Quantitative imaging for clinical dosimetry

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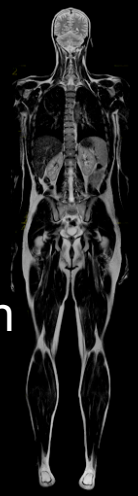
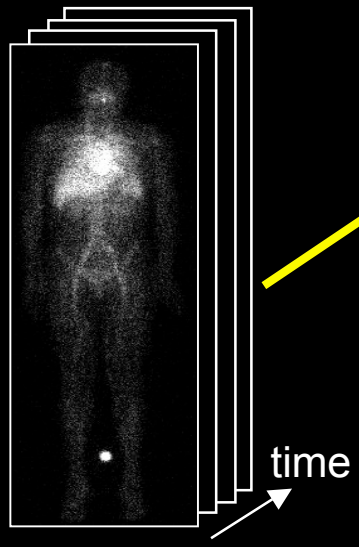
Methodology for patient-specific 3D imaging-based internal dosimetry

anatomy

- Density and composition of each voxel
- ROIs





radioactivity over time

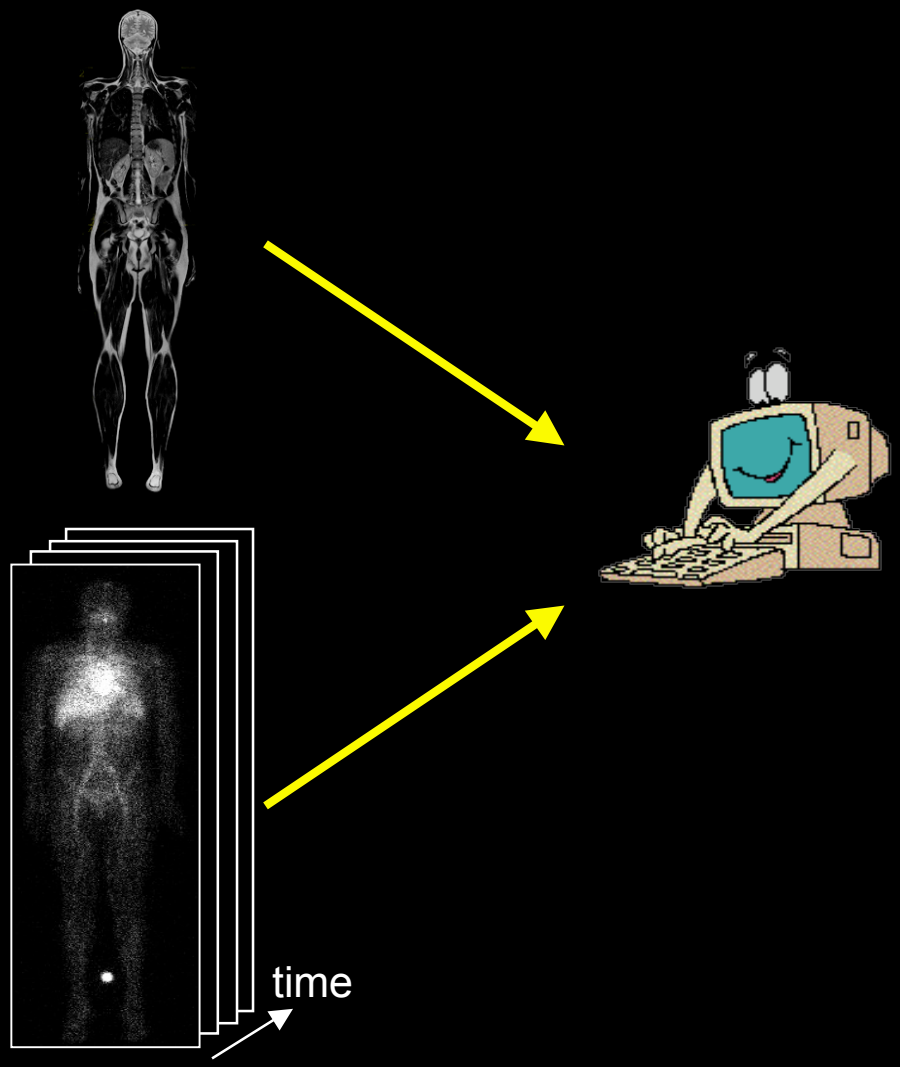
- Cumulated activity per voxel

absorbed dose calculation

spatial distribution of absorbed dose

- Dose-volume histograms
- Mean and range of absorbed dose in regions

Assumptions underlying the methodology (imaging part only) ?



