Quantitative Molecular Imaging Using PET/CT to Assess Response to Therapy

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PET/CT Applications and Challenges

Primarily for Cancer Imaging -- works very well

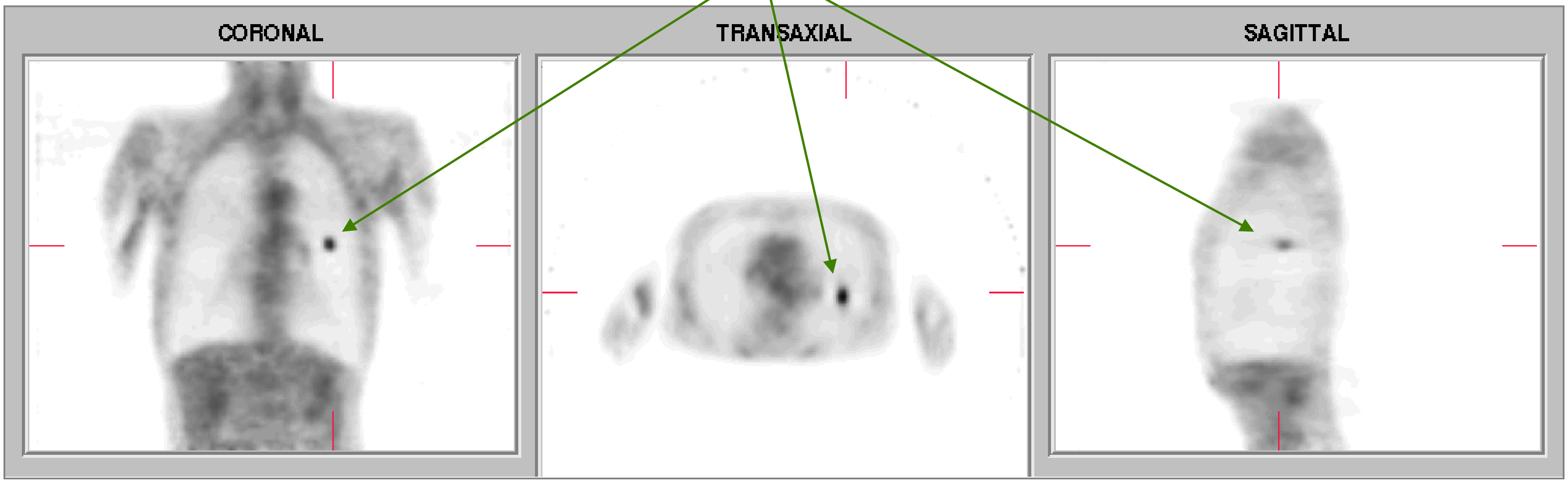
- Diagnosis and staging

Expanding Areas -- with significant challenges

- Radiation treatment planning using PET and CT
- Neurological imaging
- Cardiac imaging
- *Assessment of therapeutic response*

Do Numbers Matter in PET Images?

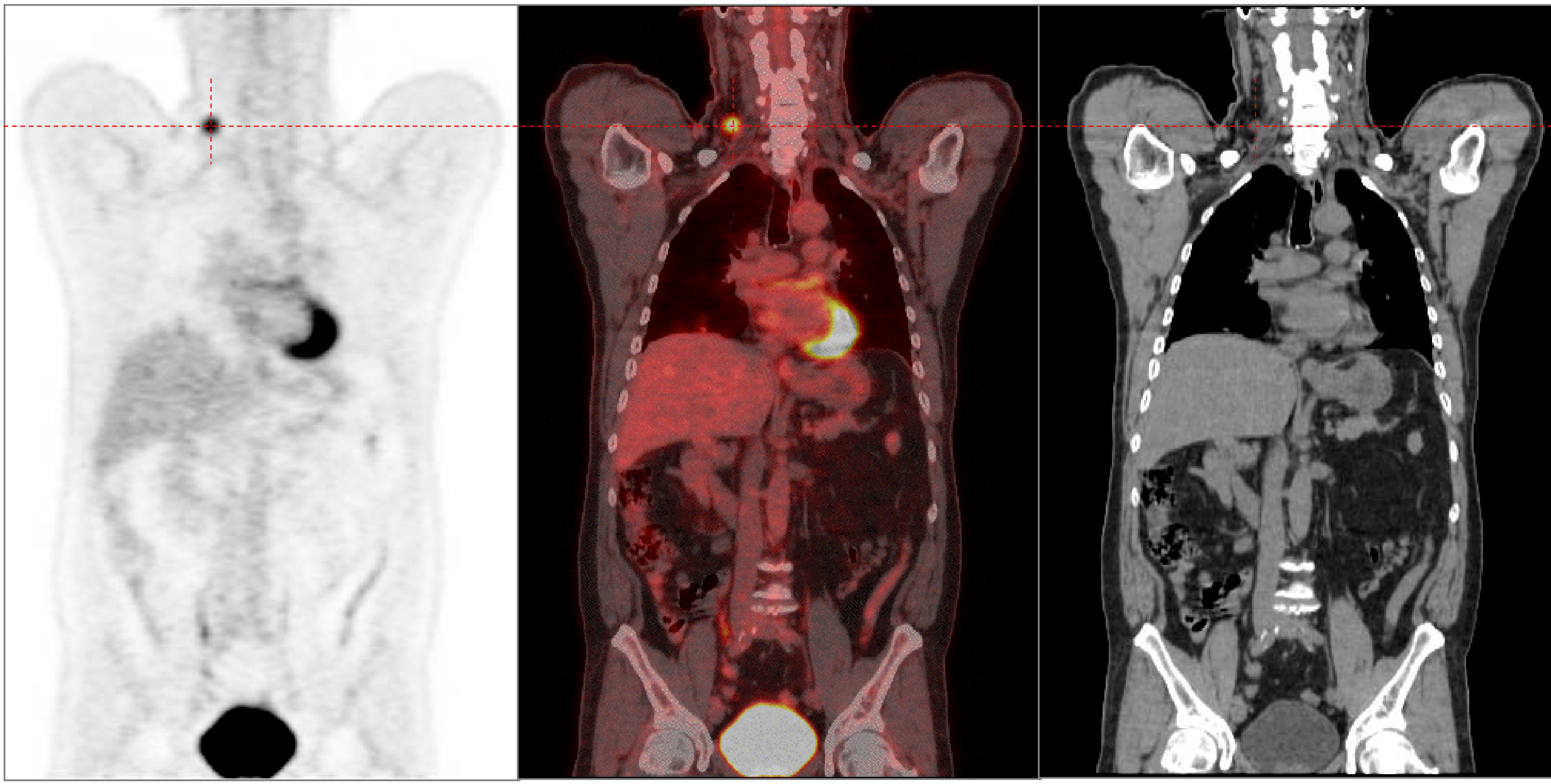
Elevated uptake of FDG (somehow related to metabolism)



- The answer to the question "Is quantitation necessary for clinical oncological PET studies interpreted by physicians with experience in interpreting PET images?" is "no."
- **Image quantitation will become increasingly important in determining the effect of therapy in many malignancies.**

R Edward Coleman Eur J Nucl Med (2002) 29:133–137

Imaging FDG uptake (PET) with anatomical localization (CT) and CT-based attenuation correction



PET Image of Function	Function+Anatomy and CT-based attenuation correction	CT Image of Anatomy

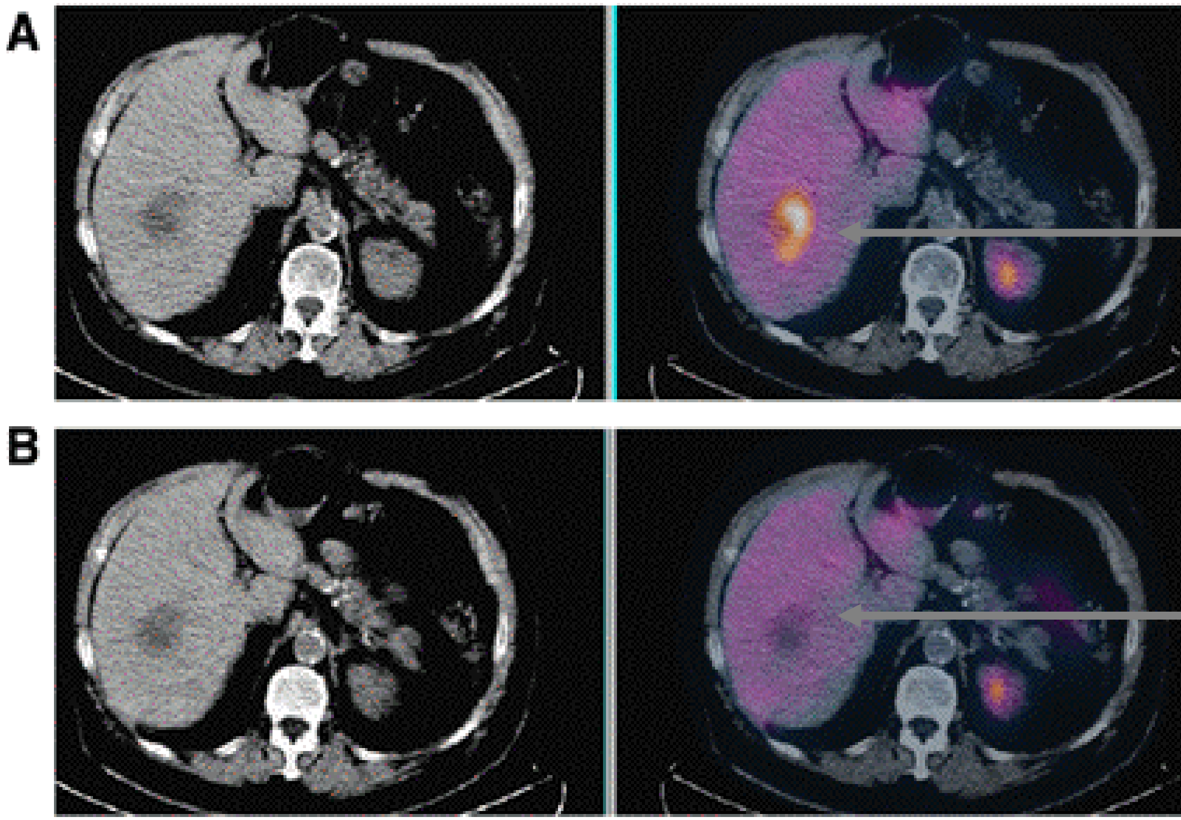
Response to therapy of liver met gastric GIST

