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sense and simplicity

Medical Imaging : Looking beyond structures

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Image Processing at Philips

- Video, motion compensation, compression
- Image-guided procedures
- Imaging & visualizing small structures : CT, MR
- Imaging physiology
- Some open problems in registration and segmentation

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Functional Imaging (The search for Istina)

- Images the metabolism of the organ
  - Nuclear Medicine
  - fMRI

- Advantages
  - Early detection (functional changes lead to structural changes)
  - Detection of dead tissue
  - Individualized therapy

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Nuclear Medicine Applications

- Oncology
  - PET (FDG) scans to identify tumors
- Cardiology
  - SPECT scans to identify
    - perfusion defects
    - Muscle Viability
    - Chronic Heart Failure
- Neurology
  - PET (Dopamine) to identify
    - Brain Plaque
    - Dementia

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Nuclear Medicine Principles

- Radiopharmaceutical injected
  - Affinity for certain organs/tissues
- Delayed imaging
  - To image a specific organ
  - Depends on physical half-life and biological half-life
- Radioactive decay measured
  - Photon emission : gamma camera (NM / SPECT)
  - Positron emission : electronic collimation (PET)

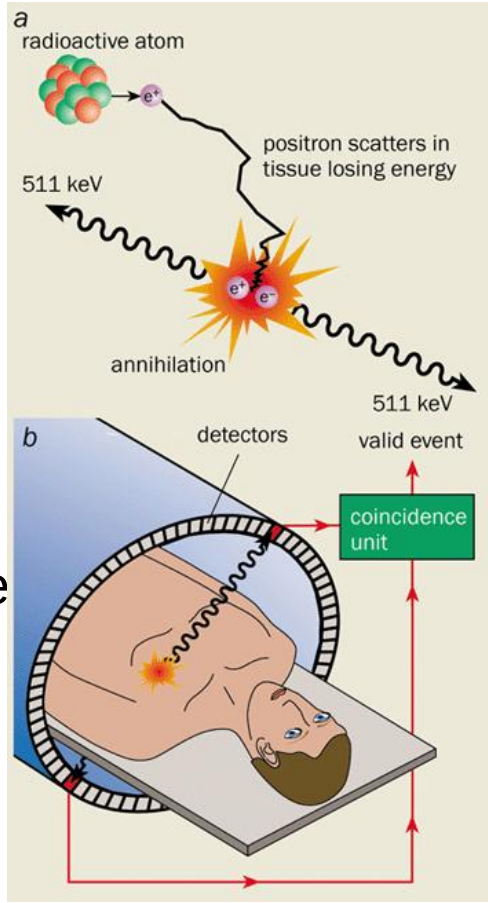

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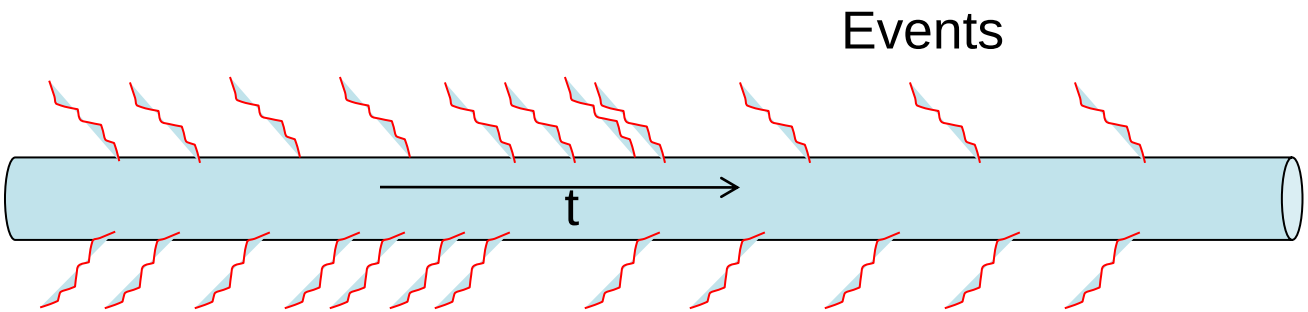
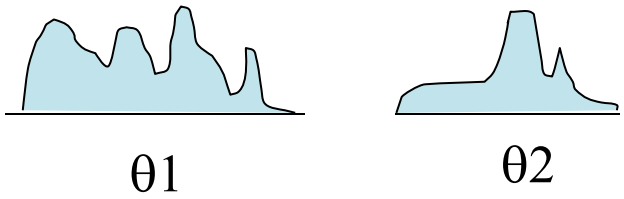
Image acquisition in NM



Collimated (2%)



“Line” integrals

Reconstruction)