1. CT can be accurately registered with the ET scan

2. Longitudinal ET scans can be accurately registered one with another

3. HU are good enough to determine density and composition

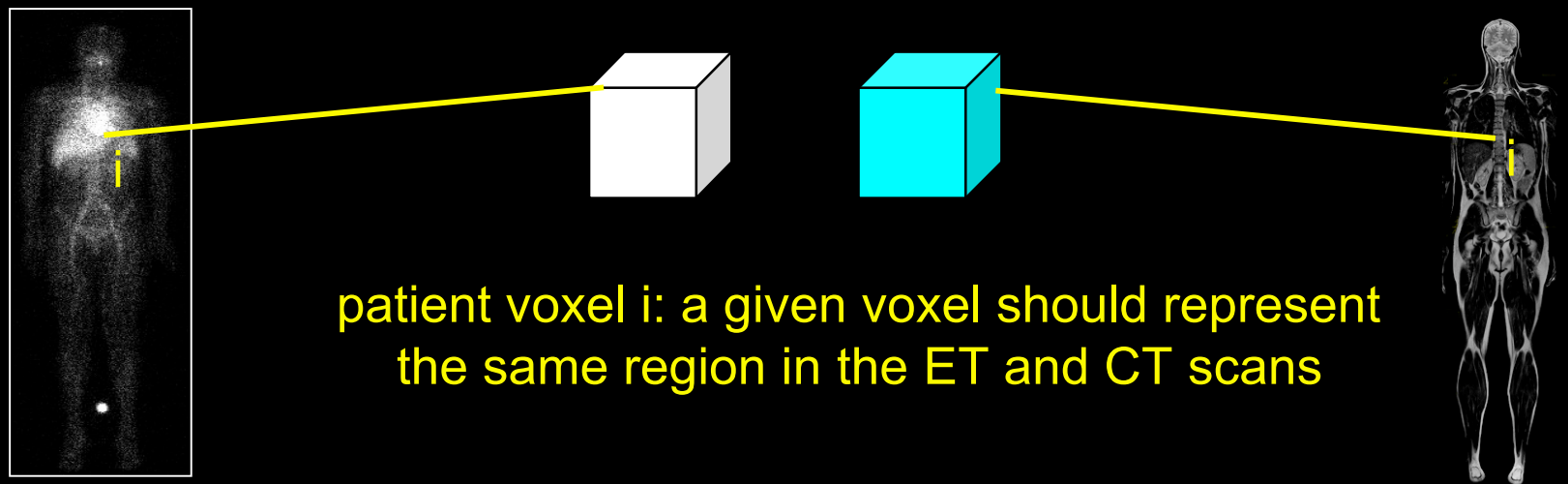
4. Unbiased activity can be estimated at the voxel level from the ET scans

5. Longitudinal sampling is sufficient to properly estimate the change in activity over time hence the cumulated activity

6. Organ region can be accurately drawn from the CT

7. Dose calculation at the voxel/organ level is sufficient

1. Accurate ET / CT registration



patient voxel i: a given voxel should represent the same region in the ET and CT scans

