# Quantitative imaging for targeted radionuclide therapy

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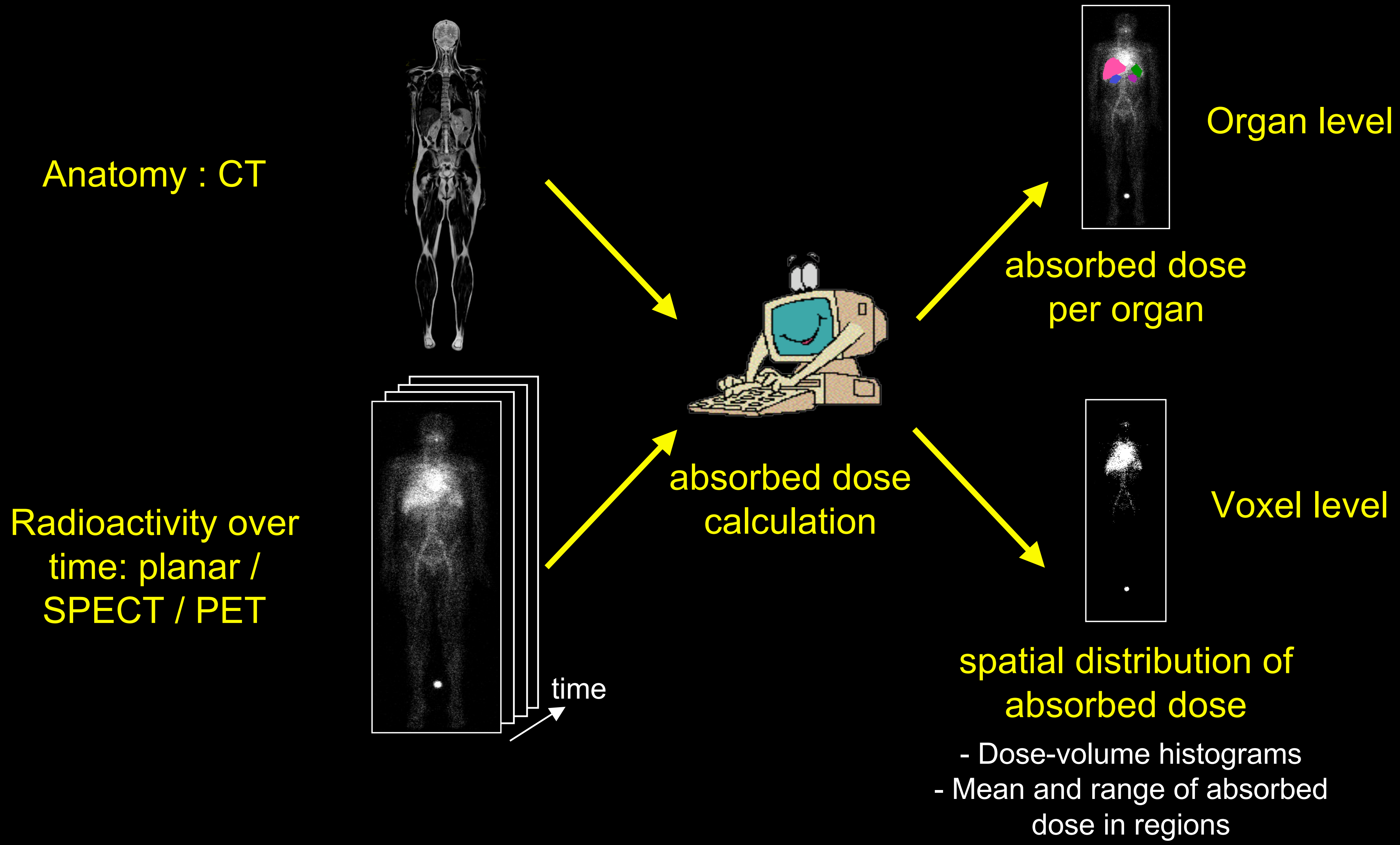
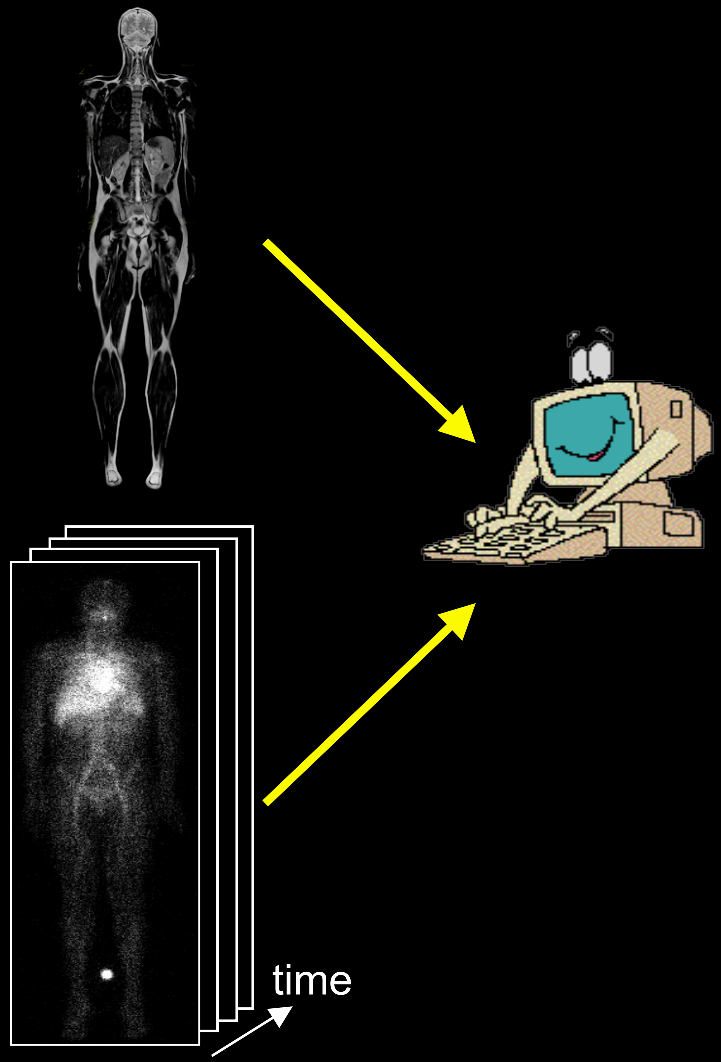
# Patient-specific imaging for internal dosimetry in TRT



