Amsterdam UMC
University Medical Centers

Possibilities and challenges in data analysis

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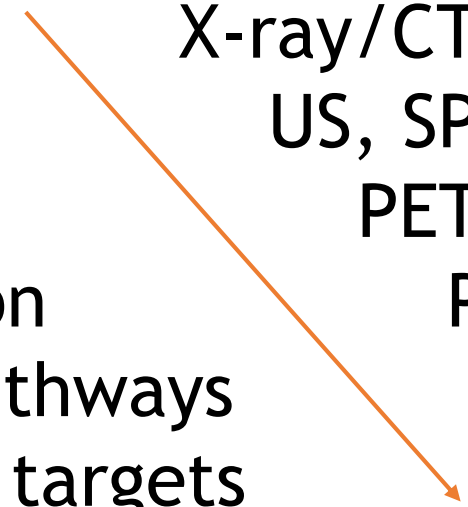
The Spectrum of Medical Imaging

Structure	X-ray/CT/MRI
Physiology	US, SPECT, PET, MRI/S
Metabolism	PET, MRS
Drug distribution	PET
Molecular pathways	PET
Molecular targets	PET, SPECT



PET: Quantitative
Picomolar Sensitivity

Jones, 1996

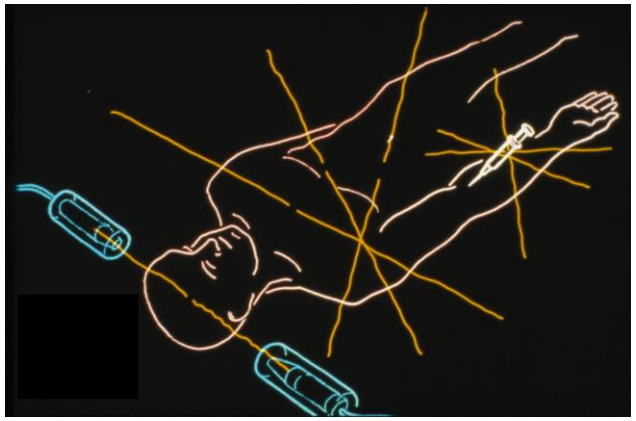
Positron Emission Tomography

1975

2015

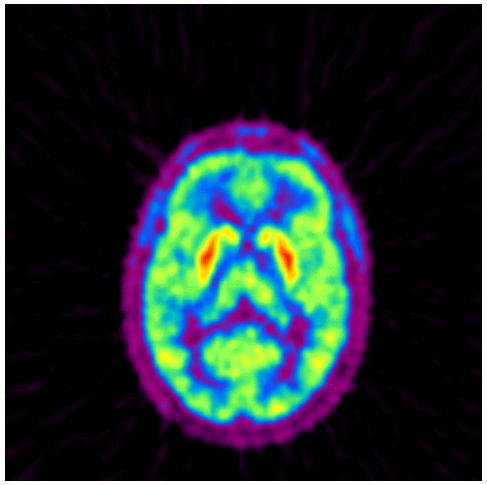
Routine Clinical Practice

Inject



Wait

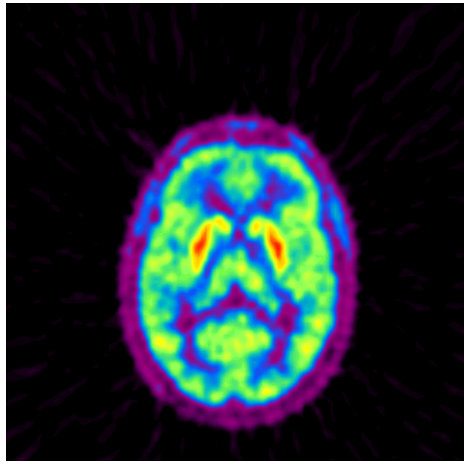
Scan



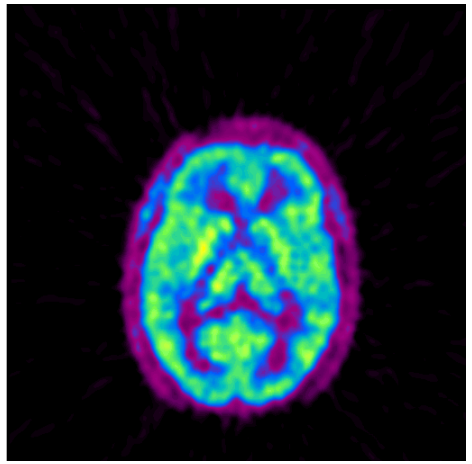
Increased uptake = increased binding
But what about:
increased flow, extraction or delivery?

Uptake (SUV)

[^{11}C]R116301: NK1 receptor ligand



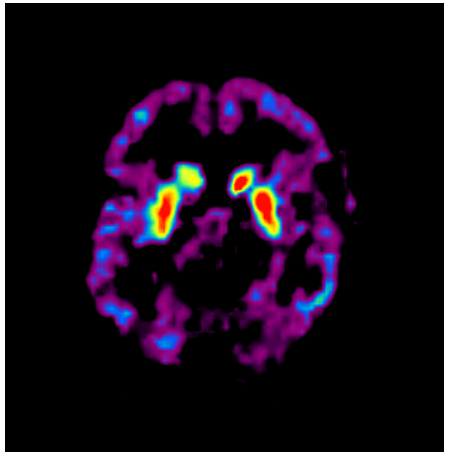
base-line

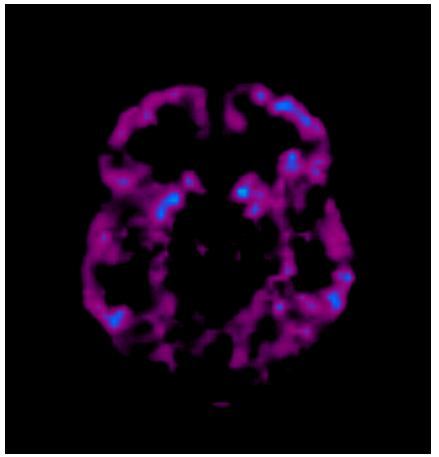


post-aprepitant
(NK1 blocker)

SUV (60-90 min)