ET : activity

CT : density

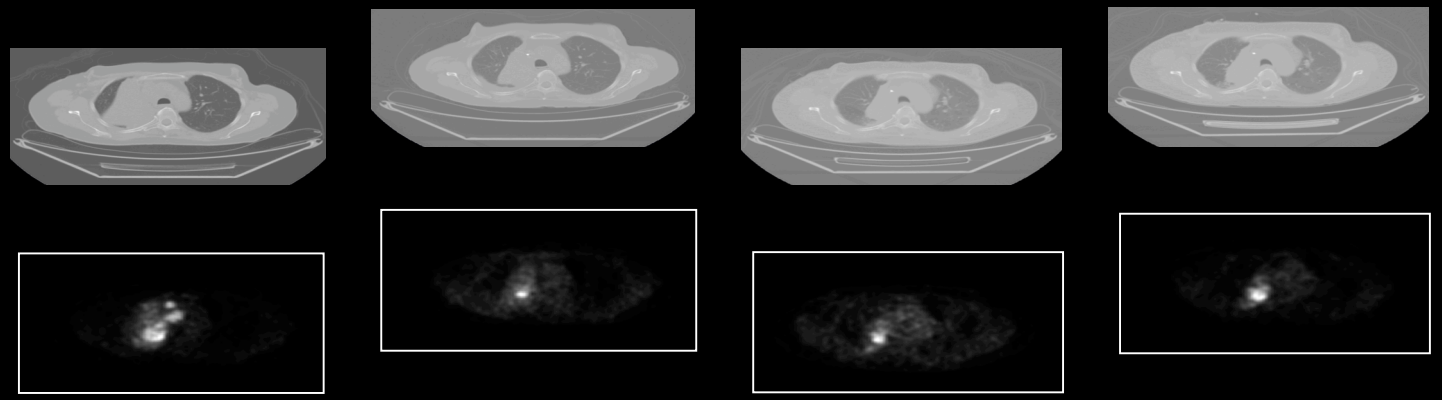
- For accurate CT-based attenuation correction
- Accurate assignement of tissue density and composition in the dose calculations

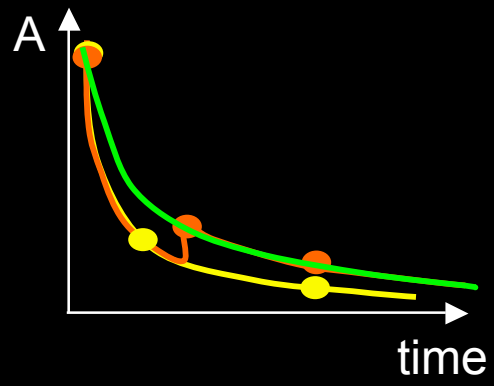
- Hybrid systems SPECT/CT and PET/CT help a lot
- Still, remaining mis-registration due to respiratory and cardiac motion:
  - In cardiac SPECT/CT, frequency of misregistration :
    None : 7%, minimal : 16%, mild : 35%, moderate : 38%, severe : 4%
  - In PET/CT : misregistration of 3.3 mm ± 1.0 mm
- WB scan registration is a real challenge

Goetze et al, J Nucl Cardiol 2007, Banos-Capilla, Med Phys 2007

2. Longitudinal ET scans accurately registered

- How accurately can successive CT be registered? (hence successive SPECT or PET)





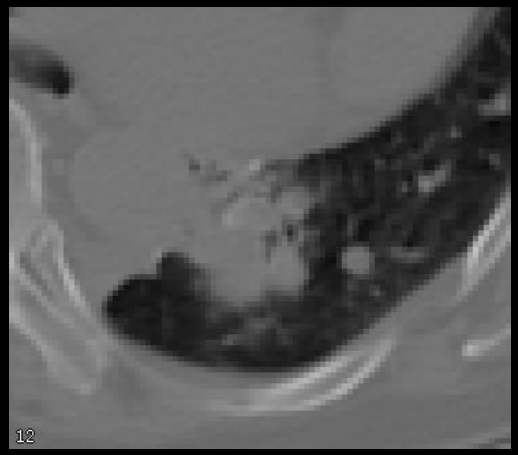
- Lack of data, eg:
  - Head and neck : 0.3 - 3.8 mm accuracy (Daisne et al, Radiother Oncology 2003)

