Model fitting of dynamic data: Implementation of perfusion models for radiotherapy analysis

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Outline

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   - Demands for a dynamic data modeling tool
2. Infrastructure concepts
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   - The model function
   - Parameter maps and modelfit-visualisation
3. Use case: perfusion MRI in glioma patients
4. Summary
   - Advantages of MITK perfusion
   - Outlook

On dynamic data modeling and perfusion imaging

Why we need dynamic data modeling: Dynamic imaging of indicator dilution

- Aim: characterize tissue physiology

- Measure dynamic distribution of an indicator

- Dynamic Contrast Enhanced MRI (DCE MRI)
  - Contrast agent
  - Microcirculation and vascularization
    - ➢ Perfusion and permeablilty

- Dynamic PET
  - Radioactive tracer with metabolite
  - Dynamic tracer uptake → Time-Activity-Curve
  - Metabolic rate and exchange constants

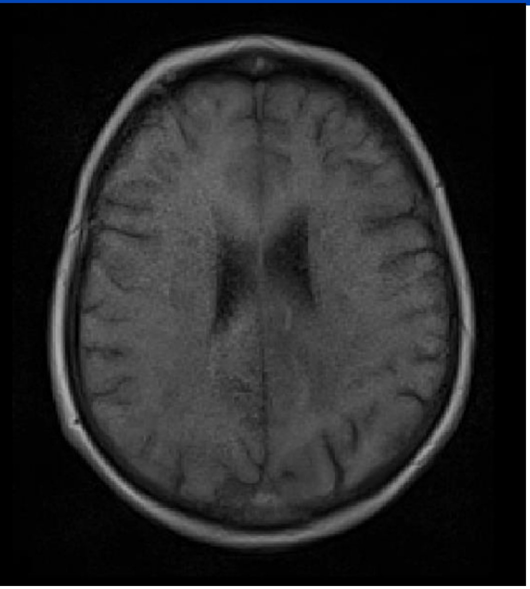
Why we need dynamic data modeling: Dynamic imaging of indicator dilution

- Acquire time series of 3D images over the time course of indicator application

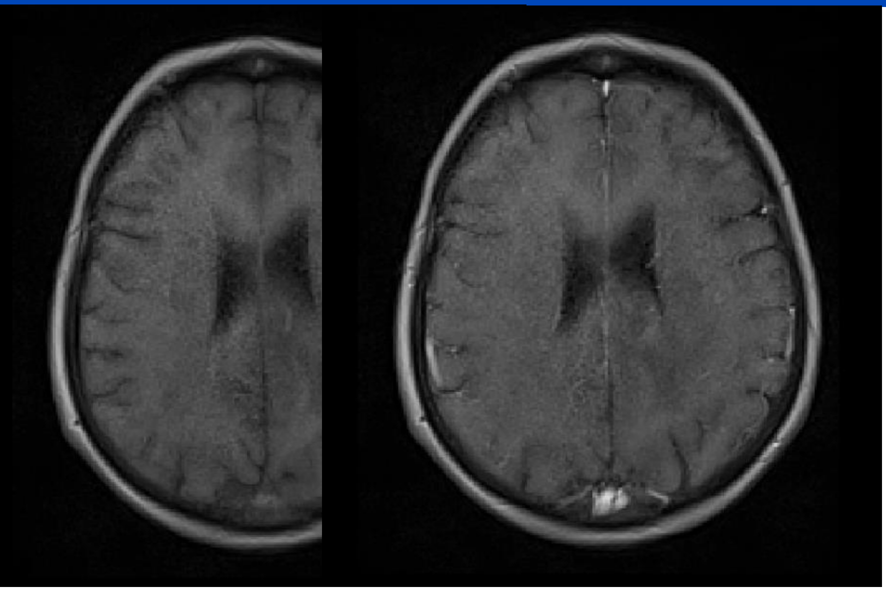
- Analyse time series with indicator dilution theory/pharmacokinetic models
  - Mathematical representation of ongoing physiological process

➢ Fitting of Signal-Time-Curves (ROI-/pixelbased)

Perfusion MRI (DCE MRI)



Perfusion MRI (DCE MRI)



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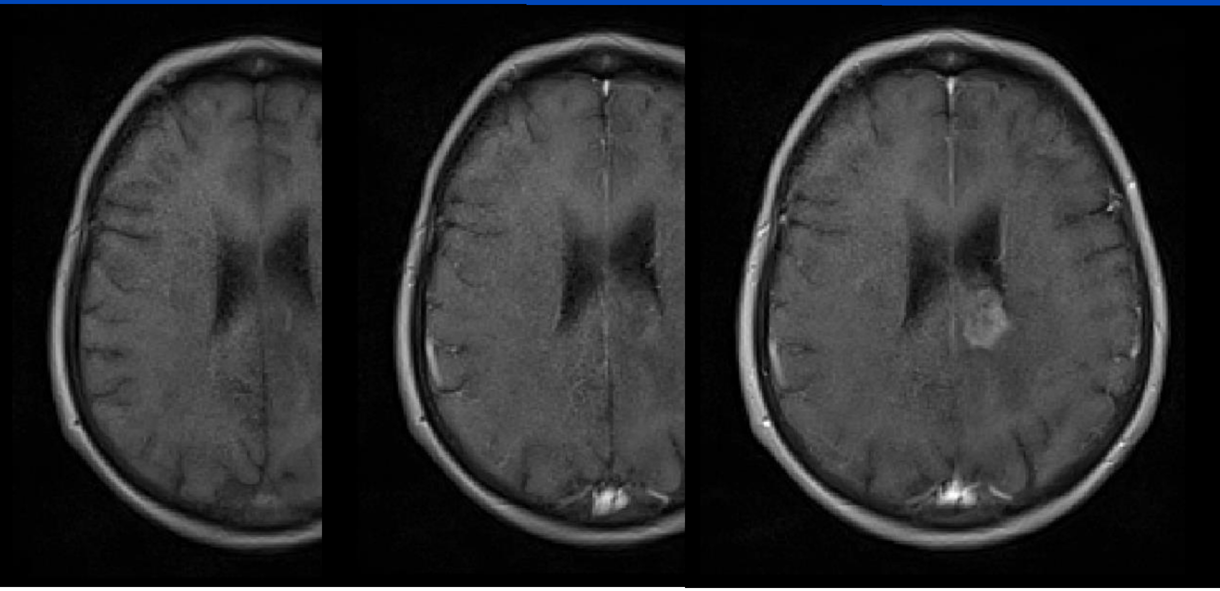