- No morphological change in the metastasis

CT PET/CT

Pre therapy

1 wk imatinib therapy

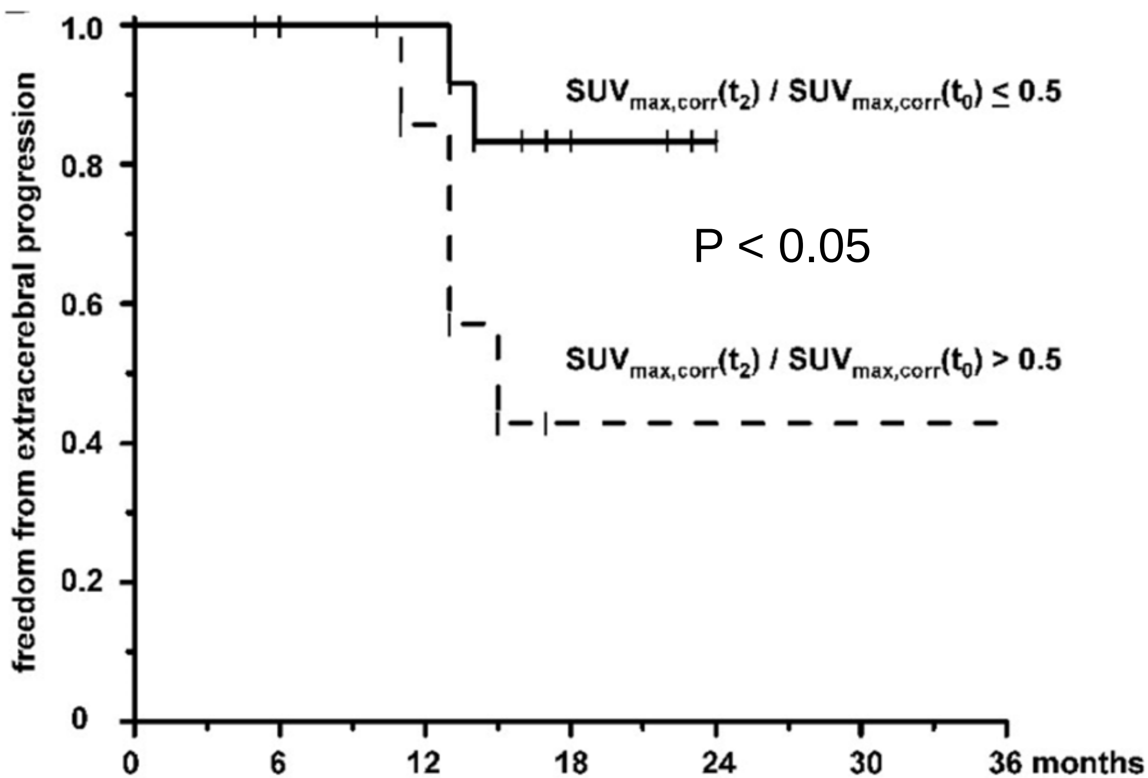


PET SUV
5 -> 1.8

Castell and Cook, British Journal of Cancer (2008)

Times to Relapse after Neoadjuvant Chemo-radiotherapy compared to PET/CT for NSCLC

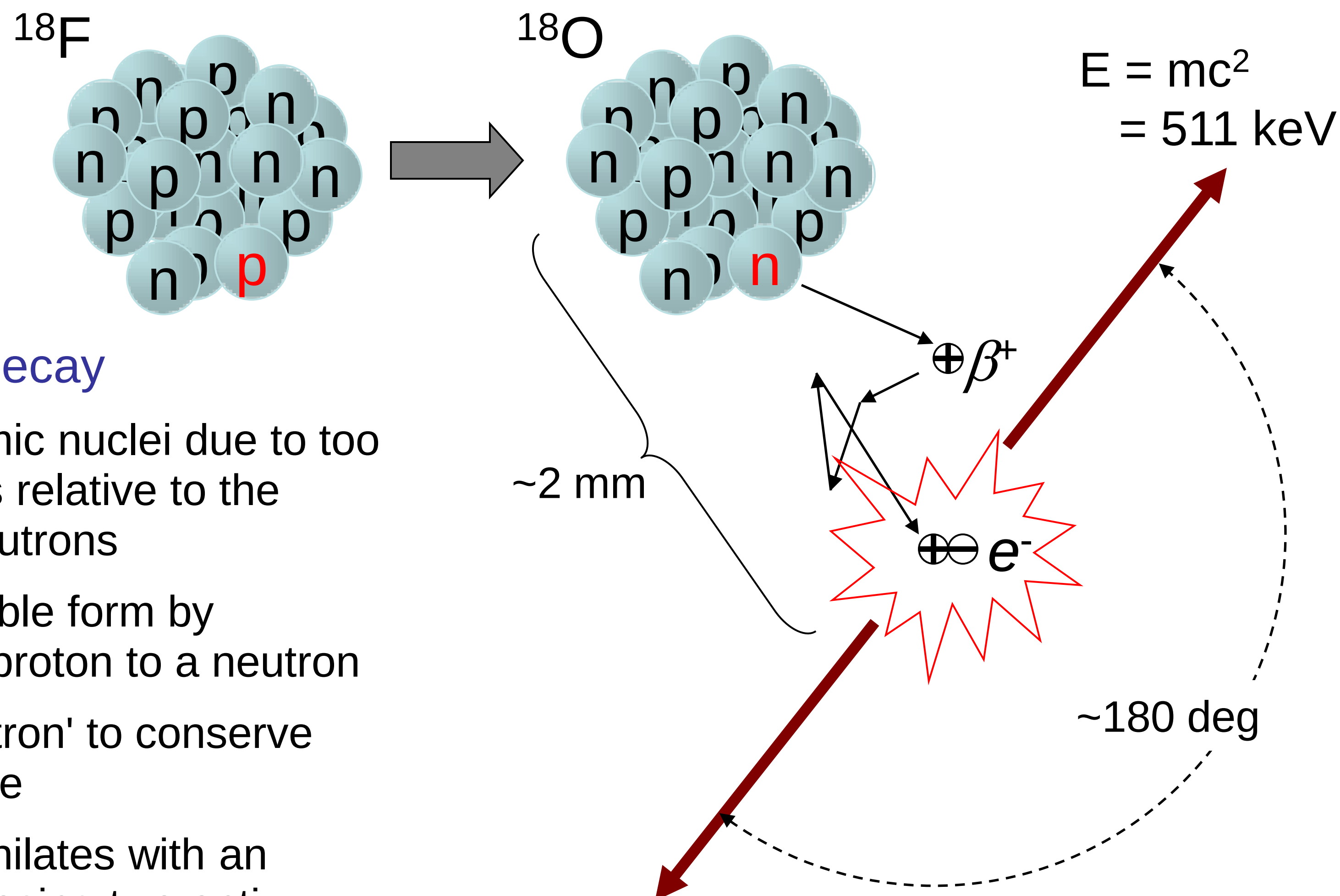
Time to extracerebral progression
Partition ratio: SUVmax*(t2)/SUVmax*(t0) ≤ 0.5



Pöttgen, et al Clinical Cancer Research, 2006

What do PET scans Measure?