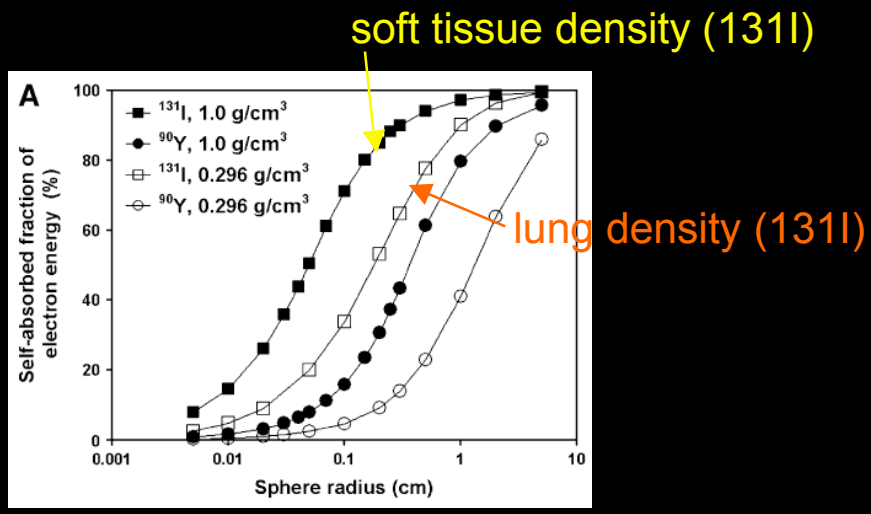
- Optimistic version : within a voxel (4 mm)
- Probably poorer for WB scans

Worth further investigations

3. HU appropriate to derive density and composition

- Density has an impact on energy deposition by electrons





The fraction of energy absorbed in a 2 cm diameter tumor decreased from 80% to 41% for 90Y for when tumor density was that of lungs compared to that of soft tissues.

Song et al J Nucl Med 2007

4. Accurate activity estimates in regions (optimistic results*)

- Scatter, attenuation, collimator (or detector) response can all be compensated rather accurately with up-to-date software, to achieve absolute quantitation based on careful calibration

- Simulation of the Zubal phantom ^{131}I (optimal ROIs):
  - mean error of -2.1% in the liver
  - mean error of -10.3% in a 59 mL sphere
  - mean error of -7.9% in a 16 mL sphere
  - mean error of -38.4% in a 7 mL sphere

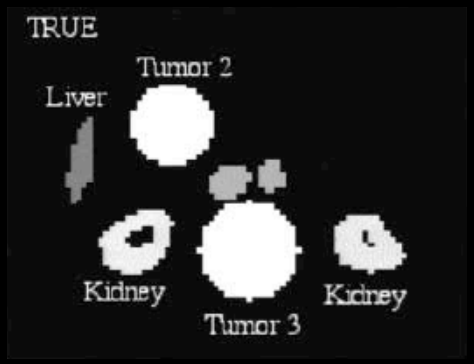
- RSD (real) phantom ^{111}In (realistic ROIs):
  - mean error of 4.1% in the liver
  - mean error of 2% in a 20.6 mL sphere
  - mean error of -12% in a 5.6 mL sphere

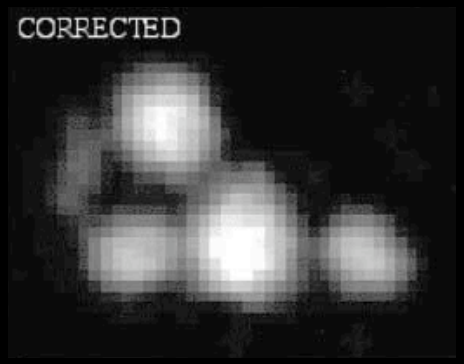
*Not all the sources of errors were included (ET/CT misregistration, ET/ET misregistration, ROI drawing, TAC fit, WB configuration)

Dewaraja et al, J Nucl Med 2005, He et al, Phys Med Biol 2005

4. Accurate activity estimate in each voxel: the big killers

- Partial volume effect :