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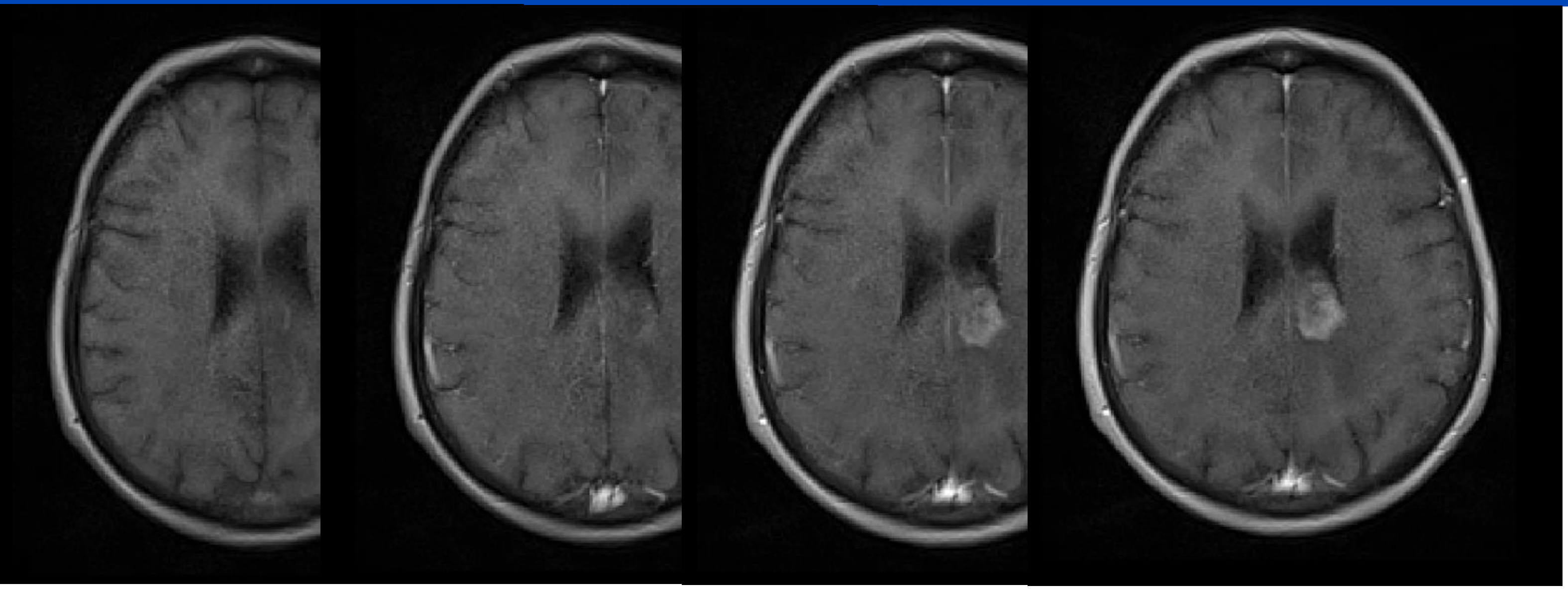

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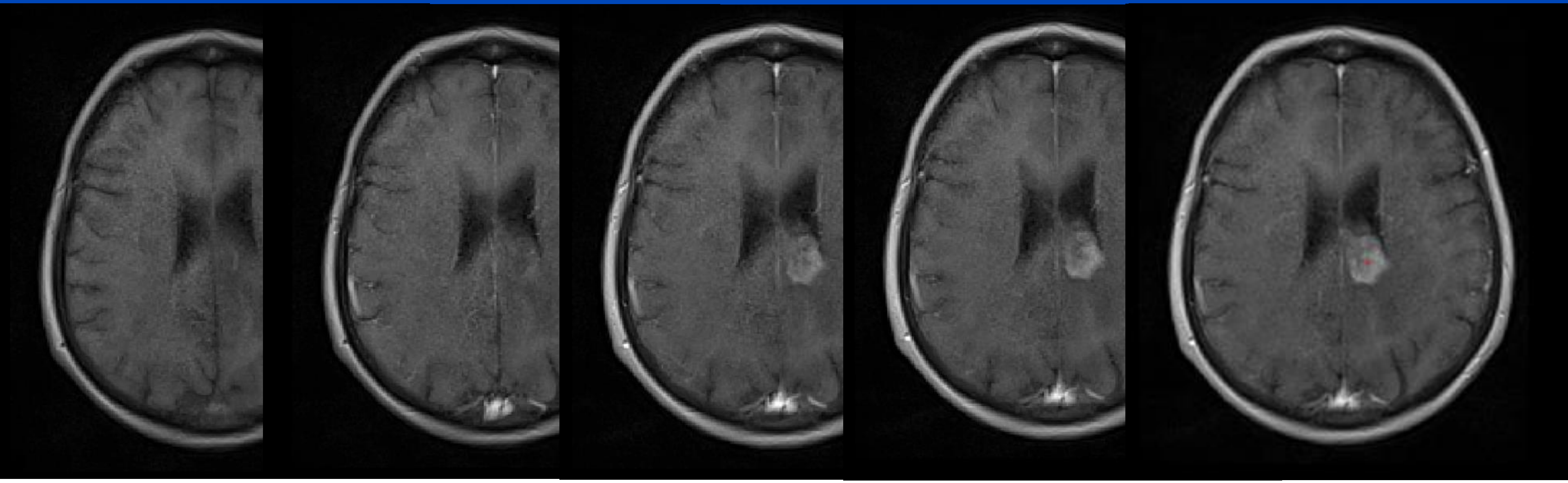

