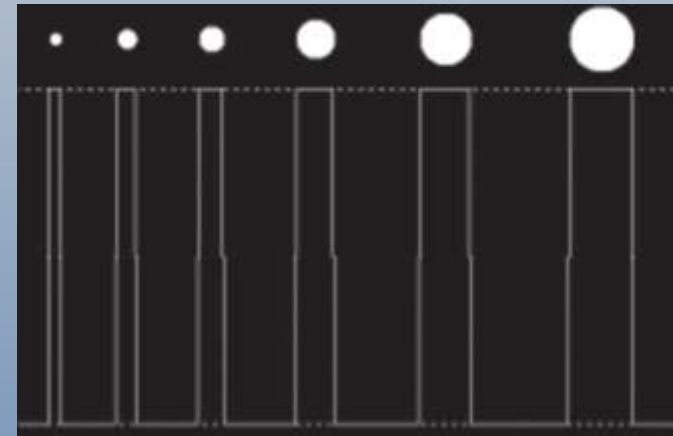
System: Reconstruction

- **Many Techniques**
 - 3DRP, OSEM, etc.
- **OSEM widely used**
 - 2-5 iterations with 8-28 subsets
 - » Time vs. Accuracy
 - » Noise increases with effective iteration number

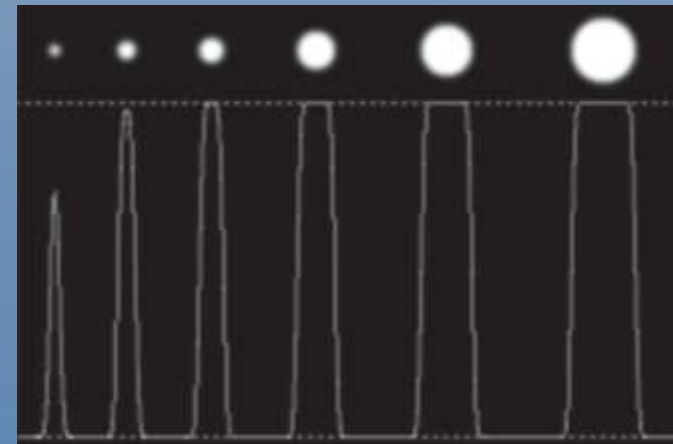


System: Filtering

- **Post-filtering 5-10mm Gaussian**
 - Metz, Hanning, Butterworth, etc.
 - Reduces SUV of small lesions
- **Recon and filtration degrade resolution by 20-50%**
- **Partial volume impacts quantification of lesions < 25mm**

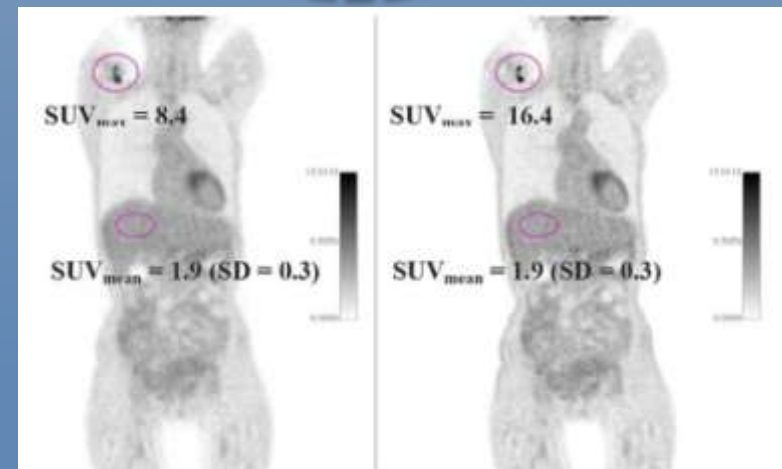
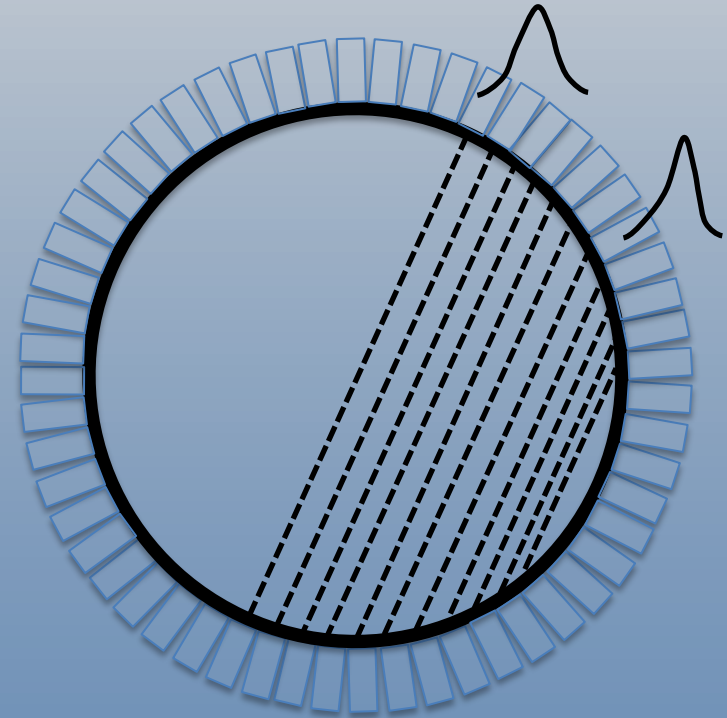


5mm blur



System: PSF Reconstruction

- PSF varies across FOV and out-of-plane
- Measure PSF through the volume and include in recon alg.
 - HD, SharpIR, Astonish
- More effective for small objects



Acquisition Modes

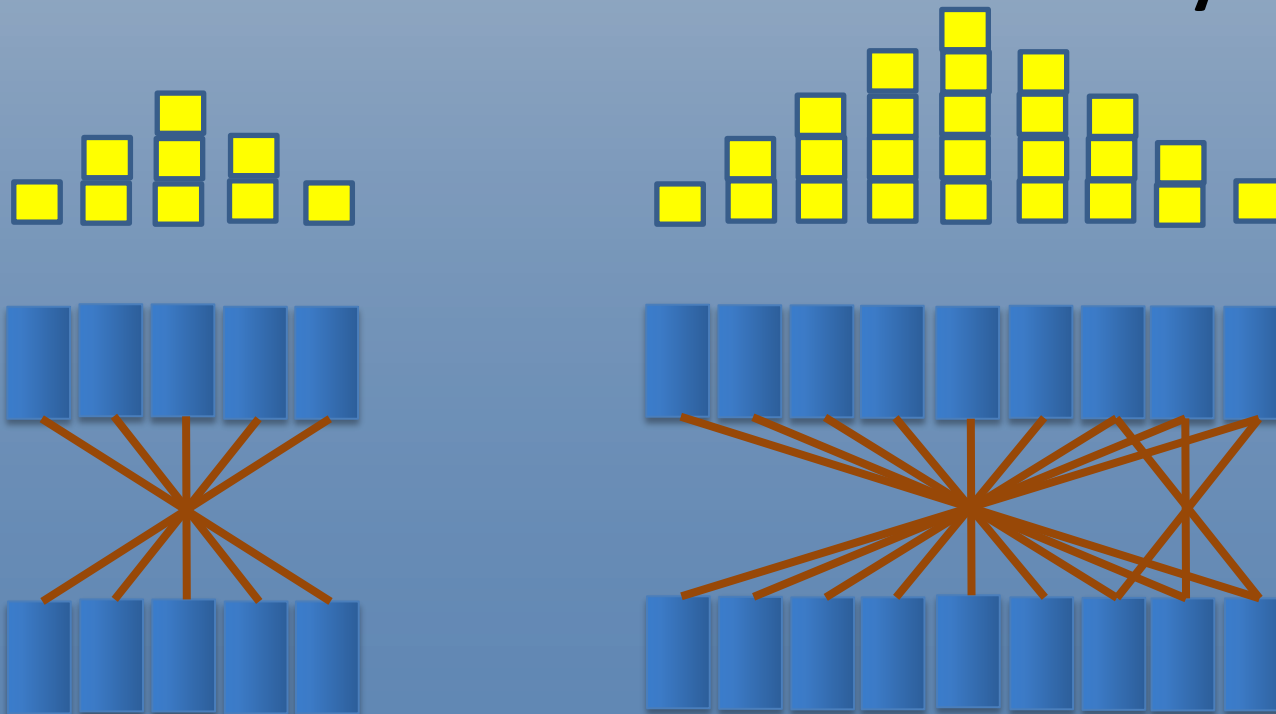
- **Frame-mode**
 - Traditionally used
 - Accumulate counts in sinogram or projection matrix
 - Fast calculation and easy reconstruction
 - May be gated, static, or dynamic
- **List-mode**
 - Becoming standard (flexibility and information)
 - List of event position, detection time, energy, etc.
 - Engineering challenges with high data rate (MB/s)
 - Can retrospectively resort data for dynamic, gated, etc.
 - Facilitates advanced reconstruction with motion compensation

Characteristics

- **Resolution**
 - Intrinsic: 2-3mm
 - System (NEMA Measured): ~5mm
 - Temporal: minutes per bed position, less for dynamic or gated
- **Sensitivity**
 - To material: 10^{-15} mol of material
 - System: 8% (0.08cps/Bq)