Simplification
questionable

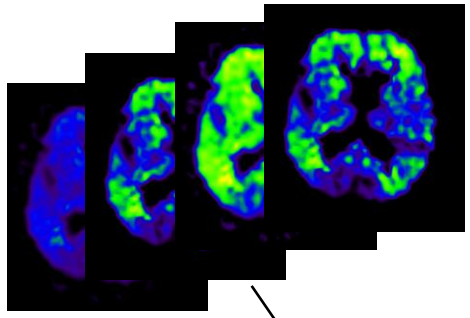




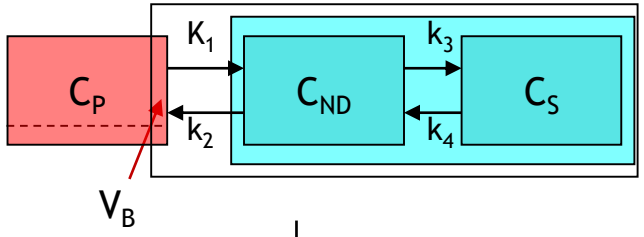
$BP_{ND} = k_3 / k_4$

Overview kinetic analysis

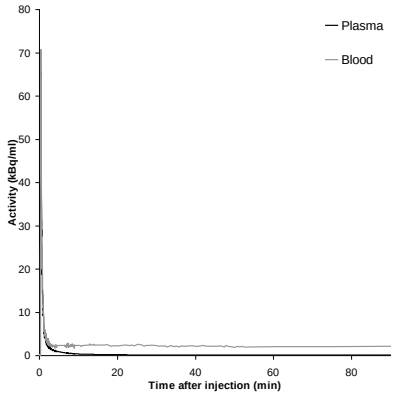
Dynamic PET scan



Kinetic model

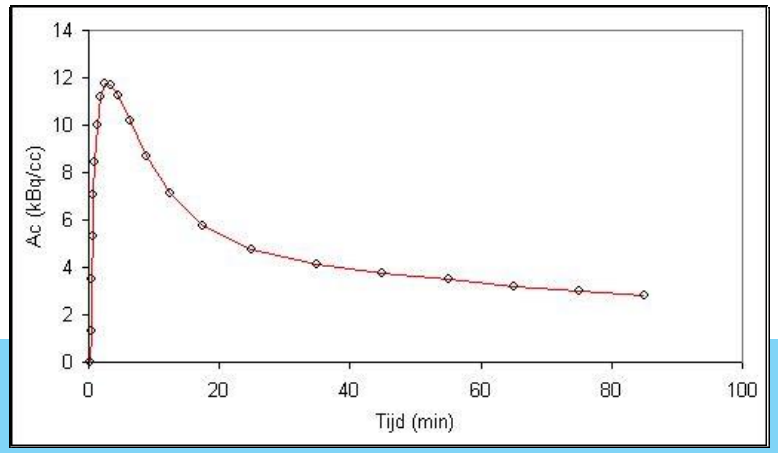


Input function



Fitting routine

Tissue time-activity curve



→ **Kinetic parameters**

$BP_{ND}=k_3/k_4=f_{ND}\cdot B_{avail}/K_d$

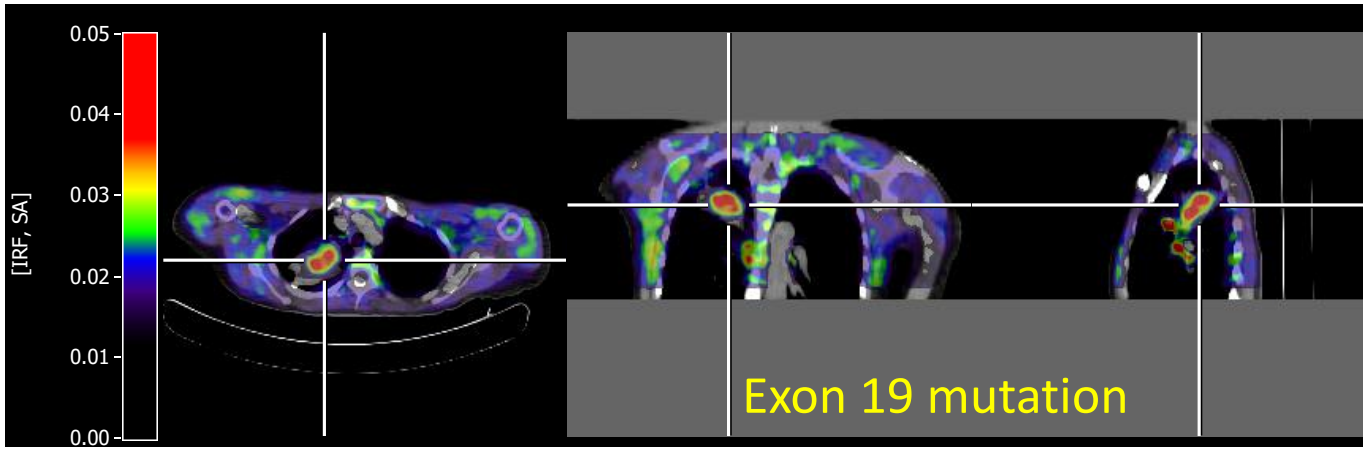