Volume

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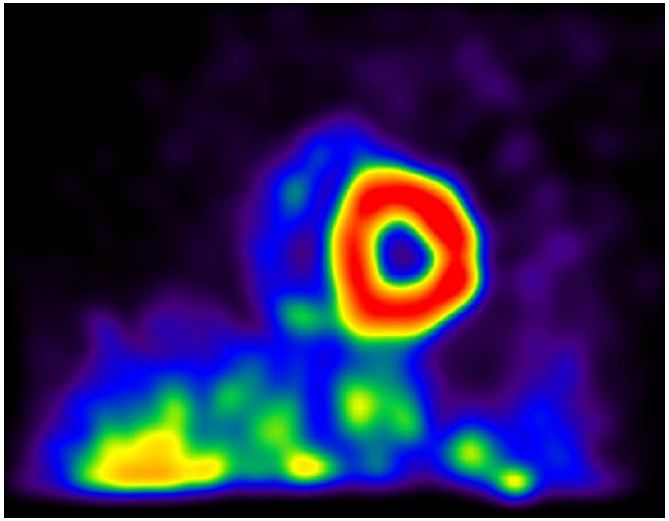
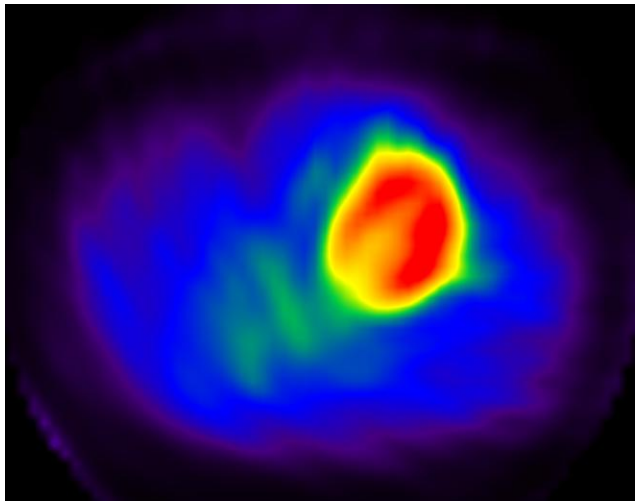
Example : Cardiac Ischemia





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Example : Lymphomas

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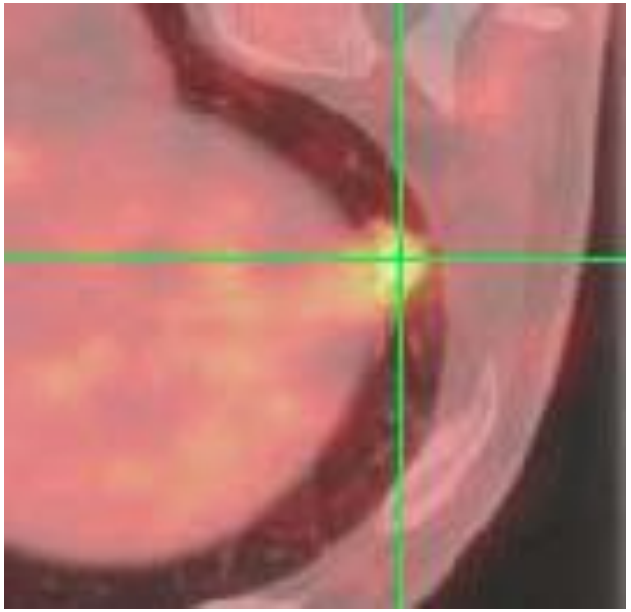
The Istina comes full circle

Fusion of hypoxia map and CT



Is tumor on the lung or on the stomach ?

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The search for Vishnu ?

- Truly early diagnosis ?
  - Diseases originate at cellular/sub-cellular level
  - Imaging happens at organ level
- Would like to
  - Connect in-vivo results with cellular-level phenomena
  - Dynamic Imaging holds the key !