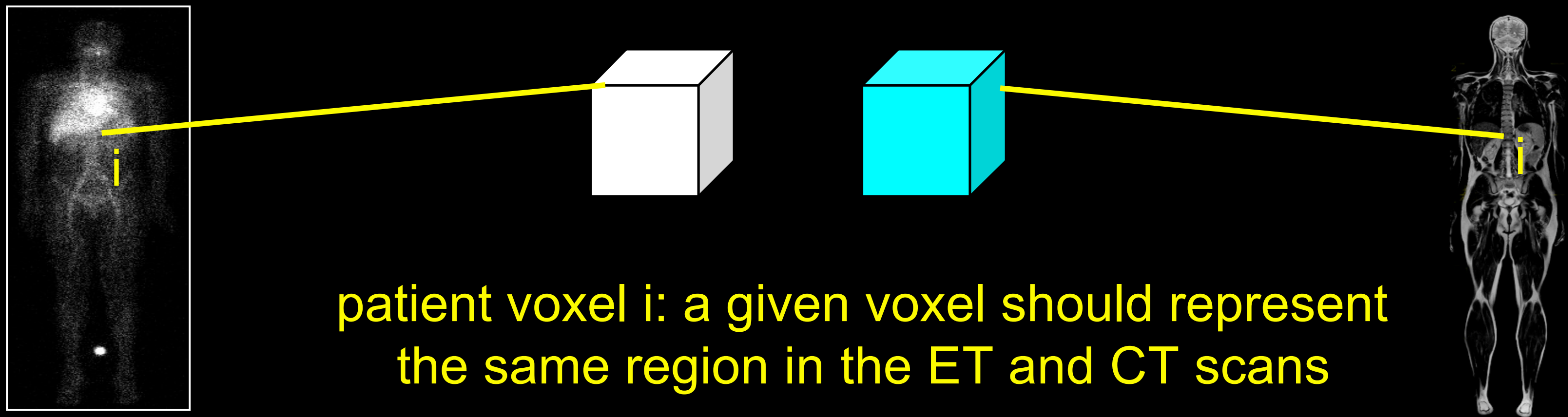
# Making the best of the imaging data for TRT