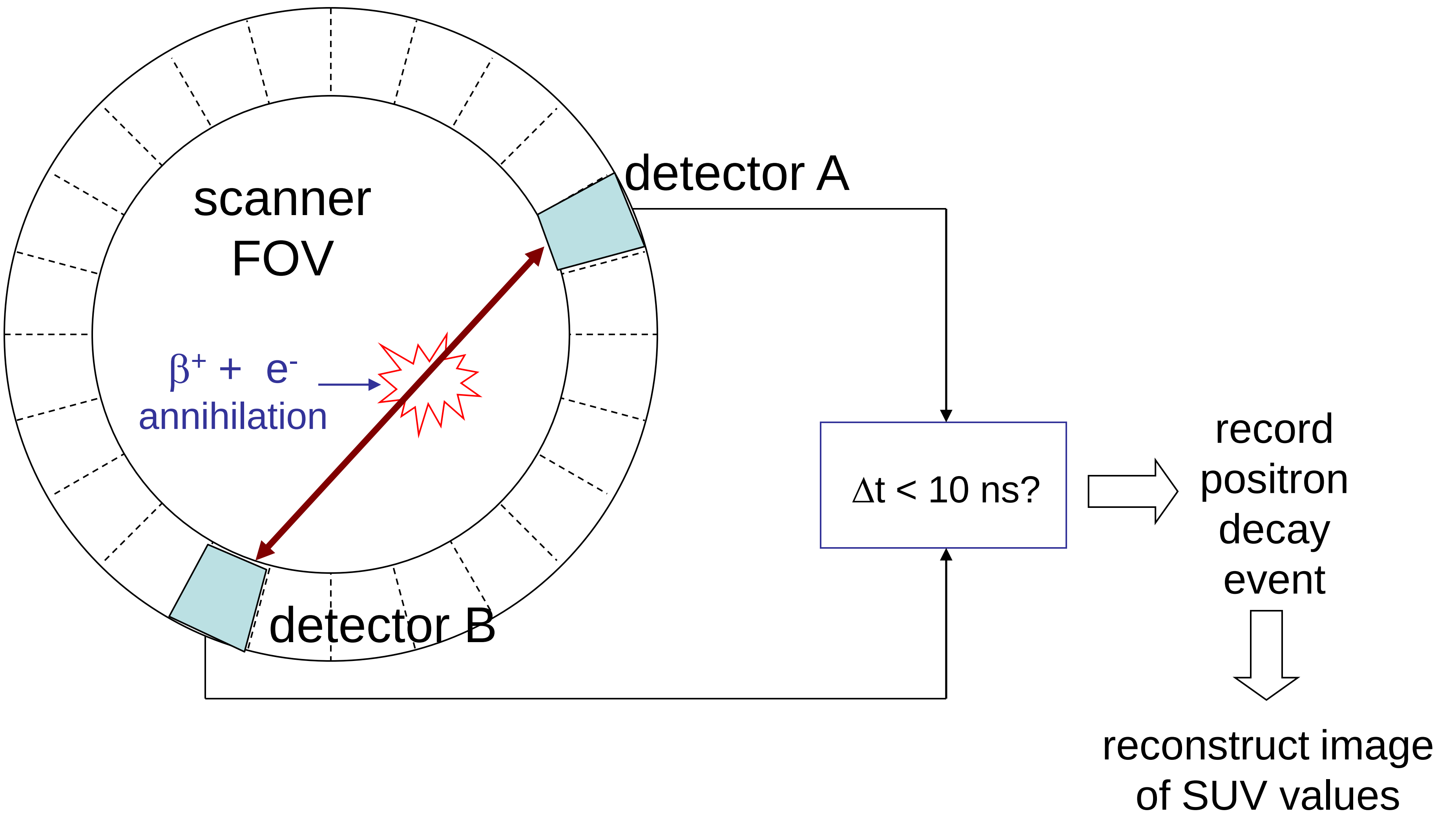
How it works: Positron Emission



Radioactive decay

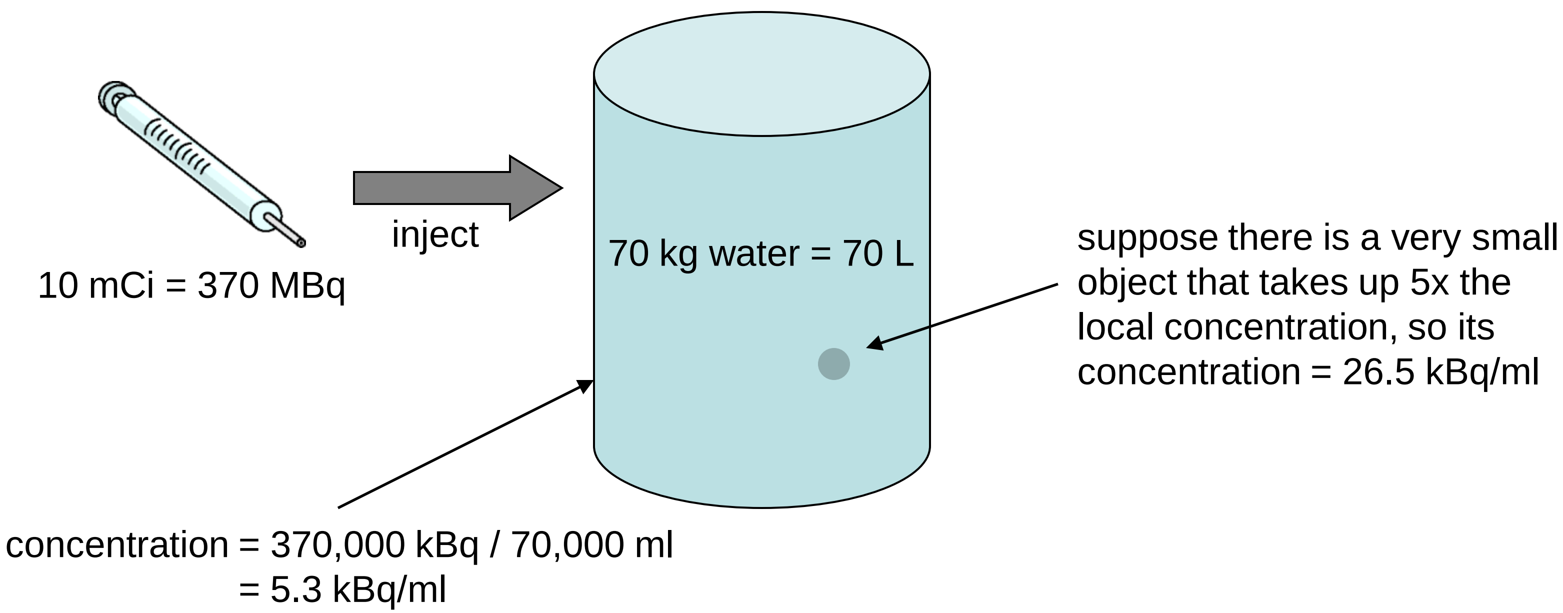
- unstable atomic nuclei due to too many protons relative to the number of neutrons
- decays to stable form by converting a proton to a neutron
- ejects a 'positron' to conserve electric charge
- positron annihilates with an electron, releasing two anti-colinear high-energy photons

How it works: Timing coincidence



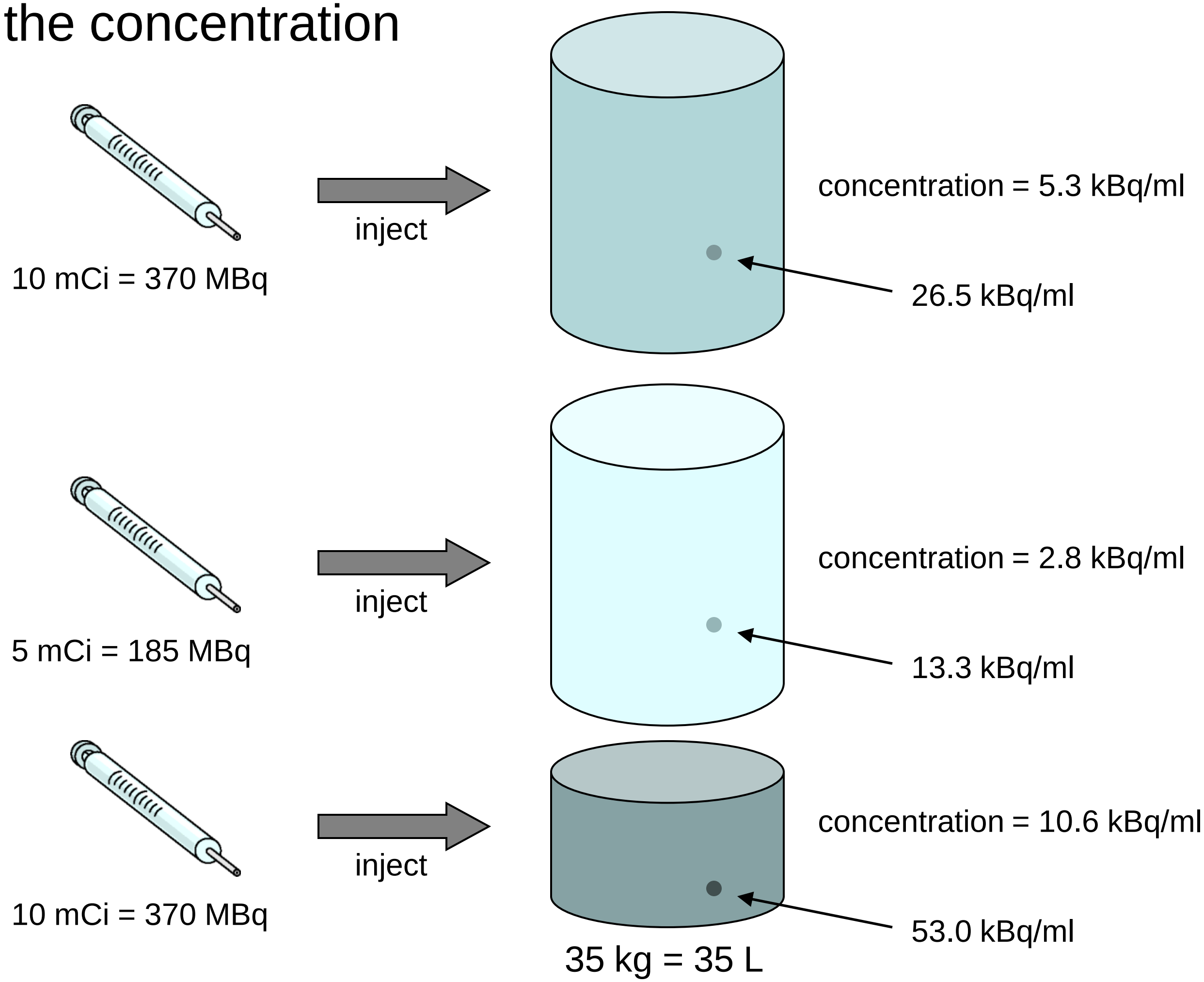
PET Scans Measure Activity Concentration

- If everything goes well, the role of the PET scanner is to measure the radioactivity per unit volume
- Typically measured as kBq/ml or μCi/ml



What if there are different activities or distribution volumes?

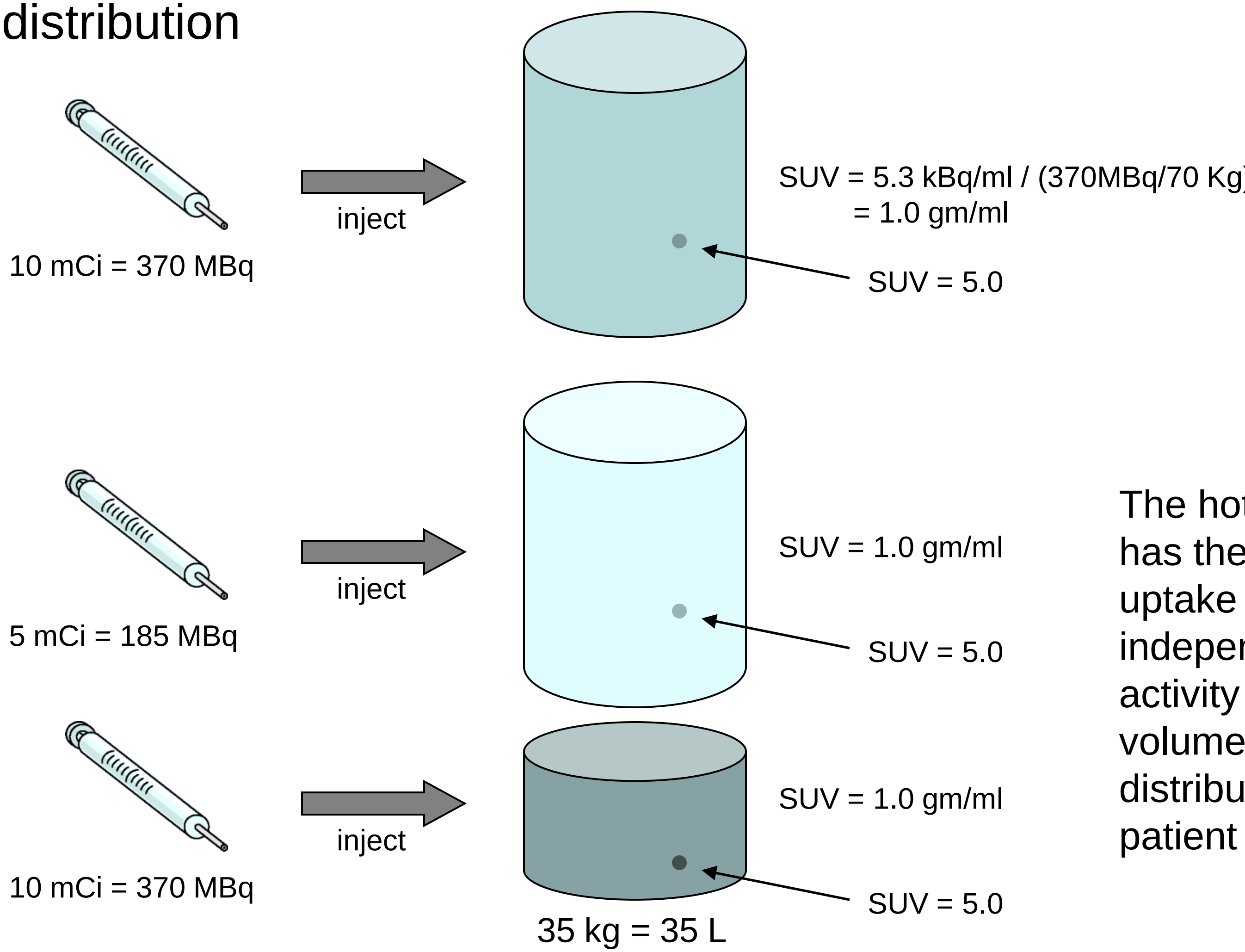
- Injecting different amounts <u>or</u> changing the volume will change the concentration