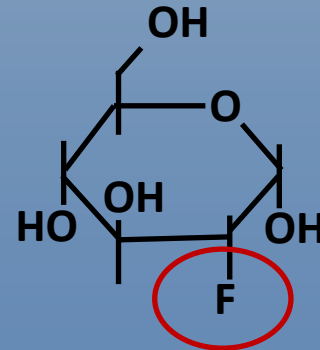
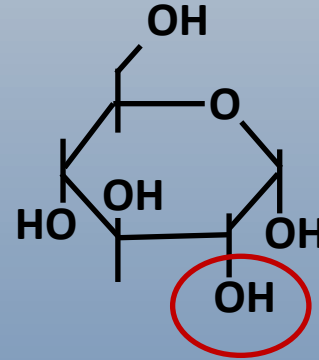
Axial Sensitivity Profile

- Sensitivity increases with axial length of scanner
 - More LOR
 - 16cm increase to 22cm increases sensitivity 78%



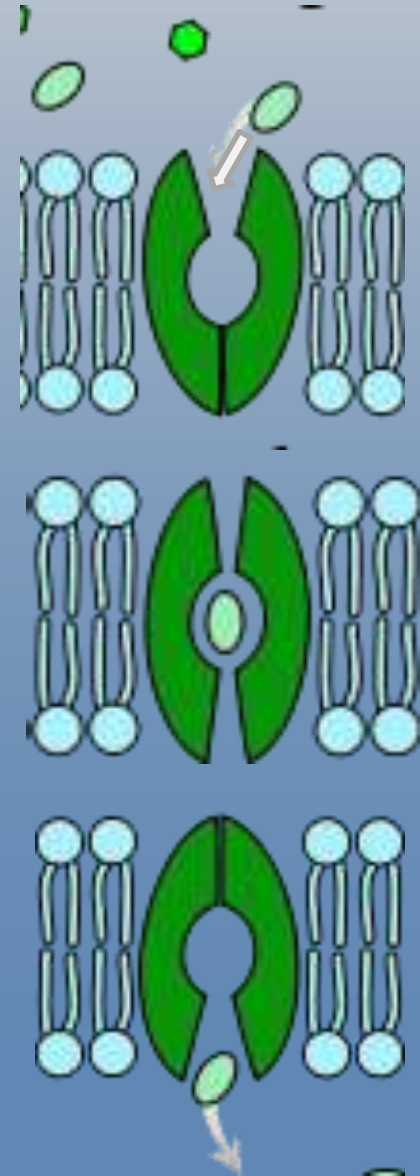
Glucose vs. FDG

- **Glucose**
 - Essential carbon supplier for tissue creation
 - Proliferation
 - Fuel for cellular respiration
 - Energy
- **Fluorodeoxyglucose**
 - Analogue of glucose



Pathophysiology: Transport

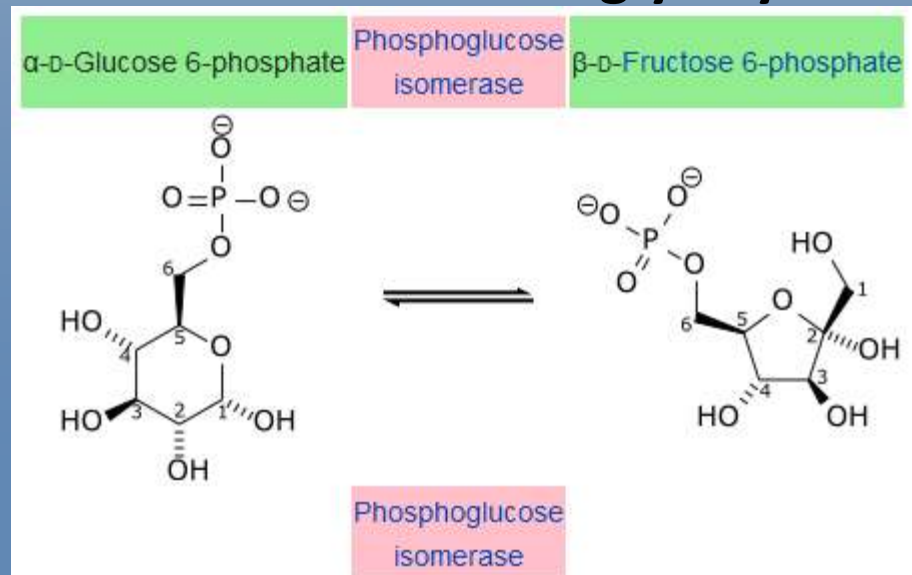
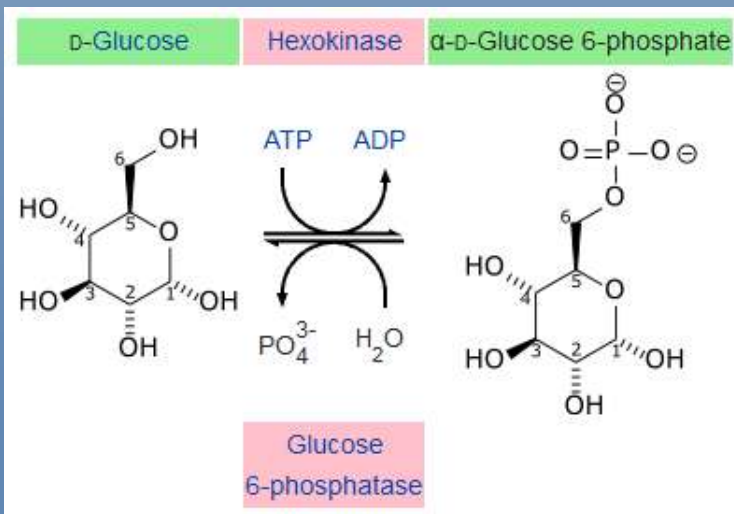
- Glucose is too big to diffuse across membrane
- Facilitated Diffusion
 - Rate increases linearly until carrier saturated (**Fasting**)
 - Competition: Glucose vs. FDG
 - Insulin increases rate 10-20x (**Diabetes**)
 - Six transporters (GLUT-1, GLUT-2, etc.) differ in location, kinetics, and sugar specificity
 - GLUT-1, 3, & 5 are overexpressed in tumors
 - GLUT-4 is in brown fat (**Artifact**)
 - GLUT-1 at Blood-Brain Barrier



Pathophysiology: Transport

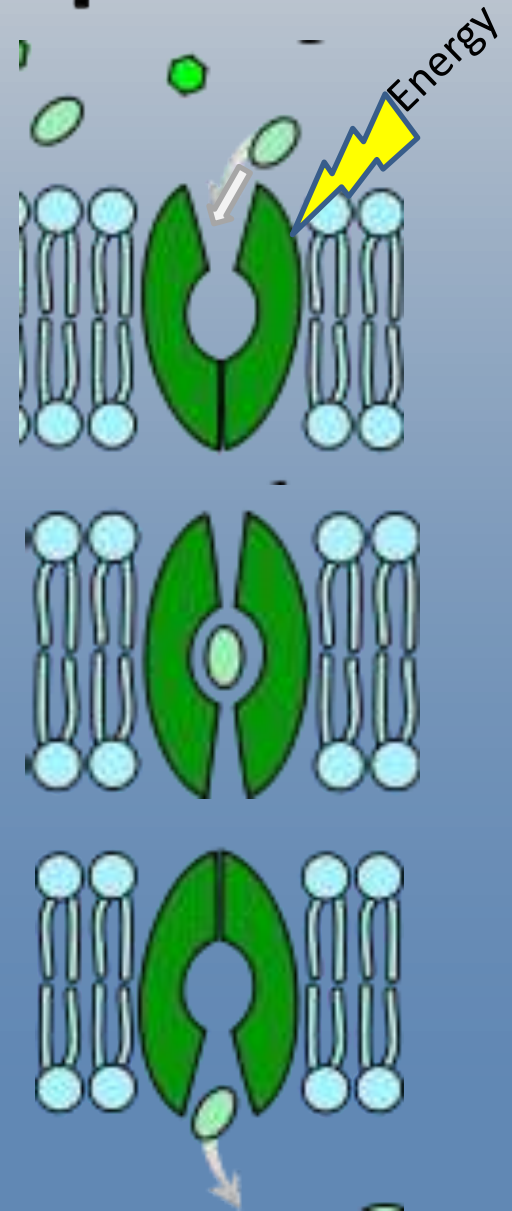
- **Facilitated Diffusion**

- Glucose is phosphorylated by hexokinase to glucose-6-phosphate → glycolysis (creates energy)
- FDG → fluorodeoxyglucose-6-phosphate cannot move on until F decays to O
 - Picks up H from environment and moves on to glycolysis