$V_T=K_1/k_2\cdot(1+BP_{ND})$

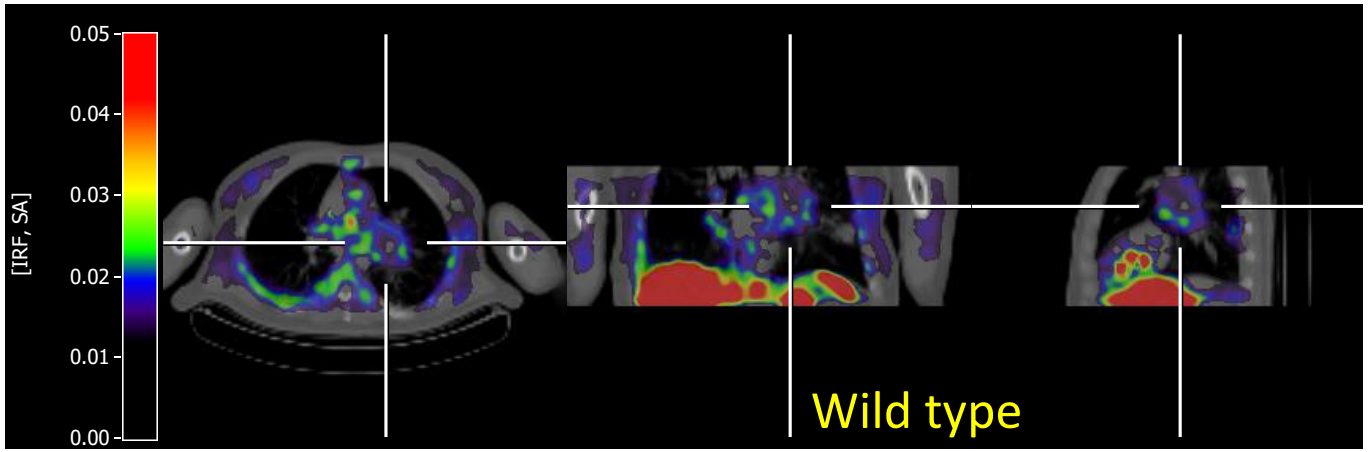
Rationale for Quantification

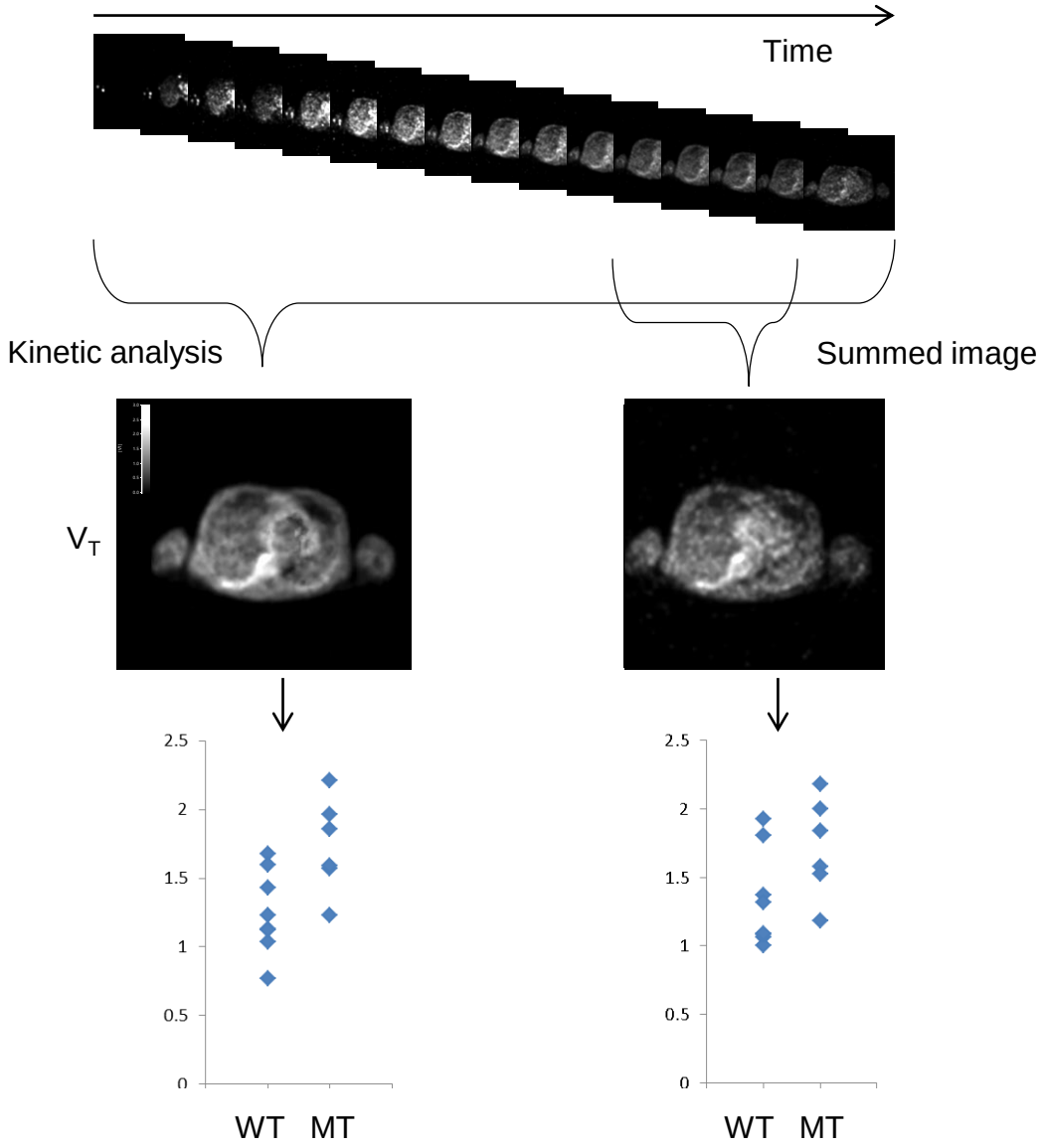
- Radiology & Nuclear Medicine: 1 image is worth more than 1000 words
- Imaging Science: 1 number is worth more than 1000 images

- Quantification:
  - Essential for correcting for confounding effects
  - Essential for identifying global effects
  - Essential for monitoring progression of disease and for monitoring response to therapy