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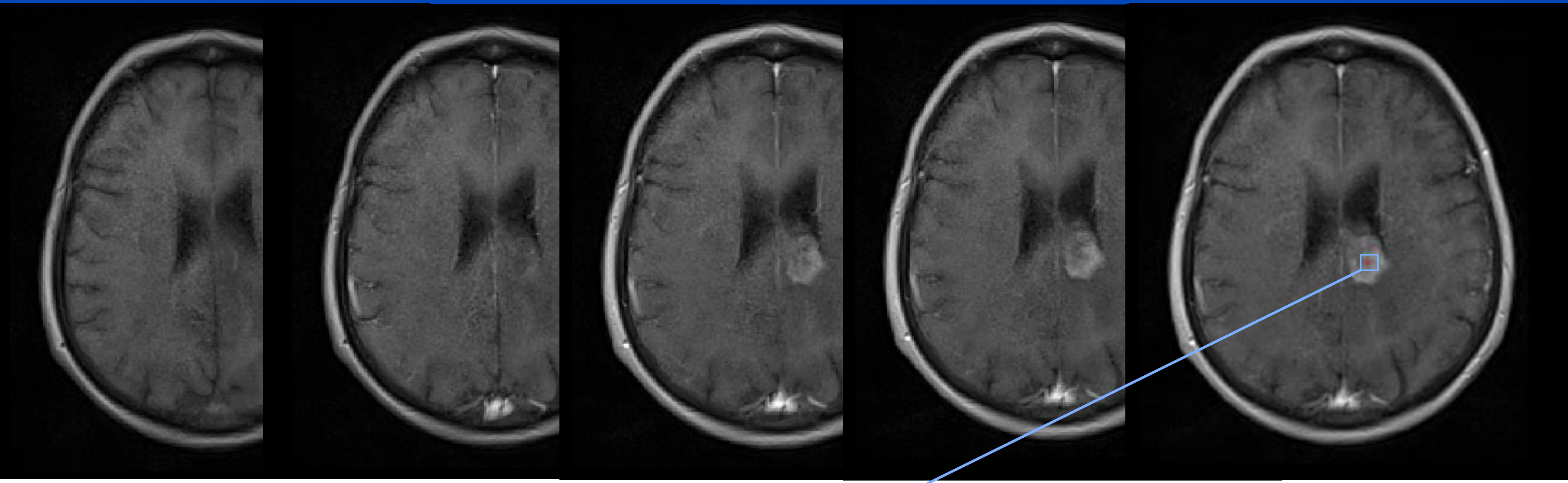