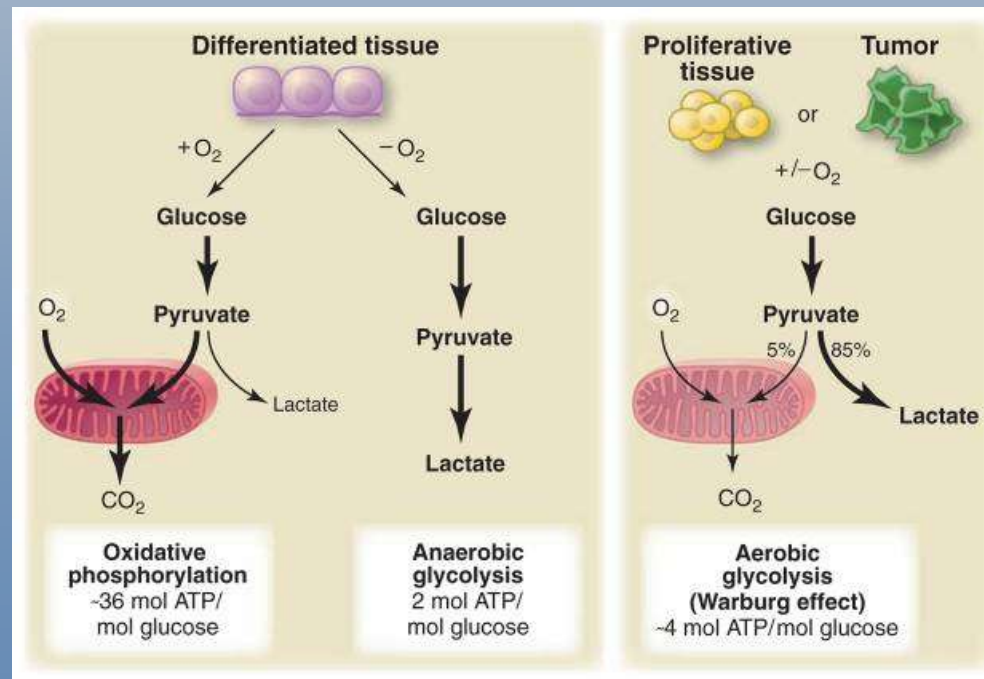
Pathophysiology: Transport

- **Active transport**
 - Requires energy and a carrier to move against concentration gradient
 - Sodium-dependent glucose transporter (SGLT) poor FDG binding
 - Glomerular filtered glucose transported into blood in distal renal tubules
 - FDG stays in urinary tract (poor recirculation) and moves to bladder



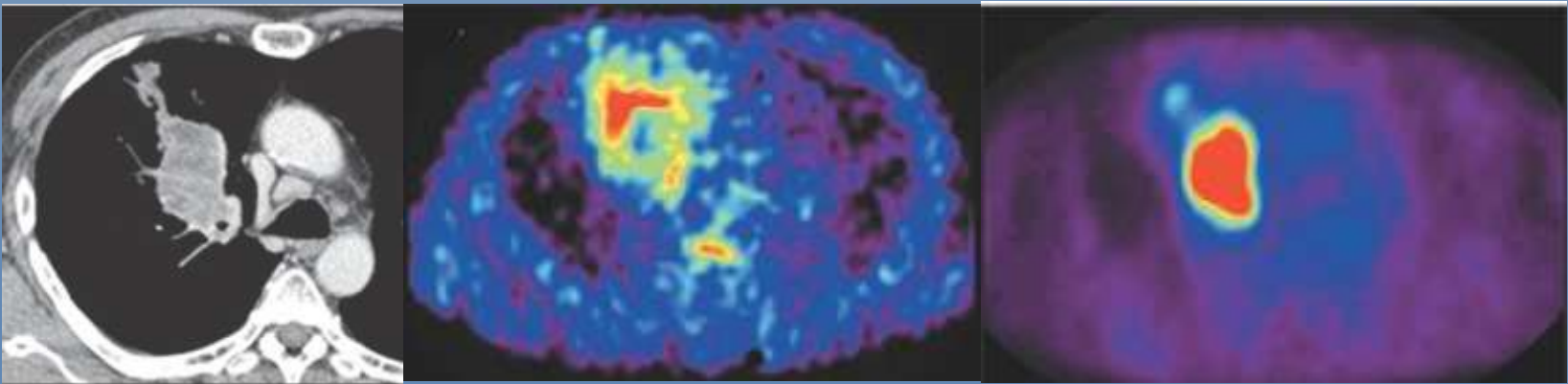
Pathophysiology: Malignancy

- Tumors use more glucose due to altered metabolism and proliferation (hyperglycolysis/Warburg effect)
 - Glycolytic capacity proportional to differentiation (**Grading/Staging**)
- Increased transporter expression and activity
- Increased production and activity of hexokinase
- Absent or low levels of phosphatase (reverse hexokinase)



Pathophysiology: Hypoxia

- Hypoxia
 - FDG uptake **increases** in acute and chronic hypoxic cells
 - Conflicting and variable results in human studies
 - Increased GLUT-1 expression through HIF-1
 - F-MISO, Cu-ASTM, F-nitroimidazoles are better agents



Pathophysiology: Necrosis

- **Necrosis**
 - Lack of uptake by necrotic tissue
 - Bright normoxic/hypoxic ring around hypointense necrosis

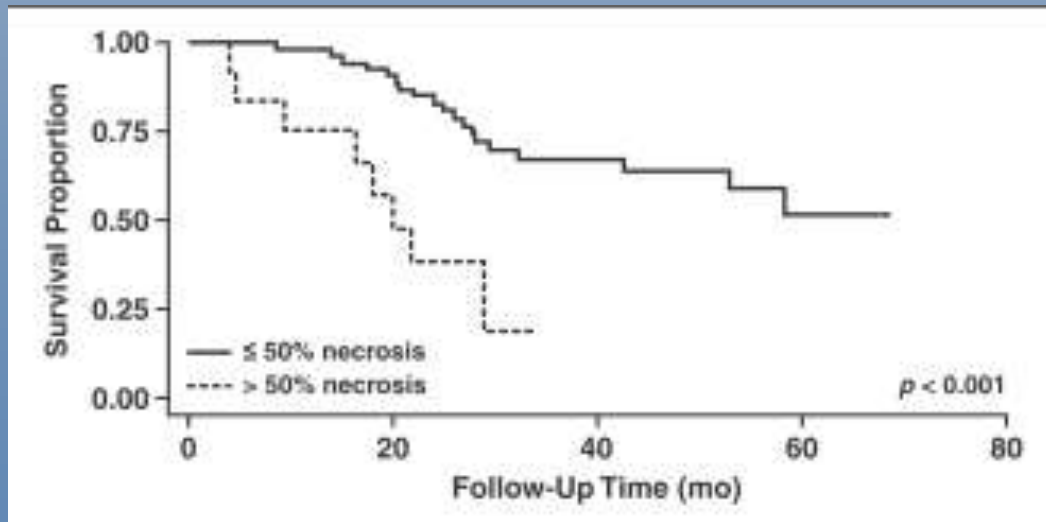
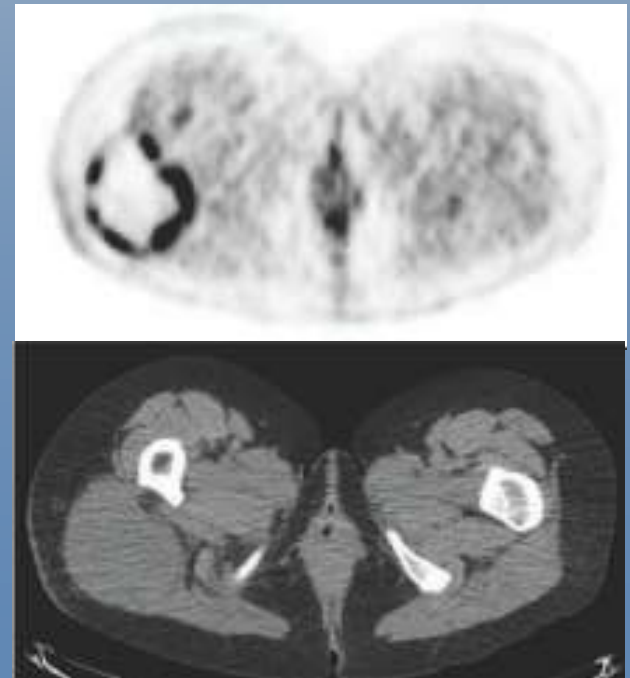
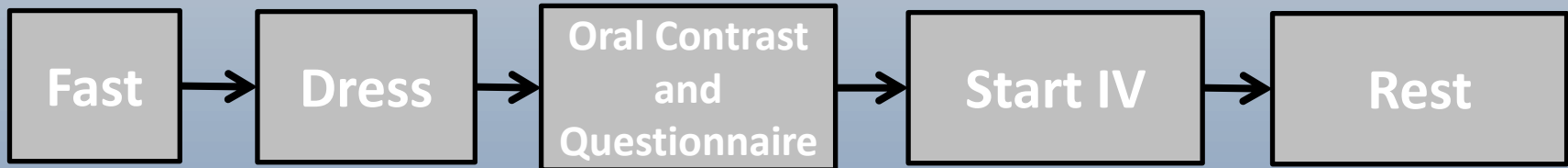


Fig. 3—Kaplan-Meier curve shows overall survival by groups in terms of necrosis volume (≤ 50% vs > 50%).