CT
- attenuation correction of ET or planar data
- estimation of tissue density and composition
- organ delineation

Planar / SPECT / PET
- activity concentration in each organ / voxel
- cumulated activity over time

# CT for accurate attenuation correction of the emission data



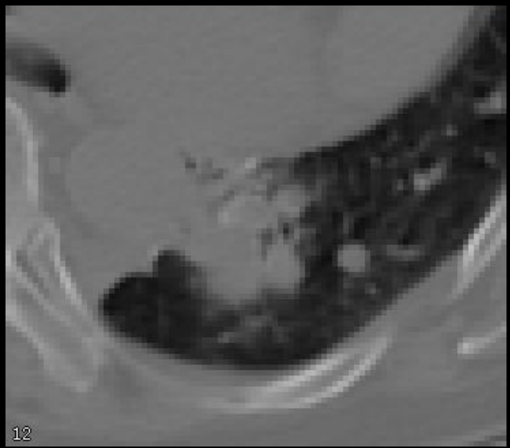

- Condition: proper alignement of the CT scan with the scintigraphic data
  - Hybrid SPECT/CT or PET/CT systems help a lot
  - ~ 1 voxel accuracy is achievable *
  - more challenging for WB scans

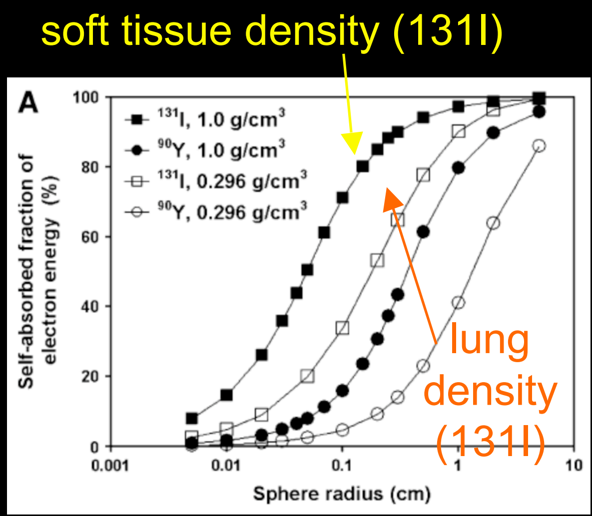
- PET and SPECT data can be accurated corrected for attenuation using vendors' software when CT is available
- Even in planar imaging, use of CT makes attenuation correction significantly more reliable than geometric mean of conjugate views #

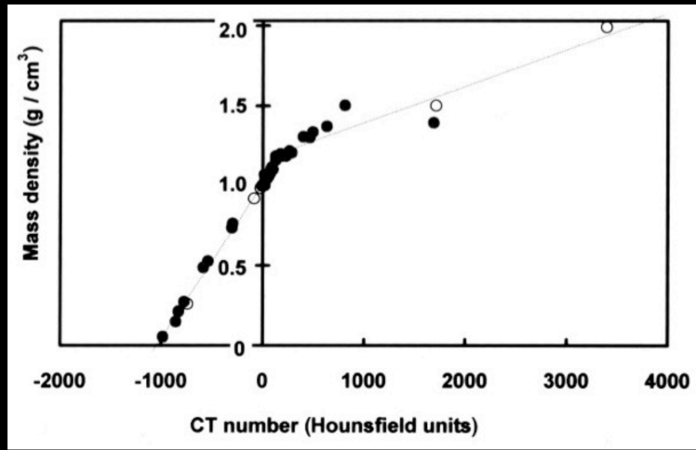
** eg, Goetze et al J Nucl Cardiol 2007, Banos-Capilla Med Phys 2007, # He et al Phys Med Biol 2006*