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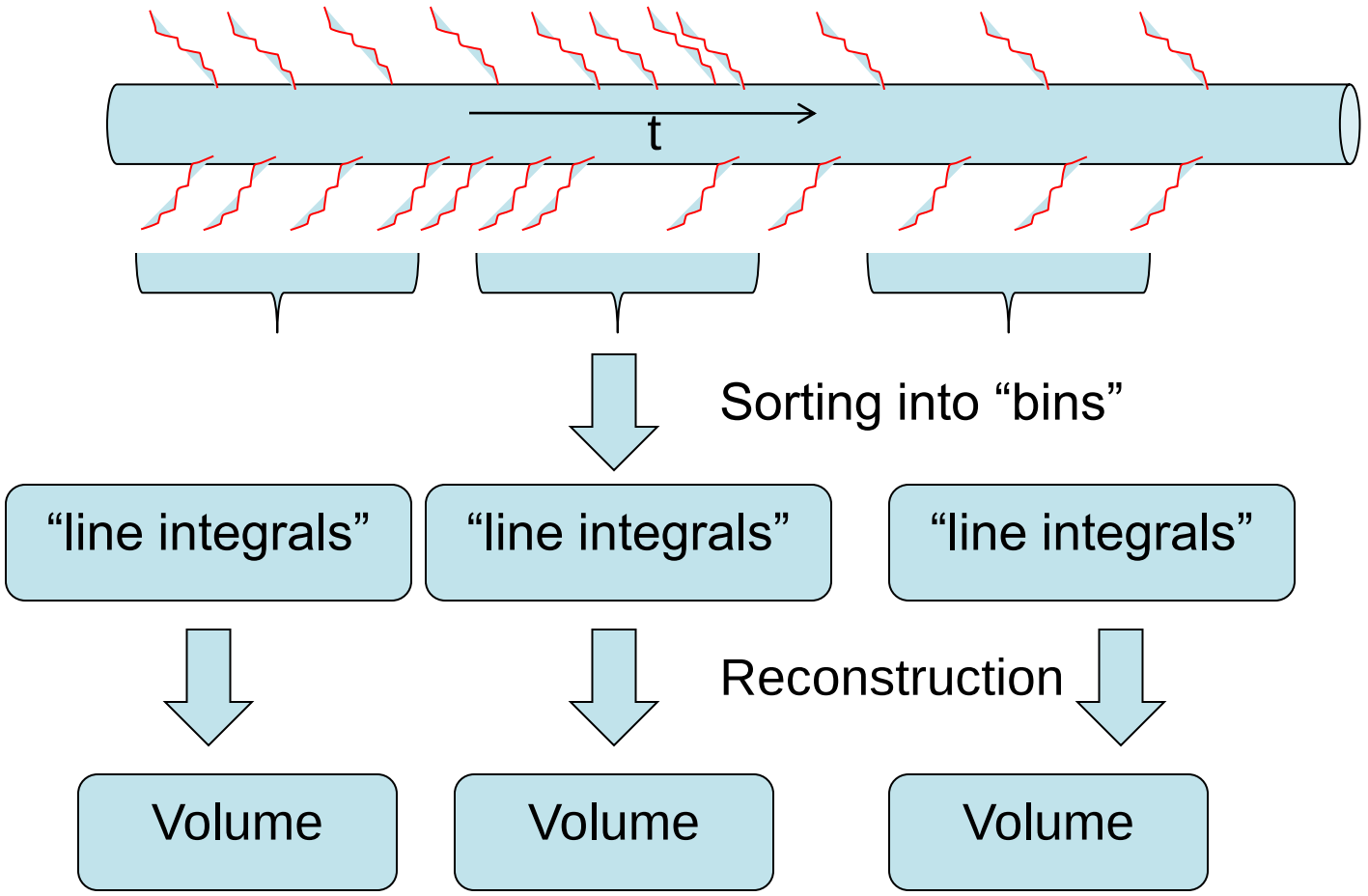
What is Dynamic Imaging ?



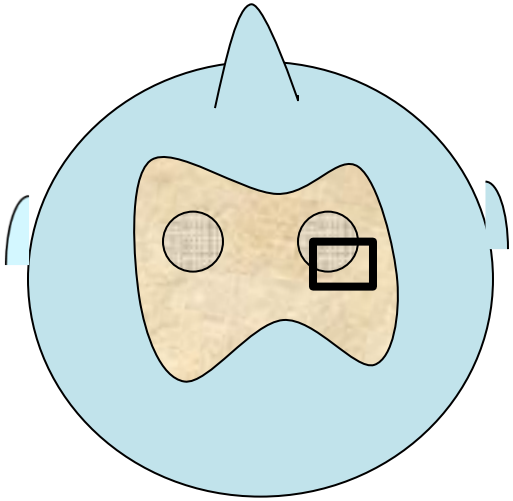
Why Dynamic Imaging ?

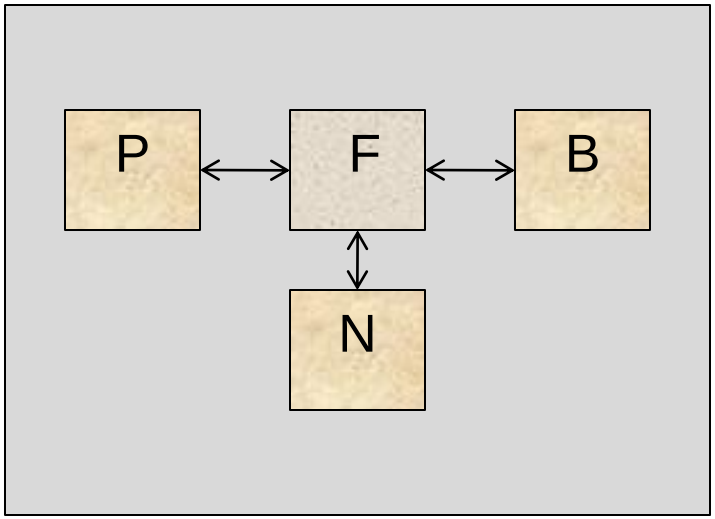
- Processes during acquisition :
  - Drug enters the organ of interest
  - Drug is metabolized
  - Drug is washed out due to excretion
- Static image gives an “average” impression
- Dynamic image gives details of each phase
  - Understanding the dynamics of drug interactions in the body

Kinetic Modeling

- Tracer in an organ undergoes various reactions : Diffusion, Absorption, Excretion
- In-Vivo imaging : images are a composite of various superimposed signals.
- Mathematical model relates the dynamics of the tracer molecule and its possible states to the in-vivo image.
- Each state : called compartment. Compartments can evolve in time but not in extent.