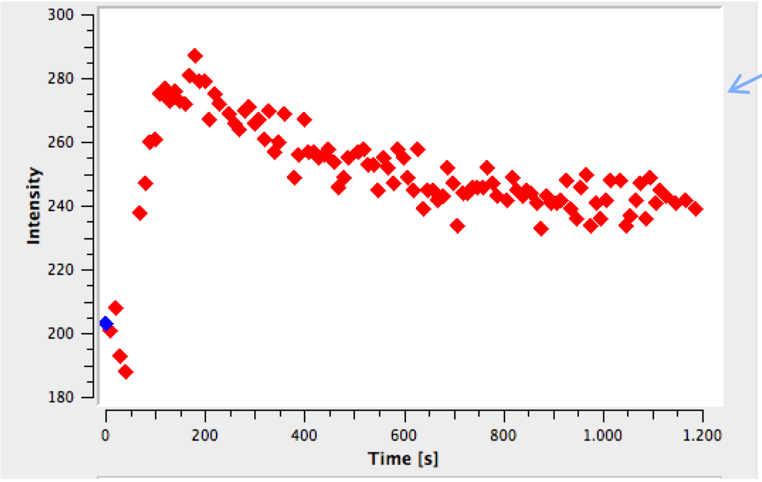

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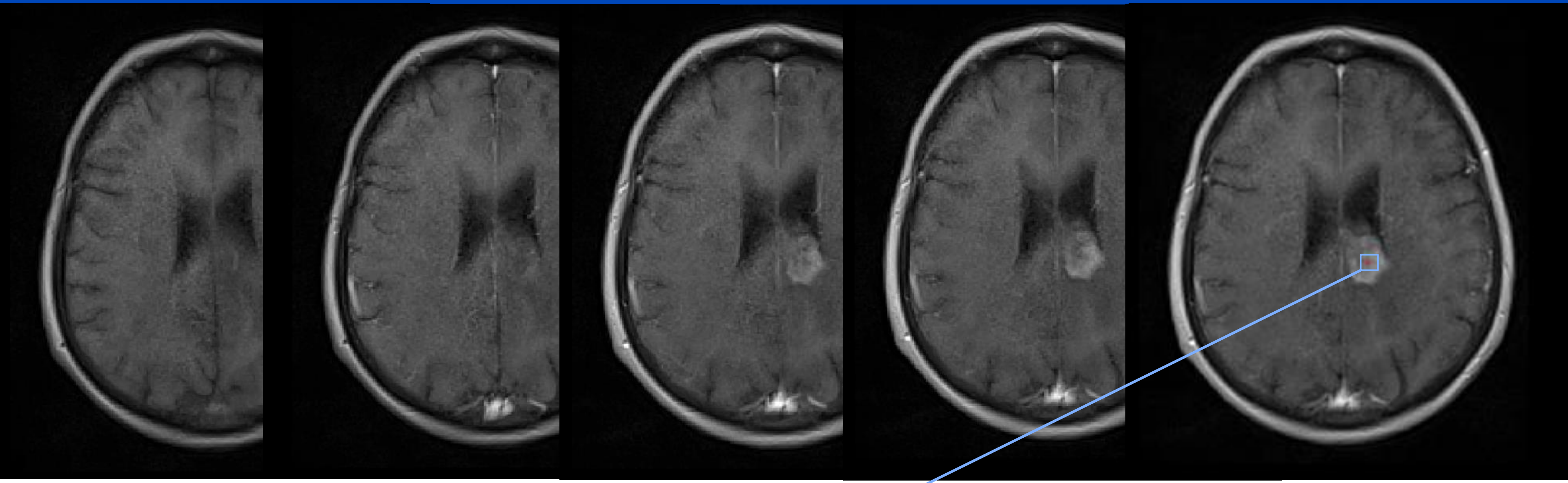
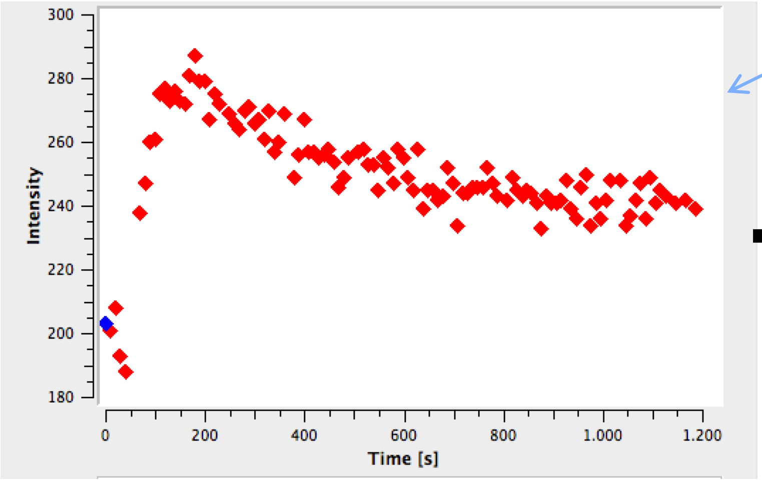
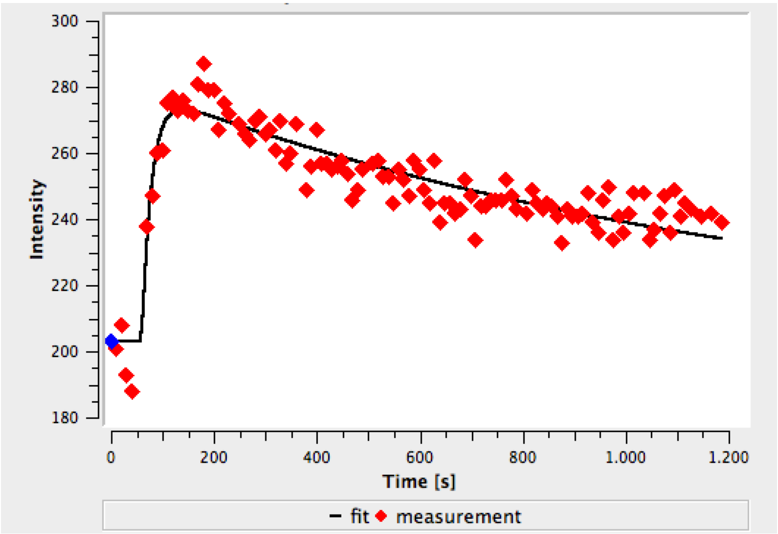
Perfusion MRI (DCE MRI)