The hot spot has different uptake values in kBq/ml even though it has the same relative uptake compared to background

Standardized uptake values (SUVs)

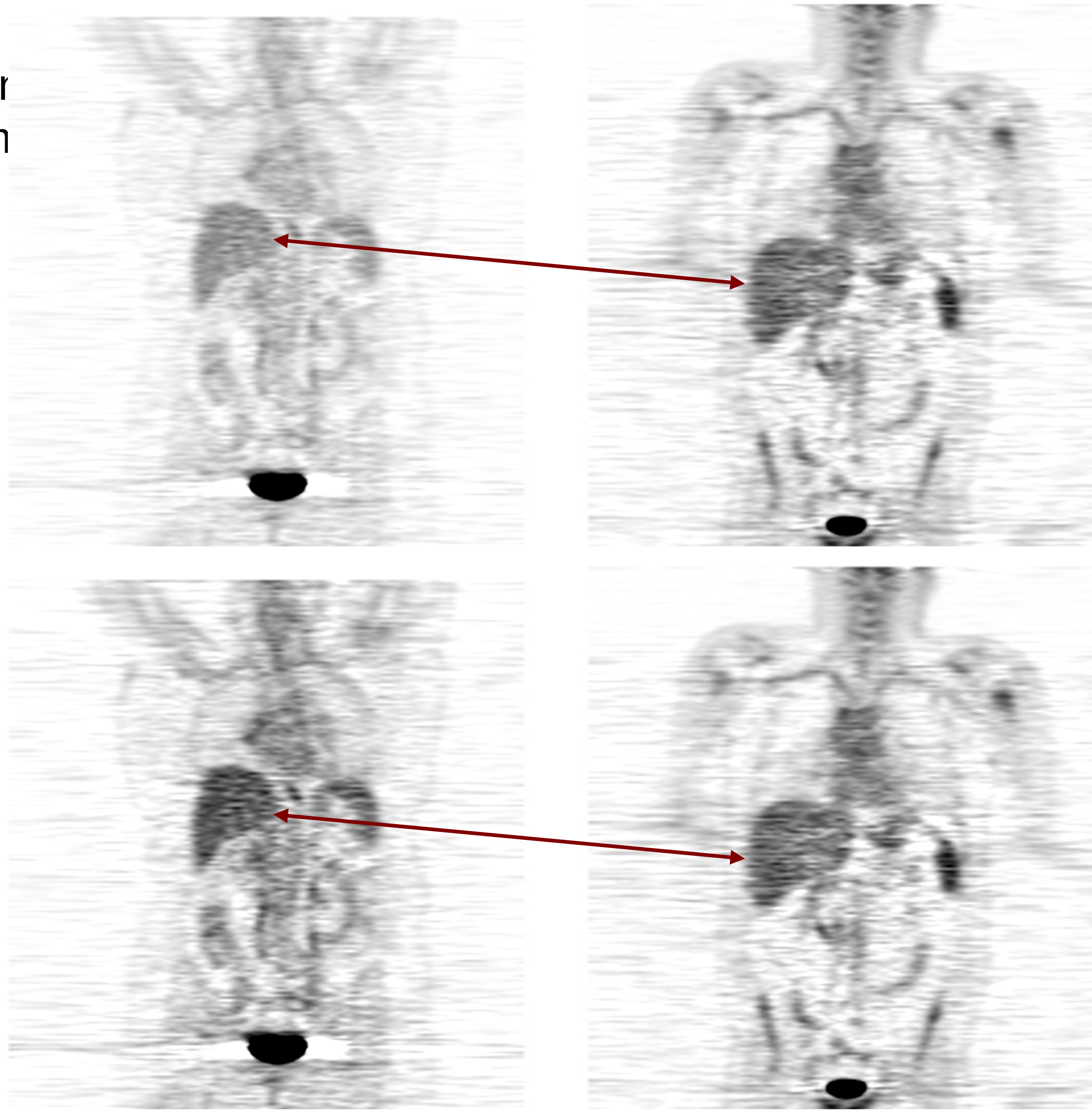
- Normalize by amounts injected per volume (i.e. weight) to get the same relative distribution with SUV = 1.0 for a uniform distribution



The hot spot now has the same SUV uptake values independent in activity injected or volume of distribution (i.e. patient size)

Measuring uptake: kBq/ml vs SUV

Same scale ir
units of kBq/n



Same scale
in units of
SUV [g/ml]

Liver values
look more
uniform
between
patients

Sources of Error in SUV Values

$$\mathrm{SUV} = \frac{\mathrm{PET}_{\mathrm{ROI}}}{D'_{\mathrm{INJ}} / V'}$$

PET = measured PET activity concentration
D′ = decay-corrected injected dose
V′ = surrogate for volume of distribution

It is important to minimize SUV errors for **serial** studies (excluding artifacts)

Some potential sources of error are:

- Determining that blood glucose levels are within range
- Changing dose uptake time
- Scanner calibration and cross calibration with dose calibrator
- Dose assay for each patient, which uses several pieces of information, all of which have to be correct:
- Correct clock settings for scanners, injection times, and assay times for correct calculations of radioactive decay and dose uptake periods
- Changing reconstruction or other processing protocols
- Changing analysis methods: How ROIs are determined and whether max or mean SUV values are reported
- Weight is typically used as a surrogate for volume of distribution, but can also be further normalized for lean body mass or body surface area, which have to be estimated

Biological Effects

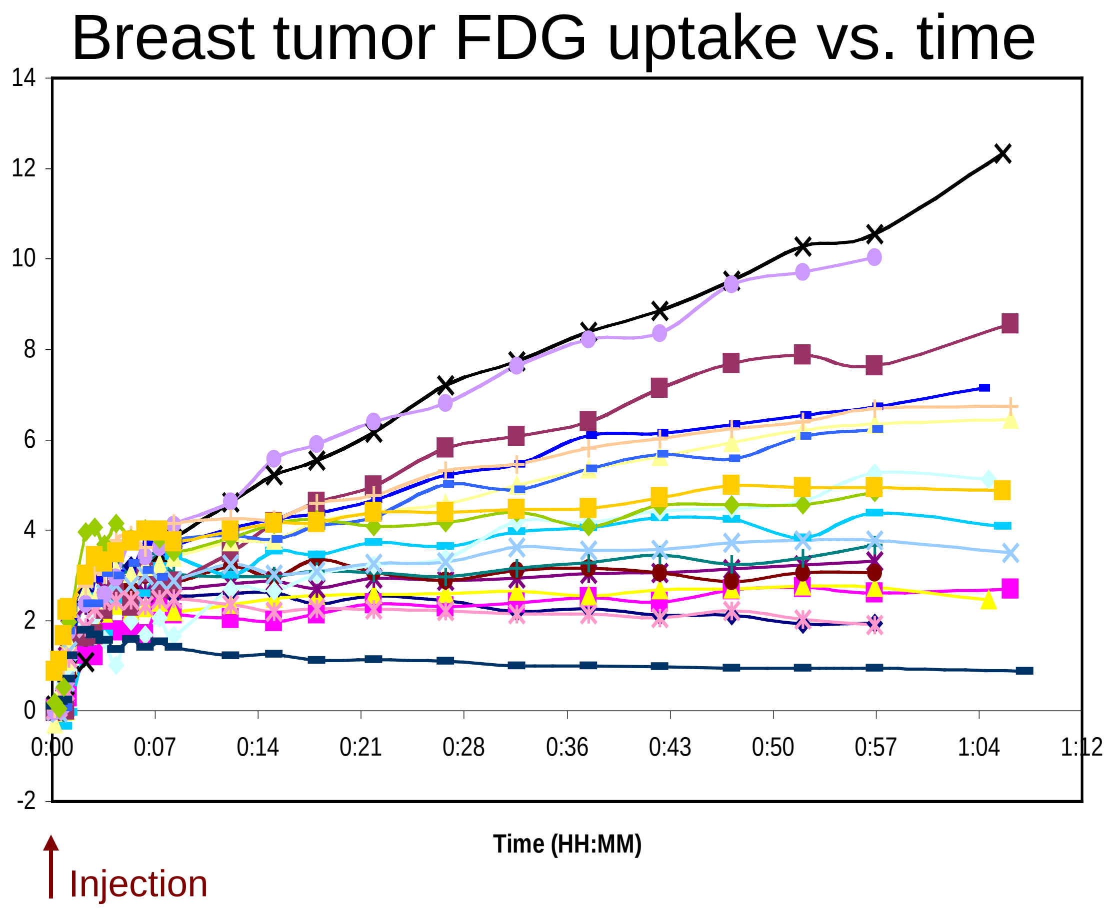
Effect of blood [Glu] on SUVs of liver mets from colorectal carcinoma