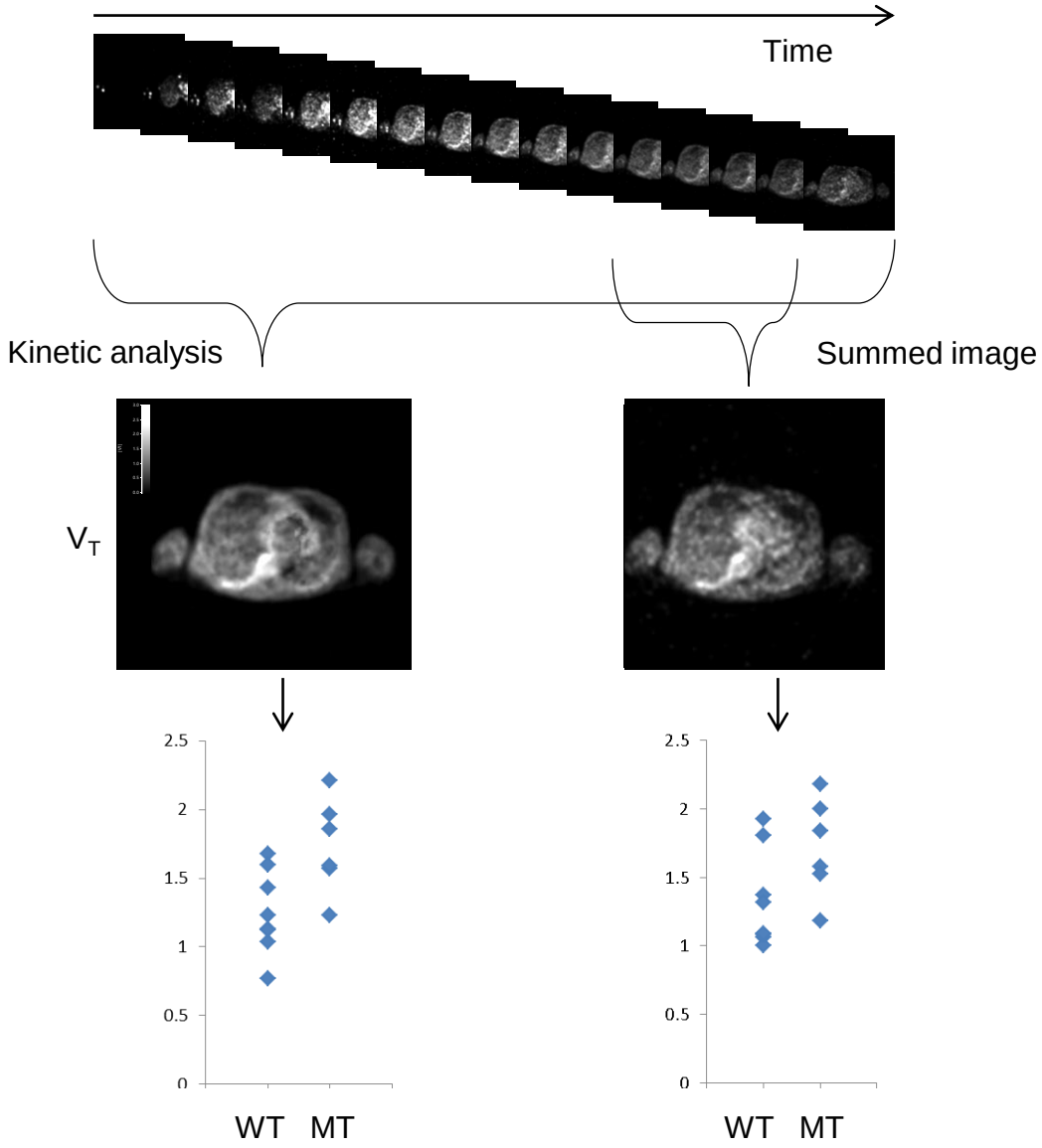
[^{11}C]Erlotinib







[^{11}C]Erlotinib

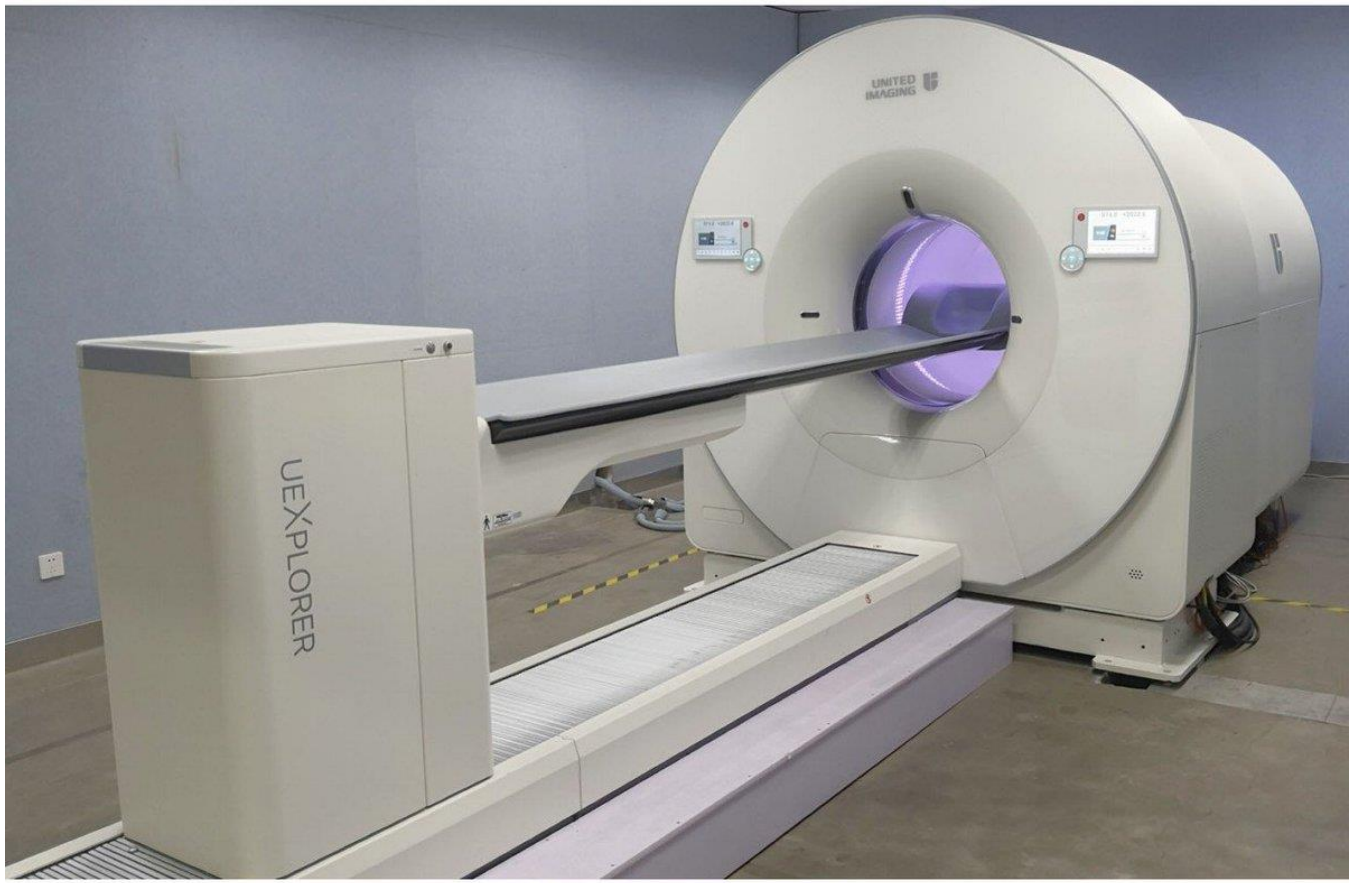


Dilemma:

