PKIN General Kinetic Modeling

Quantitative PET and SPECT

Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT) allow molecular target imaging down to picomolar concentrations. With suitable tracers and acquisition protocols, tissue properties may be quantified in absolute units. Therefore, PET and SPECT have been proven to be uniquely valuable for many in-vivo research domains. However, for exact quantification, the data have to be processed with sophisticated modeling techniques.

Modeling with PKIN

PMOD's PKIN tool is the ideal solution for the model-based analysis of PET and SPECT data. It offers a comprehensive toolbox which not only allows calculating quantitative information, but also features dedicated functionality to assess the meaningfulness of the results.

A palette of more than 50 kinetic model configurations is available.

Blood and tissue data can easily be imported into the user-friendly PKIN environment. A palette of more than 50 model configurations is available, including blood-based compartment models, reference tissue models, linearized models and many more. These models can be fitted to the data while making use of various options to ensure reliability and reproducibility. As an extension to conventional modeling, multiple data sets may be fitted at once to incorporate physiological a-priori knowledge and thus improve the outcome.

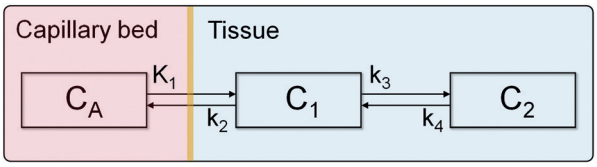
A further contribution to a meaningful result is the support and modeling of all blood-related input data such as plasma and metabolite fractions.

In daily use by hundreds of PET and SPECT researchers for more than 20 years, PKIN is arguably the best-validated modeling tool available today.

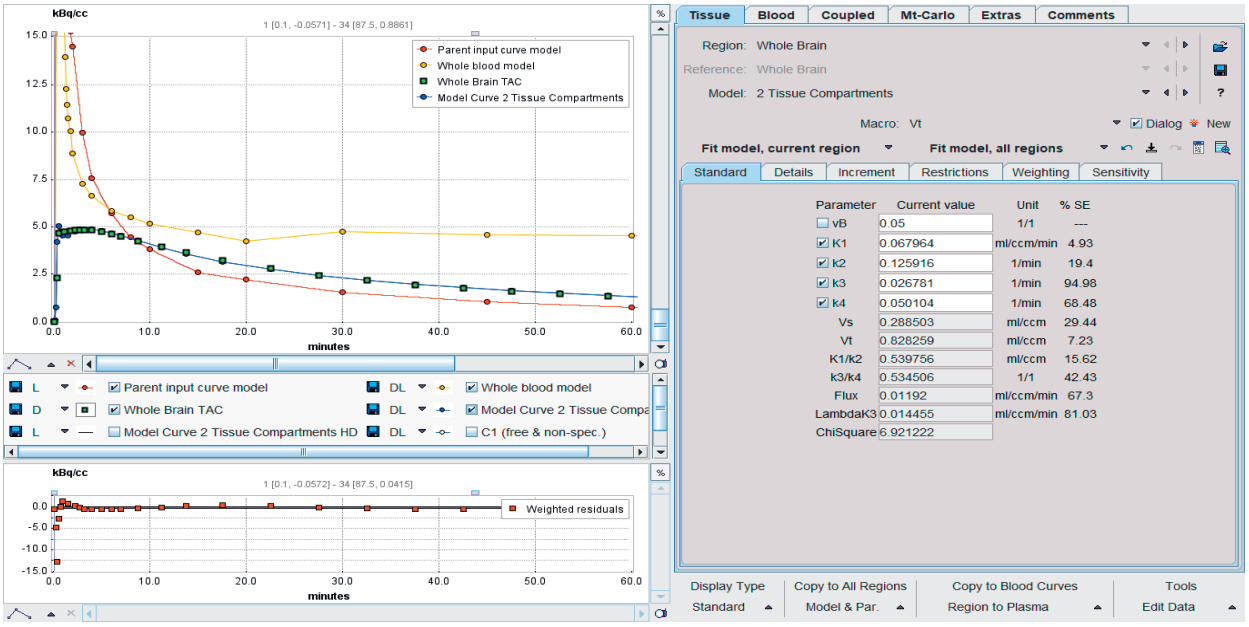
For efficient evaluation of the modeling results, the user is provided with convenient summaries and statistical decision criteria, which can easily be aggregated and transferred to the R environment for further statistical analysis.