Patient Setup – Before Injection



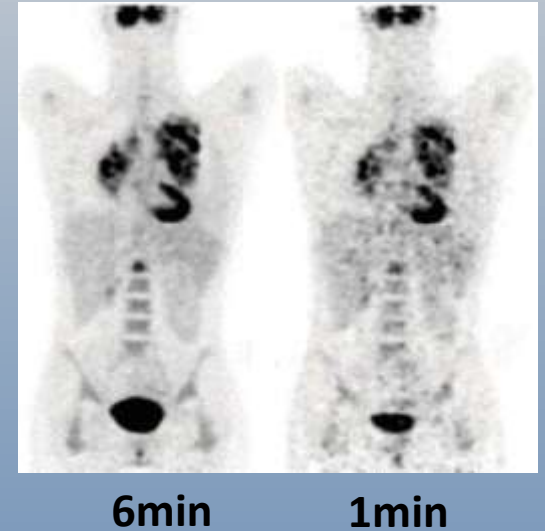
- **Fast 6hrs (2-4hrs pediatric)**
 - Glucose 80-120 mg/dL or 180-200 mg/dL for diabetic patients (**Muscle Uptake**)
- **Dress in gown and remove jewelry (**Metal Artifact**)**
- **Questionnaire and Oral CT Contrast**
 - Pregnancy, breastfeeding, fasting compliance, prior surgery, therapy, conditions, hydration
- **Start IV (22-24 gauge) contralateral to side of interest**
- **Patient may rest for up to 15min before injection**
 - Especially important in brain

Patient Setup – Before Scan



- **Injection with FDG**
 - 10-15mCi (0.081 to 0.14mCi/kg pediatric)
- **Patient rests in warm calm environment (45-60min)**
 - Warm room and blankets (**Brown Fat**)
 - No motion, talking, eating, or other stimulation (**Artifact**)
- **Void bladder just before scan (**Dose and Reproducibility**)**
- **Position patient with immobilization devices and in treatment position (**Reproducibility**)**
 - If using as simulation as well
 - Large bore size makes this easier

Patient Scan - PET



- **Whole body PET protocol**
 - 2mmx2mmx2mm voxel size
 - 1-3min per bed position
 - 12min for 4D gated
 - 5-9 bed positions (25-50% overlap)
 - OSEM reconstruction with 5mm Gaussian filter
- **CT**
 - Simulation: 120-140kVp, 100-200mAs, pitch 1.1-1.4, standard (non-enhancing) recon kernel, dose modulation (if patient is centered in bore)
 - Non-simulation: reduce mAs ~50%

Injection-Scan Interval

- Differential FDG uptake continues after injection
- Impacts SUV and apparent tumor size
 - Serial scans should be made with same injection-scan interval to ensure accurate results

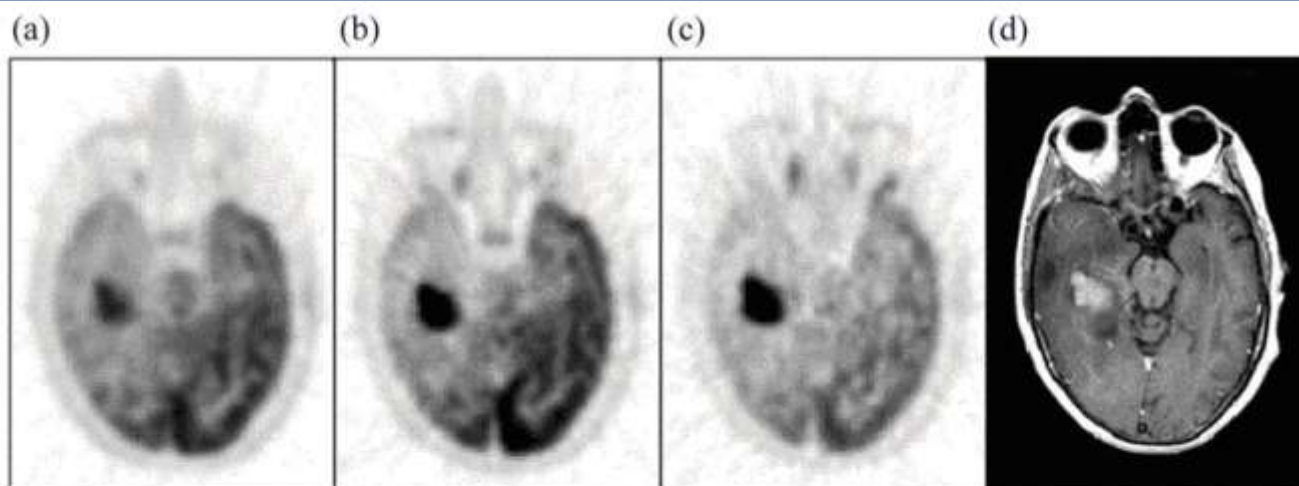


FIG. 4.11. Transaxial PET images of a patient imaged at different time points post-injection: (a) 45 min, (b) 82 min and (c) 315 min. For comparison, the axial magnetic resonance post-Gd-enhancement is shown in (d). The varying contrast between the tumour and the left (visually right) hemisphere with time post-injection should be noted.

Impact of Therapy

TABLE 2.2. CLINICAL SITUATIONS THAT AFFECT FDG UPTAKE AND FDG-PET/CT — TIMING AND RECOMMENDATIONS

Prior therapies and clinical issues	Recommended interval between therapy and PET/CT	Confounding factor	Other recommendations
Recent chemotherapy	2 weeks Interim PET 2–3 weeks from last cycle End of treatment 4–6 weeks	Marked increase in FDG uptake in the bone marrow	
Recent therapy with cytokines or growth factors	Short acting: 1 week Long acting: 3 weeks	Marked increase in FDG uptake in the bone marrow	
Inflammatory or infectious processes	Wait until inflammatory process resolved, if possible	Increase in FDG uptake in the infected or inflamed areas	
Radiation therapy	4–6 weeks	Focal increase in FDG uptake in the radiated area	
Recent surgery	4–6 weeks	Increase in FDG uptake in the surgical sites	
Granulomatous diseases such as sarcoidosis		Focal increase in FDG uptake in the affected area	
History of claustrophobia			Pretreatment

SUV

$$\text{SUV} = \frac{\text{Activity in ROI (MBq)} / \text{vol (mL)}}{\text{Injected activity (MBq)/patient weight (g)}}$$

- Areas with higher than average uptake will have SUV's >1
- Higher the SUV, greater the risk of disease
- Cannot be used as an absolute number



before chemo
SUV = 17.2



chemo day 7
SUV = 3.9



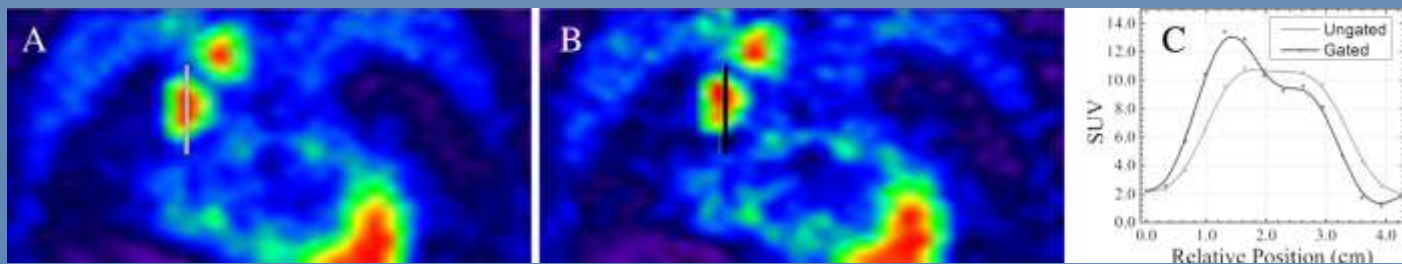
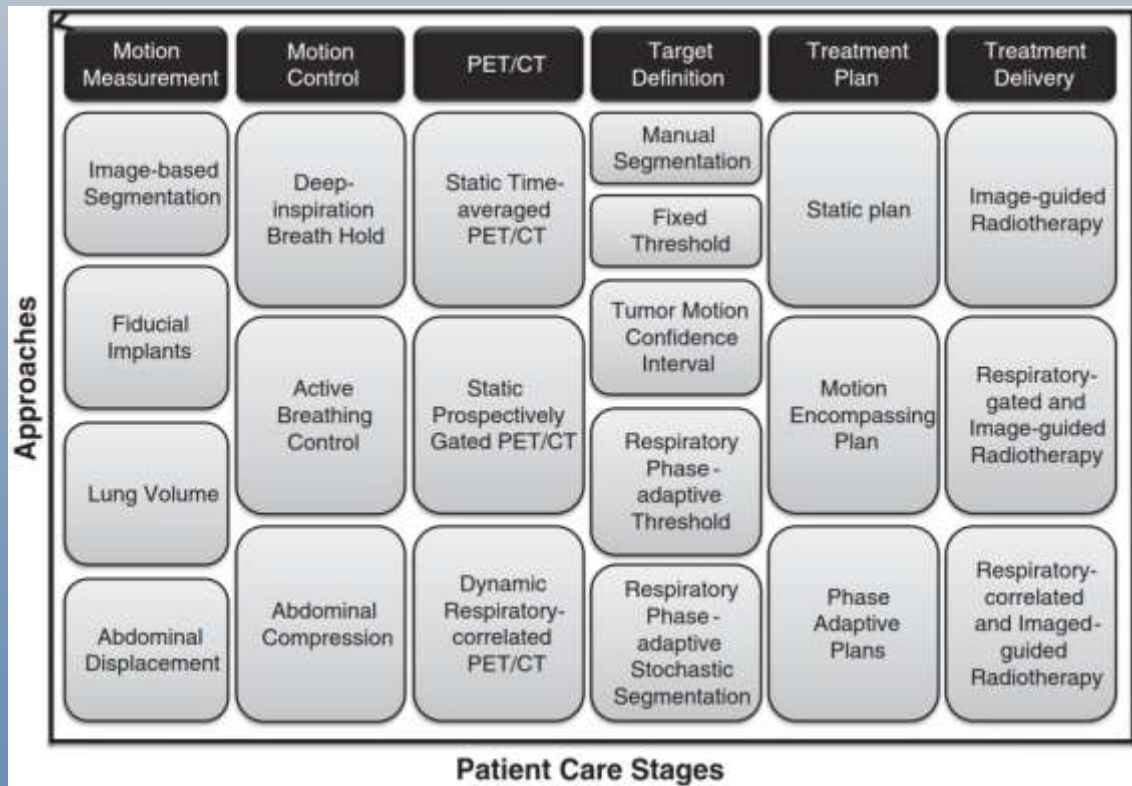
chemo day 42
SUV = 1.8