1. Static whole body scan: non-informative

2. Dynamic scan: single field of view, but no information on interlesional heterogeneity

The Solution: Total Body PET



Explorer Total Body PET/CT

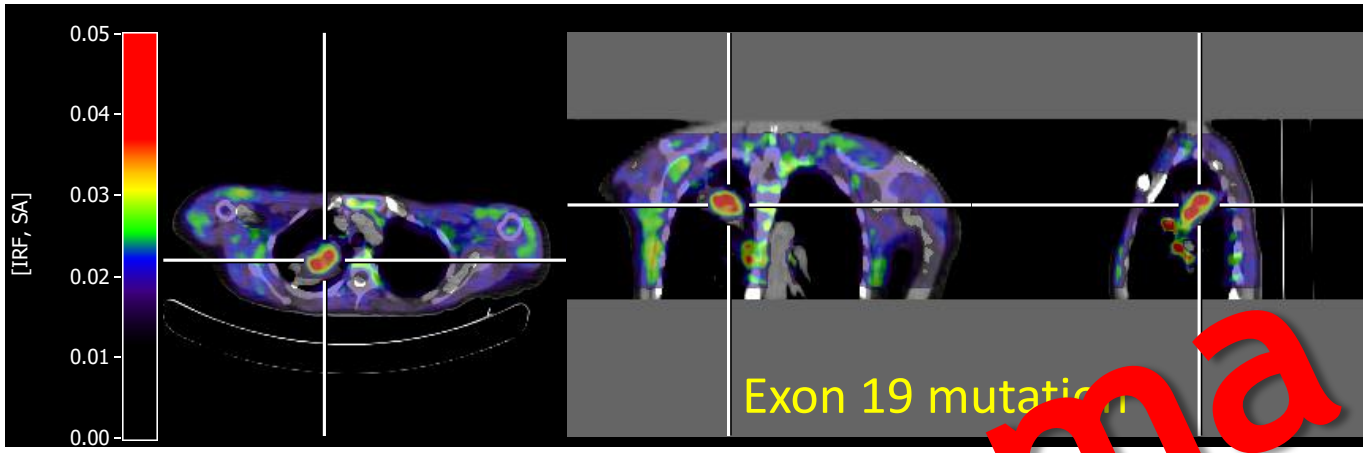
EXPLORER slides courtesy of Simon Cherry and Terry Jones, UC Davis

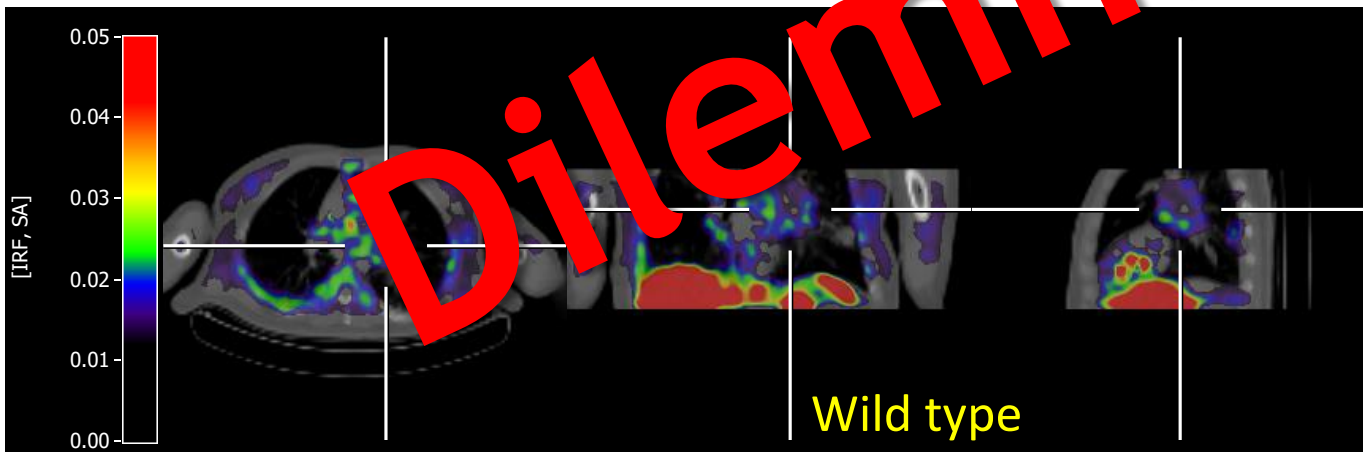
a)

b)

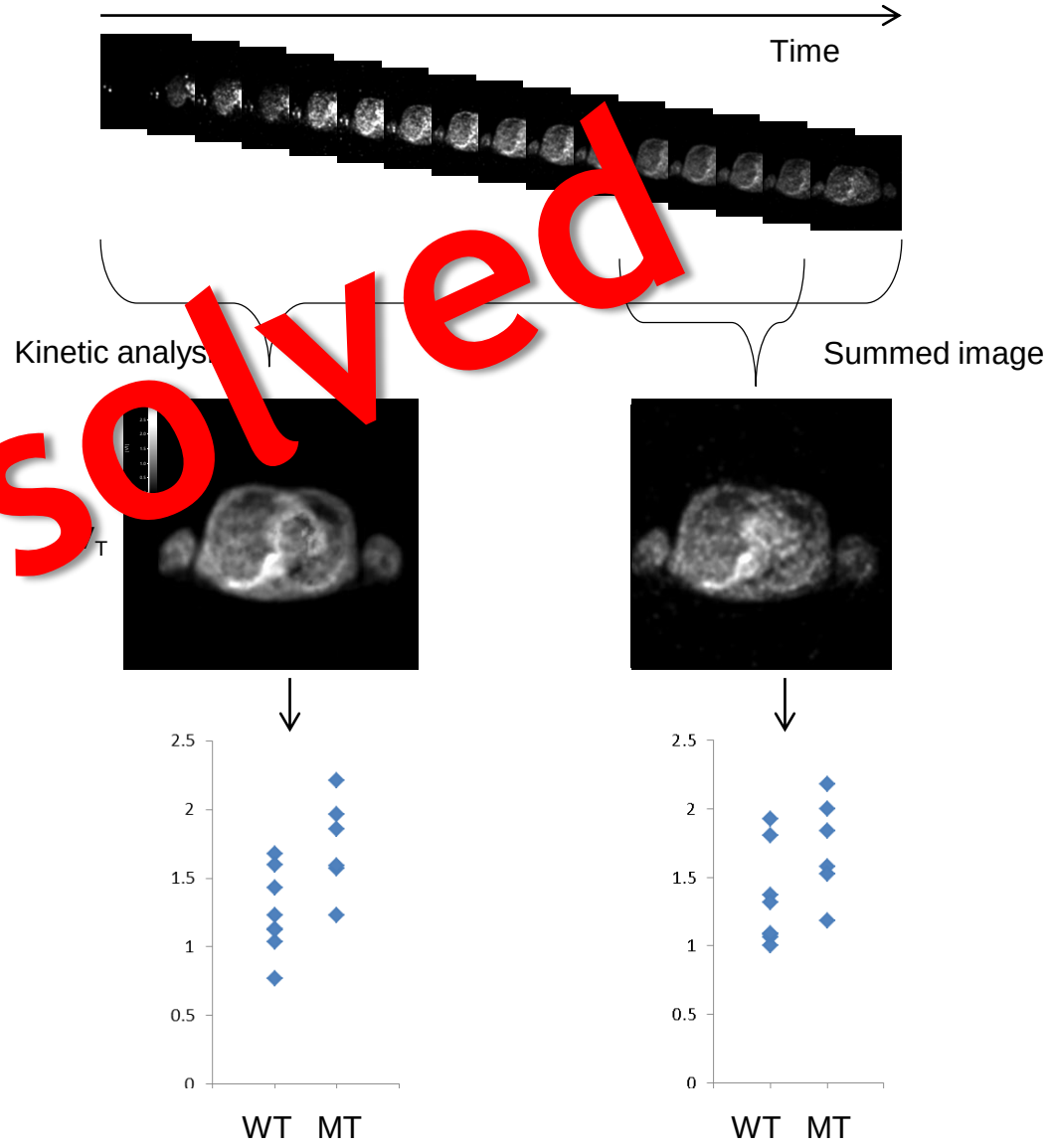
Maximum intensity projection (MIP) of late 30 min
(a) SUV; (b) indirect OSEM Patlak slope *Ki* (3 iterations 20 subsets)