FIT

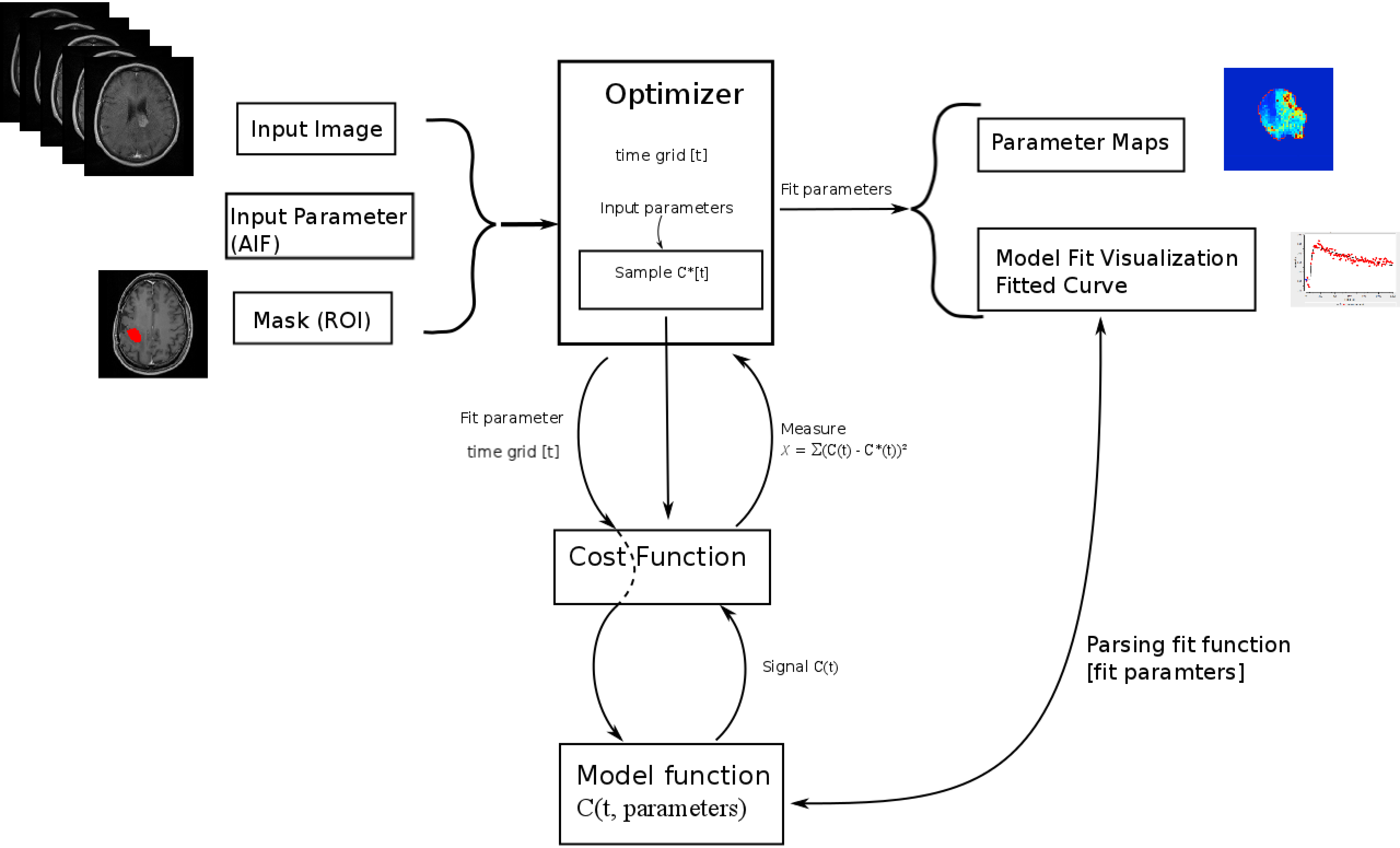


Task/Demands

- Load 4D image modality
- ROI definition (segmentation)
- Extract signal-time-curve in every voxel of ROI/ mean signal within ROI

- Model & modality independent fitting routine
    - Optimizer
    - Cost function
    - Display fitting parameters and fit quality
- Modality dependent model specifications
    - Conversion of Signal
    - Model function
    - Parameter constraints depending on model
    - Output parameters (fit parameters, measures, derived parameters, …)

Fitting routine



Infrastructure concepts

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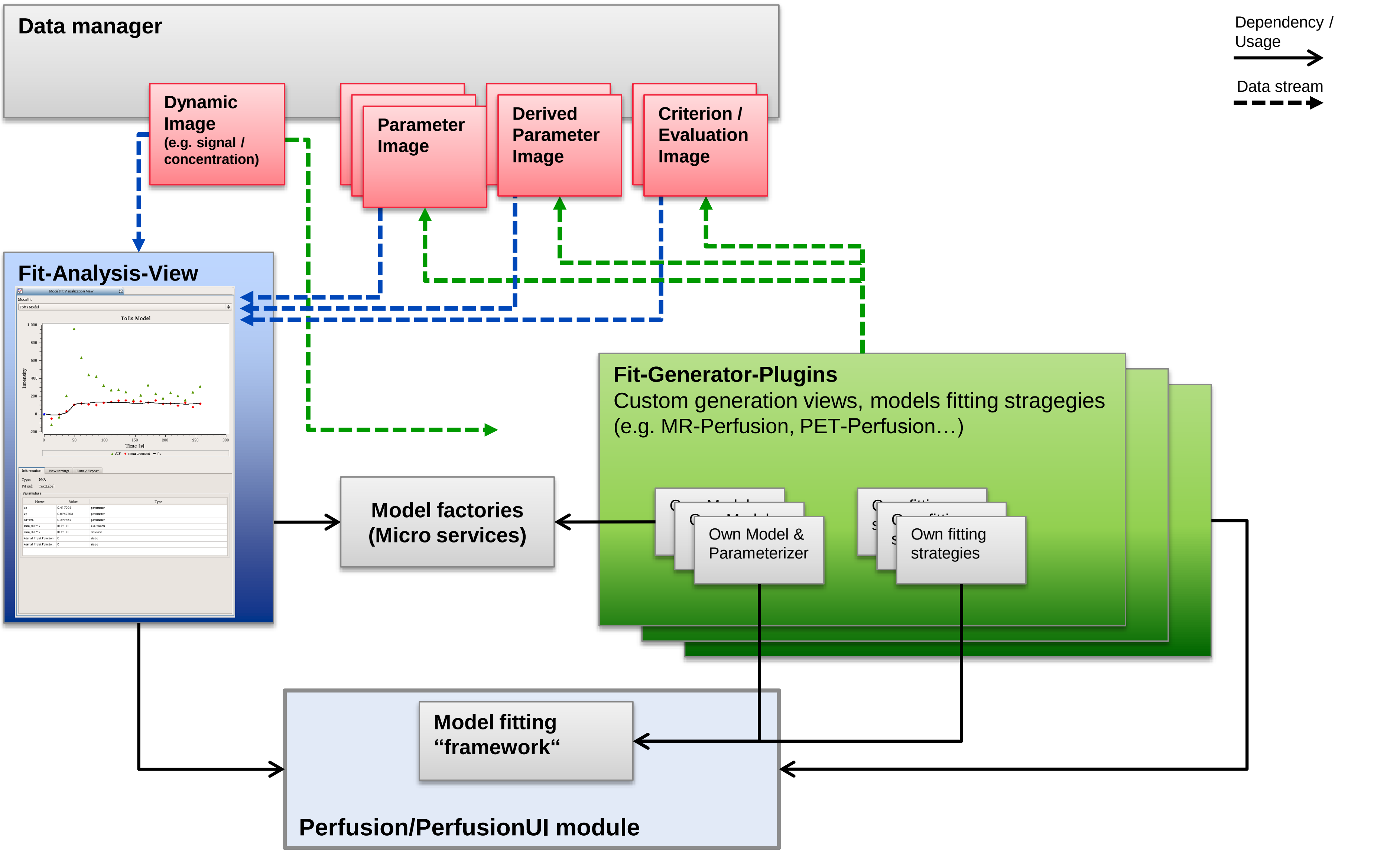
The MITK Perfusion Module: Infrastructure concepts