# CT for deriving density and composition

- Density has an impact on energy deposition by electrons



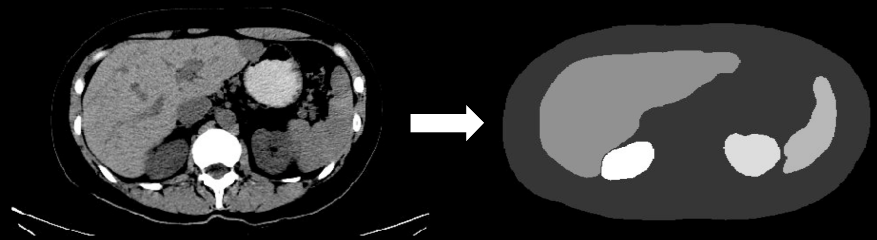

Estimates of tumor and organ density can (should) be obtained from the CT

Accurate CT/ET registration needed for dosimetry at the voxel level

*Knoos et al Radiother Oncol 1986, Sjögreen et al J Nucl Med 2002, Song et al J Nucl Med 2007*

# CT for defining organ VOI

- To assign a density to the organ / tumor
- To derive the organ / tumor mass
- To estimate dose at the organ level



- RSD phantom, mean errors in volume estimates:
  - 1.7% in the lung
  - 2.8% in the liver
  - 12.2% in a 20.6 mL sphere
  - 36.8% in a 5.6 mL sphere
- LiquiPhil phantom, errors in volume estimates:
  - -0.1% in the liver
  - 2.4% in the spleen
  - 1.4% in a 33.5 mL sphere
  - 5.8% in a 4.2 mL sphere

VOI can be accurately defined using the CT, except in small tumors
(~< 2 mL in PET, < 8 mL in SPECT)

*He et al Phys Med Biol 2005, Assie et al Cancer Biother Radiopharm 2008*

# ET for accurate activity estimate in each organ / voxel

- Feasible at the organ level with attenuation, scatter and detector response corrections (all available from vendors) and careful calibration
- Examples of mean errors in activity estimates
  - Zubal numerical phantom 131I (quantitative SPECT, optimal ROIs):
    - liver: -2.1%
    - spheres: -10.3% (59 mL), -7.9% (16 mL), -38.4% (7 mL)
  - WB anthropomorphic numerical phantom 131I (quantitative SPECT):
    - liver: -2%, spleen: -13.5%
  - RSD anthropomorphic 111In (quantitative SPECT):
    - liver: 4.1%
    - spheres: 2% (20.6 mL), -12% (5.6 mL)
  - Liqui-Phil anthropomorphic phantom 111In (quantitative SPECT & WB protocol):
    - liver: -6% (10% with WB 2D protocol)
    - spheres with quantitative SPECT: 2% (33.5 mL), -12% (4.2 mL)
    - spheres with WB 2D: -86% (33.5 mL), -80% (4.2 mL)

Results at the organ level are encouraging. SPECT more accurate than WB.

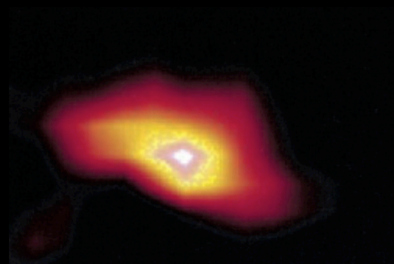
*Ljüngberg et al J Nucl Med 2002, Dewaraja et al J Nucl Med 2005, He et al Phys Med Biol 2005, Assie et al Cancer Biother Radiopharm 2008*

# ET for accurate activity estimate in each organ / voxel

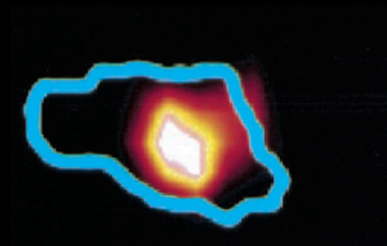
- Still two big issues for which satisfactory solutions are not available from the vendors : partial volume effect (PVE) and internal motion

Activity underestimation up to 50% or more without PV correction in structures < 3*FWHM in the images