Compartmental Analysis





Mass Balance Equations

$$\frac{\partial F(t)}{\partial t} = k_1 P(t) - k_2 F(t) \cdots$$

$$\frac{\partial B(t)}{\partial t} = k_0 \max(B, F) \cdots$$

$$\frac{\partial N(t)}{\partial t} = k_4 F(t) - k_5 N(t) \cdots$$

Key Assumptions

- Tracer (often drugs) causes no change in physiology
  - Low (trace) quantity
- Tracer is in steady-state with the tracee
  - Tracer (eg. F18) goes everywhere that tracee (eg. Glucose in the brain) goes
- No isotope effects
  - Labelling with a radio-nuclide does not alter its properties
- Parameters of the model are time-invariant

Input Function

- Tracer levels in plasma :
  - Not part of the dynamics
  - Drive the model
- Initial Condition of the system : 0
- Assumption : All tissues in the body see the same input function
  - Input : activity measured in blood plasma during the experiment

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Model Parameters

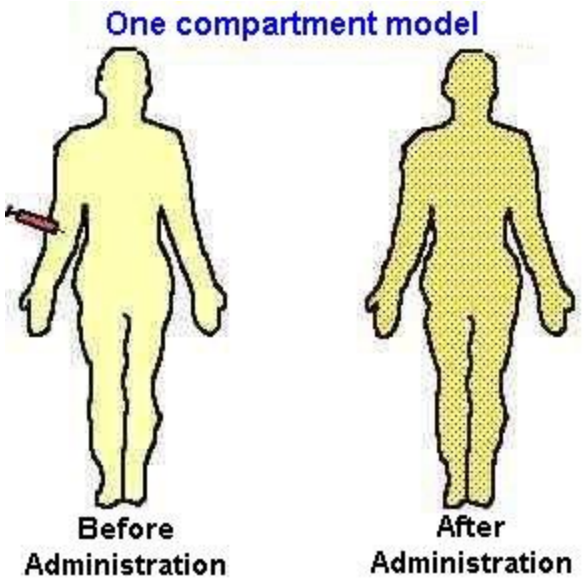
- Rate constants of various phenomena
- Can be estimated by fitting model to actual dynamic data
- Correspond to physiologically relevant parameters

Reference Tissue model

- Plasma measurement
  - Done by catheter during experiment
  - Invasive
- Alternative :
  - Define artery feeding blood to the target region as a compartment
  - “Reference” compartment activity acts as input function

One-compartment model

- Assumes whole body is a single compartment
- Can be used when drug rapidly equilibrates with the surrounding tissue
- eg. Distribution of aminoglycosides (15-30 min)
- Denotes
  - Blood flow when extraction fraction is large
  - Permeability when extraction fraction is small



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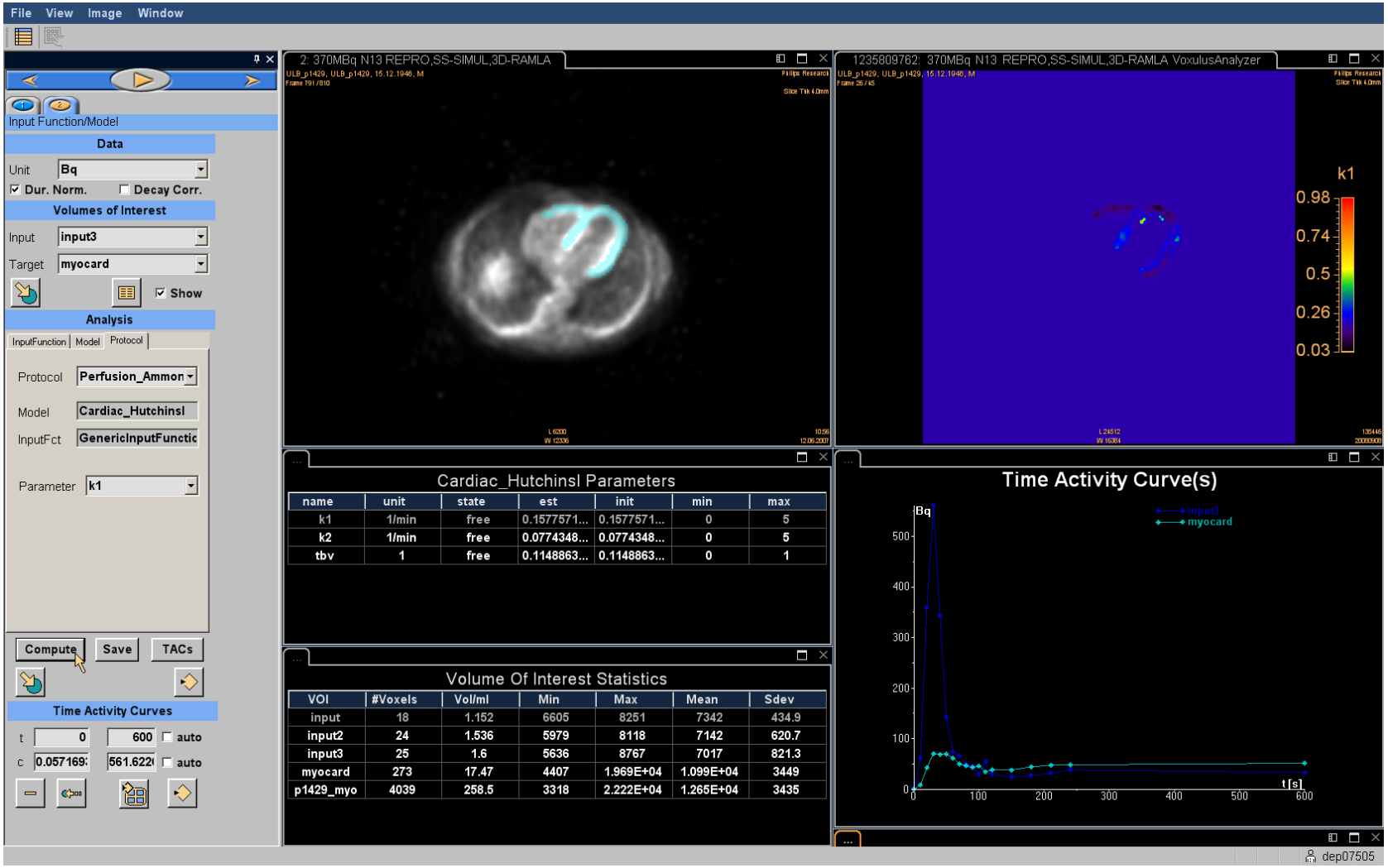
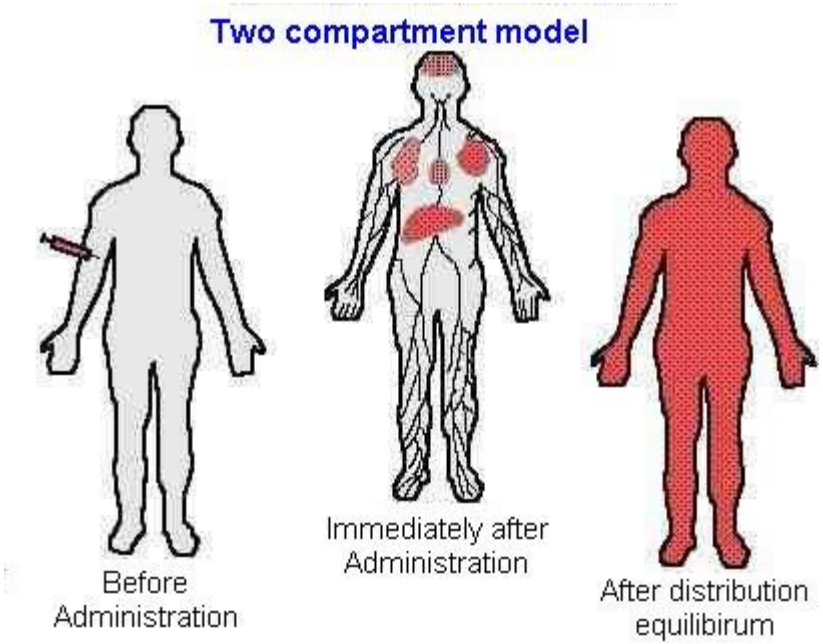
Pharmacokinetic Modeling