SUV: Confounding Factors

- **Patient size**
 - Overestimation of SUV due to fat on large patients or patients whose weight changes
 - » Use lean body mass or body surface area instead of weight
- **Glucose level**
 - High glucose level causes reduced target uptake
 - » Attempts at normalization are not recommended
- **Protocol**
 - Time from injection to scan, scanner, ROI selection, postprocessing, contrast media, resolution, etc.
 - » Keep consistent in longitudinal tracking of patient

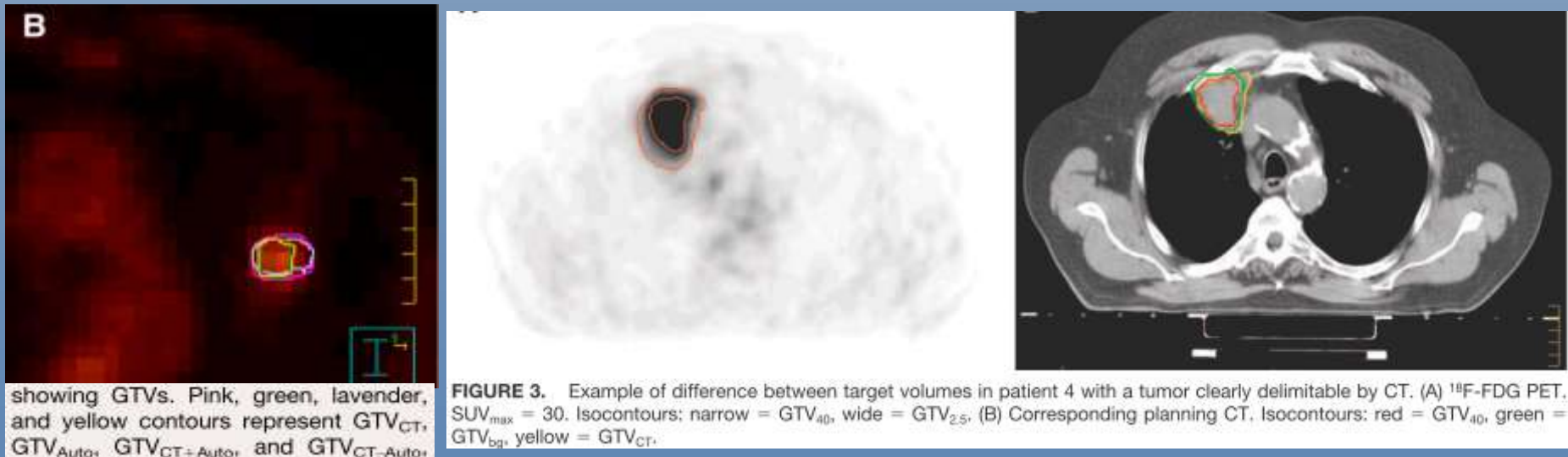
Motion Management

- **CT:**
 - Breath hold
 - Slow scan
 - Gated
- **PET**
 - Free breath
 - Gated
 - 4D



Contouring

- Independent of SUV confounding factors
- Lesion definition
- Manual, automated, semi-automated
 - Manual slower but correlates to pathologic size better



right images and ref: Nestle et al. J Nucl Med 2005;46:1342-1348.

left images and ref: Wu et al. J Nucl Med 2010;51:1517-1523

Patient Dose: Adult

- **PET**

- **ICRP 106**

	Adult	15 years	10 years	5 years	1 year
Effective dose (mSv/MBq)	1.9E-02	2.4E-02	3.7E-02	5.6E-02	9.5E-02
Bladder	1.3E-01	1.6E-01	2.5E-01	3.4E-01	4.7E-01

- **ImageWisely: 3.5-10.5mSv for 5-15mCi**

- **CT**

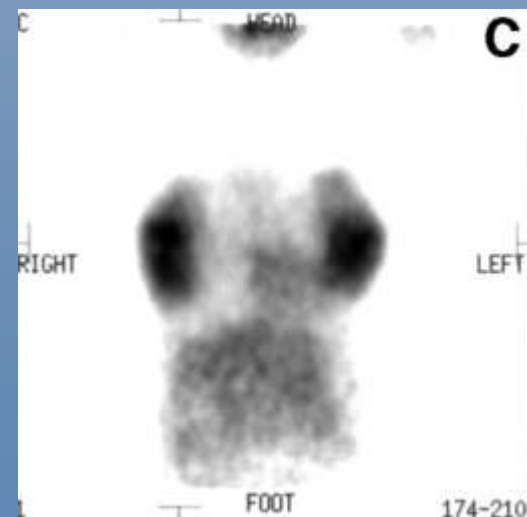
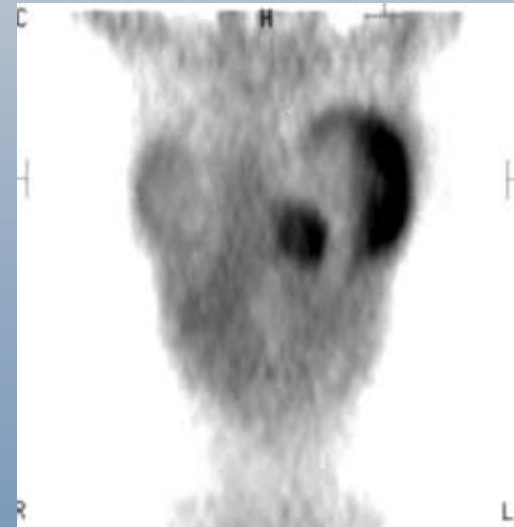
- **ImageWisely:**

Study	Injected Activity	Effective Dose Estimate
PET ^{6,7}	[5-15] mCi ¹⁸ F-FDG Injected (185-555 MBq)	3.5-10.5 mSv
CT for diagnostic purposes ⁸	[110-200] mAs ¹ CTDI _{vol} = [8-14] mGy	11-20 mSv
CT for anatomic localization ⁸	[30-60] mAs ³ CTDI _{vol} = [2-4] mGy	3-6 mSv
CT for attenuation correction only ⁸	[5-10] mAs ⁴ CTDI _{vol} = [0.3-1.0] mGy	0.5-1.0 mSv

For ease of comparison, all CT studies presented are performed with 120 kVp, pitch 1.375, 40 mm collimation, 900 mm scan range, average tube current-time product.

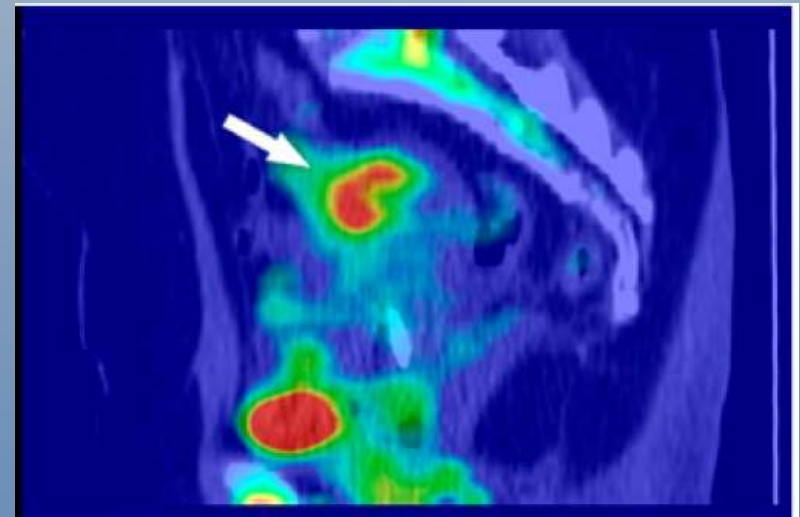
Patient Dose: Breastfeeding

- **Breastfeeding**
 - Breast uptake due to active nursing
 - Stimulates GLUT-1
 - Expressed milk: 5.54-19.3 Bq/mL/MBq
 - Uninterrupted feeding unlikely to cause dose in excess of regulatory limits
 - Infant dose largely due to proximity to breast and not ingestion of isotope
 - Delay feeding at least 4 hrs after injection
 - Express milk and have another family member bottle feed



Patient Dose: Fetal

- **FDG crosses placenta**
 - Concentrates in the brain
 - Excreted by the fetal kidneys
- **As high as 0.04mGy/MBq**
 - Photon dose 1/10th positron
 - 1/4 of dose due to mother's tissue
- **Example:**
 - 10mCi FDG gives 14.8mGy
 - 10mSv for diagnostic CT
 - **~25mSv total**



Worker Dose and ALARA

- Typical technologist effective dose
 - 6mSv/year
 - 0.02 $\mu\text{Sv}/\text{MBq}$ per unit injected activity
 - Largest dose from escorting injected patient to bathroom or scanner
- Typical technologist hand dose
 - 1.4mSv/GBq hand dose
 - 30cm forceps to reduce dose (**distance**)
 - 5mm W syringe shield drops dose by **factor of 10 (Shielding)**



Carnicer et al. Hand exposure in diagnostic nuclear medicine with ^{18}F - and $^{99\text{m}}\text{Tc}$ -labelled radiopharmaceuticals - results of the ORAMED project Radiation Measurements, 46(11) 2011 Pgs. 1277-1282A.