Activity underestimation > 10% depending on the amplitude of motion



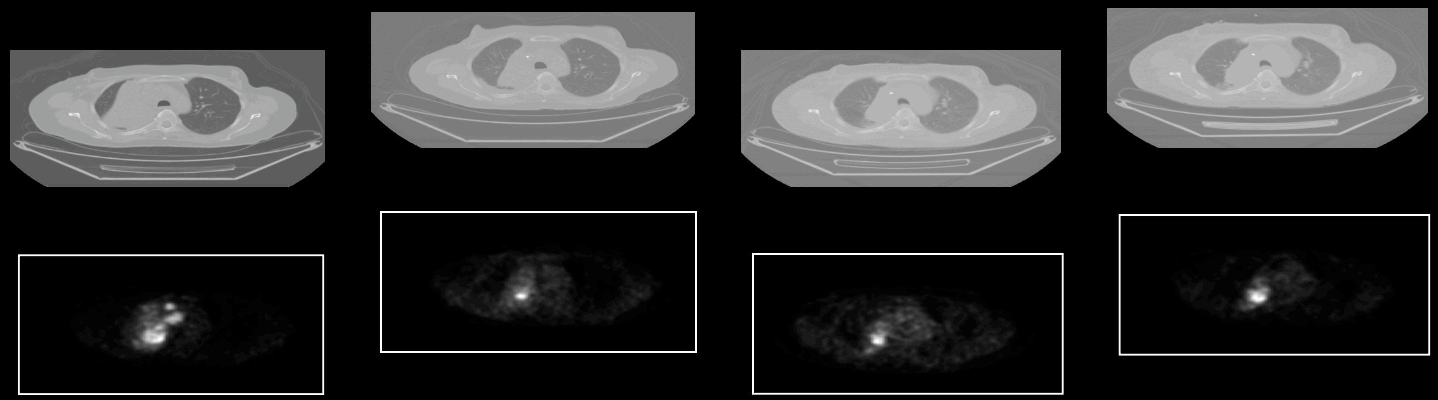
with motion



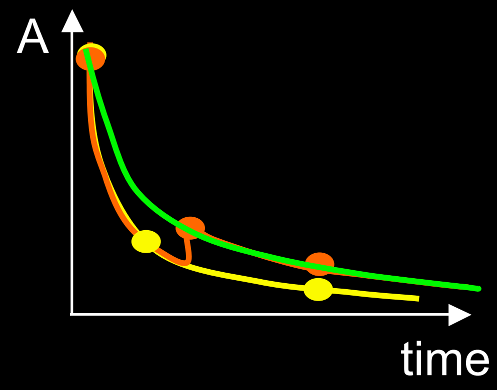
without motion

*Nehmeh et al J Nucl Med 2002, Nehmeh et al Semin Nucl Med 2008, Soret et al J Nucl Med 2007*

# Combining the longitudinal imaging studies: voxel level



D0 D1 D4 D6




- Each voxel TAC should represent the uptake and washout of the tracer in the corresponding voxel.

- Few data available, eg:
  - Head and neck: 0.3 - 3.8 mm accuracy in PET *
  - Lungs: 1-2 voxels (up to 8 mm) in PET #

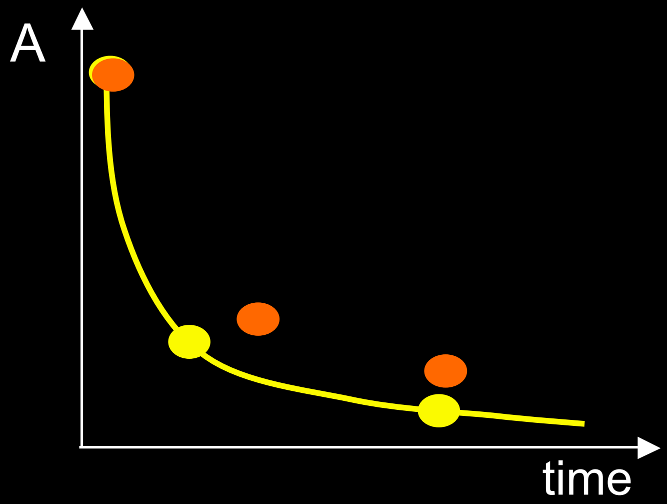
- Optimistic version: one voxel
- Poorer for WB scans