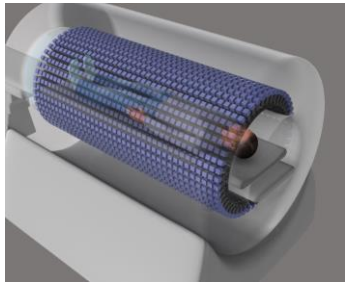
[^{11}C]Erlotinib





Dilemma solved

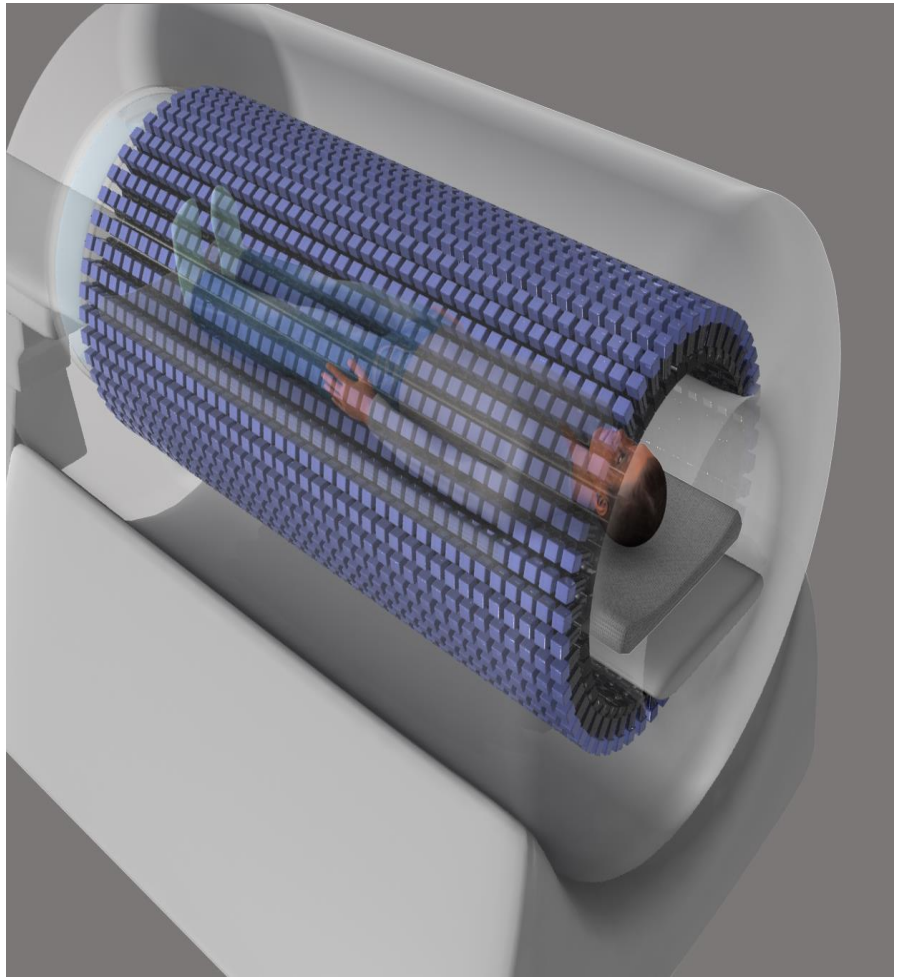




Opportunities of TB PET

- Quantitative (dynamic) scanning of total body rather than semi-quantitative (static) scanning
- Increased sensitivity

Maximizing Sensitivity
by Total-Body PET



~40-fold increase
for adult total-body imaging

~20-fold increase
for pediatric total-body imaging

~4-fold increase
for single organ imaging

EXPLORER Claim: Image Longer

- **Major increase in dynamic range**

  can image for 5 more half lives

- ^{11}C
  - ➢ 3 hours

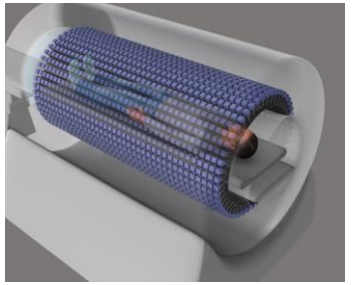
- ^{18}F

  > 16 hours

- ^{89}Zr

  > 30 days

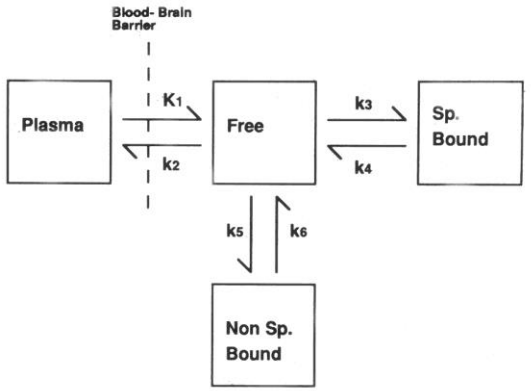
56 kg female; 6.7 mCi injected activity; 14 min acquisition



Opportunities of TB PET

- Quantitative (dynamic) scanning of total body rather than semi-quantitative (static) scanning
- Increased sensitivity
  - Longer scans possible in case of slow kinetics
  - Possibility for quantitative imaging of monoclonal antibodies (^{89}Zr labelling) in non-oncological applications
- Possibility for non-invasive measurement of arterial input function