Benatar. Radiation dose rates from patients undergoing PET: implications for technologists and waiting areas. Eur J Nucl Med. 2000;27(5)

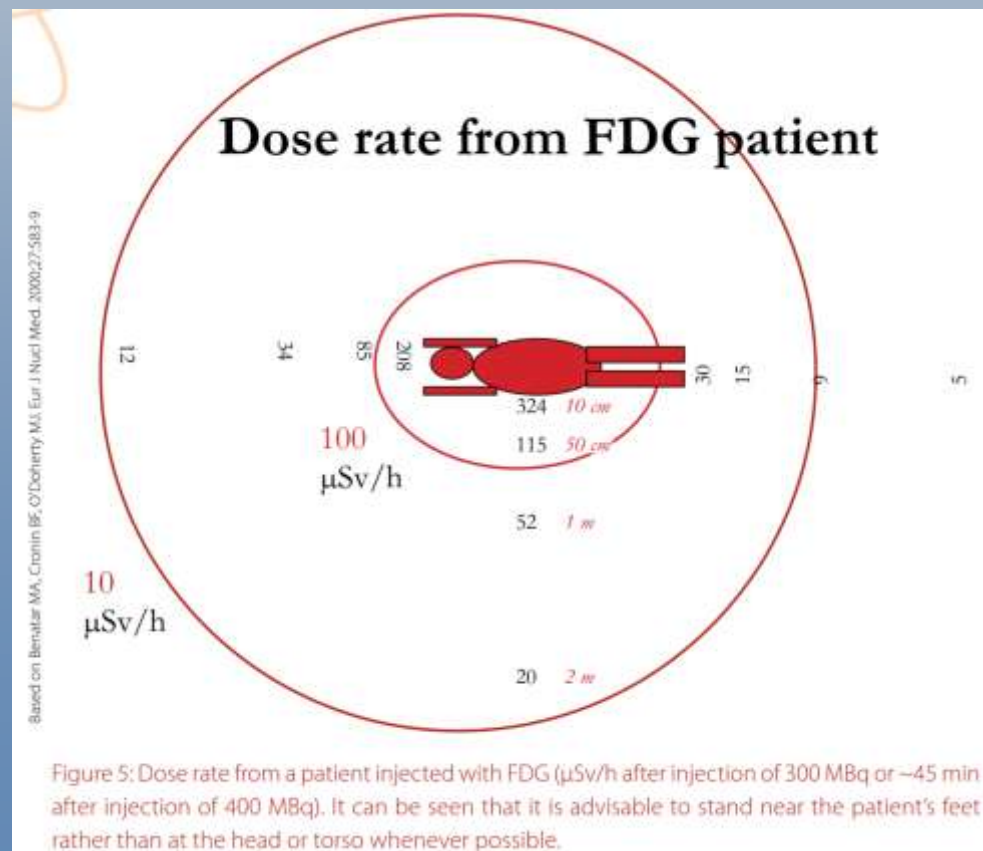
Images: William F. Sensakovic

Worker Dose and ALARA

- **Power injector**
 - 20% dose reduction (95% hand dose reduction)
 - 18.5mSv/min finger dose from unshielded syringe (10mCi)
- **Patient Bathroom**
 - 2mR/hr at surface just after patient void @60min post-injection
 - Increases through the day

Worker Dose and ALARA

- Dose from patient
 - $0.092 \mu\text{Sv}\cdot\text{m}^2/\text{MBq}\cdot\text{h}$
 - Could cause confusion after brachytherapy retraction if patient was not surveyed pre-therapy and underwent PET scan within a few hours

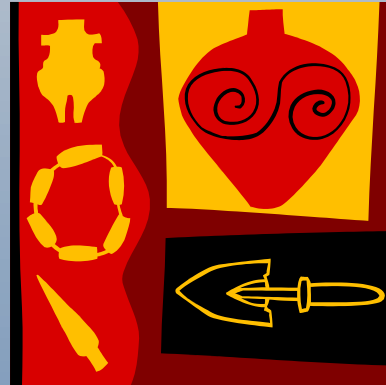


Worker Dose: Contamination

- **30cm from 1MBq point source**
 - 0.12mSv/hr skin dose from positrons
 - 0.081mSv/hr deep tissue dose from Gamma
- **0.05 ml (0.001MBq) skin contact**
 - 0.79mSv/hr skin dose
 - Skin dose due to positrons

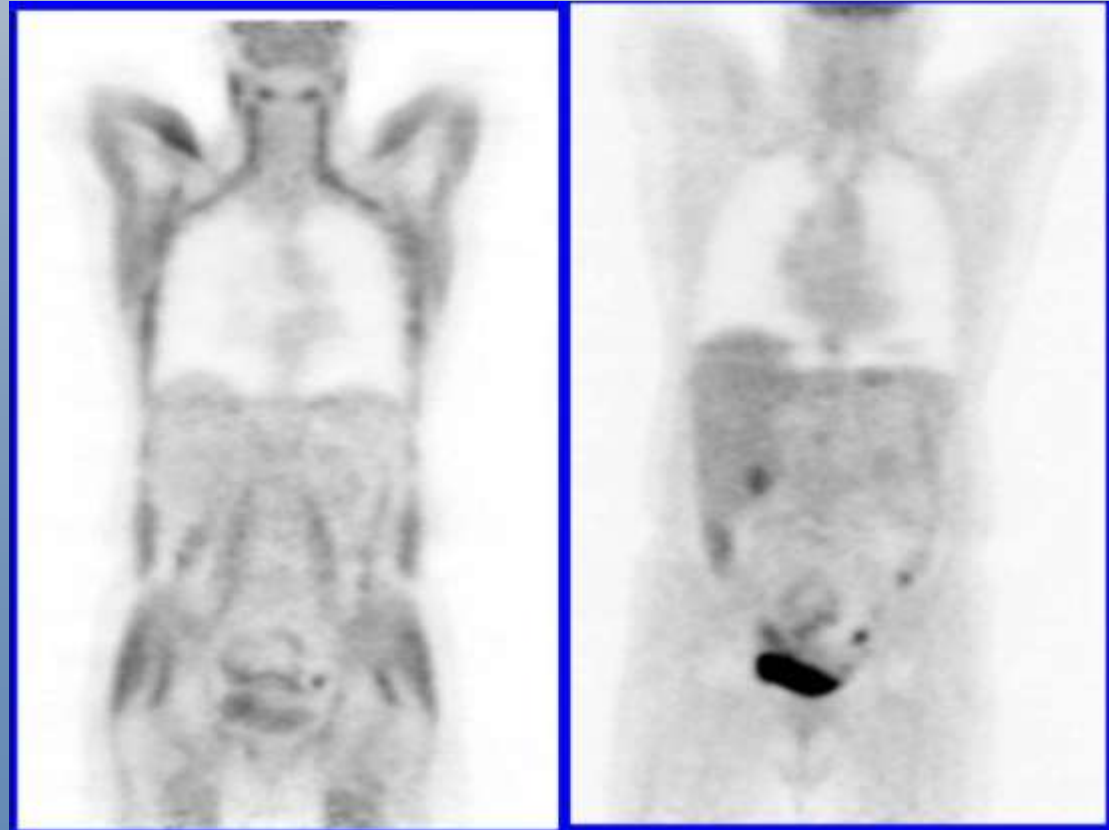


Artifacts



High Glucose Level

- Impacts visualization and SUV
- Test before scanning
- Fasting and insulin



High Glucose

Fasting Glucose

Muscle Uptake

- Impacts visualization and SUV
 - Rest in quiet room with no talking or movement
 - TV/calm music
 - Beta blocker or sedative



Talking



Hyperventilation

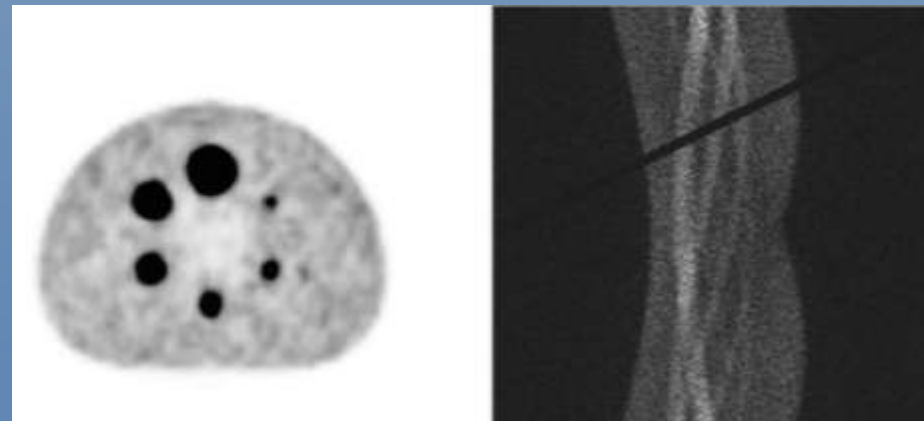
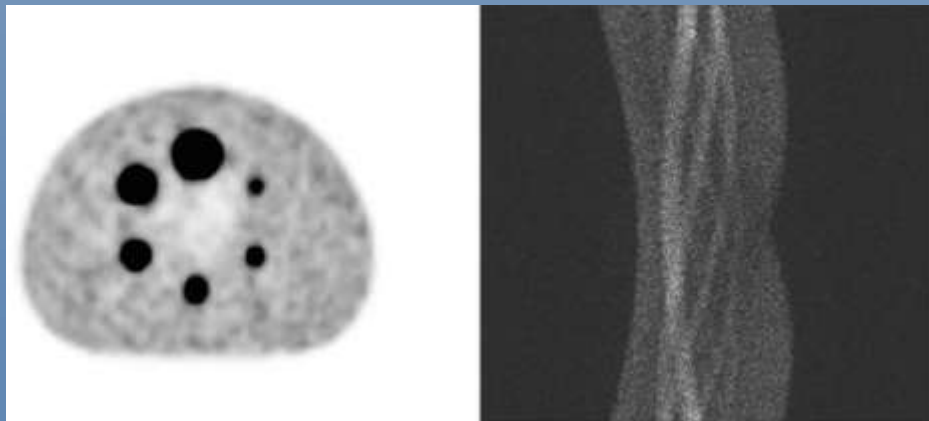
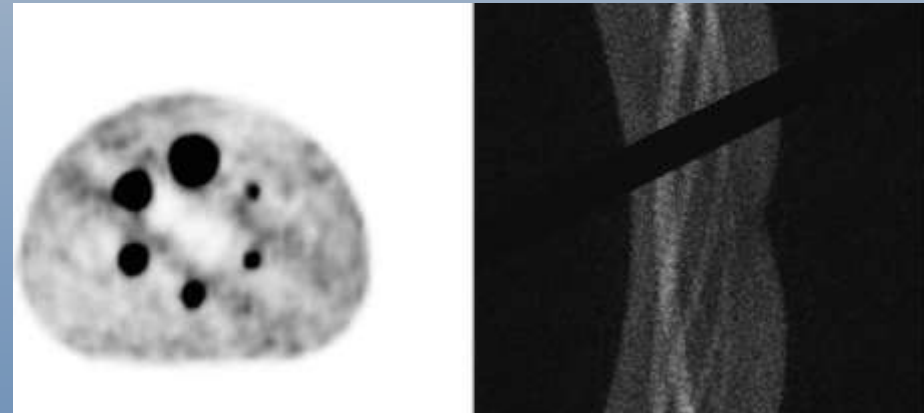
Brown Fat