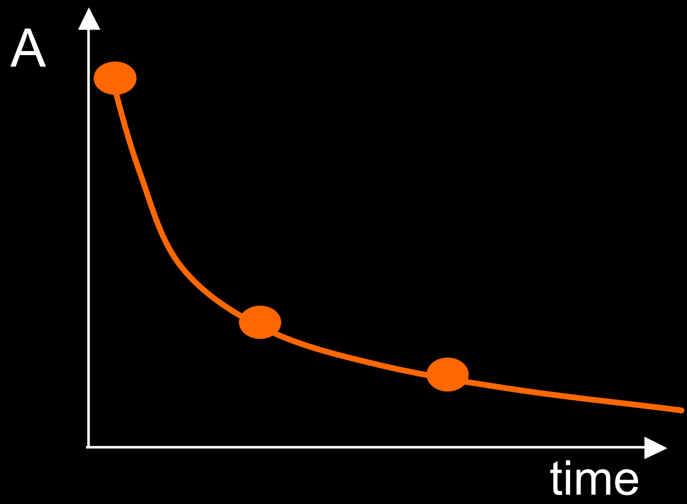
- Can be assessed in patients using consistency check #

** Daisne et al Radiother Oncology 2003, # Necib et al ISBI 2008*

# Combining the longitudinal imaging studies: voxel or organ level

- 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 the uncertainty affecting each point is known, the uncertainty affecting the dose estimate can be derived

*Flux et al, Phys Med Biol 2002*

# Error propagation from imaging to dose estimates

- 131I, Zubal phantom simulations (Not all the sources of errors were included):
  mean error of -2.1% in the liver ➡ 0% in absorbed dose
  -10.3% in a 59 mL sphere ➡ -6% in absorbed dose
  -7.9% in a 16 mL sphere ➡ -5% in absorbed dose
  -38.4% in a 7 mL sphere ➡ -31% in absorbed dose

- 131I, WB anthropomorphic numerical phantom:
  mean error of -2% in the liver ➡ +5% in absorbed dose
  -24% in the kidney ➡ -15% in absorbed dose
  +13% in the spleen ➡ -5% in absorbed dose

Magnitude of the errors in dose estimates is usually less than the magnitude of the errors in activity estimates

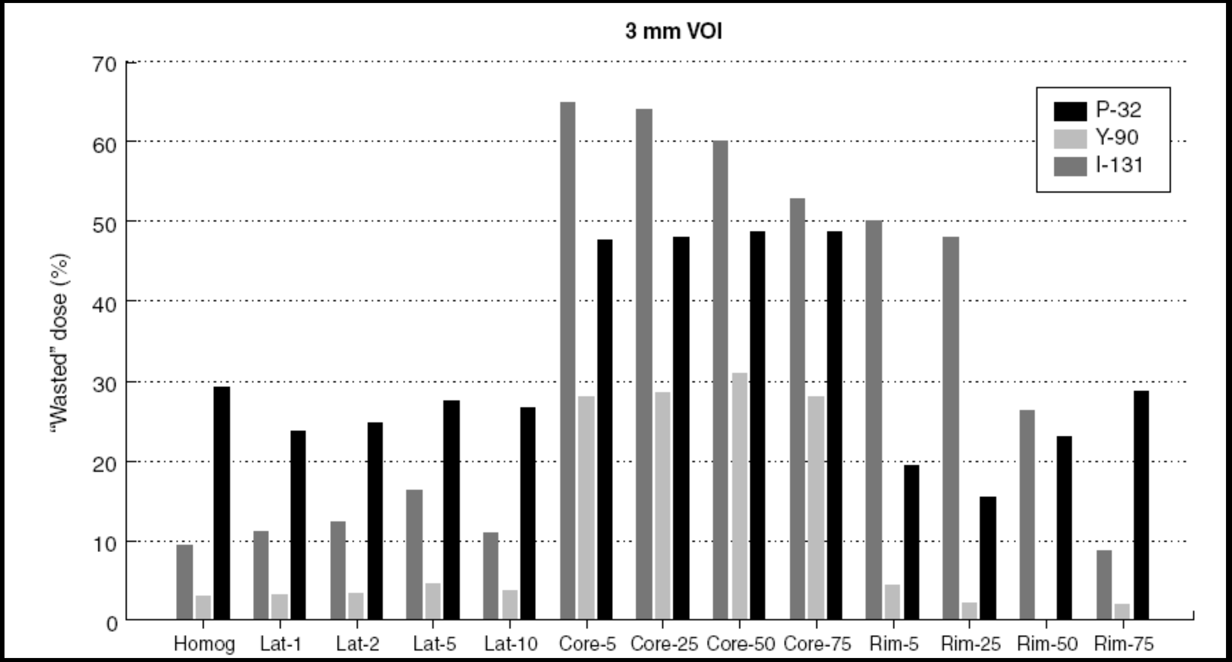
Improvement in activity estimates translates well into improvement in dose estimates