NH_3/Rb_{82} Myocardial Blood Flow



Two-compartment model

- Assumes 2 tissue (and one plasma) compartment
- Used when tracer equilibrates slowly with the surrounding tissue (1-2 hours)
- eg. FDG PET
- Rate constants denote
  - Phosphorylation in brain studies
  - Hypoxia in tumor studies



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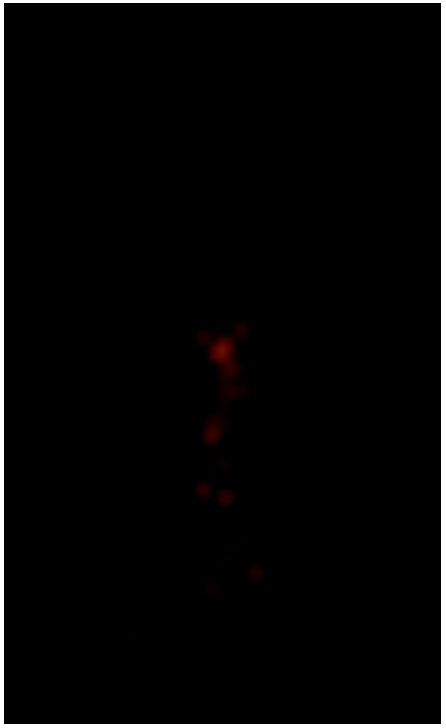
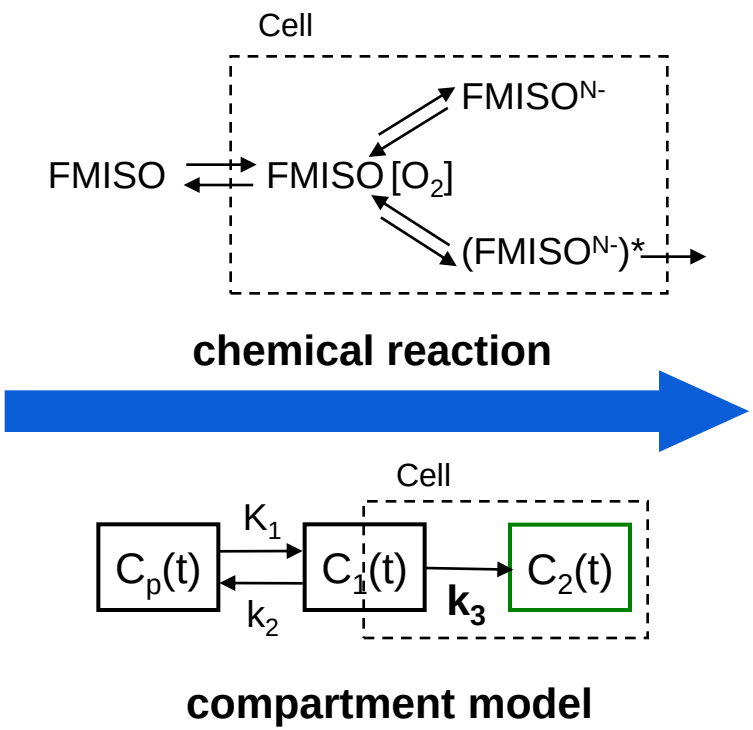
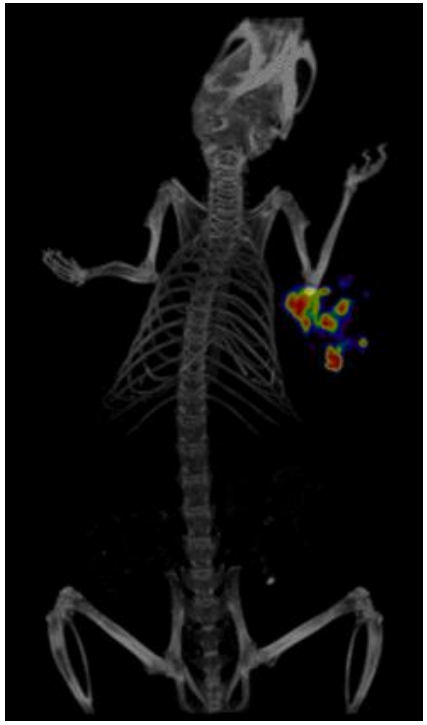
Pharmacokinetic Modeling