The fitting routine: optimizer and cost functions

- Fitting routine is decoupled from specific model and input modality
  - ➢ High re-usability
- User can choose optimizer with appropriate cost function
- Currently used: itk::LevenbergMarquard with multivalue cost function
- Cost function
  - Compares signal corresponding to current parameters with sample that is to be fitted
  - Own implementations with various „measures“/fit criterions
    - Sum of (squared) differences (χ^2)
    - Squared differences
    - …

The model function – general

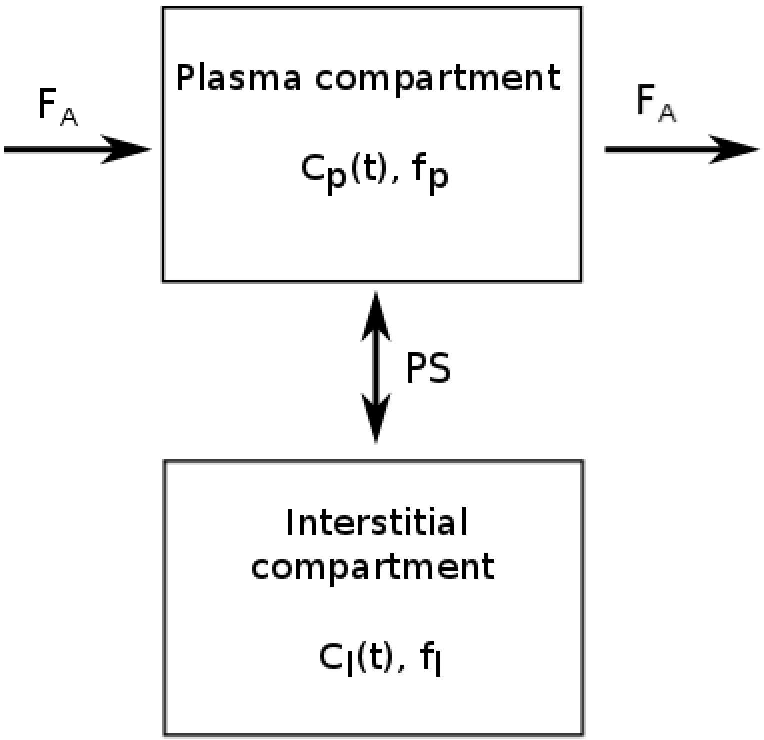
- Modality dependend, specific mathematical model for underlying physiological process
- Function declaration f(t) to describe data curve
  - Conversion of signal
- Is calculated for cost function from current fit parameters and time grid
- Resulting signal curve is needed by cost function to calculate measure

The model function – perfusion

- Function declaration gives concentration-time-curve C(t)
- Different types
  - compartment models, deconvolution analysis, semi-quantitative parameters
  - Calculation of C(t) e.g. via convolution, numeric solution of differential equations (ODE), stepwise declaration
- Currently implemented:
  - DCE MRI models: 2 compartment exchange model, extended Tofts, descriptive Brix model
  - PET: 1 and 2 tissue compartment model