*Dewaraja et al J Nucl Med 2005, Ljüngberg et al J Nucl Med 2002, Assie et al Cancer Biother Radiopharm 2008*

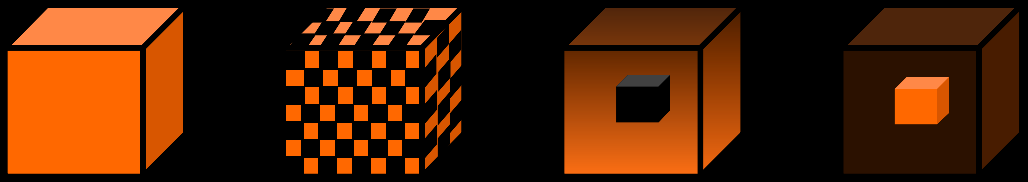
# Key point: are dose estimates at the organ / voxel level sufficient?

Necessary but not 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

*Kalogianni et al Cancer Biother Radiopharm 2007*

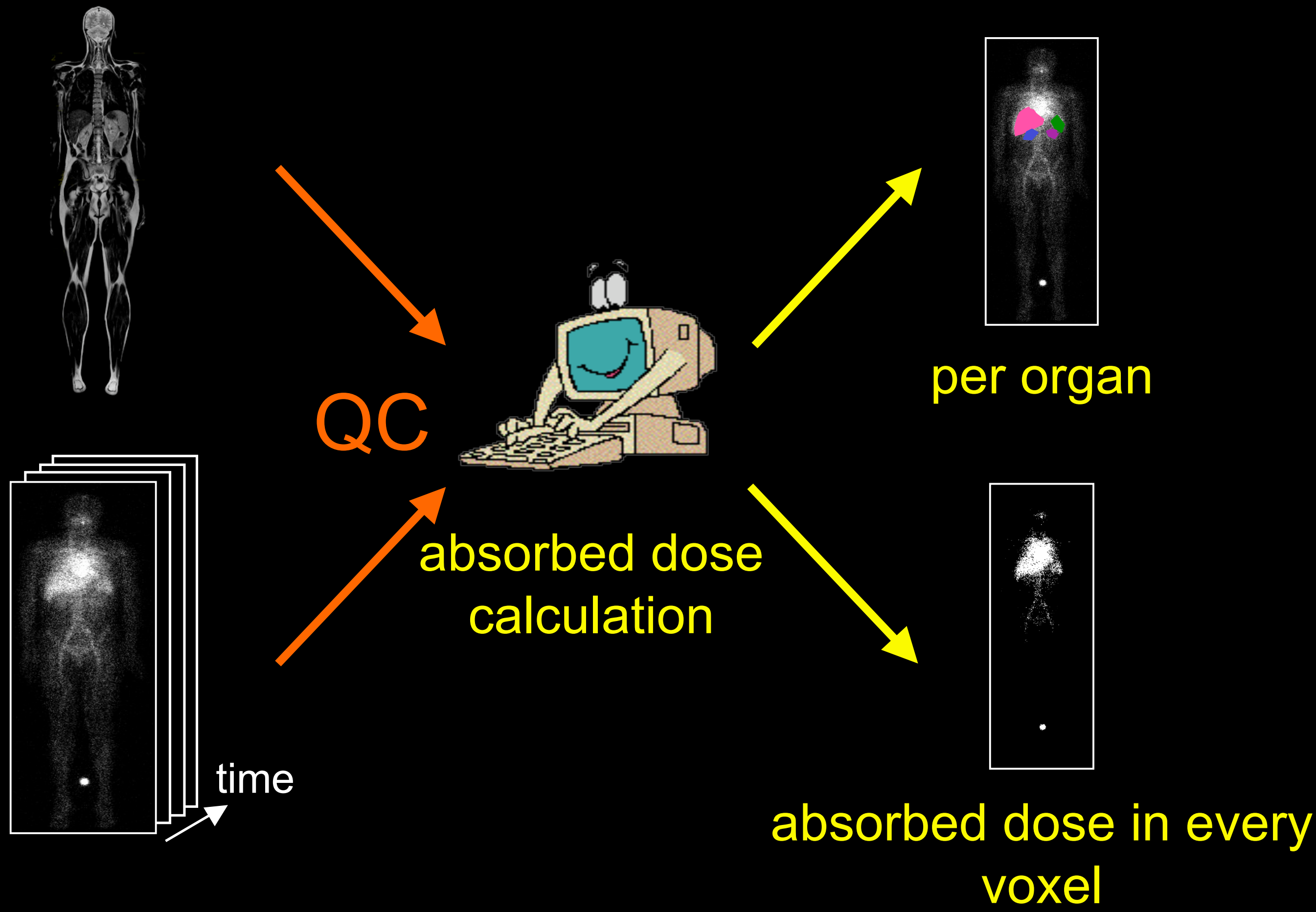
# Conclusion

- 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 using quantitative SPECT

- 3D ET/CT should be preferred for accurate activity quantitation

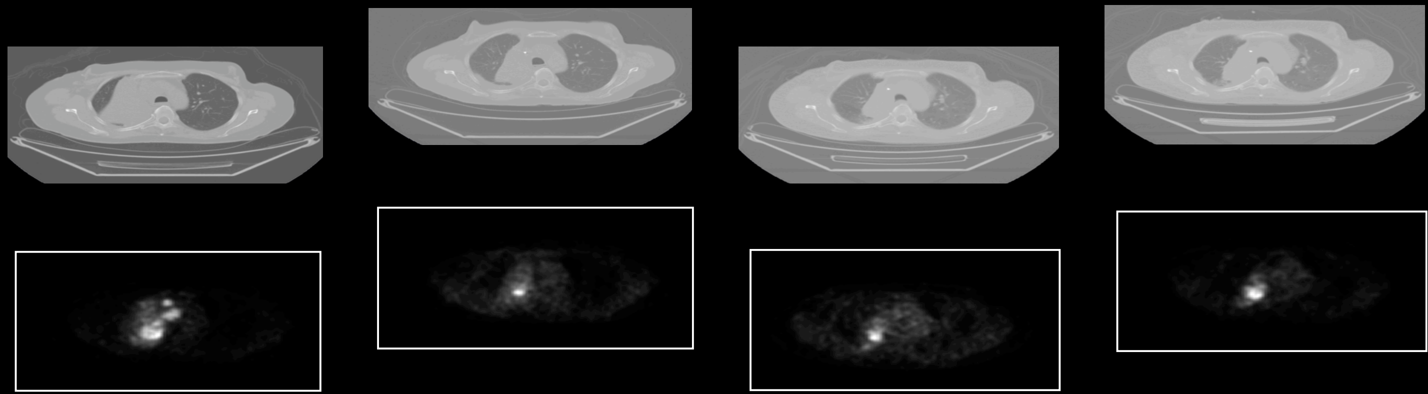
- Some effects are still often overlooked:
  - Partial volume effect and internal motion in ET : large biases (20 to 50%) in small structures (bone marrow) and voxel activity estimates
  - Activity accuracy at the voxel level ?
  - Impact of ET/ET misregistration when fitting the TAC at the voxel level
  - …

# Conclusion



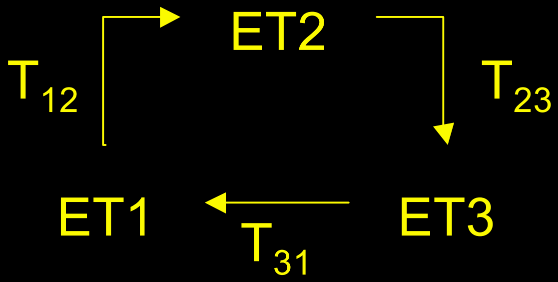

- Need for a thorough investigation of the accuracy of activity estimates for any imaging protocol
- Estimates of error propagation throughout the dose calculation scheme to assess the error affecting the final dose estimate before correlating dose with outcome

# Checking accuracy of registration of longitudinal ET scans



D0 - ET1 D1 - ET1 D4 - ET2 D6 - ET3

- Consistency measure E




$$E = I - T_{12}T_{23}T_{31}$$

*Necib et al ISBI 2008, Holden et al, IEEE Trans Med Imaging 2000*