- 8 patients w/ 20 liver metastases by CT (size 10-75 mm, mean 32 mm)
- Fasting FDG-PET scan followed 2 days later by glucose-loaded scan (i.v. glucose infusion (4 mg/kg/min for 2 hr)

	Fasting scan	Glucose loaded
[Glu] (mg/100 ml)	92.4 ± 10.2	158 ± 13.8
SUV (all lesions)	**9.4 ± 5.7**	**4.3 ± 8.3**
known lesions seen	20/20	14/20

Crippa F. et al. Tumori, 1997

Illustration of impact of changes in dose uptake duration

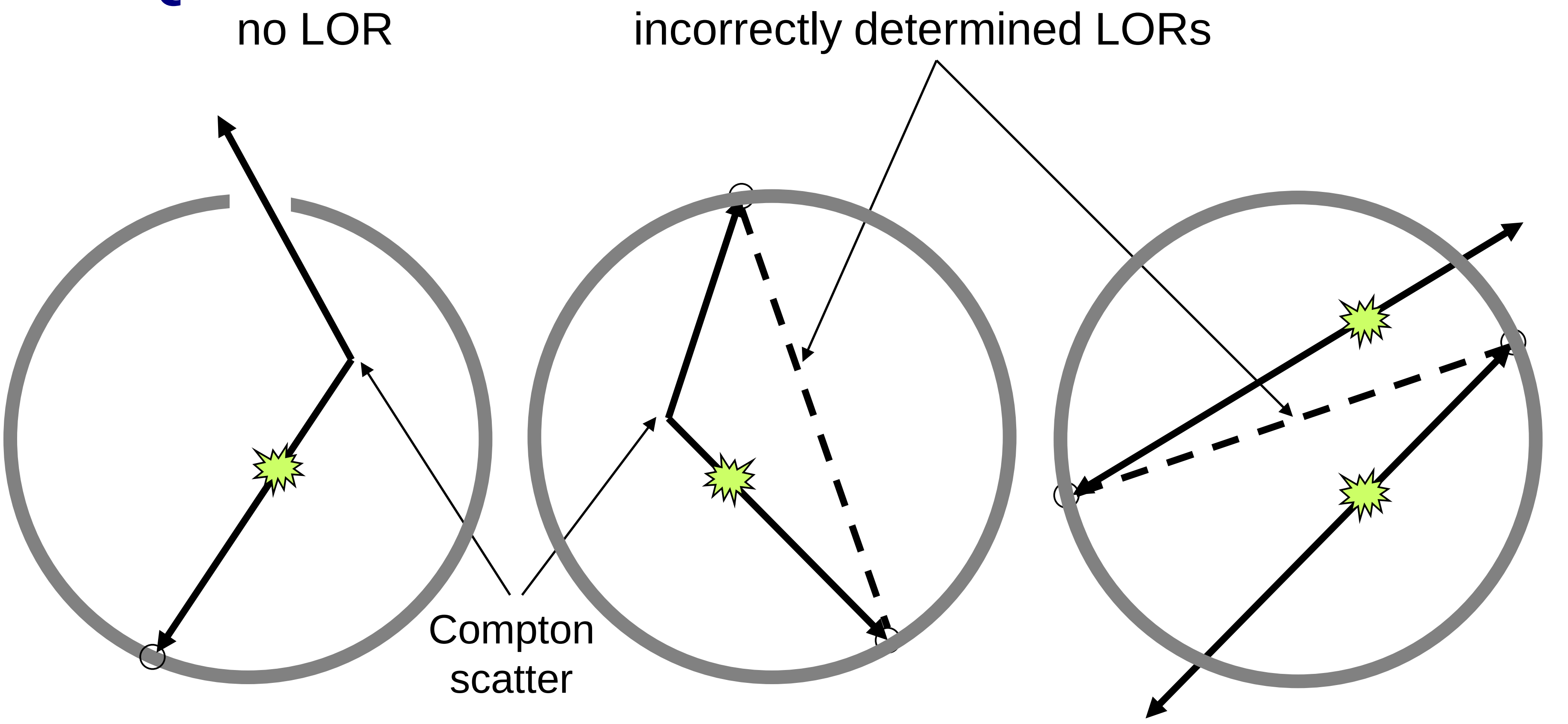


- The same study at different post-injection times will give different SUVs
- This problem is worse when two different studies are compared looking for an increase or decrease in SUVs between exams