The model function – example

- 2 compartment exchange model



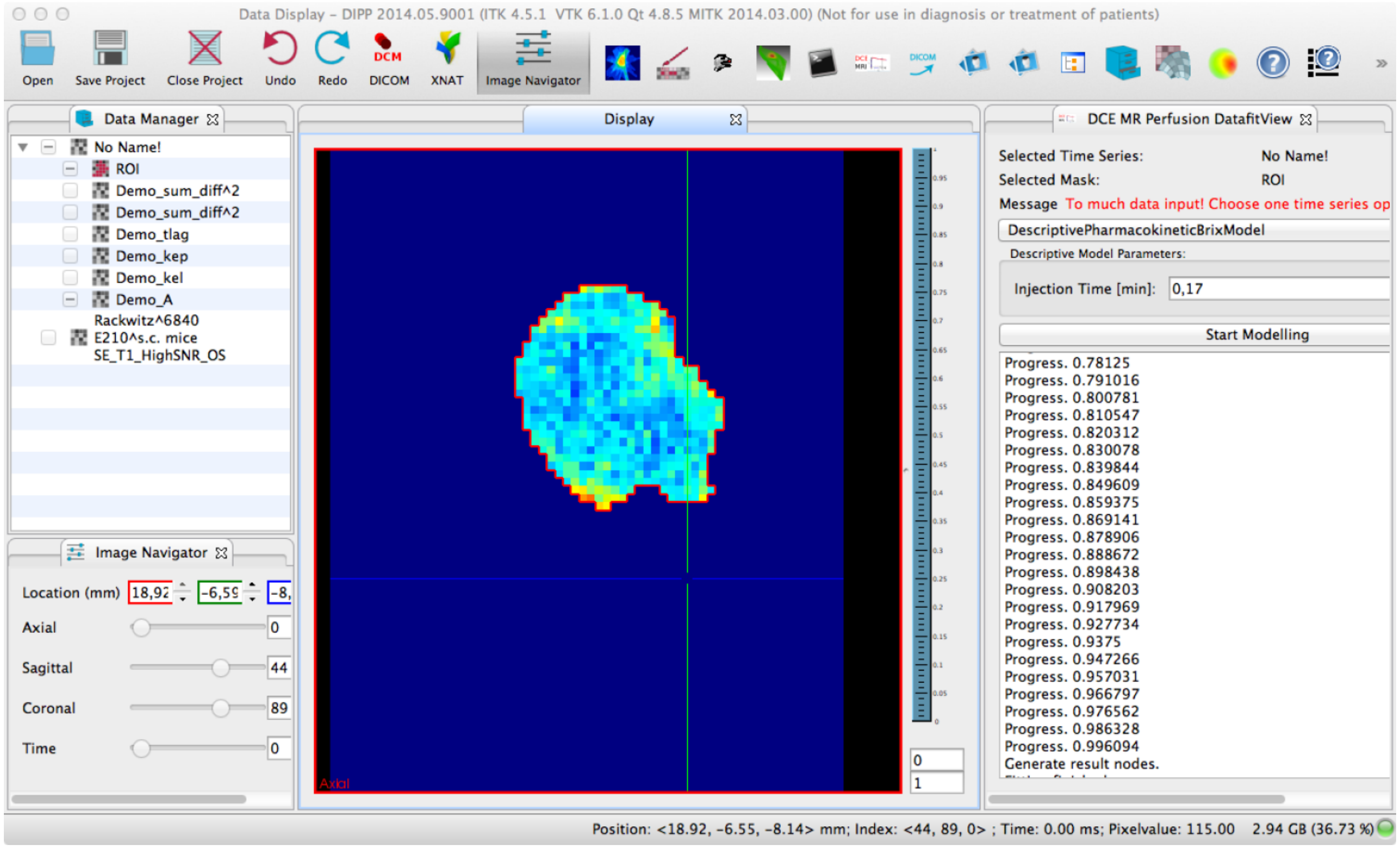
$$\frac{dC_P(t)}{dt} = \frac{F_A}{V_P}\big(C_A(t) - C_P(t)\big) \cdot \frac{PS}{V_P}\big(C_P(t) - C_I(t)\big)$$

$$\frac{dC_I(t)}{dt} = \frac{PS}{V_I}\big(C_P(t) - C_I(t)\big)$$

$$\begin{aligned} C_T(t) &= f_P C_P(t) + f_I C_I(t) \\ &= [f_P Q_P(t) + f_I Q_I(t)] * C_A(t) \end{aligned}$$

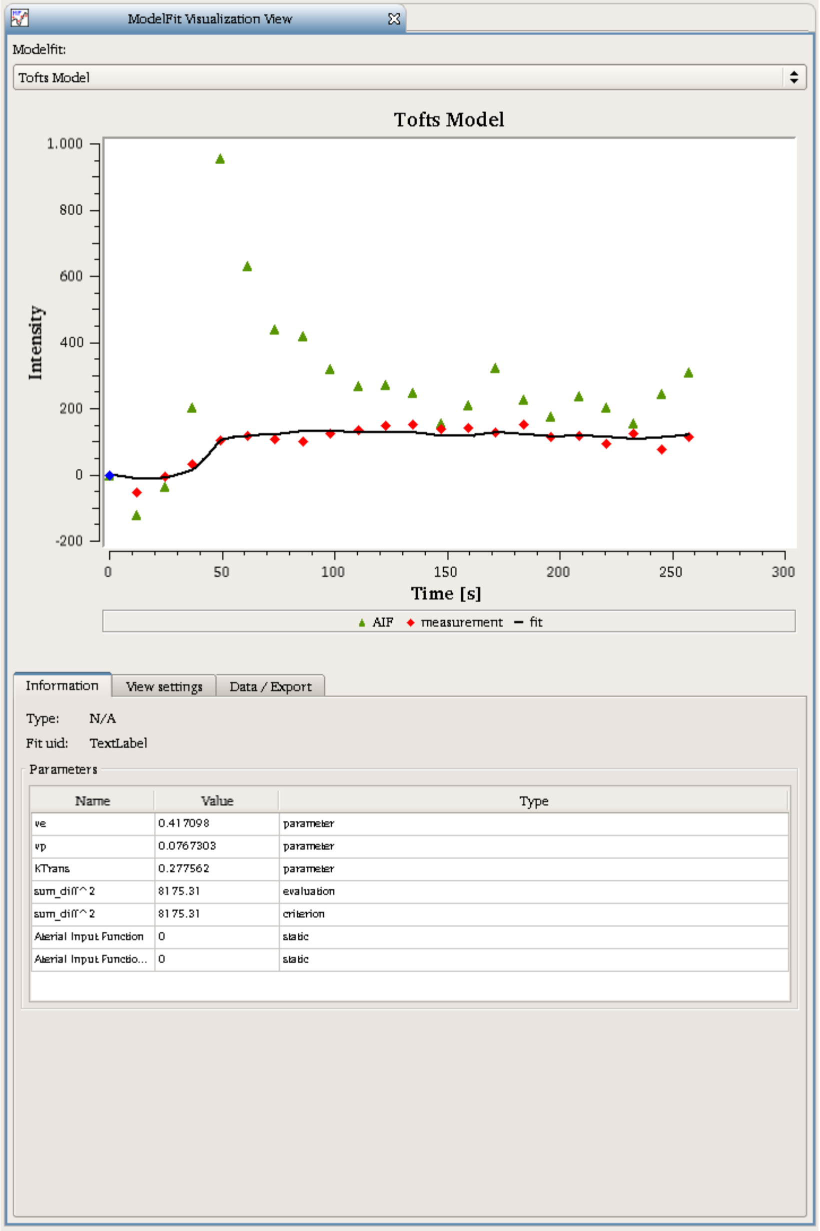
Parameter maps and modelfit visualization