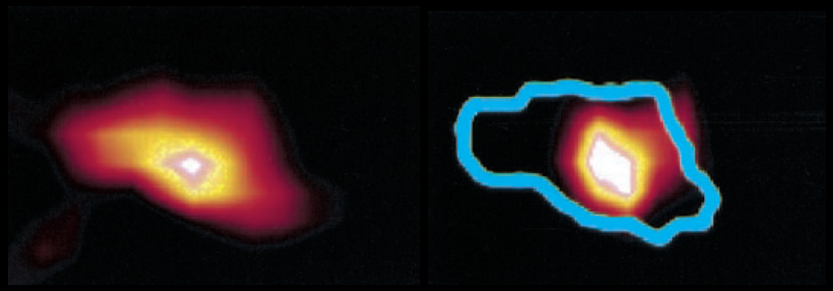




Activity underestimation up to 50% or more without PV correction

Most PV corrections are regional (unlike voxelwise), but some voxelwise corrections do exist.

- Internal motion (cardiac and respiratory) :



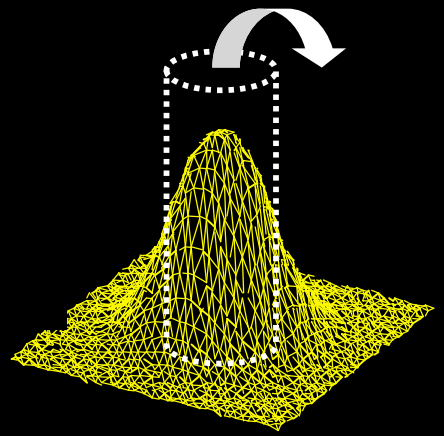
SUV	Sphere volume (mL)	% Activity concentration underestimation with the following motion phantom: Average
Mean	19.4	23.5
	11.5	24.2
	5.5	33.6
	2.0	33.1
	1.2	40.0

Dewaraja et al Comput Methods Programs Biomed 2002, Soret et al J Nucl Med 2007, Nehmeh et al J Nucl Med 2002, Boucher et al J Nucl Med 2004

4. Error propagation from activity estimates to dose estimates

- 131I, Zubal phantom simulations*:
  - mean error of -2.1% in the liver ➡ 0% in absorbed dose
  - mean error of -10.3% in a 59 mL sphere ➡ -6% in absorbed dose
  - mean error of -7.9% in a 16 mL sphere ➡ -5% in absorbed dose
  - mean error of -38.4% in a 7 mL sphere ➡ -31% in absorbed dose

Trend : underestimation of activity ➡ dose accuracy better than activity accuracy
Overestimation of activity ➡ dose accuracy poorer than activity accuracy