PKIN Validation and Usage

In daily use by hundreds of PET researchers for more than 20 years, PKIN is arguably the best-validated and most comprehensive modeling tool available today. Continuous feedback from our research users ensures that PKIN will also keep up with future advances in the field.



Schematic of a 2-tissue compartment model. Such a model is often applied for dynamic PET quantification.



PKIN user interface with the kinetic model configuration to the right, the tissue time-activity and the model curve in the upper left, and the residuals in the lower left.

Tissue Activity Models (> 50)
The tissue models in PKIN predict the dynamic uptake of the radiotracer, given a blood or reference tissue input curve. A fitting procedure varies the model parameters until the prediction most closely fits the measurement. Model categories included:
– 1-, 2-, 3-tissue compartment models
– Models with receptor saturation
– Models with additional metabolite input curve
– Models for acquisitions with multiple injections
– Graphical plots such as Patlak, Logan, Ito, RE-GP plots
– Reference tissue models
– Cardiac dual-spillover models
– Spectral analysis
– Utilities such as cumulated (organ) activity calculation or bolus/infusion optimization

Blood and Plasma Activity Models
Often, blood activity measurements are scarce and noisy. The blood models in PKIN support fitting smooth functions to such data for interpolation and noise reduction purposes. Supported functions:
– Tri-exponential function
– Modified gamma functions
– Compartment functions
– Deconvolution of dispersion for continuously sampled blood data

Plasma Fraction
PKIN supports the use of plasma fractions for the calculation of plasma activity from whole-blood activity curves. This function is particularly important when using online blood-sampling systems. Supported functions:
– Linear interpolation of measurements
– 3-exponential function
– Sigmoid function
– Hill function
– Watabe function

Parent Fraction
PKIN supports the use of parent fractions for the metabolite correction of plasma activity curves. Smooth parent fraction functions can be fitted to measured data, or used for population-based metabolite correction. Supported functions:
– Linear interpolation of measurements
– 1-, 2-, 3-exponential function
– Sigmoid function
– Hill function
– Watabe function
– Power-damped exponential function

Fitting Options
PKIN implements various approaches for improving fitting reliability, including:
– Selective fixing/fitting of parameters
– Customizable sets of initial model parameters
– History of model fits
– Initialization of compartment model parameters by a linear least-squares fit
– Randomization of initial parameters to avoid local minima
– Grid-fitting within physiologic parameter boundaries
– Macros to fit several models at once
– Coupled fitting of common parameters across regions or subjects
– Data-derived or user-defined residual weighting
– Restriction of fit range and outlier masking
– Continuous shortening of data to investigate sensitivity of parameters to acquisition duration
– Batch mode allowing application of multiple models or Monte Carlo simulations to the data of a whole population.

Options for Investigation of Results
PKIN not only provides fitting results, but also features several methods to assess their meaningfulness, such as:
– Standard error indication for resulting parameters derived from the covariance matrix
– Calculation of parameter correlation matrix and sensitivity functions
– Monte-Carlo simulations to address parameter variability
– Akaike and Schwarz criteria for comparison among models
– Parameter aggregation and transfer to R for statistical analysis

Parametric Mapping (requires PXMOD option)
When transferring pixel-wise TACs to PKIN, their location in the image is recorded. Therefore, after fitting a certain model to these TACs, maps of all model parameters can readily be generated. An advantage of this approach is the leveraging of the fully interactive PKIN environment for parametric mapping of spatially limited structures such as tumors.

Generation of Synthetic Data
Synthetic data generated from well-defined compartment models allow the user to investigate simplified analysis approaches.