- Result parameters of fitting routine are stored voxelwise as 3D parameter maps/images (one map for each parameter)



Parameter maps and modelfit visualization

- Modelfit-Visualization plug-in using factory structure to display input data points and fit voxelwise



Use Case:

Perfusion MRI in Glioma Patients

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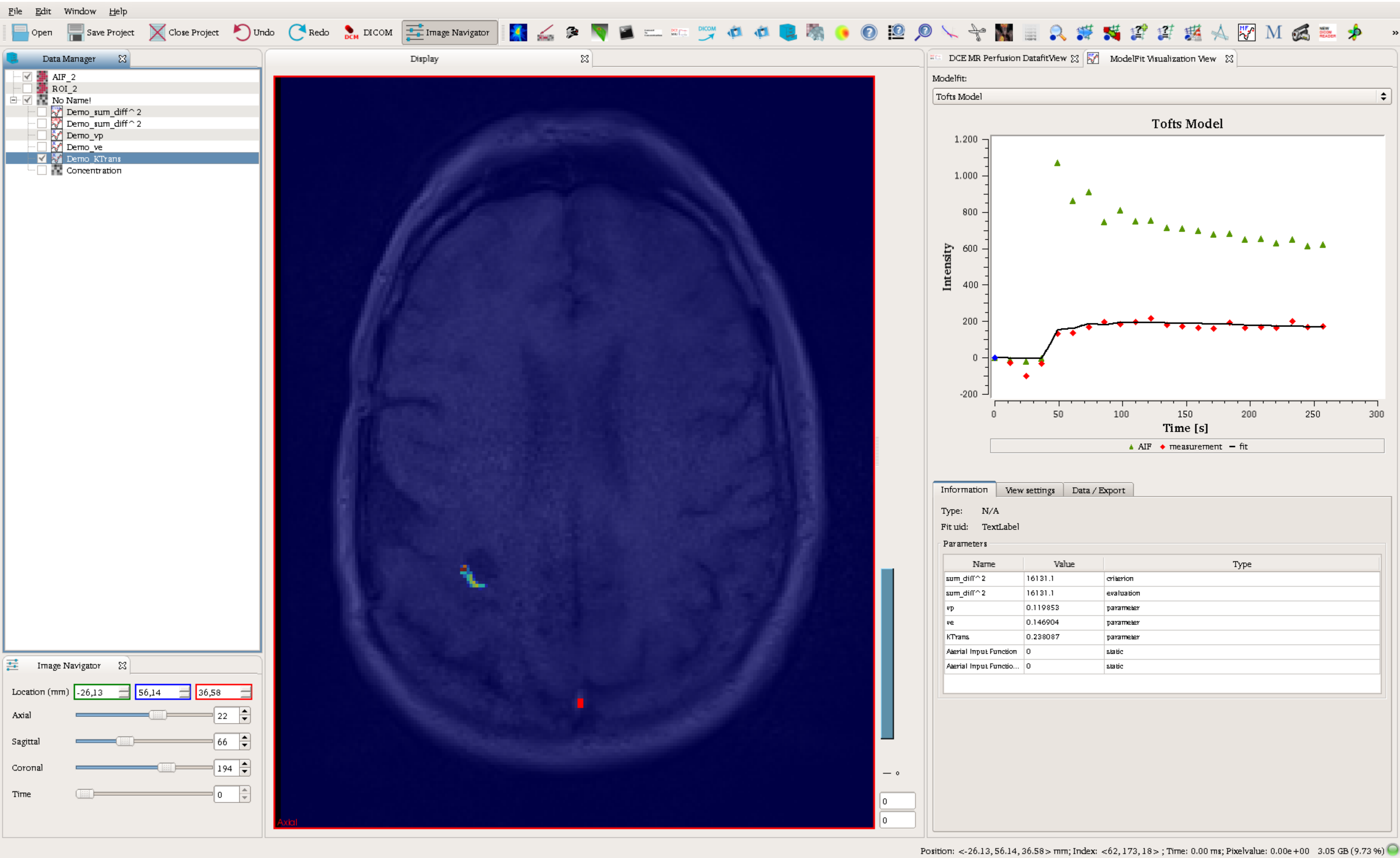

Summary

Advantages

- Modality independend tool for fitting of 4D data with given model
- Modulatrity: user can specify different parts according to his needs (cost function and optimizer, modelfunction, output parameters,…)
- User can fit data with own model implementation without concering himself with the underlying fitting routine
- Ready-to-use anaylsis software for MRI perfusion data
  - Various model implementations
  - Pixel and ROI-based fitting

Advantages

- Modelfit view for assessment of fit quality
- Countless possibilities due to combination with other MITK tools
  - Registration
  - Segmentation
  - RT Dicom import
  - Statistics
  - Comparison of different modalities and sequences

Outlook

- Validation of MRI perfusion fitting with simulated and measured data
- Studies on influence of
  - Different optimizers
  - Start parameters for fitting
- Implementation of further models (PET)
- Translation to image analysis other than perfusion
  - E.g. intravoxel incoherent motion (IVIM) models