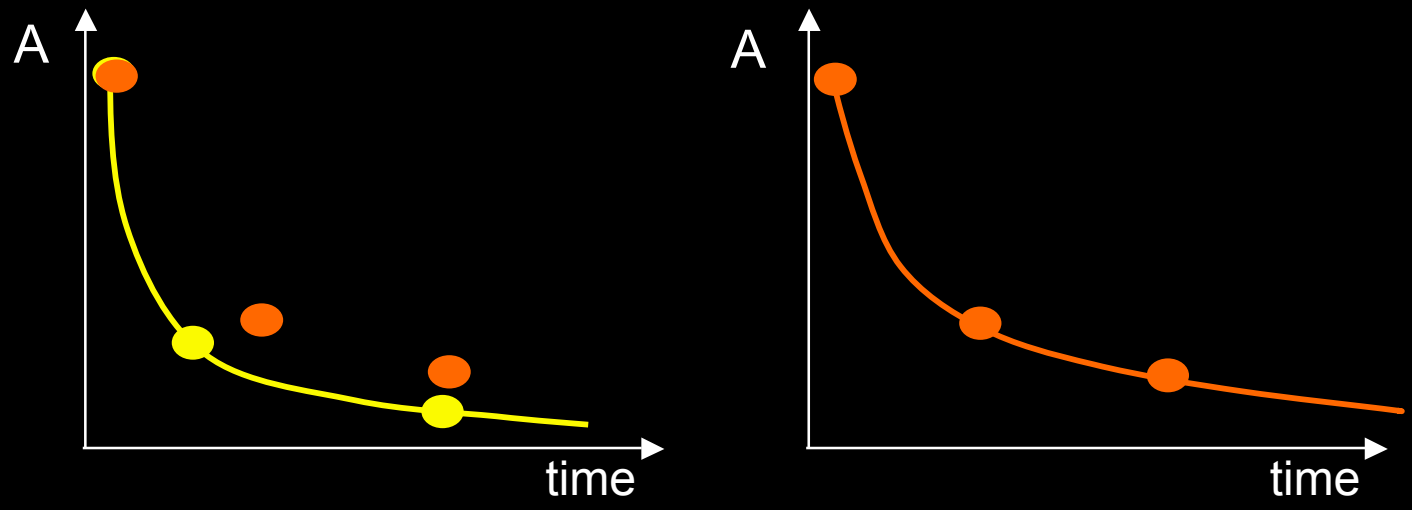


*Not all the sources of errors were included

Dewaraja et al J Nucl Med 2005

5. Longitudinal sampling appropriate to properly fit the clearance function

- Only few points (typically 3 to 5) : only a one-parameter model is reasonable (uptake is often neglected)



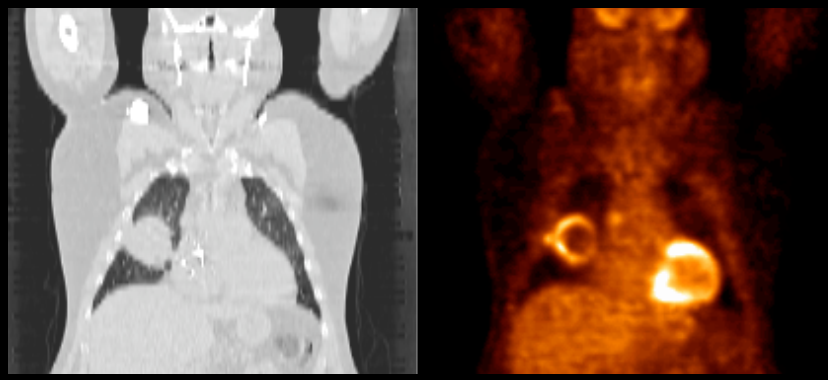
Integral of the monoexponential fit (ie linear fit) is rather robust with respect to moderate biases/noise in each individual point

- If monoexponential decrease is appropriate, additional points would help, even if systematically biased
- If the uncertainty affecting each point is known, the uncertainty affecting the dose estimate can be derived

Flux et al, Phys Med Biol 2002

6. Organ ROI can be accurately defined from the CT

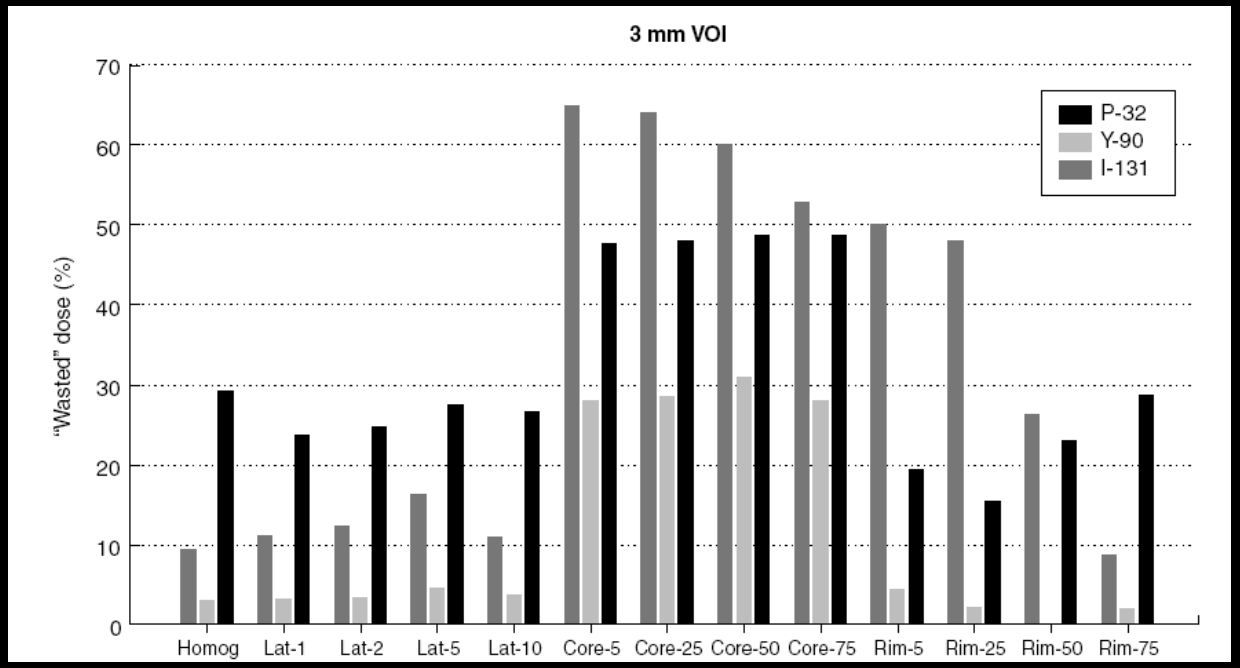
- In111, RSD phantom, errors in volume estimates:
  mean error of 1.7% in the lung
  mean error of 2.8% in the liver
  mean error of 12.2% in a 20.6 mL sphere
  mean error of 36.8% in a 5.6 mL sphere
- In111, LiquiPhil phantom, errors in volume estimates:
  error of 0.2% in the liver
  error of 2.3% in the spleen
  error of 0.1% in a 33.5 mL sphere
  error of 1.7% in a 16.7 mL sphere