Image Kinetics

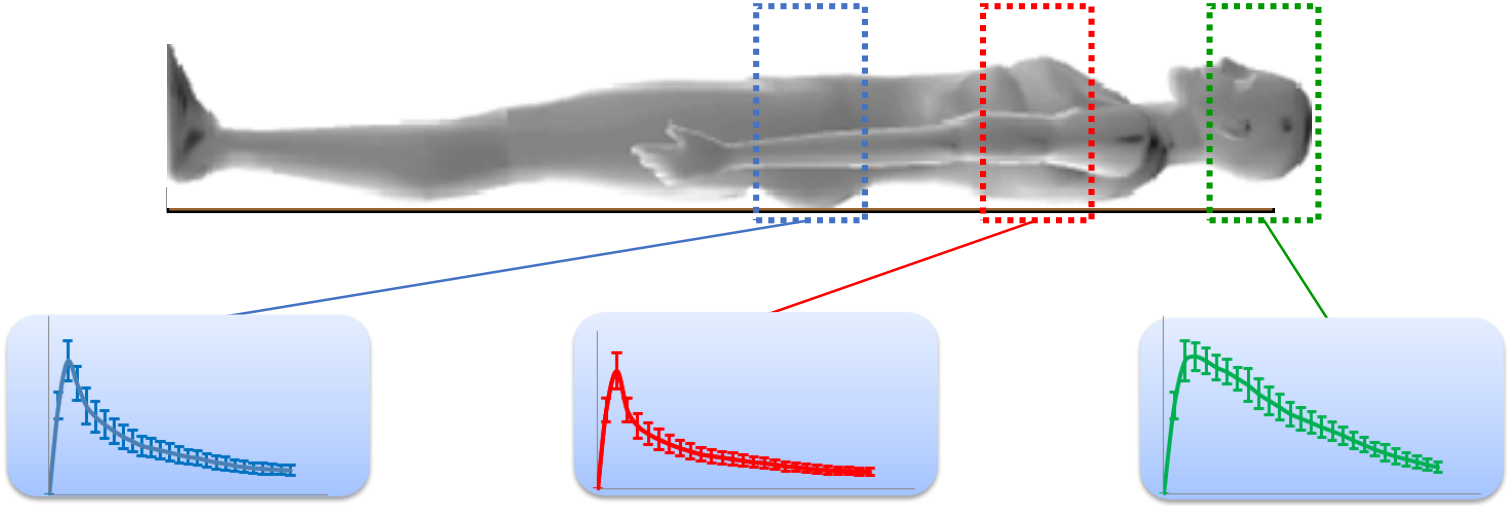


K_1 = flow x extraction (mls min^{-1} ml^{-1}),

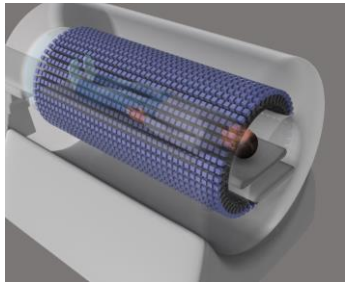
k_2 = functional efflux (min^{-1}),

k_3 = combined forward rate constant (K_{ass} x B_{max}) (min^{-1}),

k_4 = dissociation constant = k_{off} (min^{-1})



Regional tissue & arterial blood time-activity curves with high statistical quality