FMISO / FAZA tumor hypoxia



dynamic FAZA PET





CT / k_3 fusion

Image data cortesy: TU Munich, Axel Weber

Three-compartment model

- Assumes 3 tissue (and one plasma) compartment
- Used when 2 tissue compartments are not sufficient
- eg. Receptor-ligand studies (free and bound states of ligands)
- Rate constants denote
  - Binding potential

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Pharmacokinetic Modeling

Neuroreceptor binding

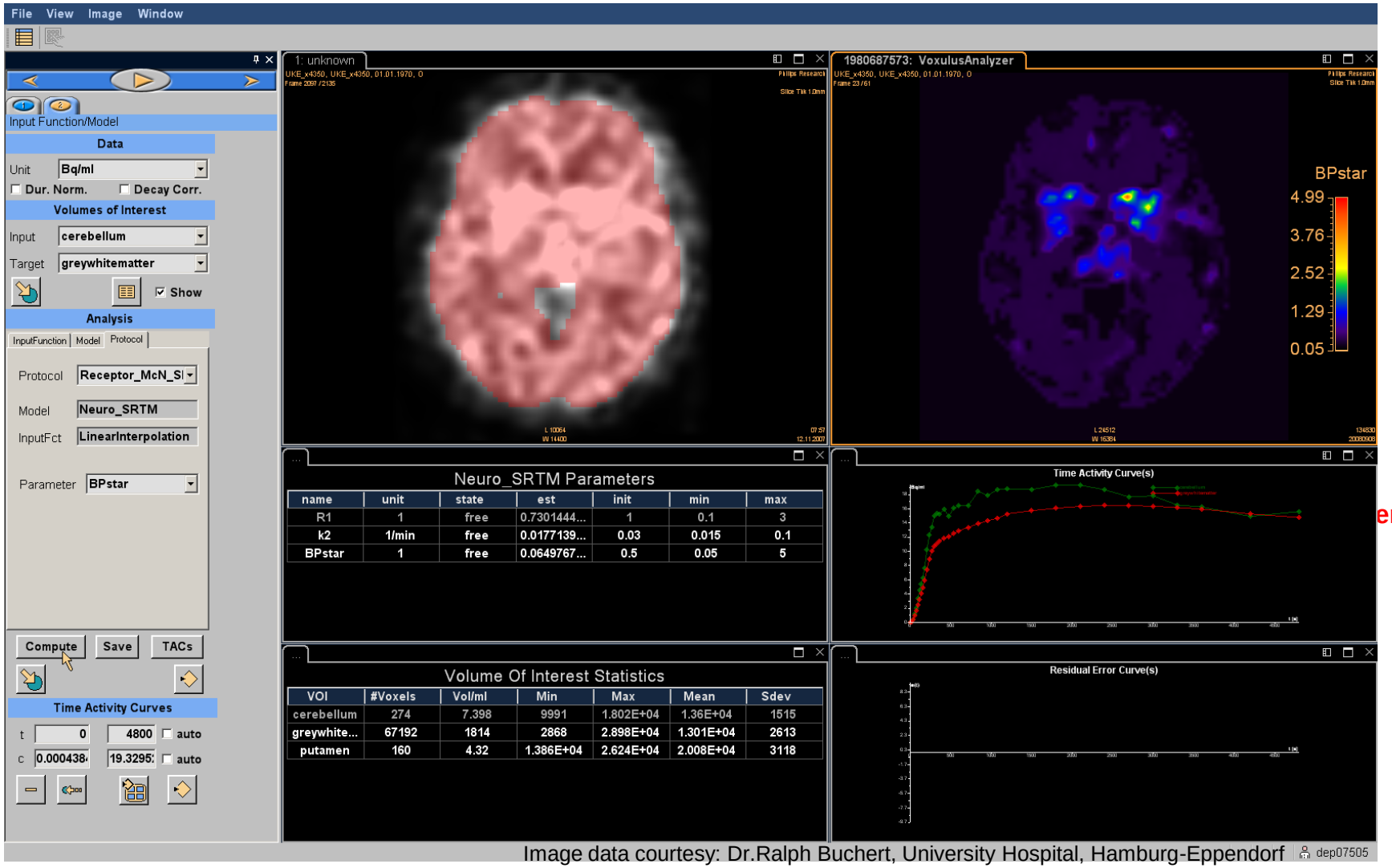

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Image data courtesy: Dr.Ralph Buchert, University Hospital, Hamburg-Eppendorf

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When intensities don’t suffice : Segmentation

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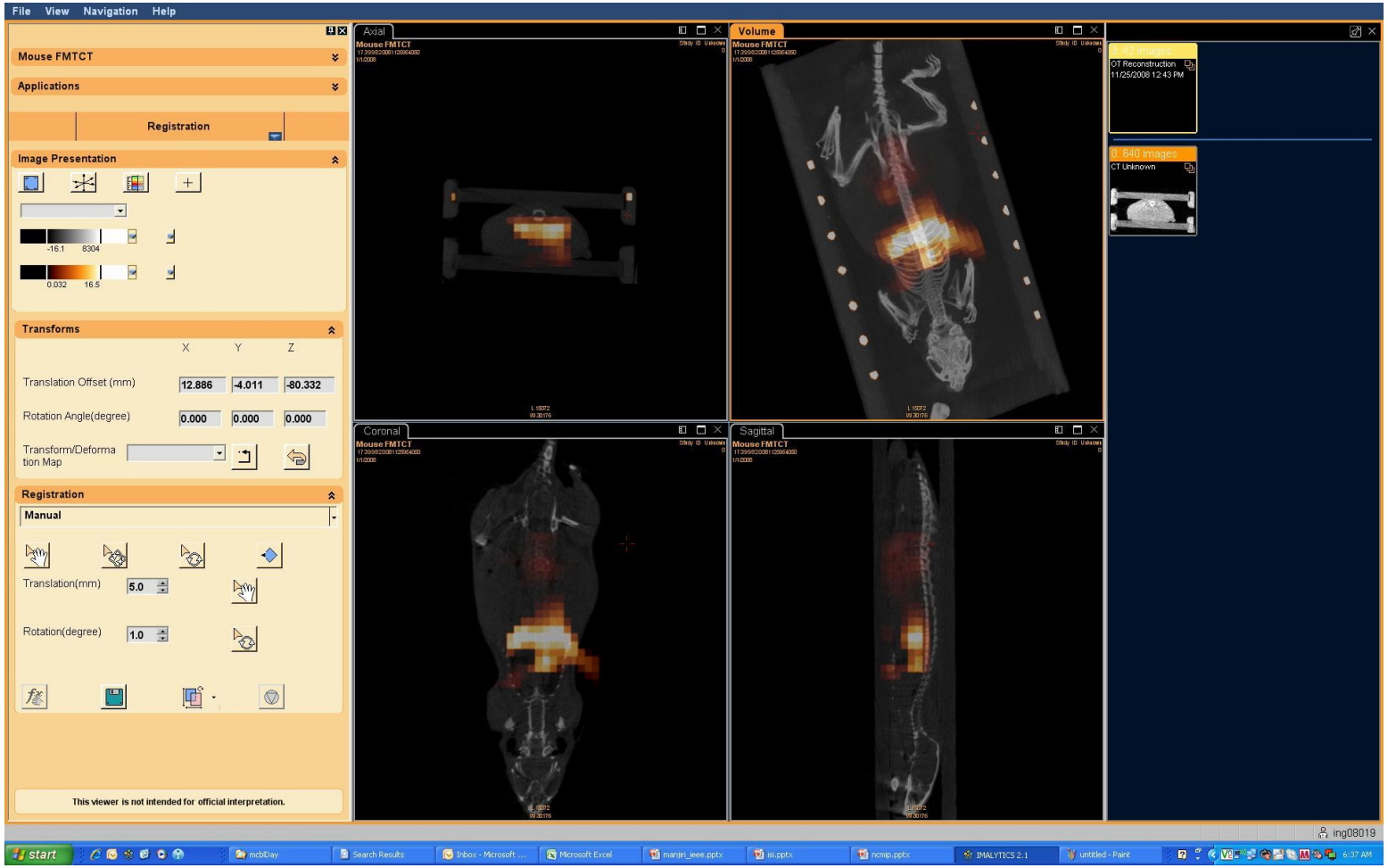
When information is orthogonal : Registration