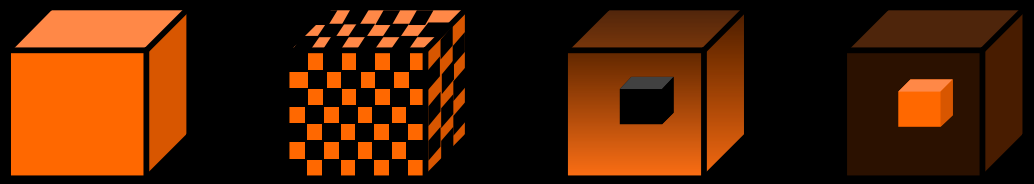
He et al Phys Med Biol 2005, Assie et al submitted

7. Dose estimates at the organ / voxel level are sufficient

% diff between effective uniform dose and biologically effective dose



Various types of heterogeneity within a voxel



The spatial resolution of the dose estimate cannot exceed that of the imaging system

Calogianni et al Cancer Biother Radiopharm 2007

Discussion

- Many improvements have been made in the imaging part of imaging-based dosimetry:
  - ET/CT imaging systems
  - activity quantitation accurate within 10% in large static organs

- Some effects are still often overlooked:
  - Partial volume effect and internal motion in ET : large biases (20 to 50%) in small structures (bone marrow) and voxel activity estimates
  - Impact of ET/ET misregistration when fitting the TAC : 3-4 mm offset
  - Impact of ET/CT misregistration in dose calculation : 3-4 mm offset
  - Reliability of TAC fit on a voxel-by-voxel basis ?
  - Activity accuracy at the voxel level ?
  - Activity accuracy over WB scans ?

- Error characterization through quality control and estimates of error propagation throughout the dose calculation scheme are absolutely needed to assess the error affecting the final dose measurement and the reproducibilty, hence assign some confidence to dose estimates before correlating them with outcome

Conclusion

• Accuracy of dose cartography is limited by the spatial resolution of the imaging systems

in human: ~7-8 mm in SPECT, ~5 mm in PET at best

in small animal: ~800 μm-1 mm in SPECT, ~1-2 mm in PET at best

and the voxel size is smaller than the spatial resolution…

• Likely to be insufficient for detailed analysis of the therapy effectiveness, as the microscopic heterogeneity of dose distribution plays a significant role

• Hopefully sufficient for a number of applications

• Models about dose heterogeneity within a voxel might help enhance the potential of imaging-based clinical dosimetry

Slides available on http://www.guillemet.org/irene