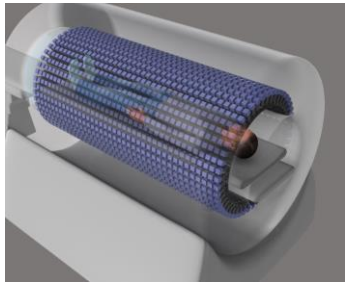
Challenges for TB PET

- Significant increase in number of lines of response

Total-Body PET: Maximizing Sensitivity

CONVENTIONAL PET

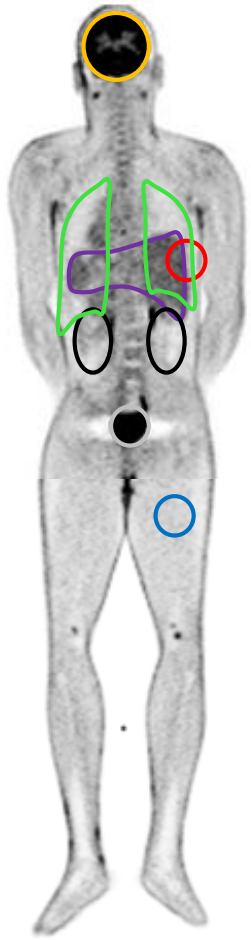
EXPLORER

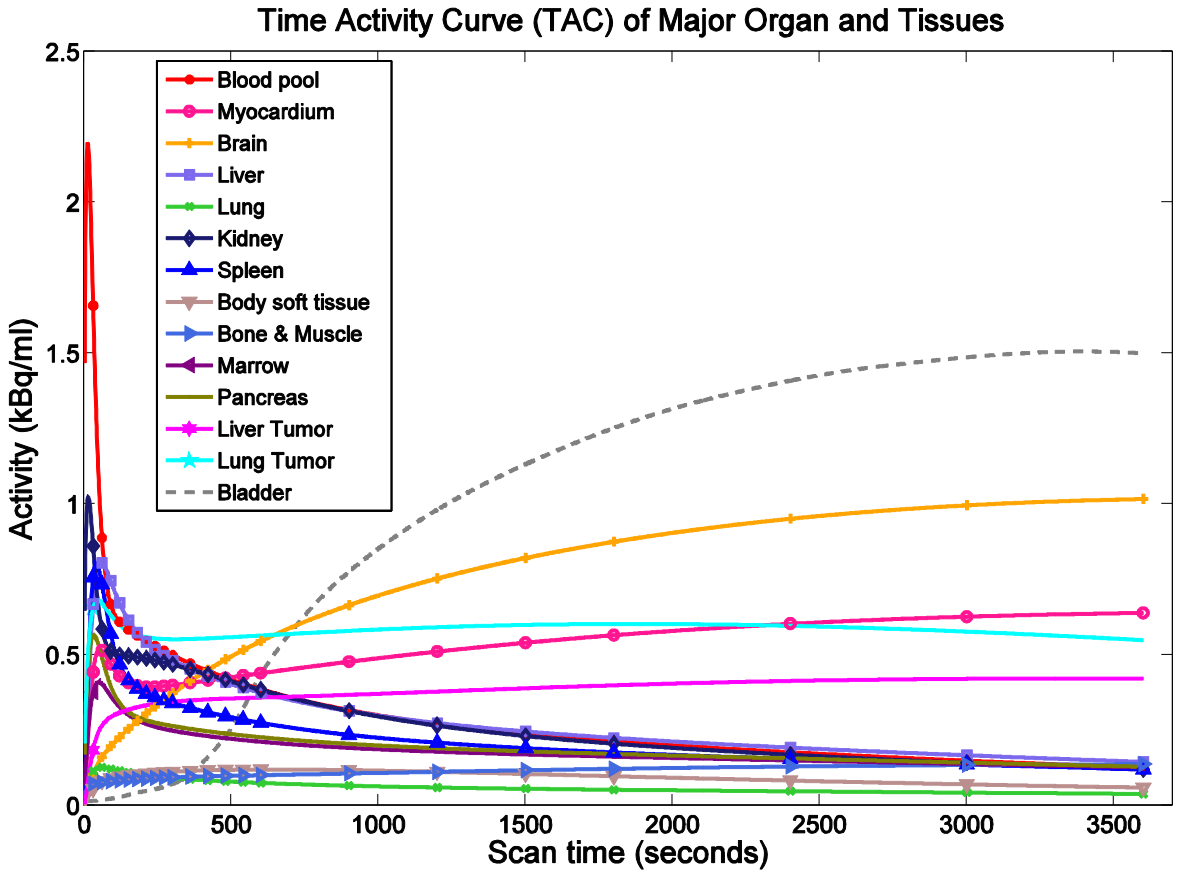


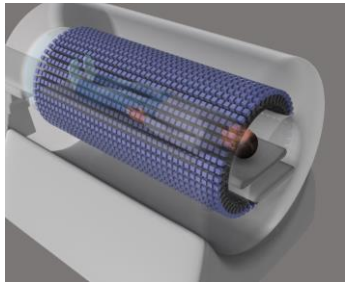
Challenges for TB PET

- Significant increase in number of lines of response → enormous datasets
- Larger axial field of view
  - More difficult for claustrophobic patients
  - Patient access: more difficult to inject tracer and to withdraw arterial blood

Total-Body Tracer Kinetics

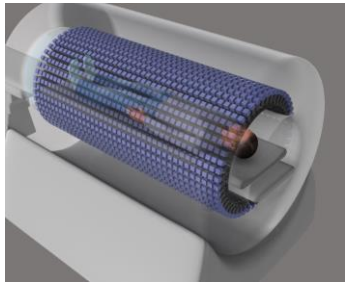






Challenges for TB PET

- Significant increase in number of lines of response → enormous datasets
- Larger axial field of view
  - More difficult for claustrophobic patients
  - Patient less accessible, i.e. difficulty to withdraw arterial blood
- Kinetic heterogeneity, i.e. different models required for different organs
- How to obtain image derived *metabolite corrected plasma* input functions?

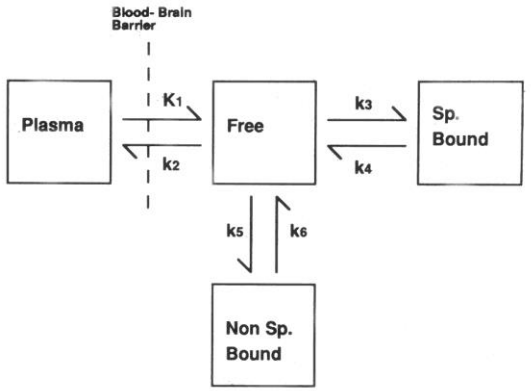


Potential Solutions

- Kinetic heterogeneity
  - Automatic segmentation of organs: cluster analysis, artificial intelligence
  - Parametric analysis: data driven methods such as spectral analysis
- Image derived metabolite corrected arterial plasma input function
  - Whole blood curve from dynamic scan: cluster analysis
  - Combine with venous plasma (metabolite) measurements
  - Derive from simultaneous fitting: same input for all voxels

Methodological building blocks already exist

Image Kinetics



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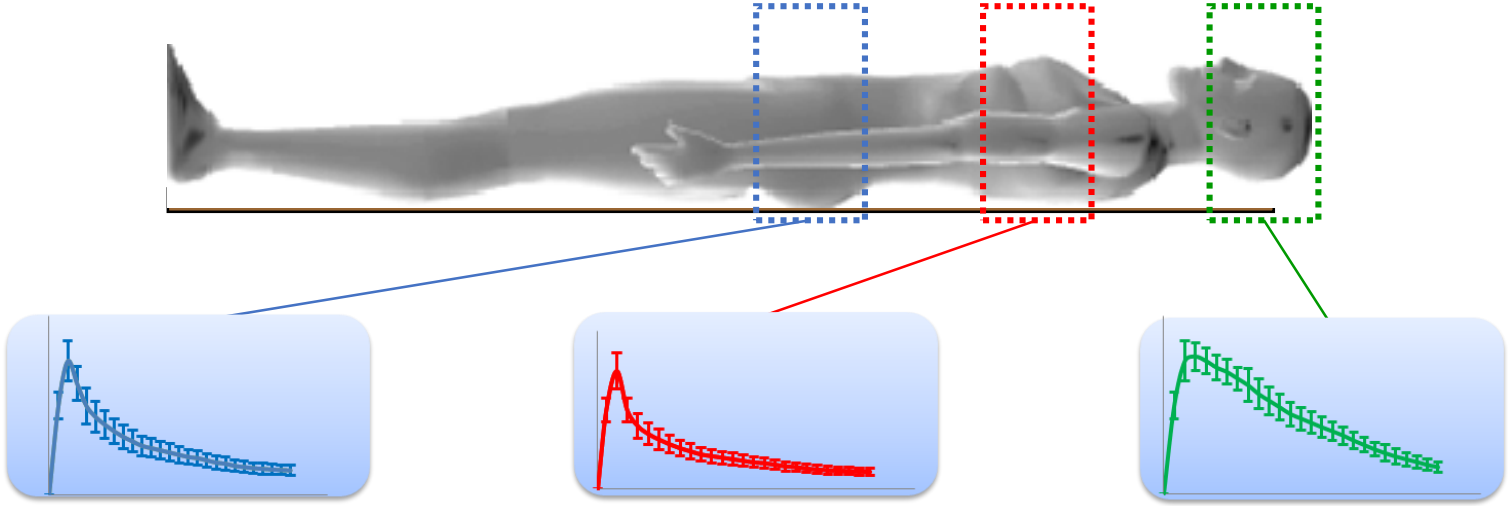

Regional tissue kinetics & arterial blood input functions with high statistical quality

Future: routine dynamic PET scanning as a non-invasive quantitative tool for clinical & research questions