Beaulieu JNM 2003

Quantitative Corrections

Quantitative errors in measurement

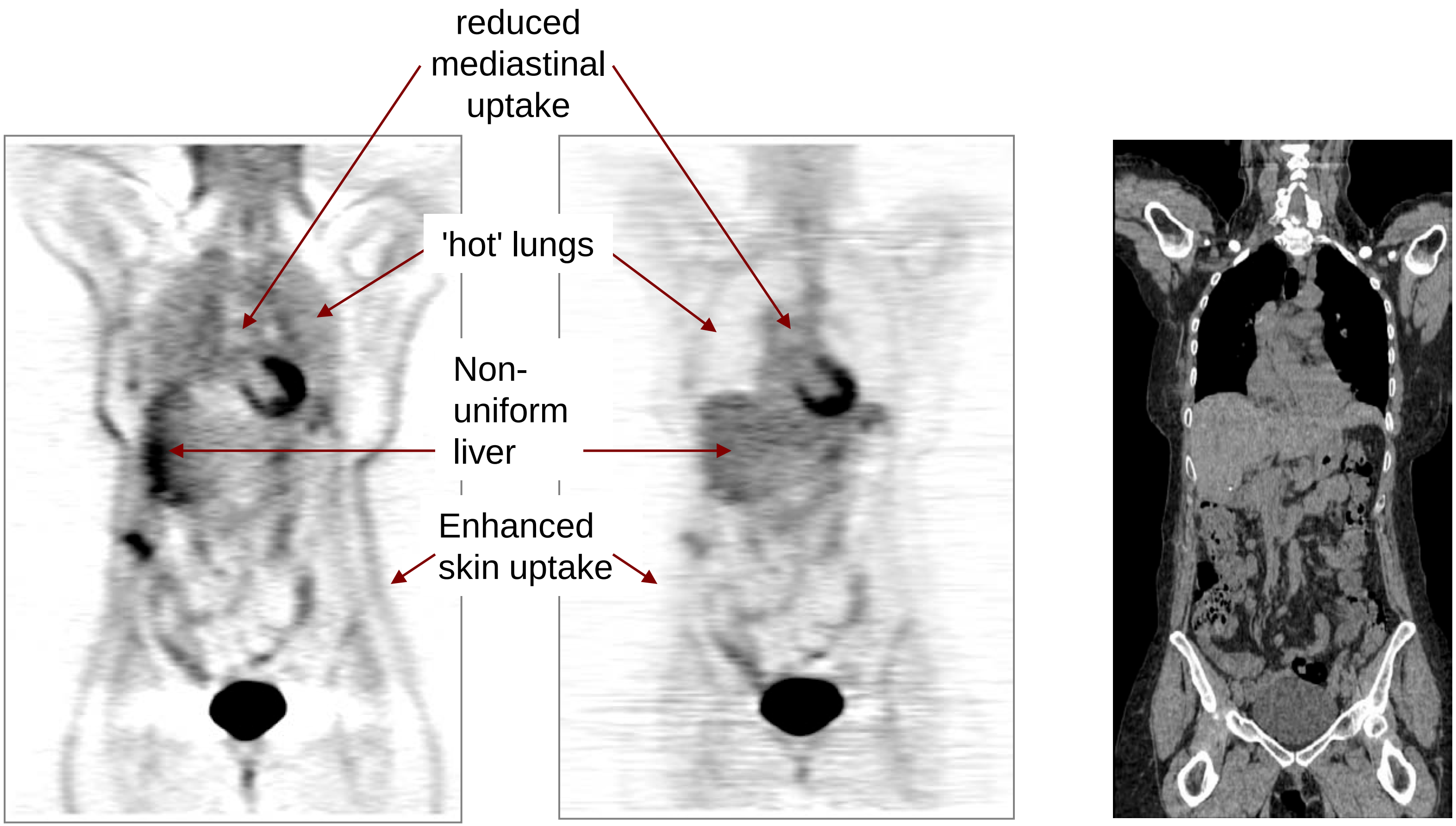


Lost (attenuated) event

Scattered coincidence event

Random coincidence event

Effects of Attenuation: Patient Study



PET: without attenuation correction

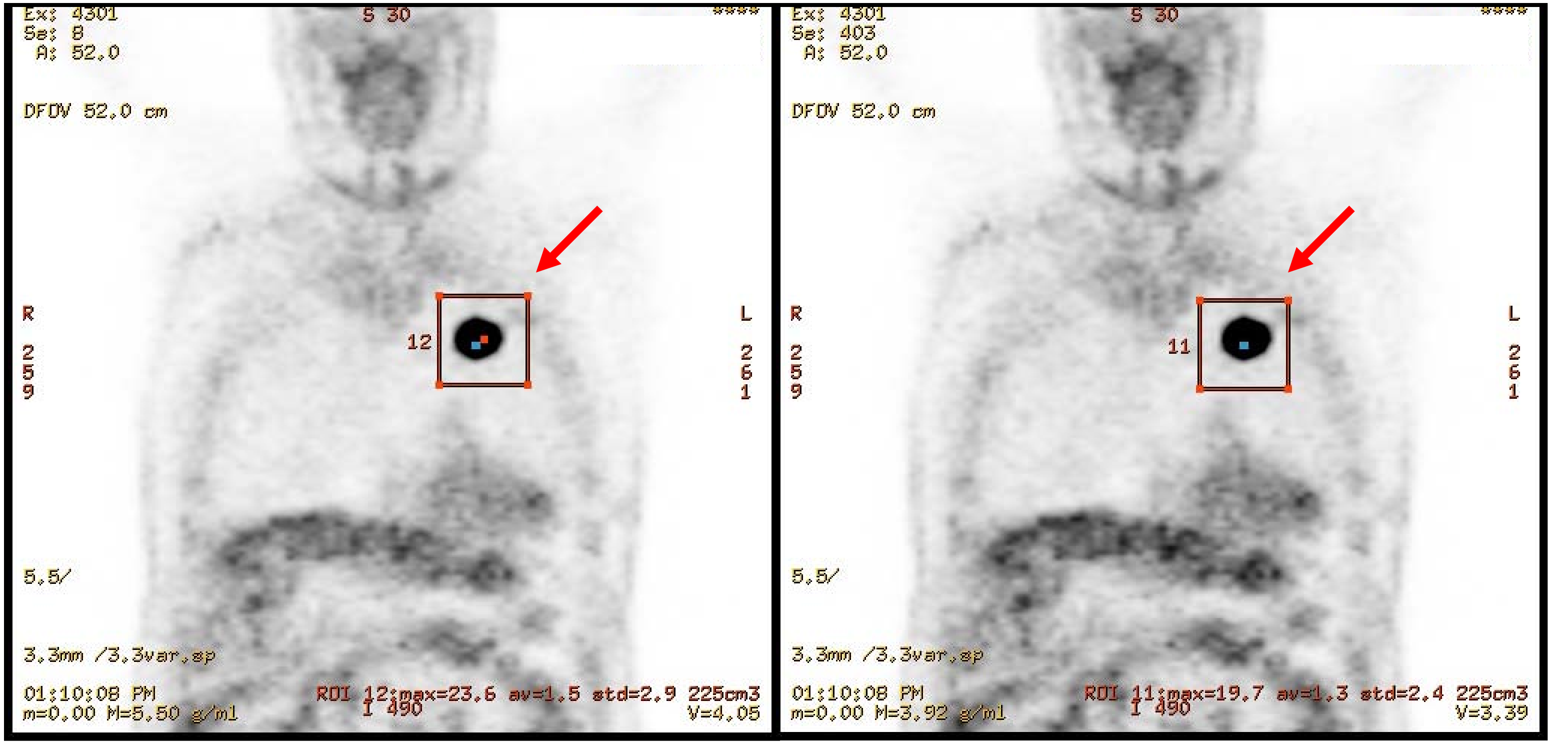
PET: with attenuation correction (accurate)

CT image (accurate)