- **Most likely in young adults**
 - Use blankets to keep patient warm
 - Match uptake to CT fat regions



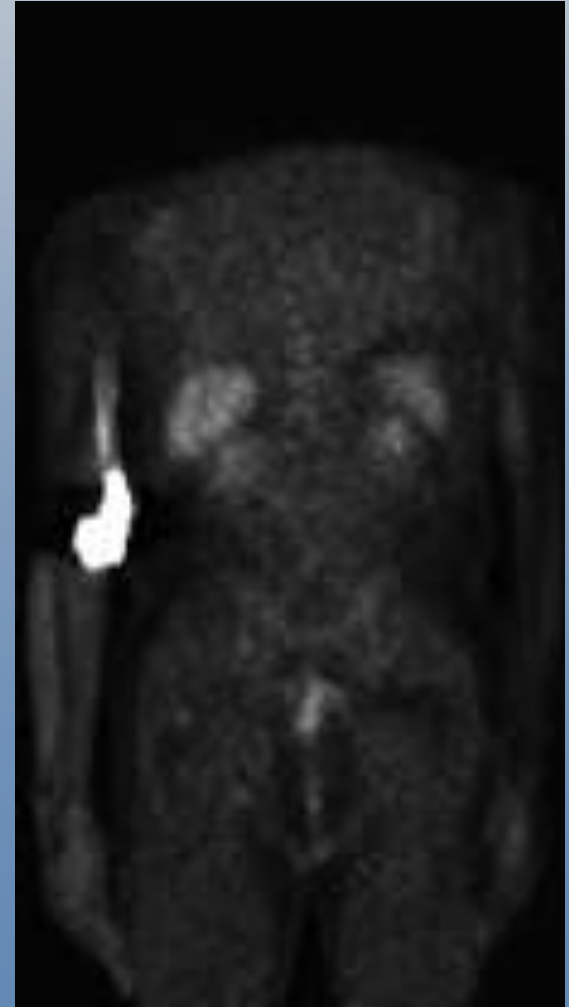
Detector Block Calibration

- Checked in daily QA
- Smaller changes can impact SUV
- Large changes necessary to impact visualization



Extravasation/Infiltration

- **11% of PET scans have some level of extravasation**
- **Calculation: 135Gy if 10mCi contained in 1mL**
- **Reality: Spreads and is absorbed by the body**
 - Does not usually cause skin damage
 - Does substantially alter SUV and visualization



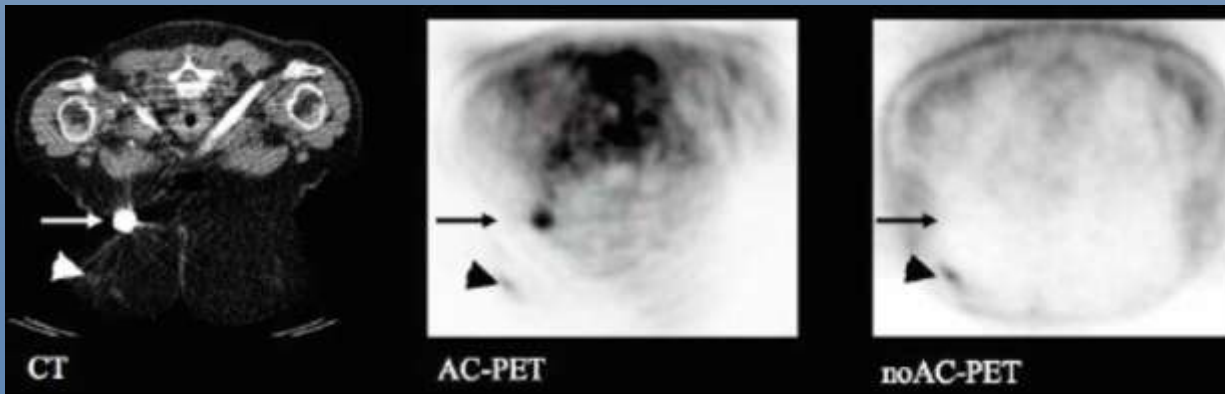
Ref: Hoop The Infiltrated Radiopharmaceutical Injection: Risk Considerations The Journal of Nuclear Medicine 32(5) 1991

Ref: Osman et al. FDG dose extravasations in PET/CT: frequency and impact on SUV measurements Frontiers in Oncology Cancer Imaging and Diagnosis 1 Article 41 2011

Image: William F. Sensakovic

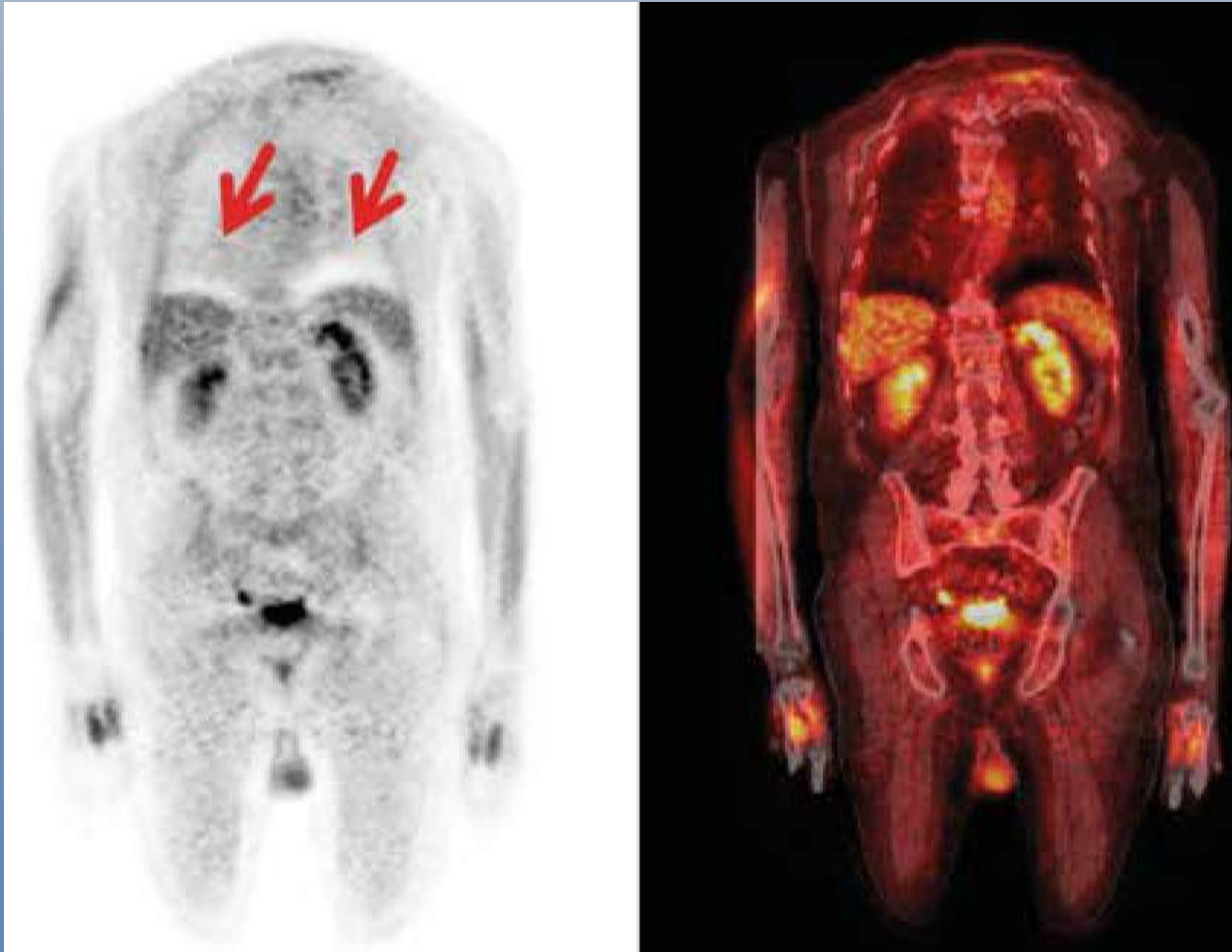
Marrow and Spleen Uptake Due to Chemotherapy