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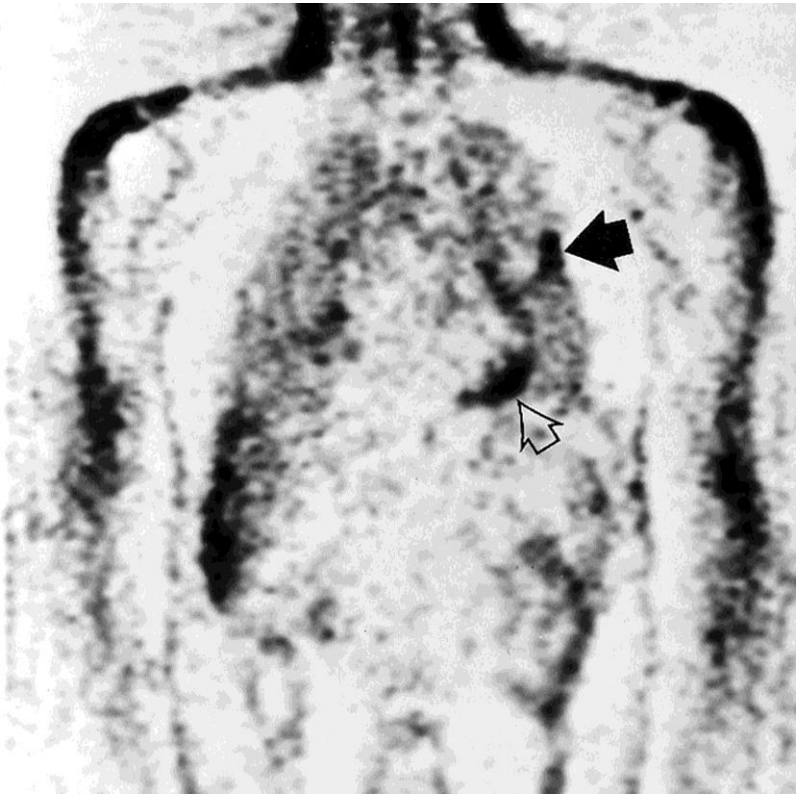
Curse of demography : Cancer or Tuberculosis ?



Western : Suspect Cancer

Asian : Suspect TB

Goo J M et al. Radiology 2000;216:117-121

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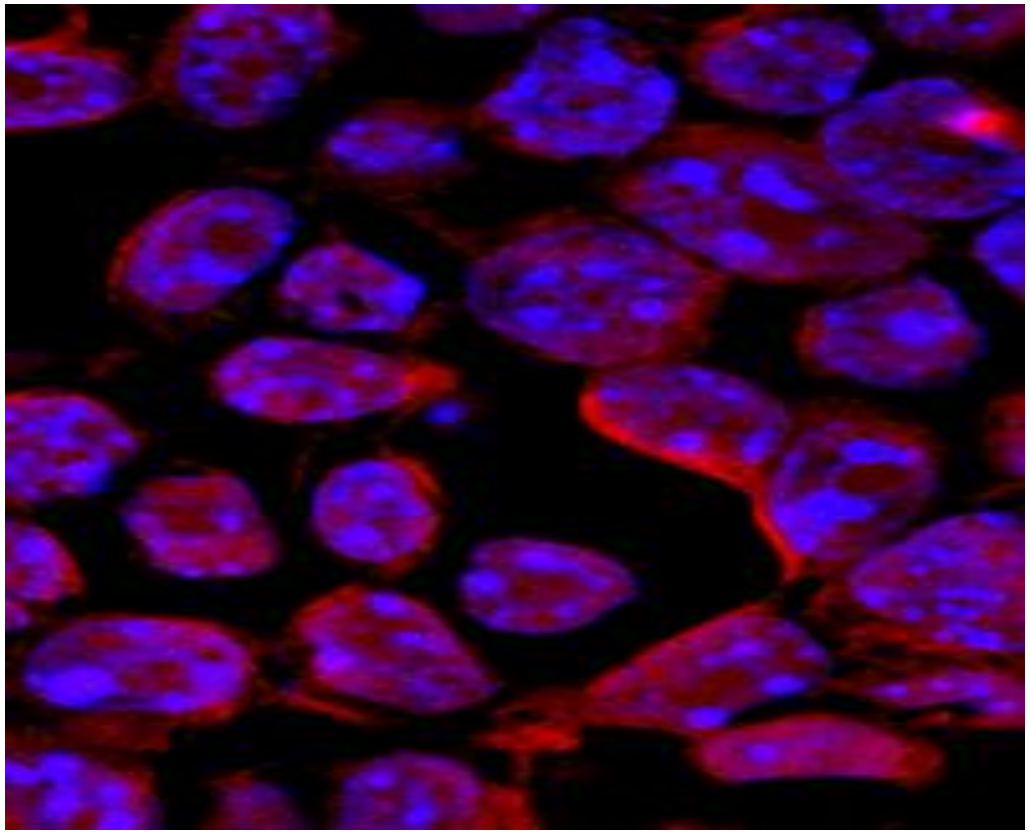
Radiology

Differential Staining of cells



At cell membrane vs in the cytoplasm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Ultrasound-Mediated Drug Delivery

- Drugs packed into microbubbles
- Released by focused US pulse