Scanner Calibration

Effect of ACF calibration error

- Can not visually see ACF (scanner activity calibration factor) error

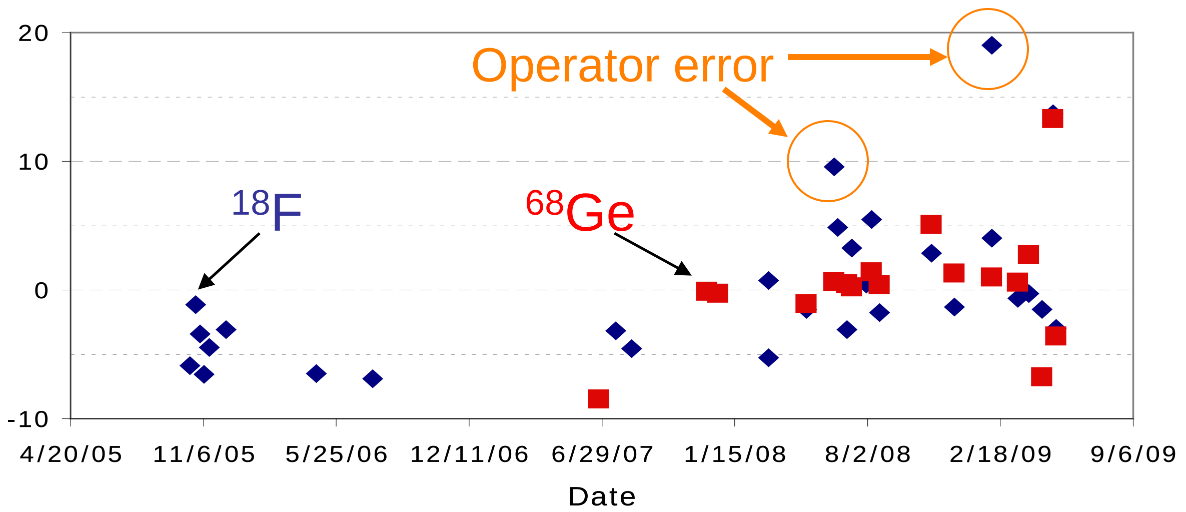


Incorrect ACF
Max SUV = 23.6

Corrected ACF
Max SUV = 19.7

Note: Both images scaled to max value

Activity Correction Factor Variation in Time



Scanner 1

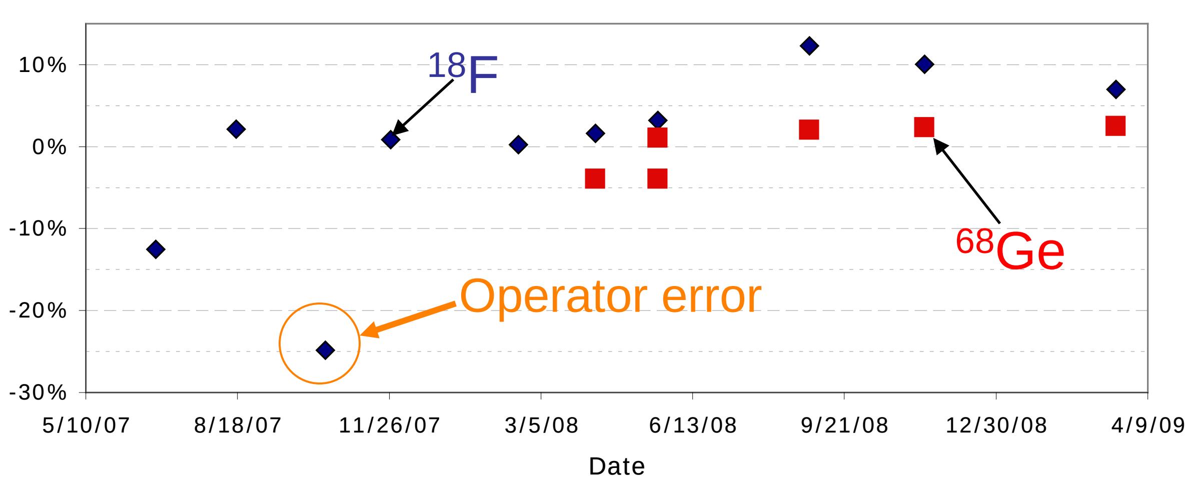
<u>Standard Deviation</u>

^{68}Ge= 3.2%

^{18}F = 6.1%

<u>Outliers Removed</u>

^{18}F = 4.1%



Scanner 2

<u>Standard Deviation</u>

^{68}Ge= 3.1%

^{18}F = 11.0%

<u>Outliers Removed</u>

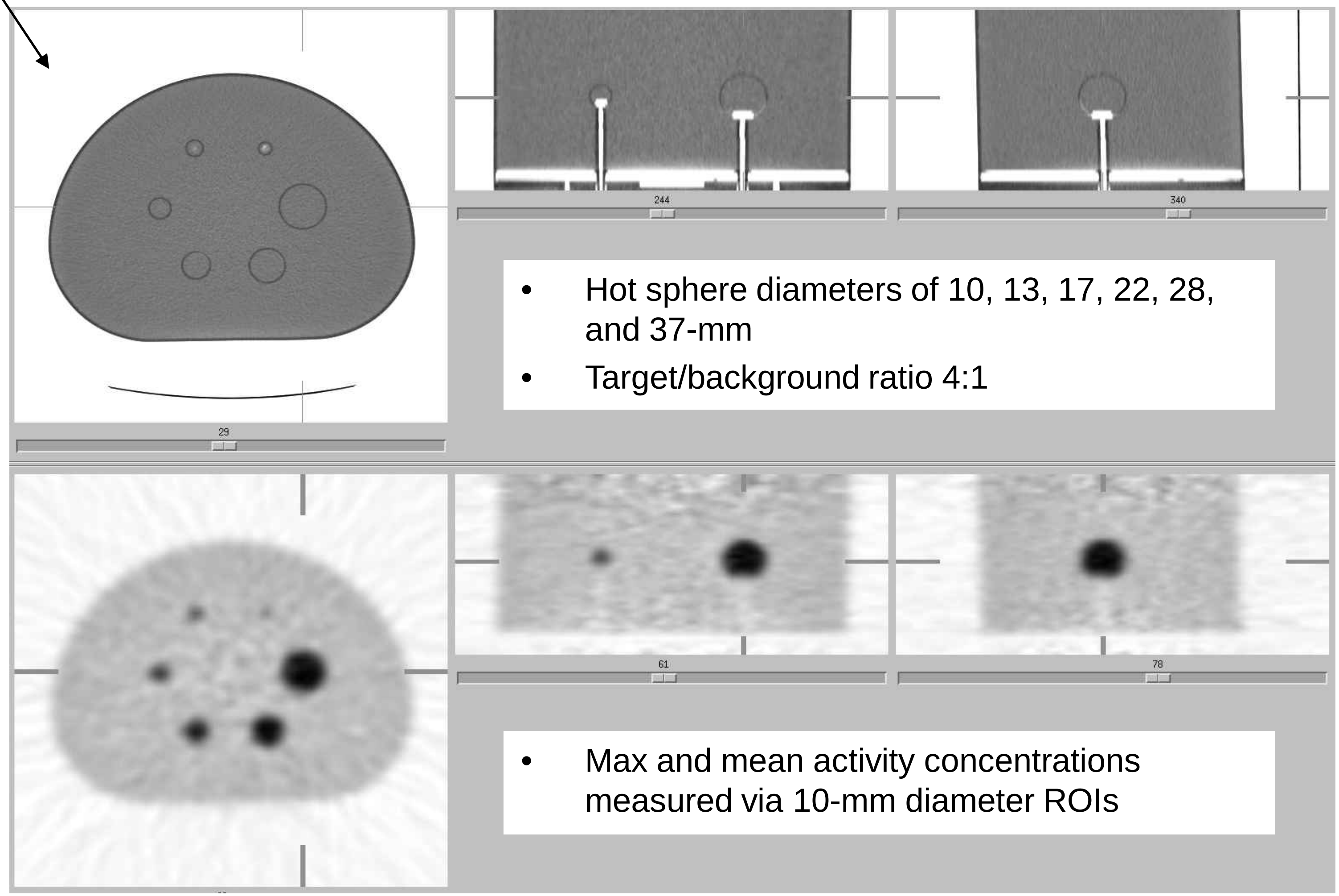
^{18}F = 7.0%

Lockhart SNM 2009

Resolution Effects

Size-Dependent Resolution Losses

similar to abdominal x-section



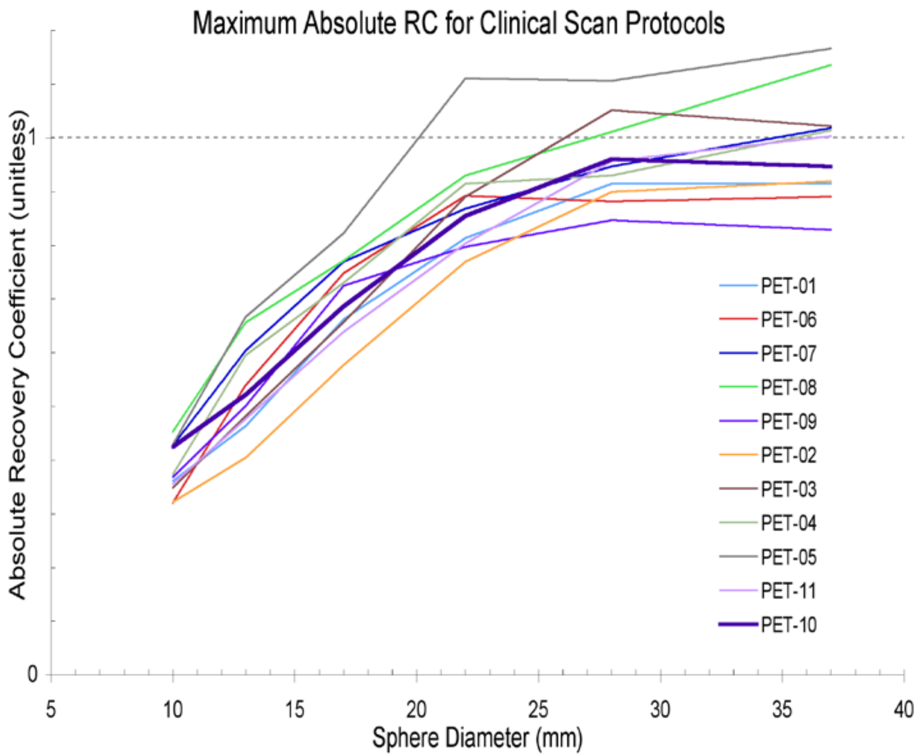
- Hot sphere diameters of 10, 13, 17, 22, 28, and 37-mm
- Target/background ratio 4:1

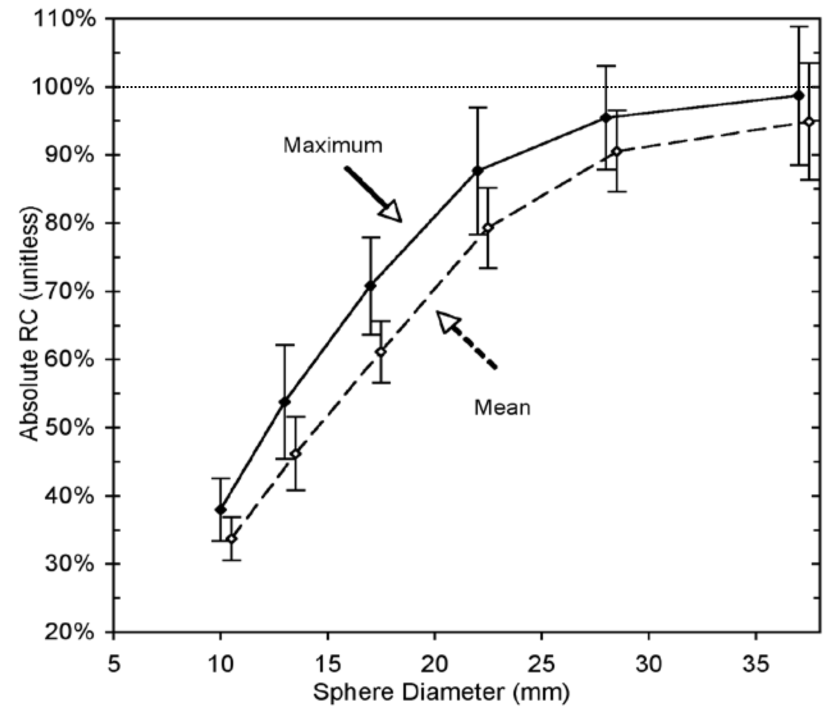
- Max and mean activity concentrations measured via 10-mm diameter ROIs

Modified NEMA NU-2 IQ Phantom

SNM Phantom: Key results of SUV measurements

Plots of recovery coefficient (RC) = measured in ROI/true





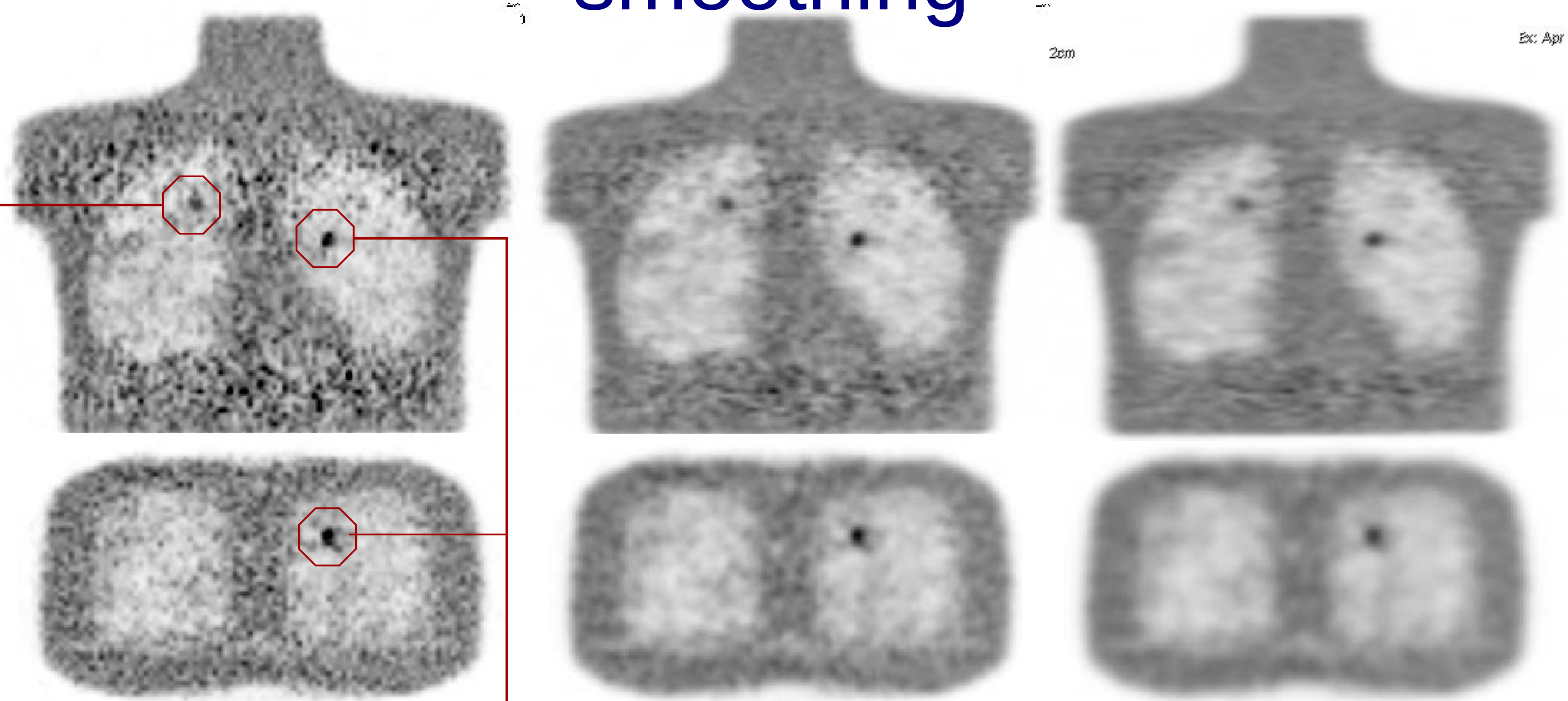
Variations are introduced by the scanner type, acquisition protocol, calibration differences, processing (e.g. image reconstruction method or smoothing) and ROI definition method.

averaged coefficients of variation

mean SUV: 8.6%, max SUV: 11.1%

Kinahan et al 2009 SNM

Effect of changing post-reconstruction smoothing



4 mm smoothing → 7 mm smoothing → 10 mm smoothing

SUVmax for 1 cm spheres

4 mm smoothing	7 mm smoothing	10 mm smoothing
3.4	2.1	1.6
3.7	3.2	2.9

SNM Chest phantom, 2 iterations, 28 subsets - True SUV (average) is 4.0

Artifacts

Regional Errors (Artifacts)