- Marrow and spleen demonstrate increased uptake
 - Higher than liver is abnormal
- Ports may cause uptake error in AC corrected images



Respiration

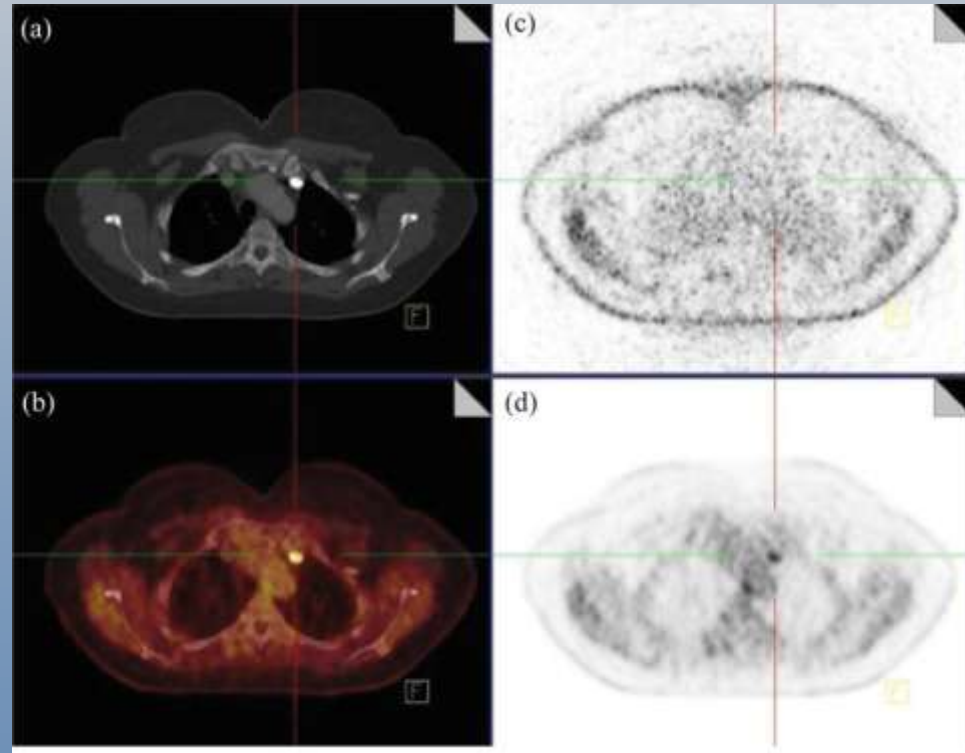
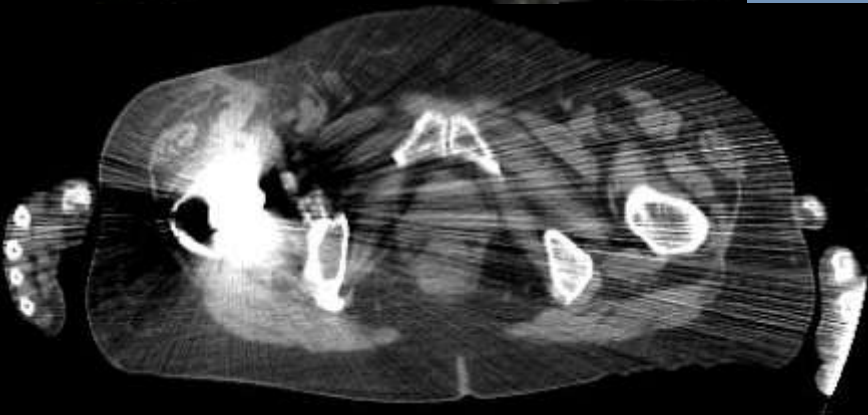
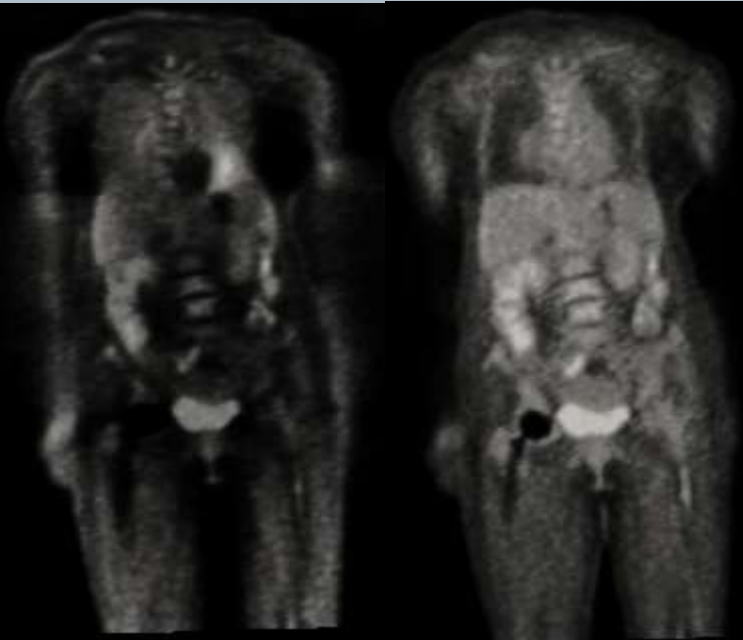
- Motion control to help



High-Z in CT

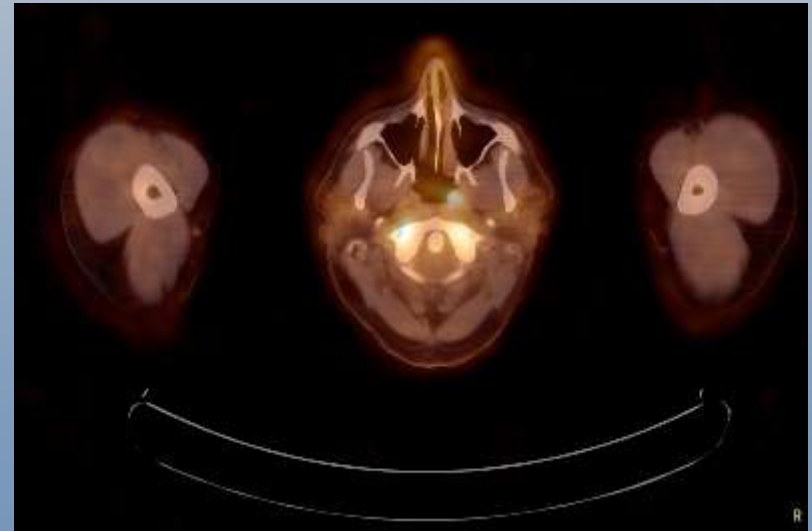
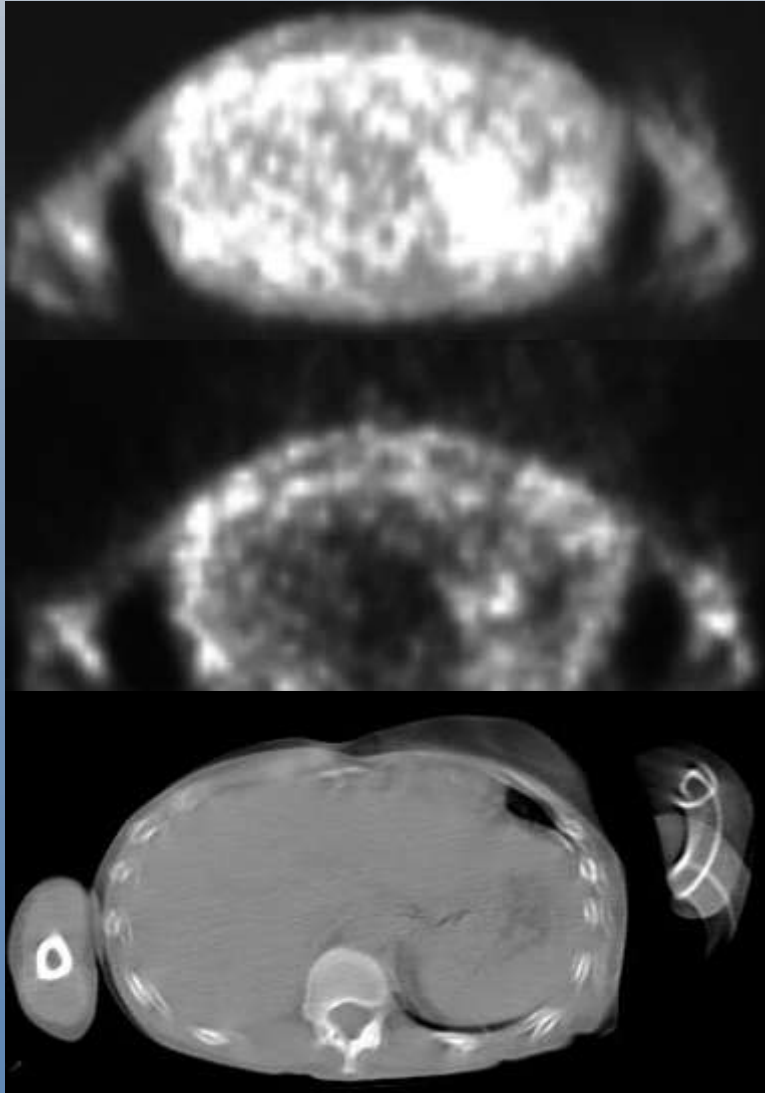
No AC

AC



- Cause major error when coupled with patient motion

Misregistration (Motion)



Truncation and Positioning

- SUV: 3.3 → 6.1
- Use extended FOV if possible