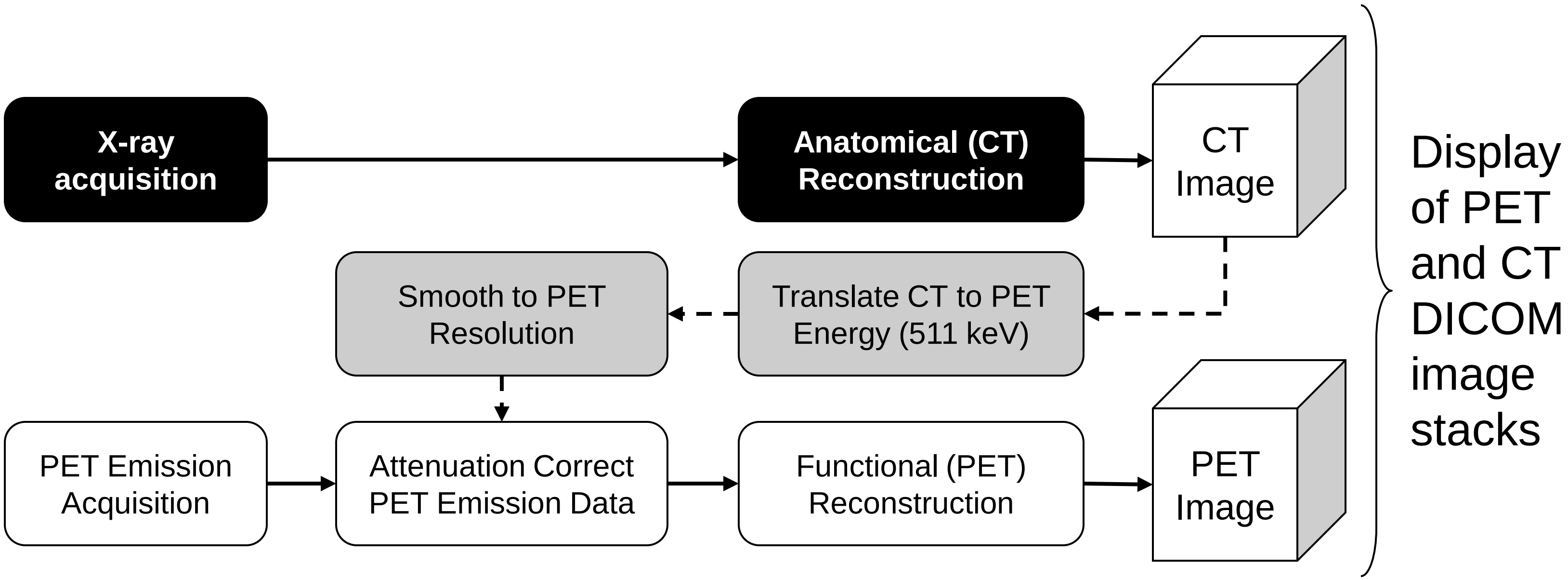
PET-based errors

- Calibration problems (localized)
- Detector failures
- Resolution and partial volume effects

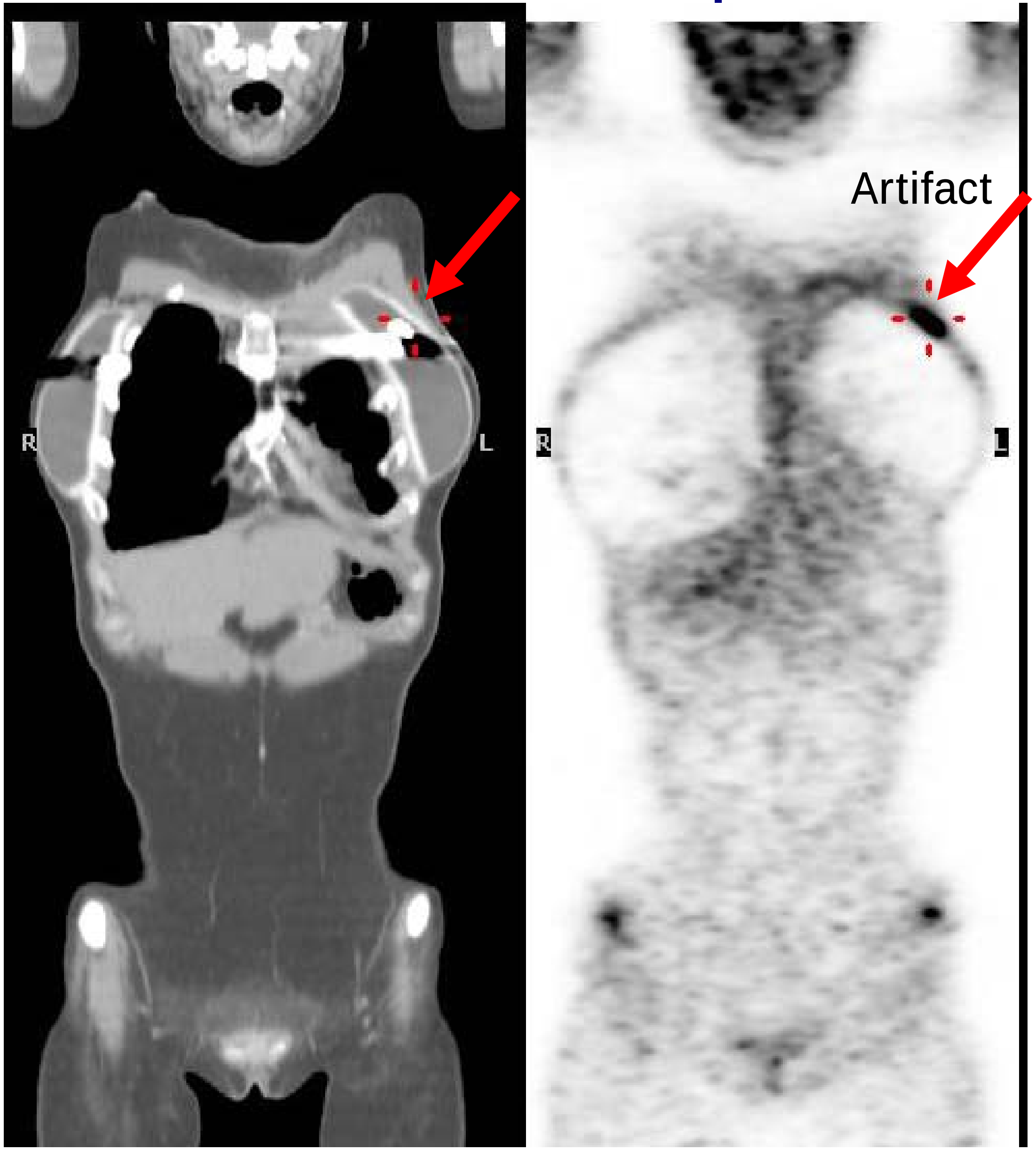
Errors from CT-based attenuation correction in PET/CT

- CT artifacts
- non-biological objects in patients
- patient motion
- truncation

Data flow for CT based attenuation correction



Metal Clip



CT

PET with CTAC

Courtesy O Mawlawi
MDACC

Patient and/or bed shifting

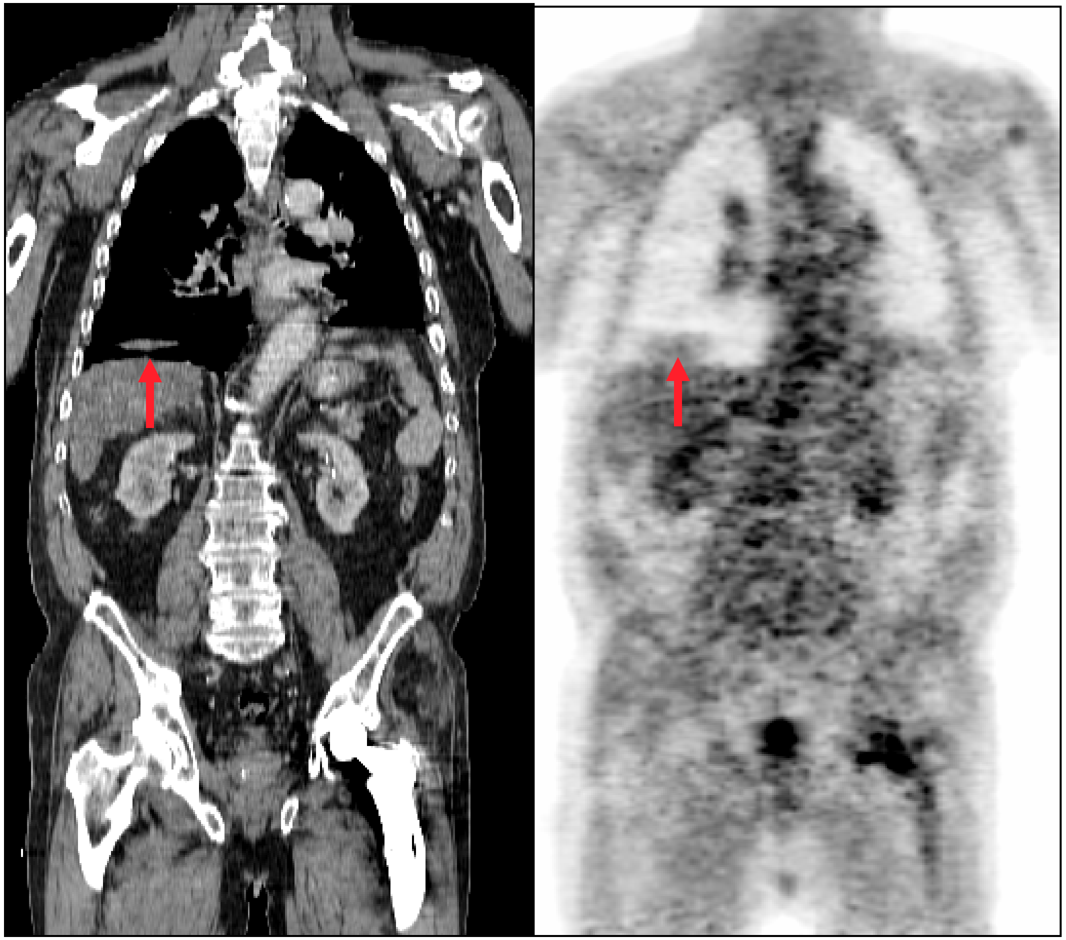
- Large change in attenuation at lung boundaries, so very susceptible to errors

PET image without attenuation correction

PET image with CT-based attenuation correction (used for measuring SUVs)

PET image fused with CT

Breathing Artifacts: Propagation of CT breathing artifacts via CT-based attenuation correction



Attenuation artifacts can dominate true tracer uptake values

Summary of Factors that Influence PET/CT Accuracy and Precision

- Biological effects: both true uptake (what we want) and biological noise
- Patient preparation: fasting, glucose levels, uptake period
- Quantitative corrections: Attenuation, scatter, randoms, detector efficiency normalization
- Resolution loss: aka partial volume errors
- Reconstruction method (smoothing and iterations)
- Analysis method: ROI definition method and SUV mean vs max
- Artifacts
  - patient motion: respiratory and other
  - incorrect SUV scaling
  - Attenuation correction with CT: truncation, motion, incorrect scaling, general CT artifacts
- Care should be used if serial studies rely only on lesion SUV values, e.g. monitoring progression of disease

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